AMINOFURAZANS (REVIEW)

V. G. Andrianov and A. V. Eremeev

UDC 547.793.2

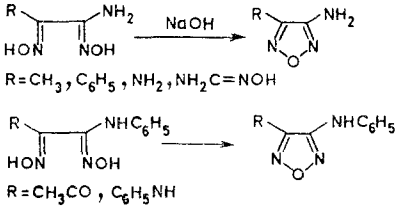
The results of investigations on the structure, methods of synthesis, and chemical properties of the aminofurazans are generalized.

In the 1880s, Holleman [1, 2], in an investigation of the reactions of 3,4-dibenzoylfuroxan with ammonia and aniline, isolated a number of compounds the structure of which was a subject of discussion for a long time. Only in 1928, by Ponzio [3], and in 1969, by Bertelson et al. [4], was it shown that the products of these reactions are aminofurazans. Recently, interest in aminofurazan derivatives has risen in connection with the discovery of their sedative, anticonvulsive, and depressant action [5-27]. However, the voluminous experimental material that has accumulated during the century of the history of the development of the chemistry of the aminofurazans has not hitherto been generalized. Methods of obtaining the aminofurazans and their chemical transformations have scarcely been considered in the reviews on furazans published previously [28-30].

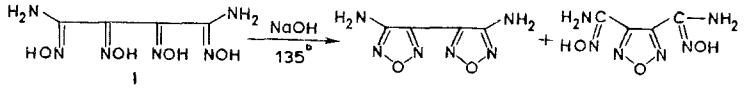
1. METHODS OF SYNTHESIZING AMINOFURAZANS

1.1. Cyclization of Aminoglyoximes

The most general and most frequently used method for obtaining aminofurazans is the dehydration of aminoglyoximes, which sometimes takes place even when their aqueous or alcoholic solutions are boiled [4, 31]. Even during its preparation, bis(phenylhydrazino)glyoxime partially cyclizes to form a furazan derivative [32]. However, considerably more severe conditions are usually required for the formation of the furazan ring. In the majority of cases, the dehydration of the aminoglyoximes is carried out by boiling them in aqueous solutions of alkalis [19, 33-38], or sometimes in ethylene glycol [35, 37, 39], or even with the use of an autoclave [35, 36, 39]



The cyclization of the tetraoxime (I) takes place in two directions, the main reaction product being 4,4'-diamino-3,3'-bifurazanyl [35]:



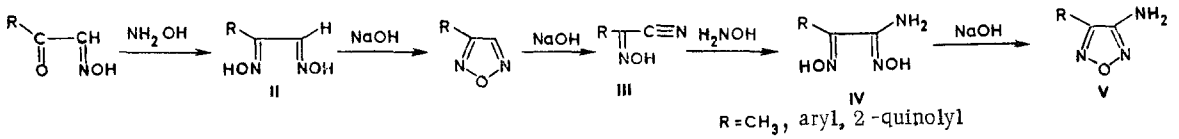
The dehydration of the α- and β- isomers of benzoylaminoglyoxime takes place readily when they are heated in 2 N ammonia solution [3]:

Institute of Organic Synthesis, Academy of Sciences of the Latvian SSR, Riga. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1155-1170, September, 1984. Original article submitted December 21, 1982.

0009-3122/84/2009-0937$08.50

In solution in 6 N ammonia at 175-180°C, methylaminoglyoxime cyclizes to 3-amino-4-methylfurazan [39]. Under similar conditions, diaminoglyoxime hydrolyzes to ammonium oxalate [39], but in caustic soda solution at 165°C it dehydrates to form diaminofurazan [35-37].

