Utilization of 1,5-disubstituted tetrazole for preparation of furo[2,3-\textit{d}]imidazole

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Synthesis of a new heterocycle, substituted furo[2,3-\textit{d}]imidazole, has been developed. The reaction of ethyl \textit{N}-(5-methoxycarbonyl-2-furyl)imidoformate and -imidoacetate, respectively, with azoimide in the presence of trifluoroacetic acid resulted in 1-(5-methoxycarbonyl-2-furyl)tetrazole and 1-(5-methoxycarbonyl-2-furyl)-5-methyltetrazole. Thermal decomposition of the latter compound provided 2-methyl-5-methoxycarbonylfuro[2,3-\textit{d}]imidazole.

Though there are several papers in the literature dealing with preparation and reactions of furo-fused heterocycles [1—3], preparation of furoimidazole derivatives has not been described so far.

In the paper [4] the classical way for the synthesis of fused imidazoles, based on cyclization of methyl 5-acetamido-4-amino-2-furancarboxylate, was tested unsuccessfully. Application of several other methods used for preparation of fused imidazole derivatives [5—12] has not led to synthesis of the furoimidazole skeleton either. Unsuccessful cyclization as well as the fact that no furo[2,3-\textit{d}]imidazole derivative has been described in the literature so far led to the conclusion that it is necessary to develop a new method based on other starting furan derivative.

The present paper describes the preparation of furo[2,3-\textit{d}]imidazole skeleton IV (Scheme 1). For its synthesis we used the reaction known with 1,5-
-diphenyltetrazole which on splitting off nitrogen at 200—230 °C provides besides diphenylcarbodiimide also 2-phenylbenzimidazole in 14 % yield [13, 14]. The starting 1,5-disubstituted tetrazoles IIIa and IIIb, not described so far, were prepared by the reaction of ethyl N-(5-methoxycarbonyl-2-furyl)imidoformate (Ia) and -imidoacetate (Ib) [15] with azoimide in the presence of trifluoroacetic acid. The primarily formed azidoazomethines (IIa, IIb) cannot be isolated because they cyclize spontaneously to 1-(5-methoxycarbonyl-2-furyl)-5-alkyltetrazoles (IIIa, IIIb), as proved by absence of the intensive absorption band in the IR spectrum at $\nu = 2250—2080$ cm$^{-1}$, characteristic of the azido group [16]. Also the UV spectra, showing only one absorption band at $\lambda = 266$ nm (IIIa) and at 257 nm (IIIb), respectively, pointed to tetrazoles, since azidoazomethines IIa, IIb should have $\lambda_{\text{max}}$ shifted by 20—30 nm to higher wavenumbers [17].

![Scheme 1](image_url)

The mass spectra of the compounds IIIa and IIIb revealed molecular ions $M^+$ of very low intensity. The further way of fragmentation provided the ion with $m/z [M^+ - 28]$, formed by splitting off of nitrogen from the molecular ion, as proved by the presence of the metastable ion maxima at $m/z = 115.7$ (IIIa) and at 142.0 (IIIb). The most intensive ion in the mass spectrum of the derivative IIIb was the
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ion with \( m/z = 80 \) (Scheme 2). The \(^1\)H NMR spectra of tetrazoles IIIa and IIIb showed a singlet of the methoxy group at \( \delta = 3.96 \) ppm and 3.95 ppm, respectively. In the spectrum of tetrazole IIIa a singlet for the tetrazole proton appeared at \( \delta = 9.2 \) ppm. The protons of the furan skeleton provided characteristic doublets at \( \delta = 6.88 \) ppm (3-H) and 7.35 ppm (4-H) with coupling constant \( J_{3,4} = 4.0 \) Hz. Tetrazoles IIIa and IIIb are considerably thermostable and can even be sublimed in vacuo. By thermolysis of the more available tetrazole IIIb at 180—185 °C in benzene with addition of copper(II)—chromium(III) catalyst, deactivated by barium (STREM CATALOGUE 1980—1981 29-0410), we prepared 2-methyl-5-methoxycarbonylfuro[2,3-d]imidazole (IVb). Without the catalyst only the unreacted tetrazole IIIb was recovered from the solution even after 4 h heating. Attempts at photochemical splitting off of nitrogen from tetrazole IIIb by irradiation of tetrazole in various solvents by medium-pressure mercury discharge

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lamp with polychromatic radiation using quartz sleeve have not led to the desired derivative IV, only to polymeric products. The structure of the new heterocycle IVb was proved by its $^1$H NMR spectrum which revealed a sharp singlet at $\delta = 7.29$ ppm for 6-H proton, a singlet for the methoxy group (3.87 ppm), and a singlet for the methyl group at $\delta = 2.50$ ppm. The mass spectrum of IVb is very characteristic. Contrary to tetrazoles IIIa and IIIb, here the most intensive ion was the molecular ion $M^{++}$ and fragmentation produced different ions than in the case of tetrazole IIIb (Scheme 3). It is evident from comparison of the UV spectra of tetrazole IIIb ($\lambda_{max} = 257$ nm) and of the substituted furoimidazole IVb ($\lambda_{max} = 301$ nm) that in the fused heterocyclic system the conjugation increased. Consequently, the absorption band was bathochromically shifted by 44 nm. The high value of the molar absorption coefficient ($\log (\varepsilon/(\text{m}^2\text{mol}^{-1})) = 3.23$) and the red shift a transition from nonpolar solvent indicated that it was a $\pi \leftarrow \pi^*$ transition.

