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SYNTHESIS AND PROPERTIES OF 4-AMINO-3-CYANOFURAZAN

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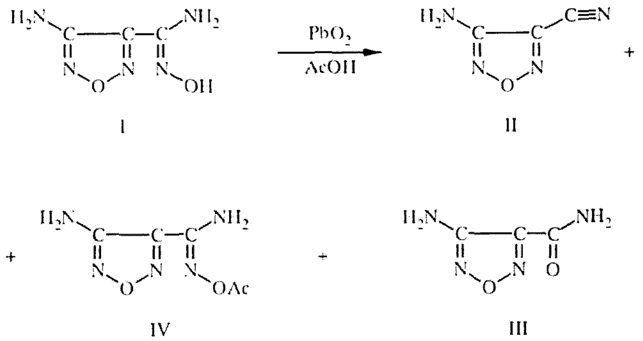
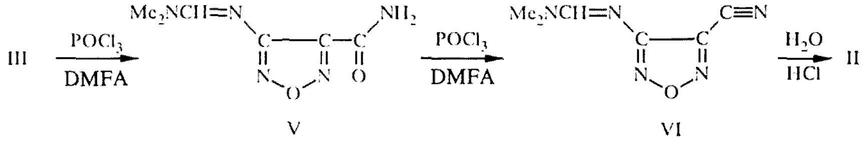
Deoximation of the amidoxime of 4-aminofurazan-3-carboxylic acid and dehydration of 4-aminofurazan-3-carboxamide gave 4-amino-3-cyanofurazan. Reactions of the cyano and amino groups were studied.

Derivatives of 4-aminofurazan-3-carboxylic acid are convenient starting materials for the synthesis of adenine [1]. A series of investigations has been devoted to the synthesis and study of the properties of derivatives of this class. The acid [1, 2] and its ester [1], amide [1, 3], amidine [3], and amidoxime [1, 2, 3], as well as the corresponding aldehyde in the form of the oxime [2], imine [3], and hydrazone [6] have been reported. However, the nitrile of 4-aminofurazan-3-carboxylic acid is presently, unknown. Cyanofurazans in general remain among the least-studied classes of furazan derivatives. Only a few members of this series are known [7-10].

In a study of the properties of the amidoximes of 4-aminofurazan-3-carboxylic acid (I), we established that treatment with lead dioxide in acetic acid solution led to the formation of a mixture of three materials, the major component of which is 4-amino-3-cyanofurazan. (II). The two others were the amide III and the O-acetylamidoxime IV.



In experiments to obtain nitrile II by dehydration of amide III, we established that the latter is very stable to the action of dehydrating agents, such as phosphorus oxychloride and thionyl chloride in this case. Dehydration succeeded only under the action of the Wilsmeier reagent (dimethylformamide and phosphorus oxychloride), in which reaction occurs at the amino group in the first step with the formation of the amidine V, which then dehydrates into the cyanofurazan VI.



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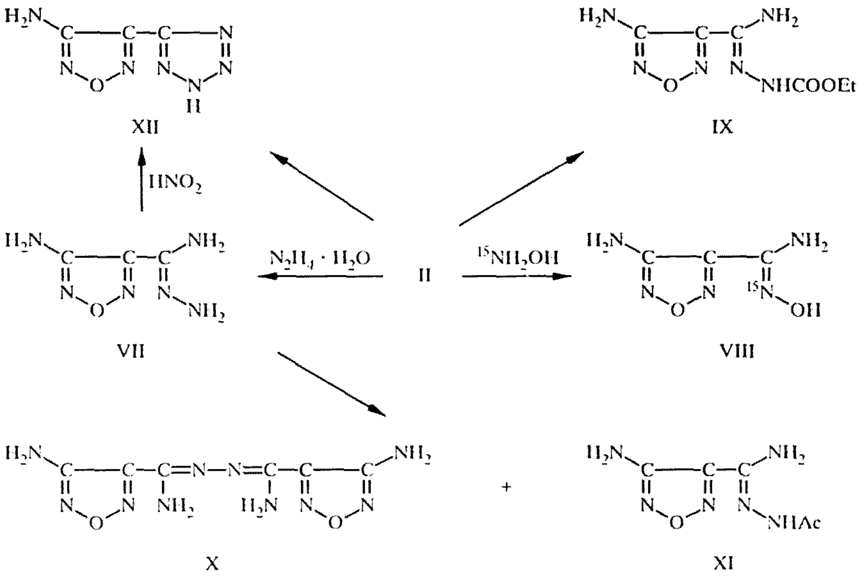
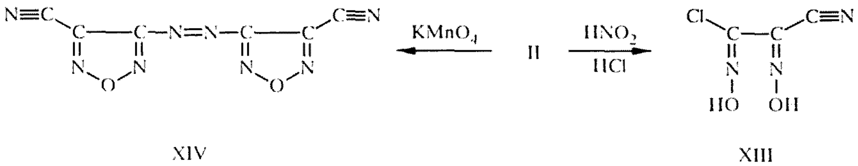
Hydrolysis of the amidine group in acidic medium leads to the cyanofurazan II.

