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# 4-Aminofurazan-3-carboxylic Acid Iminoester in Reactions with N,O-Nucleophiles

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**Abstract**–Reactions of 4-aminofurazan-3-carboxylic acid iminoester with o-aminophenol and ethylenediamine give rise respectively to 4-(1,3-benzoxazol-2-yl)- and 1-(4,5-dihydro-1*H*-imidazol-2-yl)-1,2,5-oxadiazol-3-amines, with aminoethanol arises 2-[(*Z*)-1-amino-1-(4-amino-1,2,5-oxadiazol-3-yl)methylideneamino]-1-ethanol. Treating of 3-amino-4-(1*H*-benzo[d]imidazol-2-yl)-1,2,5-oxadiazole with triethyl orthoformate in acetic anhydride yielded benzo[4,5]imidazo[1,2-*c*][1,2,5]oxadiazolo[3,4-e]pyrimidine, and alkylation with haloalkanes furnished 3-amino-4-(1-R-benzo[d]imidazol-2-yl)-1,2,5-oxadiazoles.

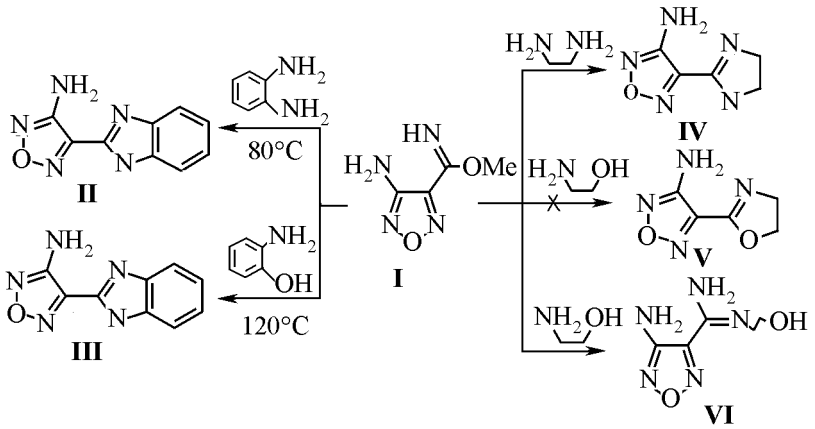
We showed formerly that application of 4-aminofurazan-3-carboxylic acid iminoester (**I**) to the synthesis of 4-(5-R-1,2,4-triazol-3-yl)furazan with various substituents in *5* position of the triazole ring was promising.

In extension of study of probable synthetic routes to polycyclic structures containing 1,2,5-oxadiazole (furazan) moiety we carried out reactions between iminoester **I** with a series of bifunctional *N*,*N* and *N*,*O*-nucleophiles, among them *o*-pheylenediamine, *o*-aminophenol, ethylenediamine, and 2-aminoethanol, for similar condensation is widely used for building up heterocyclic systems.

We showed before that heating iminoester **I** with *o*-phenylenediamine in boiling ethanol (80°C) readily yielded 3-amino-4-(1*H*-benzo[d]imidazol-2-yl)-1,2,5-oxadiazole (**II**) [2]. However in reaction of iminoether **I** with *o*-aminophenol under similar conditions did not form 4-(1,3-benzoxazol-2-yl)-1,2,5-oxadiazol-3-amine (**III**), although the basicity of *o*-aminophenol ($pK_{BH^+}$ 4.72) is somewhat higher than that of *o*-phenylenediamine ($pK_{BH^+}$ 4.52) [4].

However the raising of reaction temperature to 120°C (use of 1-butanol for the solvent) and longer reaction time resulted in preparation of compound **III** in over 75% yield.

