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Reactions of Methyl 4-Aminofurazan-3-carboximidate with Nitrogen-Containing Nucleophiles*

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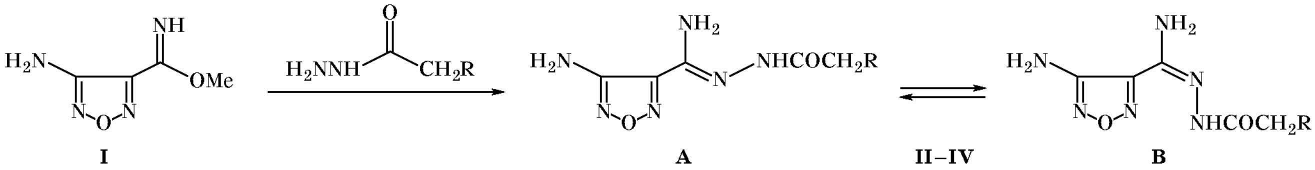
Abstract—Methyl 4-aminofurazan-3-carboximidate reacts with aromatic amines and hydrazines to give the corresponding amidines and amidrazones. The reaction of the title compound with *o*-phenylenediamine yields 3-amino-4-(2-benzimidazolyl)furazan, and with acylhydrazines N^2-acyl-4-aminofurazan-3-carbohydrazides are formed. The latter undergo thermal intramolecular cyclization with formation of 3-amino-4-(1,2,4-triazol-3-yl)furazan derivatives containing various substituents in position *5* of the triazole ring.

In continuation of our studies on the applicability of a new synthon of the 1,2,5-oxadiazole series, methyl 4-aminofurazan-3-carboximidate (**I**) [1], for preparation of various polycyclic structures possessing a 3-amino-1,2,5-oxadiazole fragment, we examined its behavior in reactions with some aromatic amines, aromatic hydrazines, and acylhydrazines. Easy reactions of carboximidate **I** with hydrazides derived from heterocyclic acids [1] led us to presume that analogous reactions are possible with aliphatic carbohydrazides containing various functional groups. In fact, heating of a mixture of compound **I** with alkanecarbohydrazide in alcohol resulted in formation of substituted carboxamidrazones **II**–**IV** in good yields (Scheme 1). According to the NMR data, amidrazones **II**–**IV** exist as two isomers, **A** and **B**. The ^{1}H NMR spectrum of compound **IV** contains signals from protons of two NH and two NH_2 groups of the amidrazone moiety, four protons of two NH_2 groups in the furazan ring, and protons of the methylene group (Fig. 1). An analogous pattern was observed in the ^{13}C NMR spectrum: there were two signals from the carbonyl carbon atoms, eight signals from carbon atoms of the furazan ring, two amidine carbon signals, and two signals from the methylene group (Fig. 2). However, we failed to assign these signals to particular isomers because of the lack of appropriate model compounds.

A fairly strong molecular ion peak with *m*/*z* 267 (I_{rel} = 40%) was observed in the mass spectrum of **IV**. The fragment ion peak with *m*/*z* 249 corresponds to elimination of water from the molecular ion. A similar pattern was observed in the mass spectra of amidrazones **II**, **III**, and **V**. This allowed us to presume easy intramolecular cyclization of compounds **II**–**V** into furazanyl-1,2,4-triazole derivatives. Indeed, heating of **II**–**V** at a temperature exceeding their melting point by 5–10°C resulted in elimination of water and formation of 3-amino-(1,2,4-triazol-3-yl)-furazans **VI**–**IX** (Scheme 2).

Scheme 1.



II, R = OMe; **III**, R = $(CH_2)_4OH$; **IV**, R = 4-aminofurazan-3-yl.