Owing to the electron acceptor properties of the furazan ring, the cyano group in derivative II is highly reactive with respect to nucleophilic agents. Alkaline hydrolysis of the cyano group to the amide group takes place very easily at 50-60°C in sodium carbonate solution. Hydrazine and hydroxylamine add rapidly and under mild conditions (room temperature) to the cyano group. The amidrazone VII is formed in the first case and the amidoxime I in the second. This reaction was used for the formation of amidoxime VIII, labelled on the nitrogen atom of the oxime group [11].



Less active nucleophiles such as ethyl hydrazinecarboxylate react with cyanofurazan II under more vigorous conditions. The amidrazone VII adds to the cyanofurazan II upon boiling in acetic acid with the formation of the dihydrazidine X. The N-acetylamidrazone XI also was formed in this reaction. It is interesting to note that X was obtained by boiling the same amidrazone VII in acetic acid. The easy addition of sodium azide to the cyano group brings about the formation of furazanotetrazole XII. The same material was formed by nitrosation of amidrazone VII.

Nitrosation of aminofurazan II in hydrochloric acid is accompanied by cleavage of the ring and formation of the chlorocyanoglyoxime XIII. This reaction is interesting since it is the first example of the cleavage of a furazan ring with the formation of glyoxime.



Oxidation of aminofurazan II with potassium permanganate in acidic medium gave the azoderivative XIV.

EXPERIMENTAL

The ${}^1H$ NMR spectra were recorded with a Bruker WH-90 in DMSO-d_6, internal standard TMS, and the IR spectra were obtained with a Perkin-Elmer 580 B in Nujol.

Elemental analyses data for C, H, and N corresponded with the calculated values.

4-Amino-3-cyanofurazan (II, $C_3H_2N_4O$). A. To a solution of 1.14 g (8 mmoles) of amidoxime I in 5 ml of acetic acid was added in portions with stirring at 20-25°C 1.78 g (7.4 mmoles) of lead dioxide. The stirring was continued at room temperature for 1.5 h, the precipitate was filtered off, the filtrate was diluted with 30 ml of water, and the product was extracted with ethyl acetate (2 × 100 ml). The extract was washed with 10% Na_2CO_3, then water, and dried over Na_2SO_4. The ethyl acetate was distilled under vacuum, the residue was suspended in 16 ml of CH_2Cl_2, and stirred for 10 min. The precipitate (a mixture of amide III and acetoxime IV) was filtered off and the filtrate was concentrated under vacuum to give 0.47 g (54%) of furazan with mp 85-87°C (from water). ^1H NMR spectrum: 7.02 ppm (2H, s, NH_2). ^{13}C NMR spectrum: 109.26 (C≡N), 127.07 (C_3), 158.27 (C_4). IR spectrum: 3415, 3345, 3251, 3206 (NH_2), 2271 (C≡N), 1645 cm^{-1} (NH_2). Mass spectrum: 110 ($M^{+\cdot}$), 80 (M−NO), 68 (N≡CC≡N → O), 58 ($H_2NC{\equiv}N \rightarrow O$), N≡CC≡N), 42 ($H_2NC{\equiv}N$).

