REACTIONS OF ETHYL ESTER OF N-(5-METHOXYCARBONYL-2-FURYL)-IMIDOFORMIC AND IMIDOACETIC ACIDS WITH AMINES

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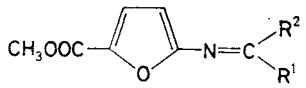
By the reaction of ethyl ester of N-(5-methoxycarbonyl-2-furyl)imidoformic (*I*) and imidoacetic (*II*) acids, resp., with ammonia, aniline, isopropylamine and methyl ester of 5-amino-2-furancarboxylic acid, resp., N,N'-disubstituted amidines were prepared.

Alkoxy group of esters of imidoacetic and imidoformic acids offers a great number of substitution reactions with nucleophilic reagents[1,2]. The most common are reactions with aliphatic or aromatic amines[3]. Some amidines prepared in this way are used as pharmaceuticals[4,5], there are known syntheses of heterocycles from ethyl esters of imidoacetic acid and N-substituted hydrazones[6].

In the presented work the reactions of ethyl ester of N-(5-methoxycarbonyl-2-furyl)-imidoformic (*I*) and imidoacetic (*II*)[7] acids with ammonia, aniline, isopropylamine and methyl ester of 5-amino-2-furancarboxylic acid, resp., are studied. N-furyl substituted amidines were prepared in this way. The compound *I* has proved to be more reactive than *II*. While *I* has changed to N,N'-bis(5-ethoxycarbonyl-2-furyl)-formamidine (*VI*) by mere contact with air moisture, *II* does not react with air moisture at all. Formamidines *IV*–*VI* were prepared from *I* by heating with amine in the solvent under an inert atmosphere. In the reaction of amines with *II* the reaction time was five times longer. The structure of the synthetised compounds was proposed on the basis of IR, UV, ^{1}H NMR and MS spectral data. In UV spectra of *I* and *II* only one absorption band λ_{max} 300 nm (log ε 3·3–3·5) was observed, while for the analogical compounds two bands are given in the literature[8,9]. In UV spectra of the compounds *III*, *IV*, *VII* red shift of 20–30 nm relatively to *I* and *II*, resp., was observed. This can be explained by the electron-donor effect of amidine group. Compounds *V*, *VI*, *VIII*, and *IX*, resp., have in UV spectra two bands with λ_{max} 260 to 290 nm and λ_{max} 347–360 nm, the second one being more intensive. The presence of the two bands indicates the conjugation of the aromatic substituent. In IR spectra of the prepared compounds an intensive band in the region 1 700–1 729 cm^{-1} (νC=O)) occurs, then a band in the region 1 600–1 625 cm^{-1} (ν(C=N)), the vibration band of NH group occurs in the region 3 100–3 400 cm^{-1}. In the case of compounds *VI* and *IX* are the signals of protons H^4, H$^{4'}$ of furan ring in ^{1}H NMR

spectra only as a diffusive band, and not as awaited, doublets, while protons H^3 and $H^{3'}$ give a doublet. We conclude therefrom that the molecules are symmetrical with a slight migration of the proton H^8. All crystalline products produced molecular ion in the mass spectra. In the mass spectra of compounds *III* and *V* a fragmentation with *m/z* 141 occurs, which arises from the molecular ion through splitting off HCN in the case of *III* ($M^{+\bullet} - 27$) and in the case of *V* C_6H_5CN ($M^{+\bullet} - 103$), with the transfer of two protons. This is proved by the existence of metastable maximum with *m/z* 118·3 and 81·4.



I, $R^1 = H$; $R^2 = OC_2H_5$
II, $R^1 = CH_3$; $R^2 = OC_2H_5$
III, $R^1 = H$; $R^2 = NH_2$
IV, $R^1 = H$; $R^2 = HN-CH(CH_3)_2$
V, $R^1 = H$; $R^2 = HN-C_6H_5$

VI, $R^1 = H$; $R^2 = HN-$ 
VII, $R^1 = CH_3$; $R^2 = HN-CH(CH_3)_2$
VIII, $R^1 = CH_3$; $R^2 = HN-C_6H_5$
IX, $R^1 = CH_3$; $R^2 = HN-$ 

EXPERIMENTAL

Melting points are uncorrected. IR spectra were measured on IR-71 and UV spectra on Specord UV-VIS in methanol. The values of ε are given in $m^2\ mol^{-1}$. Mass spectra were measured on MS 902-S, ionization 70 eV, emission 100 μA. ^1H NMR spectra were measured on BS 487 C (tetramethylsilane as a standard) in deuteriochloroform.