Aminoglyoximes are intermediates both in the preparation of aminofurazans from cyano oximes [19-21, 40, 41] and from glyoxal monooximes [15-19, 33, 40, 42] in the presence of hydroxylamine and alkali. The reaction apparently includes the following stages:

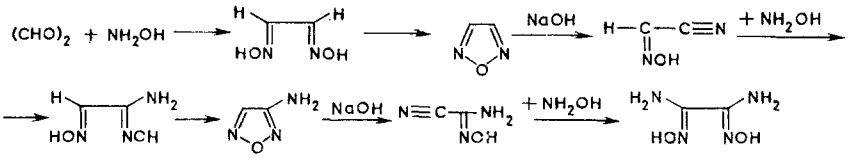


II III IV V

R = CH_3, aryl, 2-quinolyl

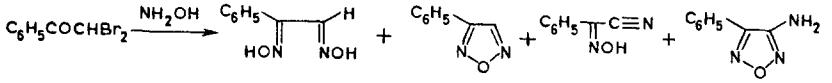
A confirmation of this scheme is the fact that — in addition to the aminofurazan — the glyoxime (II), the cyano oxime (III), and the aminoglyoxime (IV) have been isolated from the reaction mixture, and all are also converted into the aminofurazan (V) under the conditions of this reaction [33, 40].

The reaction of glyoxal with hydroxylamine takes place analogously [43]. However, in this case the final product is diaminoglyoxime, since considerably more severe conditions are required for its cyclization into diaminofurazan.

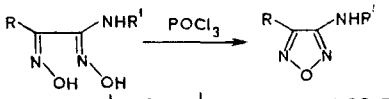


The direct method of obtaining aminofurazans from the readily accessible isonitroso ketones is of interest in the preparative respect, although, as a rule, the yields of cyclization products do not exceed 20-40%.

The reaction of dibromoacetophenone with hydroxylamine takes place by an analogous scheme. This reaction has yield phenylglyoxime, phenylfurazan, phenylisonitrosoacetonitrile, and an unidentified product with mp 98°C — apparently, 3-amino-4-phenylfurazan [44].

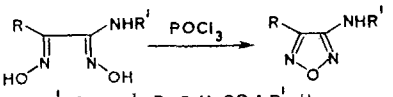


The cyclization of aminoglyoximes can also be carried out under the action of such a dehydrating agent as phosphorus oxychloride. But, in this case, depending on the configuration of the initial glyoxime, dehydration may lead either to aminofurazans or to the products of a Beckmann rearrangement — 1,2,4-oxadiazole derivatives. It has been shown that aminofurazans are usually formed from amphi-aminoglyoximes [45]:



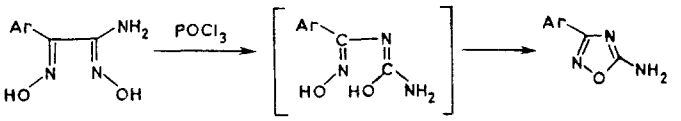
a R = C_6H_5, R' = H; b R = R' = C_6H_5; c R = C_6H_5CO, R' = H

In some cases, aminoglyoximes having the anti- configuration are also converted into aminofurazans [45]:

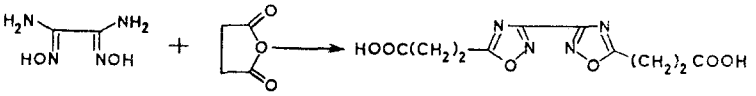


a R = R' = C_6H_5; b R = C_6H_5CO; R' = H

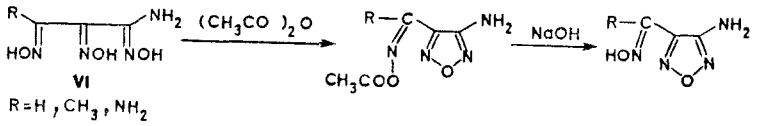
However, under the action of phosphorus oxychloride the anti- isomers of arylaminoglyoximes undergo the Beckmann rearrangement with the formation of 1,2,4-oxadiazole derivatives [46]:

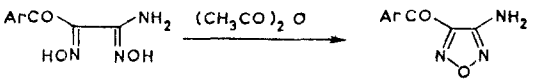


The use of acid anhydrides as cyclizing agents usually leads only to the formation of O- and N-acyl derivatives of aminoglyoximes and, under more severe conditions, to 1,2,4-oxadiazole derivatives [47]:



Exceptions are formed by certain trioximes and amphi-ketoximes which are converted into aminofurazans under the action of acetic anhydride even at room temperature [3, 48-50]:

