Utilization of 1,5-disubstituted tetrazole for preparation of furo[2,3-*d*]imidazole

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Received 8 October 1985

Paper published on the occasion of the 45th anniversary of the foundation of the Department of Organic Chemistry, Slovak Technical University, Bratislava

Synthesis of a new heterocycle, substituted furo[2,3-*d*]imidazole, has been developed. The reaction of ethyl *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-*d*]imidazole.

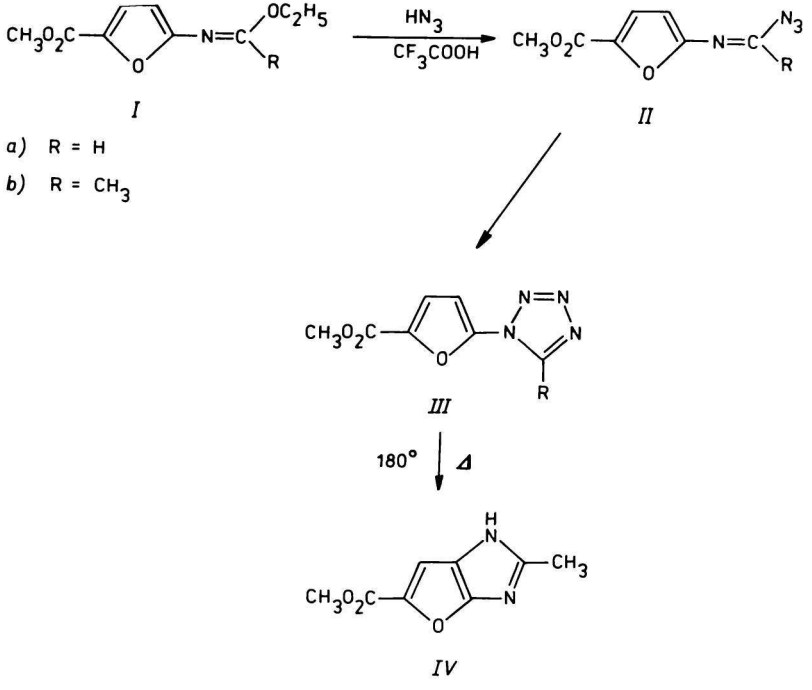
Был разработан метод синтеза нового гетероцыкла, замещенного фуро[2,3-*d*]имидазола. Этиловый эфир *N*-(5-метоксикарбонил-2-фурил)-иминомуравьиной кислоты и -иминоуксусной кислоты реагируют с ажоимидом в присутствии трифторуксусной кислоты и образуется 1-(5-метоксикарбонил-2-фурил)тетразол и в другом случае 1-(5-метоксикарбонил-2-фурил)-5-метилтетразол. Термическим путем из 1-(5-метоксикарбонил-2-фурил)-5-метилтетразола образуется 2-метил-5-метоксикарбонилфуро[2,3-*d*]имидазол.

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-*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-*d*]imidazole skeleton *IV* (Scheme 1). For its synthesis we used the reaction known with 1,5-