Similarly to *o*-phenylenediamine reacted ethylenediamine providing 3-amino-4-(4,5-dihydro-1H-imidazol-2-yl)-1,2,5-oxadiazole (**IV**) whereas the reaction of compound **I** with aminoethanol instead of expected 3-amino-4-(4,5-dihydro-1,3-oxazol-2-yl)-1,2,5-oxadiazole (**V**) furnished an amidine, 2-[(*Z*)-1-amino-1-(4-amino-1,2,5-oxadiazol-3-yl)methylideneamino]-1-ethanol (**VI**). The lack of oxazole ring closure is apparently due to considerably lower nucleophilicity of hydroxy group compared with amino group, and

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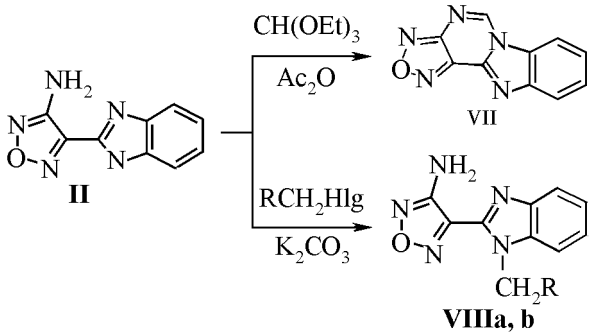
Task yields, melting points, spectral data of spectral and elemental analyses of compounds synthesized

| Compd. no. | Yield, % | mp, °C | IR spectrum, ν, $cm^{-1}$ | $^1H$ NMR spectra, δ, ppm | $^{13}C$ NMR spectrum, δ, ppm | Found, % | | | Formula | Calculated, % | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | C | H | N | | C | H | N |
| **III** | 78 | 170–171 | 3400, 3304 ($NH_2$), 2361 (CH), 1638 (C–N), 1617 (O–N–O), 1559, 1508, 1491, 1474 (C=N), 1448, 1246, 1113, 1091, 1007 (0–N) | 7.91 d (1H, Ph), 7.85 d (1H, Ph),) 7.55 t (1H, Ph), 7.51 t (1H, Ph), 6.62 s (2H, $NH_2$) | 155.71, 152.59, 150.02, 140.29, 136.84, 127.46, 125.80, 120.76, 111.66 | 54.88 | 3.61 | 28.64 | $C_9H_6N_{402}$ | 53.47 | 2.99 | 27.71 |
| **IV** | 92 | 114 | 3388 ($NH_2$), 3315 (NH), 2894 ($CH_2$), 1640 (C–N), 1608 (O–N–O), 1551, 1487, 1461 (C=N), 1334, 1288, 1184, 1136, 1013 (O–N), 978 | 6.15 in (2H, $NH_2$; 1H, NH), 3.70 in (2H, $CH_2$), 3.0 in (2H, $CH_2$) | 156.55, 156.07, 138.90, 55.92, 44.67 | 39.43 | 5.02 | 46.05 | $C_5H_7N_{50}$ | 39.22 | 4.61 | 45.73 |
| **VI** | 83 | 117–118 | 3566 (OH), 3401, 3350 (NH), 3000, 2954, 2898, 2850 ($CH_2$), 1667 (C–N), 1624 (O–N–O), 1540, 1527, 1507, 1478, 1459 (C=N), 1404, 1310, 1189, 1063 (O–N), 1012, 908 | 6.65 s (2H, $NH_2$), 6.46 s (2H, $NH_2$), 4.59 s (1H, OH), 3.65 d (2H, $CH_2$), 3.25 m (2H, $CH_2$) | 156.55, 148.68, 141.94, 62.50, 51.18 | 35.12 | 6.15 | 41.73 | $C_5H_9N_{502}$ | 35.09 | 6.30 | 40.92 |
| **VII** | 60 | 272–273 | 1650 (C–N), 1587, 1563, 1553, 1433 (C=N), 1345, 1309, 1260, 1172, 1018 (O–N), 951 | 9.85 s (1H, CH), 8.41 d(1H, Ph), 8.02 d (1H, Ph), 7.64 M (2H, Ph) | – | 57.31 | 2.57 | 32.76 | $C_{10}H_5N_{50}$ | 56.88 | 2.39 | 33.16 |
| **VIIIa** | 85 | 147 | 3401, 3299 ($NH_2$), 2985 ($CH_2$), 1633 (C–N), 1592 (O–N–O), 1471 (C=N), 1444, 1329, 1200, 1073 (O–N), 996 | 7.76 m (2H, Ph), 7.37 m (2H, Ph), 6.92 c (2H, $NH_2$), 4.71 q (2H, $CH_2$) 1.42 t (3H, $CH_3$) | – | 57.03 | 5.64 | 30.25 | $C_{11}H_{11}N_{50}$ | 57.63 | 4.84 | 30.55 |
| **VIIIb** | 93 | 168 | 3409, 3312 ($NH_2$), 2985 ($CH_2$), 1743 (C=O), 1637 (C–N), 1462 (C=N), 1378, 1280, 1229, 1177, 1022 (O–N) 986 | 7.79 m (2H, Ph), 7.39 m (2H, Ph), 6.88 s (2H, $NH_2$), 5.53 s (2H, $CH_2$), 4.19 q (2H, $CH_2$), 1.23 t (3H, $CH_3$) | – | 55.01 | 5.12 | 24.85 | $C_{13}H_{13}N_{503}$ | 54.35 | 4.56 | 24.38 |