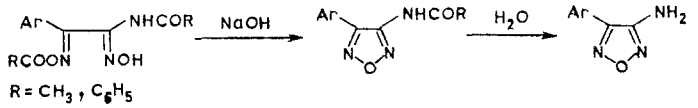




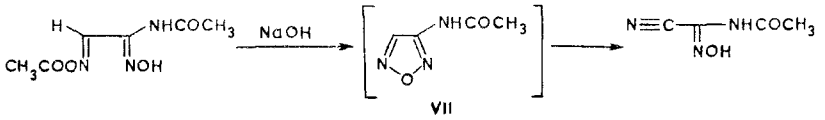
However, if in the initial compound (VI) R = OH or C(=NOH)NH_2, cyclization does not take place but O- and N-acetyl derivatives are formed [50-53].

1.2. Cyclization of Acyl Derivatives of Aminoglyoximes

In some cases, in the synthesis of aminofurazans, it is more convenient to start not from aminoglyoximes but from their acyl derivatives, which cyclize considerably more readily. The O,N-diacyl derivatives of amphi-aminoglyoximes are converted into aminofurazans on brief heating in a 20% aqueous solution of alkali [19, 54-57]:

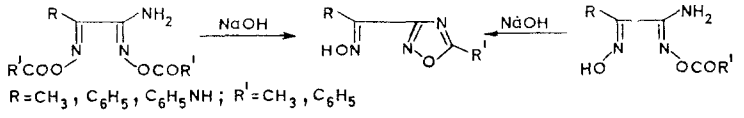


Acetyl derivatives of aminoglyoximes cyclize more readily than benzoyl derivatives. In the first stage, N-acylaminofurazans are formed which may then hydrolyze to aminofurazans. It is assumed that the aminofurazan (VII) is formed as an intermediate by analogy with the treatment of O,N-diacetylaminoglyoxime [58]:



In contrast to disubstituted furazans, monosubstituted furazans are unstable in an alkaline medium [59] and, by the opening of the ring, are converted into cyano oximes.

O-Monoacyl-, O,O-diacyl-, and O,O,N-triacyl-amphi-aminoglyoximes also cyclize to aminofurazans on treatment with alkali [54, 55, 60-62]. The carbamates of amphi-aminoglyoximes can also be used for the synthesis of furazans [56, 63].

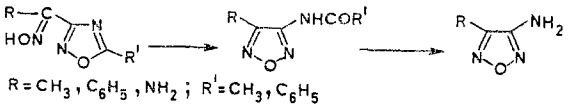


In contrast to the acyl derivatives of the amphi- isomers, on treatment with alkali, O-acyl-anti-aminoglyoximes cyclize to 1,2,4-oxadiazole derivatives [8, 14, 55-58, 64-66] or hydrolyze to the initial glyoximes [61, 63].

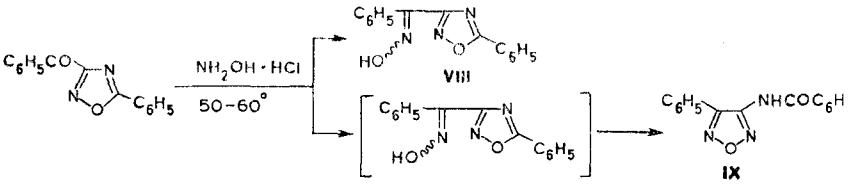
On being heated with alkali, only O,O-dibenzoyl- and O,O,N-tribenzoyl-anti-phenylaminoglyoximes cyclize to 4-benzoyl-3-phenylaminofurazan, while in the first case a 1,2,4-oxadiazole is formed simultaneously [55, 65].