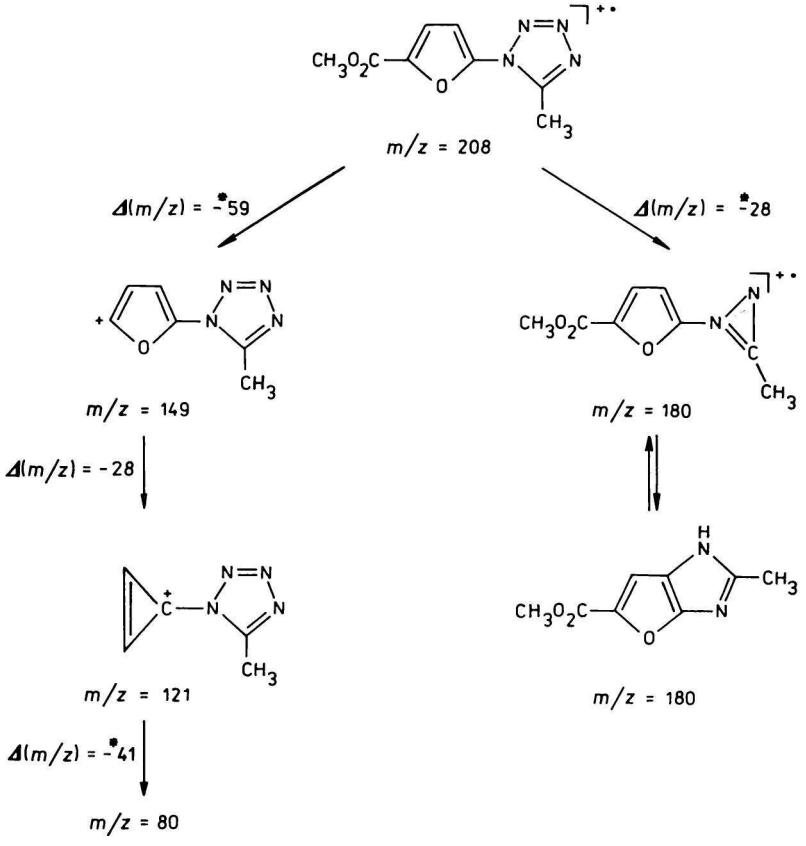
-diphenyltetrazole which on splitting off nitrogen at 200—230 °C provides beside diphenylcarbodiimide also 2-phenylbenzimidazole in 14 % yield [13, 14]. The starting 1,5-disubstituted tetrazoles *IIIa* and *IIIb*, not described so far, were prepared by the reaction of ethyl *N*-(5-methoxycarbonyl-2-furyl)imidoformate (*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 $\tilde{\nu} = 2250—2080$ 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 λ_{max} shifted by 20—30 nm to higher wavenumbers [17].



Scheme 1

The mass spectra of the compounds *IIIa* and *IIIb* revealed molecular ions $M^{+\cdot}$ of very low intensity. The further way of fragmentation provided the ion with *m/z* $[M^{+\cdot} - 28]$, 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

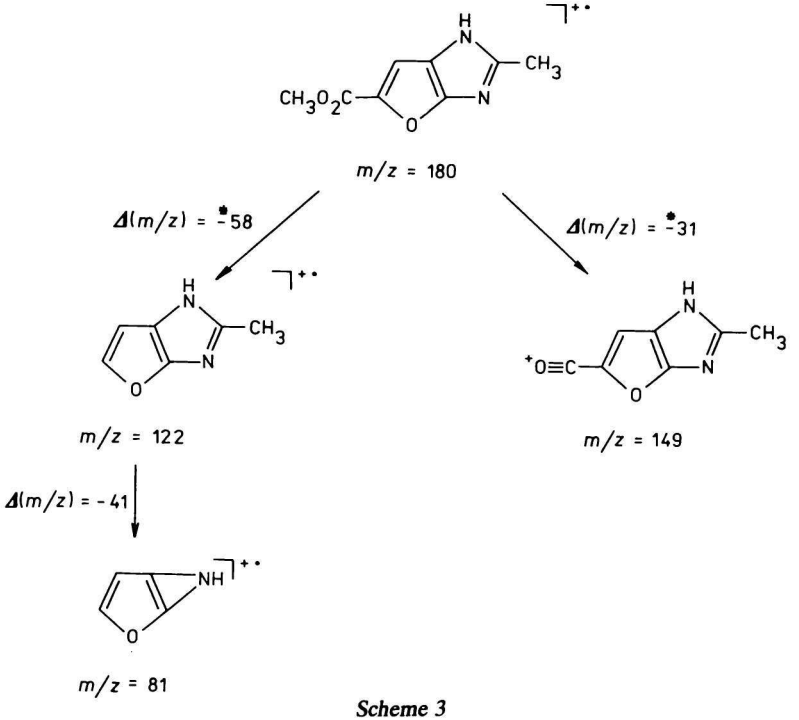
ion with $m/z = 80$ (Scheme 2). The ^{1}H NMR spectra of tetrazoles *IIIa* and *IIIb* showed a singlet of the methoxy group at $\delta = 3.96$ ppm and 3.95 ppm, respectively. In the spectrum of tetrazole *IIIa* a singlet for the tetrazole proton appeared at $\delta = 9.2$ ppm. The protons of the furan skeleton provided characteristic doublets at