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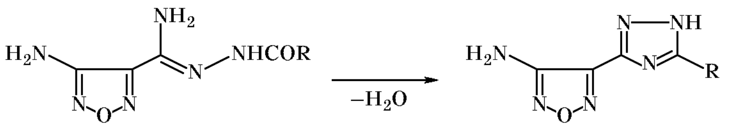
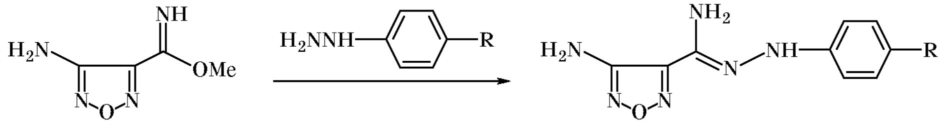
Scheme 2.



II–V **VI–IX**

II, **VI**, R = CH_2OCH_3; **III**, **VII**, R = $(CH_2)_5OH$; **IV**, **VIII**, R = 4-aminofurazan-3-ylmethyl; **V**, **IX**, R = 4-methylfurazan-3-yl.

Scheme 3.



I **X, XI**

X, R = Cl; **XI**, R = NO_2.

3-Amino-4-(1,2,4-triazol-3-yl)furazans **VI**–**IX** are NH acids, and they readily form salts on treatment with aqueous alkalies. The methoxy group in carboximidate **I** can be replaced by nitrogen-containing nucleophiles to give amidines or amidrazones. If the latter contain reactive groups and/or there are no steric hindrances, subsequent intramolecular cyclization is possible. The reactions of **I** with *para*-substituted phenylhydrazines result in formation of amidrazones **X** and **XI** (Scheme 3). The reaction with *p*-phenylenediamine stops at the stage of formation of amidine **XII** which does not undergo cyclization for steric reasons. *o*-Phenylenediamine reacts with **I** to give substituted benzimidazole **XIII** in more than 70% yield (Scheme 4). *o*-Aminophenol failed to react with carboximidate **I**, presumably because of the lower basicity (nucleophilicity) of the amino group.

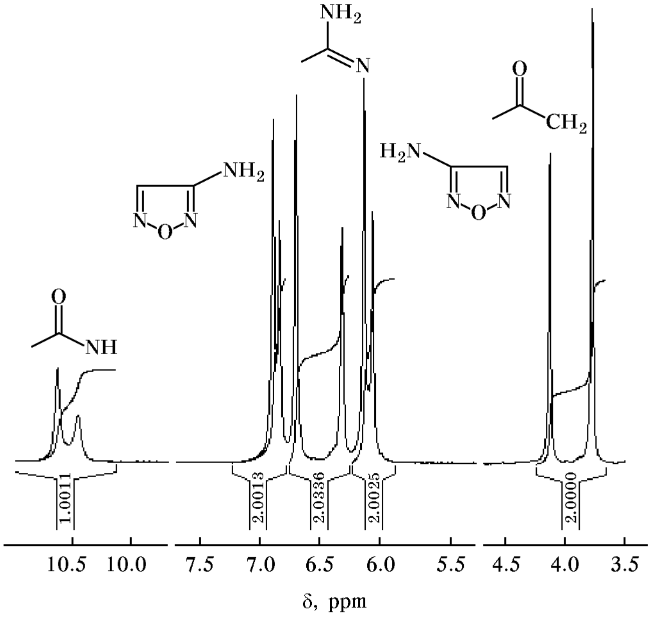


Fig. 1. ^1H NMR spectrum of N^2-(4-aminofurazan-3-ylmethylcarbonyl)-4-aminofurazan-3-carboxamide hydrazone (**IV**).