N-(5-Methoxycarbonyl-2-furyl)formamidine (*III*)

To the solution of *I* (0·5 g, 2·5 mmol) in dioxane (20 ml) dried ammonia was introduced. After 30—50 min a product precipitated. 0·3 g of *III* (71%) was obtained, m.p. 157—159°C (methanol). IR spectra (KBr, cm^{-1}): 3 367, 3 136, 1 685, 1 601, 1 498, 1 442, 1 322, 1 211, 1 143, 1 029, 980. UV spectra λ_{max} nm (log ε) 323 (3·29). For $C_7H_8N_2O_3$ (168·2) calculated: 50·00% C, 4·79% H, 16·66% N; found: 51·4% C, 4·70% H, 16·7% N. ^1H NMR spectra: 3·85 (s, 3 H, CH_3O), 5·79 (d, 1 H, $J = 3·4$ Hz, H-4 furan), 7·14 (d, 1 H, H-3 furan).

N-(5-Methoxycarbonyl-2-furyl)-N'-isopropylformamidine (*IV*)

To the solution of *I* (1 g, 5 mmol) in dioxane (20 ml) isopropylamine (0·6 g, 10 mmol) was added. The mixture was heated at 40°C under argon atmosphere for 6 hours. After distilling off dioxane, the product was obtained by column chromatography (silica gel, eluent diethyl ether, chloroform, diethyl ether–methanol). 0·45 g *IV* was obtained (43%), m.p. 58—60°C (ethanol). IR spectra (KBr, cm^{-1}): 3 300, 2 930, 1 695, 1 479, 1 308, 1 201, 1 184, 1 128, 1 010, 975, 742. UV spectra λ_{max} nm (log ε) 330 (3·34). For $C_{10}H_{14}N_2O_3$ (210·3) calculated: 57·09% C, 6·71% H, 13·33% N; found: 57·02% C, 6·66% H, 13·8% N. ^1H NMR spectra: 3·75 (s, 3 H, CH_3O), 4·13 (m, 1 H, CH), 5·59 (d, 1 H, $J = 3·5$ Hz, 4-H furan), 7·08 (d, 1 H, H-3 furan), 8·08 (s, 1 H, C—H amidine).

N-(5-Methoxycarbonyl-2-furyl)-N'-fenylformamidine (*V*)

Solution of *I* (0·5 g, 2·5 mmol) in dioxane (10 ml) and aniline (0·23 g, 2·5 mmol) was heated for 24 hours at 70°C. The product was isolated by preparative chromatography (silica gel G according to Stahl, eluent ether, benzene). 0·45 g *V* (77%) was obtained, m.p. 143—145°C (acetonitrile). IR spectra (cm^{-1}, KBr): 1 712, 1 656, 1 589, 1 492, 1 309, 1 133, 1 034, 980, 799, 745. UV spectra λ_{max} nm (log ε): 260 (2·89), 350 (3·36). For $C_{13}H_{12}N_2O_3$ (244·3) calculated: 63·89%C, 4·95% H, 11·47% N; found: 64·10% C, 5·05% H, 12·10% N. ^{1}H NMR spectra: 3·87 (s, 3 H, CH_3O), 5·83 (d, 1 H, J = 3·4 Hz, 4-H furan), 7·17 (d, 1 H, H-3 furan), 7·30 (m, 5 H phenyl), 8·66 (s, 1 H, CH amidine).