B. To a solution of 6.4 g (50 mmoles) of amide II in 40 ml of DMF was rapidly added dropwise 11.3 g (73 mmoles) of phosphorus oxychloride, resulting in an exotherm to 80°C. After 10 min, the reaction mixture was cooled and poured into 100 ml of cold water. After cooling, the solution was neutralized with sodium hydroxide and extracted with ether (3 × 30 ml). The extract was dried over Na_2SO_4 and evaporated under vacuum to give 5.7 g (69%) of amidine VI in the form of an oil. ^1H NMR spectrum: 3.09 and 3.22 (3H, s, s, CH_3), 8.41 ppm (1H, s, CH). IR spectrum: 2258 (C≡N), 1630 (C=N), 1020 cm^{-1} (furazan).

A solution of 1.65 g (10 mmoles) of amidine VI in 20 ml of 3% HCl was boiled for 5-8 min and then cooled. The compound was extracted with ether (2 × 30 ml), the extract was dried over Na_2SO_4, and evaporated under vacuum to give 0.85 g (77%) of cyanofurazan II, with properties identical to those of the material prepared by Method A.

4-Dimethylaminomethyleneaminofurazan-3-carboxamide (V, $C_6H_9N_5O_2$). To a solution of 6.4 g (50 mmoles) of amide II in 40 ml of DMF was added dropwise at room temperature 5.4 g (35 mmoles) of phosphorus oxychloride. After 10 min the reaction mixture was poured into 100 ml of cold water. Upon cooling, the solution was neutralized with sodium hydroxide solution and the precipitate was filtered off to give 6.8 g (74%) of amidine V with mp 154-156°C (from alcohol). ^1H NMR spectrum: 2.98 and 3.11 (3H, s, s, CH_3); 7.93 and 8.02 (1H, s, s, NH_2); 8.31 ppm (1H, s, CH).

4-Aminofurazan-3-carboxamidrazone (VII, $C_3H_6N_6O$). To a solution of 2.0 g (18 mmoles) of cyanofurazan II in 15 ml of acetonitrile was added with stirring 1.1 ml of hydrazine hydrate. After 6 h the precipitate was filtered off to give 1.95 g (76%) of amidrazone VII with mp 171°C (from alcohol). ^1H NMR: 5.60 (2H, c, NH_2), 5.73 (2H, c, NH_2), 6.31. IR spectrum: 3480 3418, 3320, 3223 (NH_2, NH), 1660 (NH_2), 1612 cm^{-1} (C=N).

Amidrazone VII also was obtained similarly from VI.

N′-Ethoxycarbonyl-4-aminofurazan-3-carboxamidrazone (IX, $C_6H_{10}N_6O_3$). A mixture of 0.55 g (5 mmoles) of cyanofurazan II and 0.52 g (5 mmoles) of ethyl hydrazinecarboxylate was heated at 80°C for 10 min. The reaction mixture was cooled, diluted with water, and the precipitate was filtered off to give 0.8 g (75%) of compound IX with mp 290°C (from alcohol). ^1H NMR spectrum: 1.20 (3H, t, CH_3), 4.11 (2H, q, CH_2), 6.53 (2H, s, NH_2), 6.56 (2H, s, NH_2), 9.93 ppm (1H, s, NH). IR spectrum: 3459, 3385, 3324, 3260, 3132 (NH_2, NH), 1720 (C=O), 1670 (NH_2), 1622 cm^{-1} (C=N).

4-Aminofurazan-3-carboxamidoxime-^{15}N (VIII, $C_3H_5N_5O_2$). To a solution of 0.33 g (3 mmoles) of cyanofurazan II and 0.21 g (3 mmoles) of $^{15}NH_2OH{\cdot}HCl$ in a mixture of 10 ml of water and 3 ml of ethanol was added with stirring 0.16 g (2 mmoles) of Na_2CO_3. After 1 h, the precipitate was filtered off to give 0.38 g (88%) of amidoxime VIII with mp 189-190°C (from water). ^1H NMR spectrum: 6.11 (2H, s, NH_2), 6.22 (2H, s, NH_2), 10.4 ppm (1H, d $J_{HO-{}^{15}N}$ = 2.2 Hz, OH).