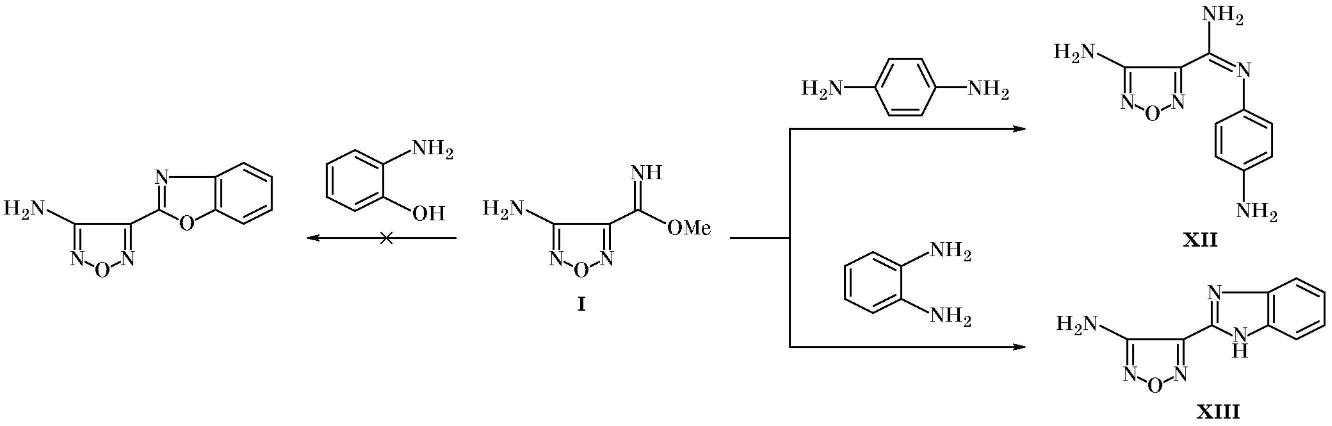
EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on a Bruker DPX-300 spectrometer using DMSO-d_6 as solvent and internal reference. The IR spectra were measured on a Perkin–Elmer Spectrum 1000 instrument from thin films on KBr support. The mass spectra were run on a Varian CH-6 spectrometer. Compound **V** was synthesized by the procedure reported in [1].

Typical procedure for reactions of methyl 4-aminofurazan-3-carboximidate (I) with aliphatic carbohydrazides. A mixture of 0.5 g (3.52 mmol) of carboximidate **I** and 3.52 mmol of appropriate hydrazide in 20 ml of alcohol was refluxed for 12 h. The mixture was cooled, and the precipitate was filtered off, washed with alcohol (2 × 5ml) and water (2 × 5ml), dried at 60°C, and recrystallized from alcohol.

N^2-(Methoxymethylcarbonyl)-4-aminofurazan-3-carboxamide hydrazone (II). Yield 85%, mp 201–202°C. ^1H NMR spectrum, δ, ppm: 10.32 and 10.24 (1H, NH), 6.98 and 6.75 (4H, $2NH_2$), 4.33 and 3.98 (2H, CH_2), 3.34 and 3.33 (3H, CH_3). ^{13}C NMR spectrum, δ_C, ppm: 170.22 (C=O), 165.56 (furazan), 154.80, 154.20, 140.74, 139.92, 136.91, 70.98 and

Scheme 4.



69.57 (CH_2), 58.77 and 58.48 (CH_3). Mass spectrum, *m*/*z*: 214 M^+, 196 $[M-H_2O]^+$. Found, %: C 33.75; H 4.41; N 39.32. $C_6H_{10}N_6O_3$. Calculated, %: C 33.64; H 4.67; N 39.25. *M* 214.

N^2-(6-Hydroxyhexanoyl)-4-aminofurazan-3-carboxamide hydrazone (III). Yield 80%, mp 189–190°C (from alcohol). ^1H NMR spectrum, δ, ppm: 10.2 and 9.79 (1H, NH), 6.75 and 6.30 (4H, $2NH_2$), 4.30 br (1H, OH), 3.40 (2H, CH_2), 2.20 t (2H, CH_2), 1.63–1.52 m (6H, $3CH_2$). ^{13}C NMR spectrum, δ_C, ppm: 173.79, 168.53, 155.09, 154.71, 140.66, 138.63, 136.45, 60.69 (CH_2OH), 34.15 (CH_2), 32.36 (CH_2), 25.36 (CH_2), 25.17 (CH_2). Mass spectrum, *m*/*z*: 256 M^+, 238 $[M-H_2O]^+$. Found, %: C 42.08; H 5.89; N 32.73. $C_9H_{16}N_6O_3$. Calculated, %: C 42.18; H 6.25; N 32.81. *M* 256.