also higher conformational lability of the hydroxyethylene chain in contrast to conformationally rigid system of *o*-aminophenol.

Benzimidazole **II** contrary to the presence in position *2* of an electron-withdrawing 1,2,5-oxadiazole ring cleanly reacted with triethyl orthoformate in acetic anhydride yielding benzo[4,5]imidazo[1,2-*c*]-[1,2,5]oxadiazolo[3,4-e]pyrimidine. It also underwent alkylation with haloalkanes in alkaline medium affording N-alkyl derivatives (**VIII**).




**VIIIa, b**

R = Me (**a**), $CH_2COOEt$ (**b**).

## EXPERIMENTAL

$^1H$ and $^{13}C$ NMR spectra were registered on spectrometer Bruker DPX-300, solvent and internal reference DMSO-$d_6$. IR spectra were measured on Perkin Elmer Spectrum BX 1000 instrument from thin film on KBr sublayer, mass spectra were recorded on Varian CH-6 device.

Melting points, elemental analyses, and spectral characteristics of compounds synthesized are presented in the table.

**4-(1,3-Benzoxazol-2-yl)-1,2,5-oxadiazol-3-amine (III).** A mixture of 0.5 g (3.5 mmol) of iminoester **I** and 0.38 g (3.5 mmol) of *o*-aminophenol in 10 ml of 1-butanol was boiled for 3 days. On cooling the separated precipitate was filtered off and dried at 60°C Yield 0.55 g.

**3-amino-4-(4,5-dihydro-1H-imidazol-2-yl)-1,2,5-oxadiazole (IV) and 2-[(*Z*)-1-amino-1-(4-amino-1,2,5-oxadiazol-3-yl)methylideneamino]-1-ethanol (VI).** A mixture of 3.5 mmol of iminoester **I** and 3.5 mmol od ethylenediamine or 2-aminoethanol in 10 ml of 2-propanol was boiled for 3 h. On cooling the solution was evaporated in air, and the residue was crystallized from a mixture chloroform–2-propanol, 2:1. Found, $M^+$: 153 (**IV**), 171 (**V**). Calculated, *M*: 153 (**IV**), 171 (**V**).

**Benzo[4,5]imidazo[1,2-*c*][1,2,5]oxadiazolo[3,4-*e*]-pyrimidine (VII).** A mixture of 0.5 g (2.48 mmol) of benzimidazole **II**, 3 ml of triethyl orthoformate, and 1 ml of acetic anhydride was boiled for 12 h. On cooling the separated precipitate was filtered off and dried at 60°C. Yield 0.31 g.

**3-Amino-4-(1-ethyl-1*H*-benzo[*d*]imidazol-2-yl)-1,2,5-oxadiazole (VIIIa) and methyl-2-[2-(4-amino-1,2,5-oxadiazol-3-yl)-1*H*-benzo[*d*]imidazol-1-yl] acetate (VIIIb).**A mixture of 0.5 g (2.48 mmol) of compound **II**, 4 mmol of alkyl halide, 1 g of anhydrous $K_2CO_3$ in 5 ml of DMF was stirred for 3 h at 20°C, then poured into 30 ml of water, the separated precipitate was filtered off, washed with water (3×10 ml), and dried in air.

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