1.3. Preparation of Aminofurazans from Other Heterocyclic Systems

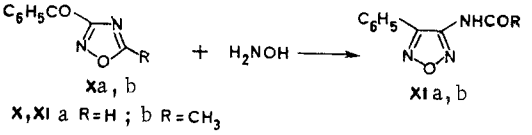
The oximes of 3-acyl-1,2,4-oxadiazoles obtained from O-acylaminoglyoximes are converted into aminofurazan derivatives on being heated in a solution of an alkali or an acid, or on fusion [8, 14, 39, 55, 56, 64-66]:



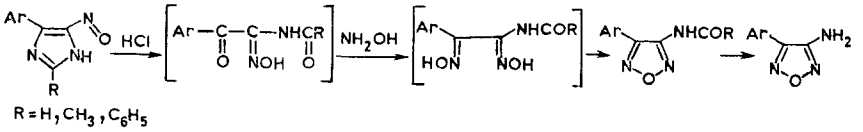
Recyclization is probably preceded by a stage involving the isomerization of the oxime group. Thus, in the reaction of 3-benzoyl-5-phenyl-1,2,4-oxadiazole with hydroxylamine hydrochloride at 60°C, Ponzio obtained a mixture of the oxadiazole (VIII) and the furazan (IX) in approximately equal amounts [65]. Since the oxime (VIII) does not undergo rearrangement to the furazan under these conditions, the hypothesis was put forward that two isomeric oximes are formed simultaneously, one of which is unstable and is converted into the aminofurazan (IX):



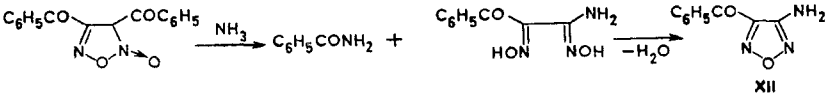
3-Benzoyl-5-methyl-1,2,4-oxadiazole (Xb) reacts with hydroxylamine hydrochloride similarly [67]. At the same time, under these conditions the unsubstituted oxadiazole (Xa) forms only the aminofurazan derivative (XIa). The reaction of the oxadiazoles (Xa, b) with free hydroxylamine leads only to the aminofurazan derivatives (XIa, b) [67]:



In the presence of hydroxylamine, 4-nitrosoimidazoles are readily converted into furazans. Here, depending on the reaction conditions, either aminofurazans or their monoacyl derivatives are obtained [9, 10, 19, 25, 67, 68]:

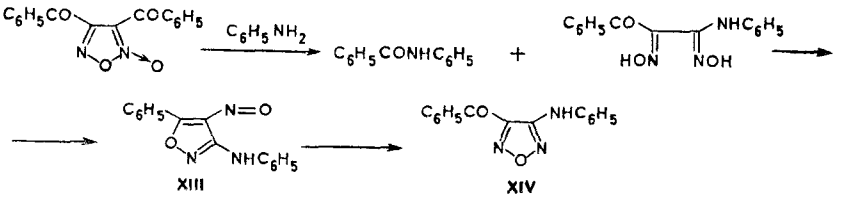


In 1887, Holleman, by the reaction of dibenzoylfuroxan with ammonia, obtained a compound with the empirical formula $C_9H_7N_2O_3$ [1, 69], to which, somewhat later [70], the structure of 5-amino-3-benzoyl-1,2,4-oxadiazole was assigned. However, in 1928, Ponzio [3] showed that the product of this reaction was actually 3-amino-4-benzoylfurazan [3]. This was apparently the first example of the synthesis of an amino-substituted furazan. In the first stage of the reaction, an unstable aminoglyoxime is formed which then cyclizes to the aminofurazan (XII):



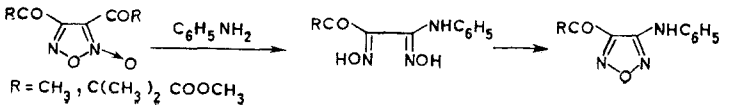
The reaction of dibenzoylfuroxan with aniline takes place in more complex fashion. In the first stage, similarly, anilinoglyoxime is formed which, under the reaction conditions,

dehydrates with the formation of an unstable colored substance readily changing into a colorless isomer [2, 4, 69, 71-74]. The structure of these compounds has caused much dispute. Only recently has it been established that the first of them is 3-anilino-4-nitroso-5-phenylisoxazole (XIII) and the second is 3-anilino-4-benzoylfurazan (XIV) [4]:

