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RESEARCH ON 2-ACYL-3-AMINOBENZOFURANS

III.* SCHMIDT REARRANGEMENT IN A SERIES OF 2- AND 3-ACYLBENZOFURAN DERIVATIVES

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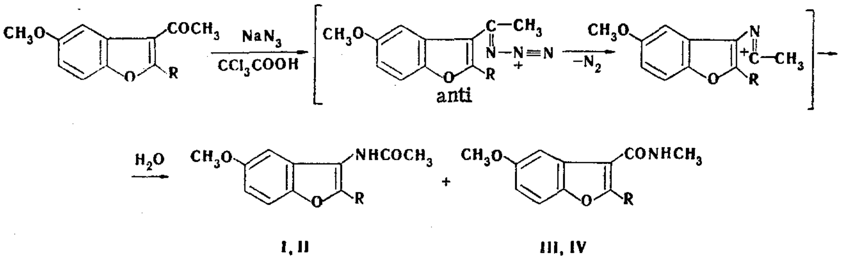
It is demonstrated that, depending on the position of the acetyl substituent in the furan ring of benzofuran, the Schmidt rearrangement leads to benzofuran-2-carboxylic acid methylamide or to 3-acetamidobenzofuran derivatives.

It is known that 3-acetylbenzofuran oximes behave "anomalously" under the conditions of the Beckmann rearrangement and that the formation of the usual rearrangement products – amides – is not observed in this case [2, 3]. We have studied the possibility of the synthesis of 3-acetamidobenzofurans by means of the Schmidt rearrangement. It was established that the direction of the rearrangement depends on the position of the acyl substituent in the benzofuran system. Thus 3-acetamidobenzofuran derivatives (I and II, respectively) are formed in good yields in the reaction of sodium azide in trichloroacetic acid with 3-acetyl-5-methoxybenzofuran and 2-methyl-3-acetyl-5-methoxybenzofuran. The structures of I and II were proved by means of spectral methods and by alternative synthesis [4]. The formation of small amounts of the isomeric 5-methoxybenzofuran-3-carboxylic acid methylamide (III) was established by thin-layer chromatography (TLC).

A different direction of Schmidt rearrangement is observed when the reaction is carried out with 2-acetylbenzofuran under the same conditions, and benzofuran-2-carboxylic acid methylamide (V) is formed in 80% yield.



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[*] See [1] for communication II.

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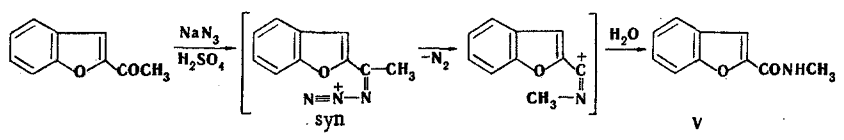

I, III R=H; II, IV R=CH_3

The structure of methylamide V was proved by alternative synthesis [5]. The highest yield of methylamide V was obtained when the reaction was carried out in chloroform in the presence of concentrated sulfuric acid.

It is interesting to note that benzofuran-2-carboxylic acid methylamide V is also formed in the Beckmann rearrangement of 2-acetylbenzofuran oxime [6, 7]. Our results provide a basis for the assumption that the heteroring in the intermediate particle formed during the condensation of hydrazoic acid with 3-acetylbenzofuran derivatives is in the anti position with respect to the departing nitrogen molecule, whereas in the case of 2-acetylbenzofuran this position is occupied by the methyl group. Consequently, the heteroring migrates in the first case, and the alkyl group migrates in the second.

Thus the Schmidt rearrangement of 3-acetylbenzofurans may serve as a good method for the synthesis of 3-acetamidobenzofurans.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-10 spectrometer. The UV spectra of $2 \cdot 10^{-5}$ M solutions of the compounds (layer thickness 10 mm) were recorded with a Pye-Unicam spectrophotometer. Chromatography was carried out in a thin layer of activity II Al_2O_3 in a carbon tetrachloride–ethanol system (10 : 1).

3-Acetamido-5-methoxybenzofuran (I). Powdered sodium azide [1 g (0.015 mole)] was added in portions with stirring at 60° to a solution of 1.9 g (0.01 mole) of 3-acetyl-5-methoxybenzofuran [7] in 15 g of trichloroacetic acid, after which the mixture was stirred at 60° for 4 h. It was then cooled and treated with 75 ml of water and 10 ml of 25% ammonium hydroxide, and the resulting precipitate was removed by filtration and washed on the filter with water and petroleum ether to give 1.6 g (78%) of I with mp 164-166° (from isopropyl alcohol) and R_f 0.45. IR spectrum: 1560, 1662 (C=O); 3280 cm^{-1} (N–H). UV spectrum, λ_{max} (log ε): 219 (4.46), 250 (4.07), 257 (4.1), 291 (3.84), and 301 nm (3.81). Found: C 64.3; H 5.5; N 6.9%. $C_{11}H_{11}NO_3$. Calculated: C 64.4; H 5.4; N 6.8%.