N,N'-(5-Methoxycarbonyl-2-furyl) formamidine (*VI*)

The mixture of *I* (0·5 g, 2·4 mmol) and methyl ester of 5-aminofuran-2-carboxylic acid in dioxane (20 ml) was refluxed for 2 hours. 0·69 g *VI* (94%) was obtained, m.p. 203—205°C (acetonitrile). IR spectra (KBr, cm^{-1}): 3 152, 2 975, 1 721, 1 660, 1 498, 1 442, 1 309, 1 134, 989. UV spectra λ_{max} nm (log ε): 277 (3·01), 360 (3·57). For $C_{13}H_{12}N_2O_6$ (292·3) calculated: 53·41% C, 4·14% H, 9·59% N; found: 52·98% C, 4·18% H, 9·36% N. ^{1}H NMR spectra: 3·81 (s, 6 H, CH_3O), 6·32 (broad band, 2 H, H-4,4'-furan), 7·32 (d, 2 H, J = 3·6 Hz, H-3,3'-furan), 8·31 (s, 2 H, CH amidine).

N-(5-Methoxycarbonyl-2-furyl)-N'-isopropylacetamidine (*VII*)

The solution of *II* (1 g, 4·7 mmol) in tetrahydrofurane (20 ml) was heated with isopropylamine (0·32 g, 5·5 mmol) in the glass autoclave at 100°C for 48 hours. Then the mixture was separated by preparative TLC (silica gel G according to Stahl, diethyl ether). 0·2 g of *VII* (19%) was obtained, oil. IR spectra (chloroform): 2 981, 1 706, 1 608, 1 410, 1 369, 1 308, 1 138, 1 012. UV spectra λ_{max} nm (log ε): 320 (3·15). For $C_{11}H_{16}N_2O_3$ (224·4) calculated: 58·88% C, 7·14% H, 12·49% N; found: 57·95% C, 6·89% H, 13·05% N. ^{1}H NMR spectra: 1·22 (d, 6 H, J = 6·4 Hz, CH_3 isopropyl), 2·12 (s, 3 H, CH_3- acetamidine), 3·87 (s, 3 H, CH_3O), 4·23 (m, 1 H, CH — isopropyl), 5·59 (d, 1 H, J = 3·5 Hz, H-4 furan), 7·18 (d, 1 H, H-3 furan).

N-(5-Methoxycarbonyl-2-furyl)-N'-fenylacetamidine (*VIII*)

Prepared similarly as *VII*, by heating at 70°C for 5 days. 0·28 g (48%) was obtained, m.p. 197 to 199°C (acetonitrile). IR spectra (KBr, cm^{-1}): 3 001, 1 727, 1 658, 1 596, 1 539, 1 311, 1 278, 1 127, 1 015, 979. UV spectra λ_{max} nm (log ε) 206 (3·89), 292 (3·31). For $C_{14}H_{14}N_2O_3$ (258·4) calculated: 65·06% C, 5·46% H, 10·84% N; found: 63·80% C, 5·46% H, 11·10% N. ^{1}H NMR spectra: 2·2 (s, 3 H, CH_3 acetamidine), 3·86 (s, 3 H, CH_3O), 5·75 (d, 1 H, J = 3·5 Hz, H-4 furan), 6·5 (broad band, 1 H, NH), 7·18 (d, 1 H, H-3 furan), 7·26 (m, 5 H, phenyl).

N,N'-(5-Methoxycarbonyl-2-furyl)acetamidine (*IX*)

Solution of *II* (1 g, 4·7 mmol) in dioxane (20 ml) and methyl ester of 5-amino-2-furancarboxylic acid (0·7 g, 5 mmol) was heated at 100°C for 24 hours under argon. After cooling 1·3 g *IX* (98%) was obtained, m.p. 198—199°C (methanol). IR spectra (KBr, cm^{-1}): 3 274, 1 728, 1 625, 1 588, 1 627, 1 838, 1 335, 1 306, 1 132, 1 009. UV spectra λ_{max} nm (log ε): 290 (3·11), 347 (3·51). For $C_{14}H_{14}N_2O_6$ (306·4) calculated: 54·87% C, 4·60% H, 9·13% N; found: 54·40% C, 4·67% H, 9·69% N. ^{1}H NMR spectra: 2·31 (s, 3 H, CH_3 acetamidine), 3·81 (s, 6 H, CH_3O), 5·91 (broad band, 2 H, H-4,4' furan), 7·21 (d, 2 H, J = 3·5 Hz, H-3,3' furan).

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