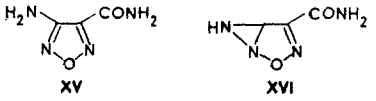


XIII XIV

The reaction of dibenzoylfuroxan with aliphatic amines gives only nitrosoisoxazoles [75]. On reacting with aniline, dialkanoylfuroxans form stable aminoglyoximes which, on heating, dehydrate to give aminofurazans [4]:

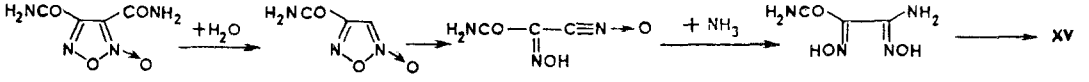


In 1905, Ulpiani [76], by boiling an aqueous solution of furoxandicarbonamide, obtained, together with other reaction products, a compound (mp 175°C), which he called "β-fulminuramide" [76]. Its hydrolysis led to an acid (mp 196°C), and its esterification led to an ester (mp 103-105°C). Ulpiani suggested two possible structures for the compound obtained — (XV) and (XVI), inclining rather to the structure (XVI) [76, 77].

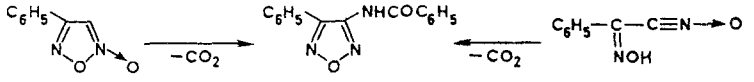


XV XVI

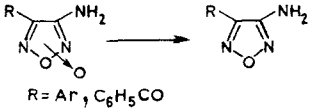
Probably, in actual fact, he was dealing with 3-aminofurazan-4-carbonamide (XV). This is confirmed by the fact that the 3-aminofurazan-4-carboxylic acid derivatives obtained by other methods had melting points close to those given by Ulpiani [38, 50]. The formation of the aminofurazan (XV) can be represented by the following scheme [76, 77]:



At the same time, it has recently been shown that a series of compounds to which the structures of 3-aminofurazan-4-carboxylic acid derivatives were ascribed [78] actually possess a different structure [79]. In 50% ethanol, 4-phenylfuroxan and isonitrosophenylacetonitrile N-oxide are converted into 3-benzoylamino-4-phenylfurazan [80-82]. The mechanisms of these reactions have not been established:

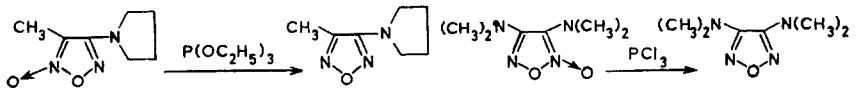


Aminofurazans can also be obtained by the reduction of aminofuroxans. Zinc, tin, and stannous chloride in acid media reduce both aminofuroxan isomers [3, 5-7, 18, 19, 34, 57]:



It is interesting to note that stannous chloride does not reduce phenylaminofuroxans unsubstituted in the phenyl nuclei [57].

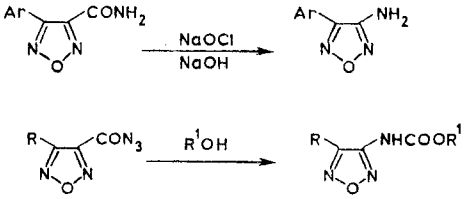
Compounds of trivalent phosphorus are also used as reducing agents [83, 84]:



The reduction of 3-amino-4-phenylfuroxan with hydrogen over a platinum catalyst is accompanied by the cleavage of the furoxan ring and leads to amphi-phenylaminoglyoxime [34]. The reduction of 4-anilino-3-butylfuroxan likewise leads to aminoglyoxime [85].

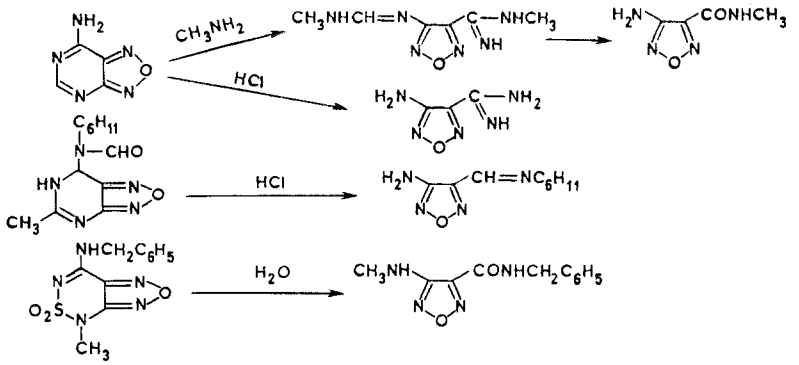
1.4. Other Methods for Obtaining Aminofurazans