Scheme 2

$\delta = 6.88$ 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

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 $M^{+\cdot}$ and fragmentation produced different ions than in the case of tetrazole *IIIb* (Scheme 3). It is evident from comparison of the UV spectra of



Scheme 3

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 ($\log(\varepsilon/(m^2\ mol^{-1})) = 3.23$) 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 $m^2\ mol^{-1}$. Mass spectra were measured on an MS 902-S AEI Manchester spectrometer at 100 μA and 70 eV and ^{1}H 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 cm^3) ethyl *N*-(5-methoxycarbonyl-2-furyl)imidoformate *Ia* (10 mmol) and ethyl *N*-(5-methoxycarbonyl-2-furyl)imidoacetate *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 $C_7H_6N_4O_3$ (M_r = 194.15) w_i(calc.): 43.30 % C, 3.16 % H, 28.86 % N; w_i(found): 43.37 % C, 3.40 % H, 28.56 % N. IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 3102, 1708, 1531, 1423, 1305, 1132, 1064, 1009, 960, 810, 744. UV spectrum, λ_{max}/nm (log {ε}): 266 (2.12). ^{1}H NMR spectrum, δ/ppm: 3.96 (s, 3H, CH_3—O), 6.88 (d, $J_{3,4}$ = 4 Hz, 1H, 3-H-furan), 7.35 (d, 1H, 4-H-furan), 9.2 (s, 1H-tetrazole). Mass spectrum *m/z* (I_r/%): $M^{+\cdot}$ 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 $C_8H_8N_4O_3$ (M_r = 208.17) w_i(calc.): 46.15 % C, 3.87 % H, 26.91 % N; w_i(found): 46.19 % C, 3.90 % H, 26.99 % N. IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 3125, 1730, 1610, 1525, 1433, 1295, 1210, 1145, 1010, 985, 795, 760. UV spectrum, λ_{max}/nm (log {ε}): 257 (2.12). ^{1}H NMR spectrum, δ/ppm: 2.76 (s, 3H, CH_3), 3.95 (s, 3H, CH_3—O), 6.85 (d, $J_{3,4}$ = 4 Hz, 1H, 3-H-furan), 7.35 (d, 1H, 4-H-furan). Mass spectrum *m/z* (I_r/%): $M^{+\cdot}$ 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 cm^3) 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 LS_{5-40} cemented with 13 % plaster, eluent ether). Yield of *IVb* 330 mg (38 %), m.p. = 257—259 °C (methanol). For $C_8H_8N_2O_3$ (M_r = 180.16) w_i(calc.): 53.32 % C, 4.47 % H, 15.65 % N; w_i(found): 53.67 % C, 4.11 % H, 15.30 % N. IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 3367, 1725, 1653, 1545, 1360, 1302, 1212, 770. UV spectrum, λ_{max}/nm (log {ε}): 303 (3.23). ^{1}H NMR spectrum, δ/ppm: 2.50 (s, 3H, CH_3), 3.87 (s, 3H, CH_3—O), 7.29 (s, 1H). Mass spectrum *m/z* (I_r/%): $M^{+\cdot}$ 180 (100), 149 (50), 122 (15), 81 (20), 80 (25), 68 (22), 53 (36).

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Translated by A. Kardošová