RESEARCH ON IMIDAZO[1,2-a]BENZIMIDAZOLE DERIVATIVES.

19.* ACTION OF EXCESS NITROUS ACID ON 9-METHYL-2-PHENYLIMIDAZO[1,2-a]BENZIMIDAZOLE

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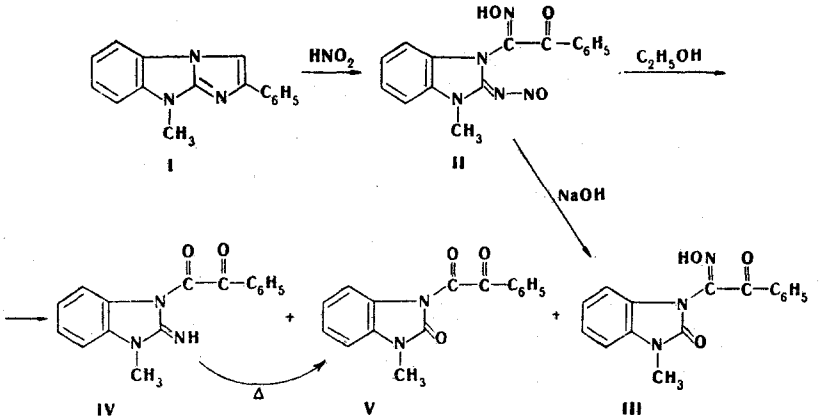
The action of excess nitrous acid on 9-methyl-2-phenylimidazo[1,2-a]benzimidazole results in opening of the outer imidazole ring and the formation of unstable 1-methyl-2-nitrosimino-3-oximinophenacylbenzimidazoline. The products of cleavage of this compound in alkali, acid, and alcohol solutions were studied.

During a study of the nitrosation [2] of 9-methyl-2-phenylimidazo[1,2-a]benzimidazole (I) it was noted that the introduction of the nitrosating agent in amounts that exceed the equimolar amount leads to a proportional decrease in the yield of the final 3-nitroso derivative. It was found that the C_3 atom is initially nitrosated by the action of excess sodium nitrite on I in acetic acid, after which the nitrosyl cation attacks the nitrogen atom in the 1 position, which leads to opening of the outer imidazole ring and the formation of 1-methyl-2-nitrosimino-3-oximinophenacylbenzimidazoline (II). Absorption bands of C=C (1498 and 1602), C=N (1540 and 1570), C=O (1685), and N=O (1435 cm^{-1}) groups are observed in the IR spectrum of II in mineral oil. The absorption of the OH group is observed in the form of a broad band at 2600-3300 cm^{-1}.

The nitrosimine obtained, like some 2-nitrosiminothiazolidines [3-5], is rather unstable: it explodes at 114°C, it is converted to the previously described [2] 1-methyl-3-oximinophenacylbenzimidazolone (III) when it is added to a 10% solution of alkali at 20°C, and it is readily denitrosated to give 2-imino-1-methyl-3-oximinophenacylbenzimidazoline when it is heated in 10% hydrochloric acid solution.

Compound II also decomposed violently when we attempted to recrystallize it from ethanol, and 2-imino-3-(β-phenyloxalyl)-1-methylbenzimidazoline (IV), which is only slightly soluble in many organic solvents, precipitated from solution in 37% yield. The IR spectrum of IV contains, in addition to a band at 1690 cm^{-1}, which is characteristic for the keto group of the phenacyl grouping, a band at 1765 cm^{-1}, which can be described by absorption of a C=O group bonded to the ring nitrogen atom. The NH group absorbs at 3080 cm^{-1}. The formation of diketone IV can probably be explained by the ease of splitting out of a nitroso



*See [1] for Communication 18.

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group from II, as a result of which the alcohol undergoes nitrosation to give ethyl nitrite, which, as is well-known [6], can serve as a deoximating agent for oximino ketones.

Light-yellow needles of 1-methyl-3-(β-phenyloxalyl)benzimidazolone (V) — the product of hydrolysis of imine IV — were isolated from the filtrate in 45% yield after separation of imine IV from the hot solution. This compound can also be obtained by heating imine IV to 160-170°C or by brief refluxing of IV in dimethylformamide (DMF). The band of stretching vibrations of the NH group vanishes in the IR spectrum of benzimidazolone V, and another band of carbonyl absorption at 1720 cm^{-1}, which is close to the ν_{CO} absorption in the spectra of other benzimidazolone derivatives [7], appears.

Another small amount of III (7% yield), as well as a mixture of a number of products of more profound cleavage of nitrosimine II, judging from the results of chromatographic analysis of the mother liquor and the formation of ethyl benzoate in the reaction mixture, can be isolated from the reaction mixture. However, the structures of these substances cannot be established because of their low yields and the difficulties involved in separation of the mixture.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer.

1-Methyl-2-N-nitrosimino-3-oximinophenacylbenzimidazoline (II). A solution of 0.7 g (10 mmole) of sodium nitrite in 2 ml of water was added slowly at 10-15°C to a solution of 1.24 g (5 mmole) of 9-methyl-2-phenylimidazo[1,2-a]benzimidazole in 10 ml of glacial acetic acid. The color of the reaction solution gradually changed from colorless at the start of the reaction to dark cherry-red in the middle of the reaction, and to orange at the end of the reaction. Water (30 ml) was then added with stirring to the solution, and the bright-yellow precipitate was removed by filtration, washed thoroughly with water, and air dried to give 1.5 g (93%) of product. The compound was moderately soluble in ether, acetone, chloroform, and ammonia and insoluble in water and mineral acids. During determination of the melting point the compound exploded at 114°C. Found: N 21.8%. $C_{16}H_{13}N_5O_3$. Calculated: N 21.7%.