The Hofmann [12, 13] and Curtius [22, 86] rearrangements are also used for the introduction of an amine function into the furazan ring:

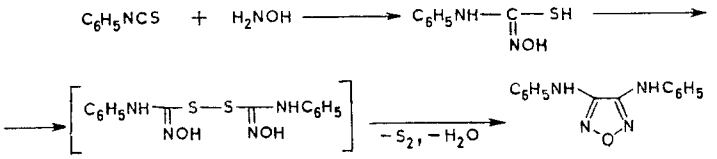


These methods may be useful in the preparation of functional derivatives of aminofurazans when the corresponding aminoglyoximes are difficult of access.

Functionally substituted aminofurazans can be obtained by opening the six-membered rings in furazano[3,4-d]pyrimidines [87] and furazano[3,4-c][1,2,6]thiadiazines [88]:



Dianilinofurazan is formed by the reaction of hydroxylamine with phenyl isothiocyanate [89]:



2. PROPERTIES OF THE AMINOFURAZANS

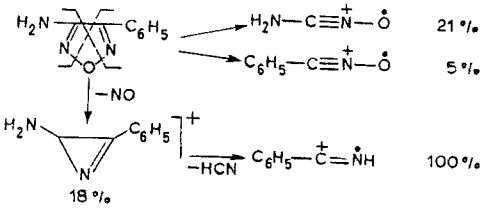
2.1. Structure and Physicochemical Properties of the Aminofurazans

An x-ray investigation of the 3-amino-4-methylfurazan molecule [90] showed that the furazan ring is planar. The elementary cell consists of two independent molecules differing little in geometry. The chain of conjugation comprises, mainly, the N=C–C=N bonds. The furazan ring is unsymmetrical, the N–O bond in the H_2N–C=N–O chain being 0.025 Å longer than in the CH_3–C=N–O chain. The results of a quantum-chemical calculation of the aminofurazan molecule [91] also show that the orders of the bonds in the H_2N–C=N–O fragment are lower than in H–C=N–O. In 3-amino-4-methylfurazan the amino group is rotated in relation to the plane of the ring, the dihedral angle amounting to 11.5° for one molecule and 24° for the other [90]. In the second molecule, the amino group is not completely planar (the sum of the valence angles at the nitrogen atom amounts to 355°). The deviations from planarity are most prob-

ably connected with distortion in the crystalline state, since the result of a quantum-chemical calculation of the aminofurazan molecule by the MO SCF MINDO/3 method with complete optimization of the geometry showed that the minimum of the potential energy of the molecule corresponds to a coplanar arrangement of the amino group and of the furazan ring [91]. The calculation also showed that the conjugation of the amino group with the ring in aminofurazan is smaller than in aniline. As a result, the π-electron density on the nitrogen atom in aminofurazan is higher than in aniline. However, because of the presence of three electronegative heteroatoms in the ring, furazan possesses stronger electron-accepting properties. The total negative charge on the amino group of aminofurazan therefore proves to be lower than in aniline [91].

The introduction of an amino group, which is capable of conjugation with the furazan ring, leads to a fall in the energy of the π—π* transition and to a shift in the absorption maximum into the 214-284 nm region [92]. With an increase in the electronegativity of the substituents in 4-substituted 3-aminofurazans, a hypsochromic shift of the absorption band is observed, the position of the maximum correlating with the σ°_{M} constants of the substituents [92]. Protonation at the amino group leads to a fall in the intensity of absorption and to the appearance of an absorption band of the protonated form in the short-wave region [92].