N^2-(4-Aminofurazan-3-ylmethylcarbonyl)-4-aminofurazan-3-carboxamide hydrazone (IV). Yield 73%, mp 223–224°C (from alcohol). Mass spectrum, *m*/*z*: 267 M^+, 249 $[M-H_2O]^+$. Found, %: C 31.79; H 4.81; N 47.57. $C_7H_9N_9O_3$. Calculated, %: C 31.46; H 3.37; N 47.19. *M* 267.

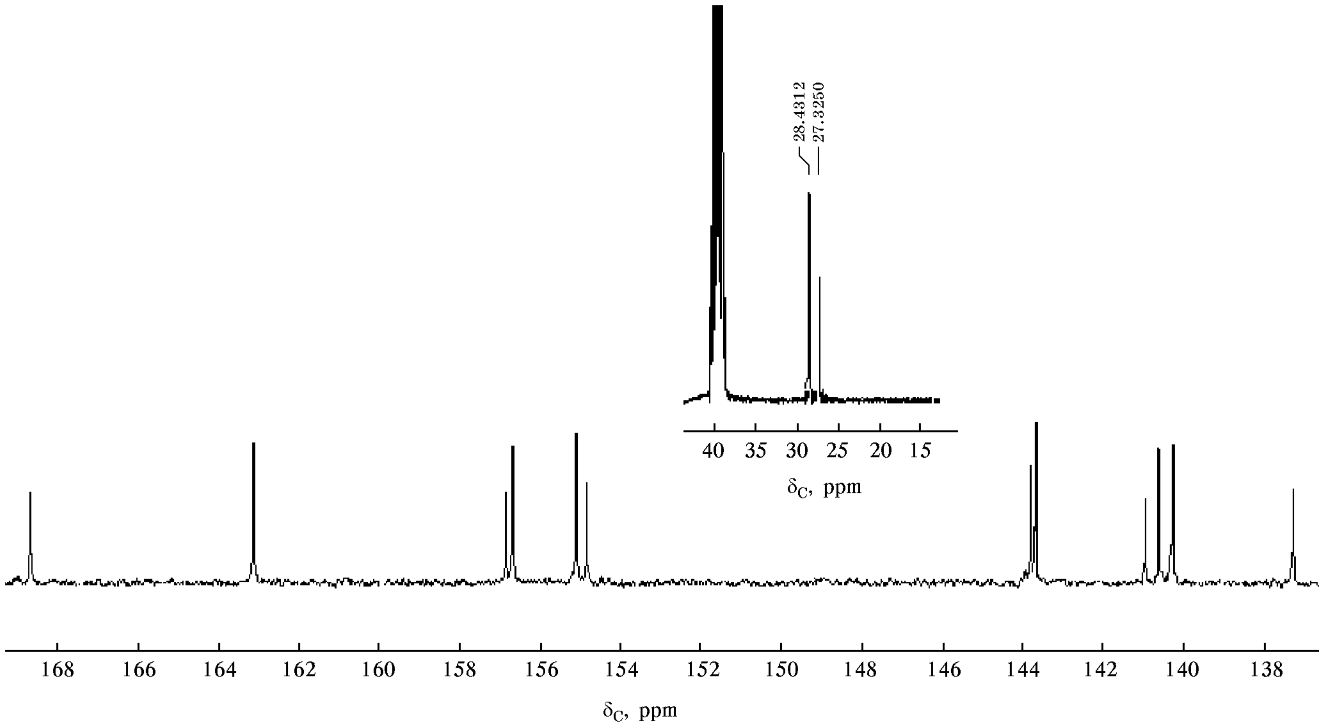


Fig. 2. ^{13}C NMR spectrum of N^2-(4-aminofurazan-3-ylmethylcarbonyl)-4-aminofurazan-3-carboxamide hydrazone (**IV**).