**Experimental**

Melting points were determined on a Kofler block. IR spectra were measured on an IR–71 spectrophotometer, UV spectra were recorded in methanol on a Specord UV VIS
apparatus, the ε values are given in m² mol⁻¹. Mass spectra were measured on an MS 902-S AEI Manchester spectrometer at 100 μA and 70 eV and ¹H NMR spectra were obtained with a Tesla BS 487 spectrometer in deuterated chloroform using tetramethylsilane as standard.

1-(5-Methoxycarbonyl-2-furyl)tetrazoles IIIa, IIIb

Into the solution of azoimide (10 mmol) in benzene (10 cm³) ethyl N-(5-methoxycarbonyl-2-furyl)imidoformate Ia (10 mmol) and ethyl N-(5-methoxycarbonyl-2-furyl)imidooacetate Ib (10 mmol), respectively, were added. The mixture was stirred till dissolution of Ia and Ib. Then trifluoroacetic acid (10 mmol) was added and the reaction mixture was allowed to stand at room temperature for 24 h. The solution was evaporated in vacuo and the product was isolated by column chromatography (silica gel, eluent chloroform—methanol, volume ratio = 8 : 2).

1-(5-Methoxycarbonyl-2-furyl)tetrazole (IIIa): yield = 89 %, m.p. = 90.5—101 °C, sublimed at 2 kPa. For C₇H₆N₄O₃ (Mᵣ = 194.15) w(calc.): 43.30 % C, 3.16 % H, 28.86 % N; w(found): 43.37 % C, 3.40 % H, 28.56 % N. IR spectrum (KBr), v/cm⁻¹: 3102, 1708, 1531, 1423, 1305, 1132, 1064, 1009, 960, 810, 744. UV spectrum, λₘₐₓ/nm (log ε): 266 (2.12). ¹H NMR spectrum, δ/ppm: 3.96 (s, 3H, CH₃—О), 6.88 (d, J₃,₄ = 4 Hz, 1H, 3-H-furan), 7.35 (d, 1H, 4-H-furan). Mass spectrum m/z (I(%): M⁺ 194 (4), 166 (27), 152 (5), 135 (100), 108 (48), 80 (10), 79 (54), 67 (45), 63 (88).

1-(5-Methoxycarbonyl-2-furyl)-5-methyltetrazole (IIIb): yield = 88 %, m.p. = 95.5—96 °C (methanol). For C₉H₈N₄O₃ (Mᵣ = 208.17) w(calc.): 46.15 % C, 3.87 % H, 26.91 % N; w(found): 46.19 % C, 3.90 % H, 26.99 % N. IR spectrum (KBr), v/cm⁻¹: 3125, 1730, 1610, 1525, 1433, 1295, 1210, 1145, 1010, 985, 795, 760. UV spectrum, λₘₐₓ/nm (log ε): 257 (2.12). ¹H NMR spectrum, δ/ppm: 2.76 (s, 3H, CH₃), 3.95 (s, 3H, CH₂—O), 6.85 (d, J₃,₄ = 4 Hz, 1H, 3-H-furan), 7.35 (d, 1H, 4-H-furan). Mass spectrum m/z (I(%): M⁺ 208 (1), 180 (40), 149 (45), 137 (25), 122 (50), 121 (38), 109 (18), 93 (30), 80 (100), 67 (40), 59 (50), 52 (65).

2-Methyl-5-methoxycarbonylfuro[2,3-d]imidazole IVb

The mixture of IIIb (1 g; 4.8 mmol) and copper(II)—chromium(III) catalyst, deactivated by barium (100 mg), in anhydrous benzene (100 cm³) was heated in a pressure tube at 180—185 °C for 11/2 h. After the reaction was completed, the catalyst was filtered off, benzene was distilled off in vacuo and the product was obtained by chromatography on thin layer plates (silica gel LS₅₄₀ cemented with 13 % plaster, eluent ether). Yield of IVb 330 mg (38 %), m.p. = 257—259 °C (methanol). For C₈H₇N₂O₂ (Mᵣ = 180.16) w(calc.): 53.32 % C, 4.47 % H, 15.65 % N; w(found): 53.67 % C, 4.11 % H, 15.30 % N. IR spectrum (KBr), v/cm⁻¹: 3367, 1725, 1653, 1545, 1360, 1302, 1212, 770. UV spectrum, λₘₐₓ/nm (log ε): 303 (3.23). ¹H NMR spectrum, δ/ppm: 2.50 (s, 3H, CH₃), 3.87 (s, 3H, CH₂—O), 7.29 (s, 1H). Mass spectrum m/z (I(%): M⁺ 180 (100), 149 (50), 122 (15), 81 (20), 80 (25), 68 (22), 53 (36).
References


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