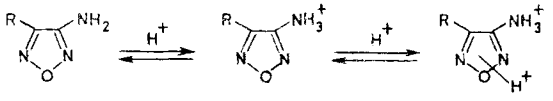
Fragmentation of the ring of 3-amino-4-phenylfurazan under the action of electron impact takes place in three directions [93]:



In the ^{13}C NMR spectrum of diaminofurazan the signal of the two carbon atoms is observed at 150.9 ppm [75]. The IR spectra of a number of aminofurazans have been described [94-96]. The heats of combustion of the aminofurazans have been measured, and it has been shown that the deviation of the experimental values from those calculated on the basis of increments amounts to 2-7.5 kcal/mole [97]. In an investigation of the kinetics of the thermal decomposition of diaminofurazan and of 3-amino-4-nitrofurazan it was established that the stability of these compounds, as of other derivatives of the furazan series, is limited by the cleavage of the N—O bond of the furazan ring [98, 99].

2.2. Acid—Base Properties of the Aminofurazans

The low electron density on amino group attached to a furazan ring [91] is the cause of the low basicity of the aminofurazans. The calculated value of the proton affinity of aminofurazan is 12.2 kcal/mole lower than that of aniline [91]. This is in harmony with the results of an investigation of the basicities of the aminofurazans [92, 100]. A study of the UV spectra of solutions of aminofurazans in sulfuric acid indicates the existence of the equilibrium:

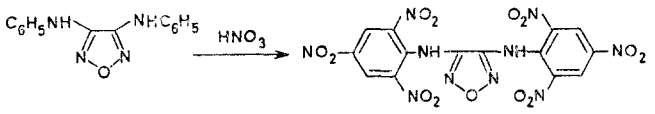


The value of pK_{a_1} is in the range from −1.94 to −4.46, which is approximately 7-9 units lower than for aniline. The value of the constant pk_{a_2}, corresponding to protonation in the ring, is less sensitive to the influence of substituents and is in the range from −4.81 to −5.34. The pK_a values of substituted 3-amino-4-phenylfurazans published previously were 3.1-3.4 [42], which apparently does not correspond to reality.

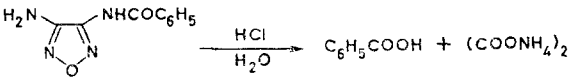
The values of pK_{a_1} correlate well with the σ°_{m} and σ°_{p} constants of the substituents, the influence of a substituent bearing mainly an induction nature [92].

2.3. Reactions of Aminofurazans with Acids

Aminofurazans are stable to the action of acids. This is demonstrated, for example, by their formation on the hydrolysis of acylaminofurazans in boiling 20% hydrochloric acid. 3-Amino-4-phenylfurazan does not change under the action of concentrated hydrochloric and sulfuric acids, but it reacts with concentrated nitric acid with the cleavage of the furazan ring and the formation of p-nitrobenzoic acid [55]. Under the action of concentrated nitric acid at 90°C, dianilinofurazan nitrates to form 3,4-di(picrylamino)furazan [35]:

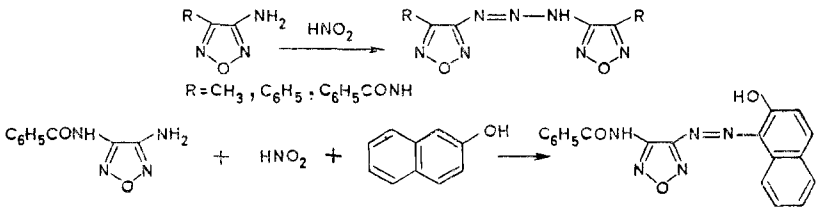


Cleavage of the furazan ring was observed in an attempt to obtain diaminofurazan by the hydrolysis of 3-amino-4-benzoylaminofurazan in 20% hydrochloric acid [39]. This led to the erroneous conclusion that diaminofurazan was unstable.

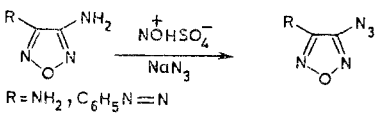


The hydrolysis of 3-benzoylamino-4-phenylfurazan in 15% hydrochloric acid led to the formation not only of 3-amino-4-phenylfurazan, but also to that of hydroxylamine through the partial cleavage of the furazan ring [68].