Typical procedure for synthesis of 1,2,4-triazoles VI–IX. *N*-Acylcarboxamidrazone **II**–**V**, 0.75 g, was heated on a metal bath to 5–10°C above its melting point, kept for 1–2 min at that temperature, and cooled. The melt was dissolved in 20% aqueous sodium hydroxide, the undissolved material was filtered off, and the filtrate was acidified to pH 1 by adding concentrated hydrochloric acid. The precipitate was filtered off and dried in air.

3-Amino-4-(5-methoxymethyl-1,2,4-triazol-3-yl)-furazan (VI). Yield 70%, mp 189–190°C. ^{1}H NMR spectrum, δ, ppm: 6.70 s (2H, NH_2), 4.64 s (2H, CH_2), 3.36 s (3H, OCH_3). ^{13}C NMR spectrum, δ_C, ppm: 155.55 (furazan), 155.33 and 150.66 (triazole), 139.35 (furazan), 64.99 (CH_2), 58.42 (CH_3). Found, %: C 36.53; H 4.78; N 42.61. M^+ 196. $C_6H_8N_6O_2$. Calculated, %: C 36.74; H 4.11; N 42.84. *M* 196.

3-Amino-4-[5-(5-hydroxypentyl)-1,2,4-triazol-3-yl]furazan (VII). Yield 80%, mp 156–157°C. ^{1}H NMR spectrum, δ, ppm: 14.3 br (1H, NH), 6.40 s (2H, NH_2), 4.33 br (1H, OH), 3.39 s (2H, CH_2), 2.80 s (2H, CH_2), 1.73–1.36 m (6H, $3CH_2$). ^{13}C NMR spectrum, δ_C, ppm: 173.79, 168.53, 155.09, 154.71, 140.66, 138.63, 136.45, 60.69 (CH_2OH), 34.15 (CH_2), 32.36 (CH_2), 25.36 (CH_2), 25.17 (CH_2). Found, %: C 45.48; H 5.12; N 35.21. M^+ 238. $C_9H_{14}N_6O_2$. Calculated, %: C 45.37; H 5.92; N 35.27. *M* 238.

3-(4-Aminofurazan-3-yl)-5-(4-aminofurazan-3-ylmethyl)-1,2,4-triazole (VIII). Yield 60%, mp 180–181°C. IR spectrum, ν, cm^{-1}: 3617, 3534, 3455, 3344, 3194, 3041, 2896, 2784, 1640, 1602, 1552, 1532, 1461, 1439, 1401, 1357, 1279, 1245, 1172, 1131, 1049, 1007, 975, 892, 860, 795, 769, 718, 690. ^{1}H NMR spectrum, δ, ppm: 14.72 br (1H, NH), 6.42 s (2H, NH_2), 6.35 s (2H, NH_2), 4.36 s (2H, CH_2). ^{13}C NMR spectrum, δ_C, ppm: 156.97 and 156.07 (furazan), 144.94 (triazole), 21.10 (CH_2). Found, %: C 33.52; H 3.16; N 50.35. M^+ 249. $C_7H_7N_9O_2$. Calculated, %: C 33.74; H 2.83; N 50.59. *M* 249.

3-(4-Aminofurazan-3-yl)-5-(4-methylfurazan-3-yl)-1,2,4-triazole (IX). Yield 75%, mp 214–215°C. ^{1}H NMR spectrum, δ, ppm: 16.11 br (1H, NH), 6.50 s (2H, NH_2), 2.70 s (3H, CH_3). ^{13}C NMR spectrum, δ_C, ppm: 153.33, 151.42, 9.34 (CH_3). Found, %: C 36.02; H 2.76; N 47.95. $C_7H_6N_8O_2$. Calculated, %: C 35.90; H 2.58; N 47.85.