4-Aminofurazan-3-carboxylic Acid Dihydrazidine (X, $C_6H_8N_{10}O_2$). A solution of 5.0 g (35 mmoles) of amidrazone VII in 20 ml of acetic acid was boiled for 40 min and cooled. The precipitate, containing a mixture of dihydrazidine X and acetylamidrazone XI, was filtered off and suspended in a solution of 2.0 g of sodium hydroxide in 20 ml of water. The insoluble material was the dihydrazidine X. The basic solution was neutralized with hydrochloric acid and the precipitate of acetylamidrazone XI was filtered off.

Dihydrazidine X: Yield 1.86 g (41%), mp 269-271°C (from a 1:1 mixture of alcohol and water). ^1H NMR spectrum: 6.31 (2H, s, NH_2), 6.80 ppm (2H, s, NH_2). IR spectrum: 3437, 3416, 3300, 3213 (NH_2), 1653 (C=N), 1010 cm^{-1} (furazan).

Acetylamidrazone XI: Yield 2.3 g (36%)m mp 236-238°C (from water). ^1H NMR spectrum: 1.93 (3H, s, CH_3), 6.67 (4H, s, NH), 10.1 ppm (1H, c, NH).

The reaction of amidrazone VI with cyanofurazan II proceeded analogously.

4-Amino-3-(5-tetrazolyl)furazan (XII, $C_3H_3N_7O$). A. To a solution of 1.0 g (7 mmoles) of amidrazone VII in 20 ml of 2% HCl at 0-5°C was added dropwise with stirring a solution of 0.5 g (7.2 mmoles) of sodium nitrite in 4 ml of water. After 2 h, the precipitate was filtered off to give 0.7 g (65%) of compound XII with mp 211-212°C (from water). ^1H NMR spectrum: 6.35 ppm (2H, s, NH_2). IR spectrum: 3460, 3360 (NH_2), 1642 (NH_2), 1033 cm^{-1} (furazan).

B. To a solution of 5.5 g (50 mmoles) of cyanofurazan in 10 ml of DMF was added 4.0 g (62 mmoles) of sodium azide and the mixture was stirred at 80-90°C for 30-50 min. The mixture was cooled and poured into 70 ml of water, which was then treated with hydrochloric acid to pH 3-4. The product was extracted with ether (2 × 100 ml) and the ether was evaporated under vacuum to give 6.0 g (78%) of compound XII.

Chlorocyanoglyoxime (XIII, $C_3H_2ClN_3O_2$). To a solution of 1.1 g (10 mmoles) of cyanofurazan II in 20 ml of 10% HCl at 0-5°C was added with stirring a solution of 0.73 g (11 mmoles) sodium nitrite in 4 ml of water. After 1 h, the mixture was extracted with ether, the extract was dried over sodium sulfate, and evaporated under vacuum to give 0.68 g (46%) of glyoxime XIII with mp 148-149°C (from water). ^1H NMR spectrum: 11.0 (1H, s, OH), 12.1 ppm (1H, s, OH). IR spectrum: 3210, 3200, 3159 (OH), 2271 ($C\equiv N$), 1600 cm^{-1} (C=N).

3,3'-Dicyano-4-4'-azofurazan (XIV, $C_6N_8O_2$). To a solution of 1.1 g (10 mmoles) of furazan II in 50 ml of 20% HCl was added dropwise with stirring at room temperature a solution of 1.57 g (10 mmoles) of potassium permanganate in 20 ml of water. After 10 min, oxalic acid was added to dissolve the manganese dioxide, and the mixture was extracted with ether. The extract was dried over sodium sulfate and evaporated to give 0.93 g (86%) of azofurazan XIV with mp 150-152°C (from a 1:1 mixture of ethanol and water). IR spectrum: 2271 ($C\equiv N$), 1633 (N=N), 1036 cm^{-1} (furazan).

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