Decomposition of N-Nitrosimine II. A) In Alkali. A 0.32-g (1 mmole) sample of nitrosimine II was dissolved in 5 ml of 10% KOH solution at 20°C, during which voluminous nitrogen evolution was observed. When gas evolution was complete, the yellow solution was acidified with concentrated HCl, and the precipitated snow-white cubic crystals of 1-methyl-3-oximinophenacylbenzimidazolone were removed by filtration and washed with water to give 0.29 g (quantitative yield) with mp 216°C (dec., from alcohol). No melting-point depression was observed for a mixture of this product with an authentic sample [2].

B) In Acid. A 0.32-g (1 mmole) sample of II was refluxed in 10 ml of 10% hydrochloric acid solution for 1 h, after which the mixture was cooled. The resulting precipitate of 2-imino-1-methyl-3-oximinophenacylbenzimidazoline hydrochloride was identical to the compound described in [2]. The product had mp 184°C and was obtained in 93% yield. Nitrosation of the product in glacial CH_3COOH converted it to the starting nitrosimine.

C) In Ethanol. A suspension of 0.97 g (3 mmole) of II in 20 ml of ethanol was heated to the boiling point, during which the solid dissolved and a spontaneous reaction commenced. The spontaneous reaction was accompanied by voluminous gas evolution and the formation of an alcohol-insoluble precipitate, which was identified as bright-orange plates of 2-imino-3-(β-phenyloxalyl)-1-methylbenzimidazoline (IV). The solution was cooled to 40-45°C, and the compound obtained was immediately removed by filtration. The product was insoluble in most organic solvents, alkalis, and acids and crystallized from dimethylformamide (DMF) with partial decomposition. The yield was 0.31 g (37%). During determination of the melting point, the compound became lighter in color at ∿160°C and melted at 189°C. The substance scintillated in a stream of oxygen. Found: C 68.5; H 4.4; H 15.3%. $C_{16}H_{13}N_3O_2$. Calculated: C 68.8; H 4.7; N 15.0%.

The mother liquor after separation of imine IV was allowed to stand in a refrigerator overnight, and the precipitated pale-yellow shiny needles of benzimidazolone V were removed by filtration and washed with a small amount of cold alcohol to give 0.38 g (45%) of a product with mp 189°C (from alcohol). The same compound was obtained by heating imine IV, which was described above, in a test tube in a glycerol bath at 160-170°C (the reaction was carried

out until the starting orange compound became completely colorless) and also by refluxing IV in DMF (the mixture was refluxed until the solution turned orange). Found: C 68.5; H 4.3; N 10.0%. $C_{15}H_{12}N_2O_3$. Calculated: C 68.6; H 4.3; N 10.0%.

The alcohol solution after separation of V was evaporated to dryness, and the residue was treated with diethyl ether to remove the ethyl benzoate and crystallized twice from dioxane to give snow-white cubic crystals with mp 216°C that were identified as 1-methyl-3-oximinophenacylbenzimidazolone (III). The yield was 0.06 g (7%).

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RESEARCH ON THE CHEMISTRY OF 2-HETARYLBENZIMIDAZOLES.

2.* SYNTHESIS AND PROPERTIES OF 1-METHYL-2-(1'-METHYL-2'-PYRROLYL)BENZIMIDAZOLE

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The condensation of 1-methyl-2-formylpyrrole with o-phenylenediamine gave 2-(1'-methyl-2'-pyrrolyl)benzimidazole, which was subjected to methylation. The alkylation product was subjected to electrophilic substitution. The substituent is incorporated in the 4 or 5 position of the hetaryl ring; however, bromination of 1-methyl-2-(1'-methyl-2'-pyrrolyl)benzimidazole leads to the formation of the mono-, di-, and tribromo derivatives, depending on the conditions. The acidophobic properties of the pyrrole ring are partially lost as a consequence of the effect of the benzimidazole ring.

We have previously studied electrophilic substitution in the furan and thiophene rings in 2-(2'-furyl)benzimidazole (I) and 2-(2'-thienyl)benzimidazole (II) [1]. Despite the acidophobic properties of the furan and thiophene rings and the rather severe conditions of the transformations, electrophilic substitution reactions in these compounds proceed smoothly and give the products in high yields.

It seemed of interest to study the behavior of 2-(2'-pyrrolyl)benzimidazole in electrophilic substitution reactions and to compare the relative reactivities of the furan, thiophene, and pyrrole rings in π conjugation with the benzimidazole ring.

2-(2'-Pyrrolyl)benzimidazole (III) was obtained [2] by reaction of o-phenylenediamine with 2-formylpyrrole and subjected to methylation. In this reaction III reacts only at the NH group of the imidazole ring to give 1-methyl-2-(2'-pyrrolyl)benzimidazole (IV). 2-(1'-Methyl-2'-pyrrolyl)benzimidazole (V) was therefore synthesized from 1-methyl-2-formylpyrrole. The product (VI) of methylation of the latter at the N atom of the imidazole ring was sub-

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