Typical procedure for reaction of carboximidate I with aromatic hydrazines. A mixture of equimolar amounts of compound **I** and substituted phenylhydrazine in alcohol was refluxed for 5 h. The mixture was cooled, and the precipitate was filtered off, washed with cold alcohol (10 ml) and water (10 ml), and dried in air.

***N*^{2}-(4-Chlorophenyl)-4-aminofurazan-4-carboxamide hydrazone (X).** Yield 79%, mp 165°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 8.95 s (1H, NH), 7.25 d (2H, H_{arom}), 6.95 d (2H, H_{arom}), 6.43 s (2H, NH_2), 6.41 s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 154.63 (furazan), 144.74 (amidrazone), 140.85 (furazan), 135.53, 129.05, 121.82, 113.41 (C_6H_4). Found, %: C 42.52; H 3.75; Cl 14.08; N 33.99. M^+ 252. $C_9H_9N_6OCl$. Calculated, %: C 42.78; H 3.59; Cl 14.03; N 33.26. *M* 252.

***N*^{2}-(4-Nitrophenyl)-4-aminofurazan-4-carboxamide hydrazone (XI).** Yield 88%, mp 279–280°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 9.85 s (1H, NH), 8.12 d (2H, H_{arom}), 7.03 d (2H, H_{arom}), 6.78 s (2H, NH_2), 6.40 s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 154.74 (furazan), 150.68 (amidrazone), 140.84 (furazan), 138.11, 138.05, 126.30, 111.11 (C_{arom}). Found, %: C 41.05; H 3.94; N 37.31. M^+ 263. $C_9H_9N_7O_3$. Calculated, %: C 41.06; H 3.45; N 37.26. *M* 263.

3-Amino-*N*^{2}-(4-aminophenyl)furazan-4-carboxamidine (XII). A mixture of 0.5 g (3.5 mmol) of compound **I** and 0.4 g (3.5 mmol) of *p*-phenylenediamine in 10 ml of alcohol was refluxed for 3 days. The mixture was cooled, and the precipitate was filtered off and dried in air. Yield 0.63 g (83%), mp 177°C (from alcohol). ^{1}H NMR spectrum, δ, ppm: 6.75 d (2H, H_{arom}), 6.70 s (2H, NH_2), 6.58 d (2H, H_{arom}), 6.55 s (2H, NH_2), 4.9 s (2H, NH_2). Found, %: C 50.24; H 5.44; N 39.48. M^+ 218. $C_9H_{10}N_6O$. Calculated, %: C 49.54; H 4.58; N 38.53. *M* 218.

3-Amino-4-(2-benzimidazolyl)furazan (XIII). A mixture of 0.5 g (3.5 mmol) of compound **I** and 0.35 g (3.5 mmol) of *o*-phenylenediamine in 10 ml of ethanol was refluxed for 20 h. The mixture was cooled, and the precipitate was filtered off, washed with alcohol (2 × 5 ml), and dried in air. Yield 0.42 g. An additional amount (0.08 g) can be isolated by dilution of the filtrate with water. Overall yield 71%, mp 264–265°C (from alcohol). ^{1}H NMR spectrum, δ, ppm: 13.6 s (1H, NH), 7.7 m (2H, H_{arom}), 7.3 m (2H, H_{arom}), 6.8 s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 155.60 and 138.63 (furazan), 140.31 (imidazole), 142.71, 134.34, 124.28, 122.85, 119.67, 112.20 (C_{arom}). Found, %: C 53.76; H 2.98; N 34.92. M^+ 201. $C_9H_7N_5O$. Calculated, %: C 53.73; H 3.51; N 34.81. *M* 201.

REFERENCE

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