2-Methyl-3-acetamido-5-methoxybenzofuran (II). This compound [1.7 g (80%)], with mp 152-153° (from aqueous isopropyl alcohol) and R_f 0.42, was obtained from 2 g of 2-methyl-3-acetyl-5-methoxybenzofuran [7] by the preceding method. IR spectrum: 1620, 1670 (C=O); 3260 cm^{-1} (N–H). UV spectrum, λ_{max} (log ε): 217 (4.42), 252 (4.17), 257 (4.15), 291 (3.89), and 300 nm (3.81). Found: C 65.8; H 6.8; N 6.5%. $C_{12}H_{13}NO_3$. Calculated: C 65.8; H 6.0; N 6.4%.

5-Methoxybenzofuran-3-carboxylic Acid Methylamide (III). A solution of 1.9 g (0.01 mole) of 5-methoxybenzofuran-3-carboxylic acid in 1.8 ml of thionyl chloride and 10 ml of absolute dioxane was heated at 60° for 2 h and refluxed for 30 min, after which it was allowed to stand at room temperature overnight. The excess thionyl chloride and the solvent were removed by distillation, and the residue was dissolved in 40 ml of absolute ether. The solution was filtered, and a solution of 0.93 g (0.03 mole) of methylamine in 10 ml of absolute alcohol was added dropwise with stirring to the filtrate. The mixture was cooled and stirred for 30 min, after which it was allowed to stand at room temperature overnight. The solvent was removed by vacuum distillation, 50 ml of water was added to the residue, and the mixture was heated to 40°C. The precipitate was removed by filtration and washed with water to give 1.4 g (68.5%) of a product with mp 105-106° (from hexane–benzene) and R_f 0.42. IR spectrum: 1575, 1640 (C=O); 3296 cm^{-1} (N–H). UV spectrum, λ_{max} (log ε): 217 (4.42), 250 (4.11), 255 (4.08), and 295 nm (3.92). Found: C 64.5; H 5.3; N 6.8%. $C_{11}H_{11}NO_3$. Calculated: C 64.4; H 5.4; N 6.8%.

2-Methyl-5-methoxybenzofuran-3-carboxylic Acid Methylamide (IV). This compound [1.3 g (64%)], with mp 128-130° (from benzene–cyclohexane) and R_f 0.52, was obtained from 2 g of 2-methyl-5-methoxybenzofuran-3-carboxylic acid by the method used to prepare methylamide III. IR spectrum: 1612, 1645 (C=O); 3272 cm^{-1} (N–H). UV spectrum, λ_{max} (log ε): 215 (4.4), 251 (4.08), 254 (3.8), and 292 nm. Found: C 65.6; H 6.1; N 6.3%. $C_{12}H_{13}NO_3$. Calculated: C 65.8; H 6.0; N 6.4%.

Benzofuran-2-carboxylic Acid Methylamide (V). A 1.3-g (0.02 mole) sample of sodium azide was added in portions at 50° in the course of an hour to a mixture of 1.6 g (0.01 mole) of 2-acetylbenzofuran, 50 ml of chloroform, and 10 ml of concentrated sulfuric acid, after which the mixture was stirred at 50° for 3 h. It was then cooled, the organic layer was separated, and the aqueous phase was extracted with chloroform. The combined chloroform extracts were dried with sodium sulfate, and the solvent was removed by distillation to give 1.4 g (80%) of methylamide V with mp 107-108° (from aqueous alcohol) [5] and R_f 0.57. IR spectrum: 1658 (C=O) and 3270 cm^{-1} (N–H). UV spectrum, λ_{max} (log ε): 216 (4.06) and 269 nm (4.03).

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PECULIARITIES OF THE MANIFESTATION OF THE K ABSORPTION BANDS IN THE UV ABSORPTION SPECTRA OF AZOMETHINE BASES

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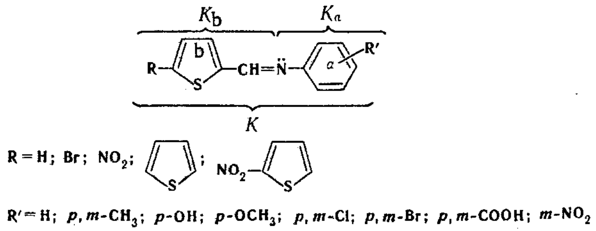
The structure of the UV spectra of azomethine bases of the thiophene and dithienyl series was examined on the basis of the concept of the nonplanar structure of azomethine bases. A peculiarity of the manifestation of the K absorption bands associated with stabilization of the wavelengths of the K bands, which is determined by an increase in the angle of acoplanarity of the azomethine system above 30°, was revealed.

In the present research we investigated the structure of the UV absorption spectra of azomethine bases of the general formula



Their interpretation became possible after the assumption on the basis of UV absorption spectra, of the nonplanar structure of benzylideneaniline [1] as a result of rotation of the *a* ring about the bond with the nitrogen atom at a certain angle θ [2-5]. The acoplanarity of this molecule was recently confirmed by the results of x-ray diffraction analysis [6]. The long-wave absorption band in the spectra of the azomethines usually corresponds to the $\pi \rightarrow \pi^*$ electron transition of the entire conjugated system of the azomethine (the K band) [1, 2, 4,

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