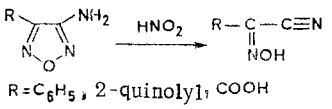
With nitrous acid, aminofurazans form diazonium salts, which readily take part in azo-coupling reactions [33, 39, 40, 66]:



Azidofurazans have been synthesized by the nucleophilic substitution of the diazonium grouping [101], but it was impossible to replace the diazonium group by a hydroxy group [41].

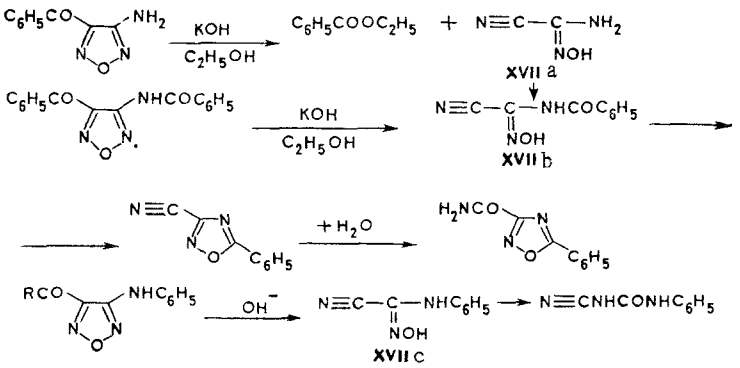


In a number of cases, dediazotization leads to the opening of the furazan ring with the formation of isonitrosoacetonitrile derivatives [40, 41, 77]:



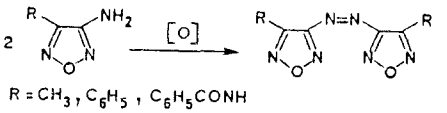
2.4. Action of Alkalies on Aminofurazans

Aminofurazans are stable to the action of alkalies. This is demonstrated, for example, by their formation in the cyclization of aminoglyoximes in a hot 20% solution of alkali or in a solution of ammonia at 175°C. Exceptions are 3-amino-4-benzoylfurazan derivatives; these readily undergo cleavage under the action of potassium ethanolate with the formation of an intermediate cyanoformamide oxime (XVII), which then either cyclizes into a 1,2,4-oxadiazole derivative [70, 102-104] or undergoes the Beckmann rearrangement [4, 73, 74]:

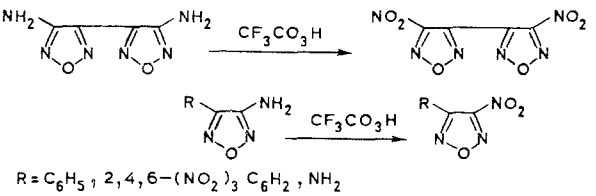


2.5. Oxidation and Reduction of Aminofurazans

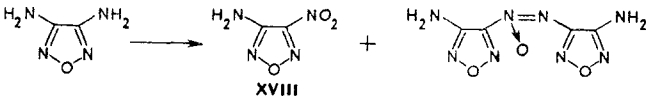
Aminofurazans are readily oxidized by potassium permanganate, chromium trioxide, and sodium hypochlorite with the formation of azo compounds [39, 55, 66]:



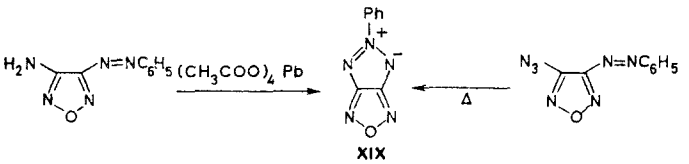
Oxidation with trifluoroperacetic acid leads to nitrofurazans [35, 105-107]:



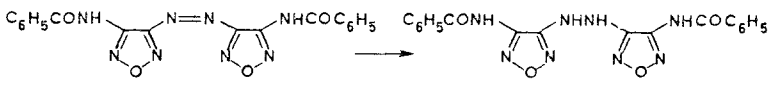
Under these conditions, in diaminofurazan only one amino group is oxidized. When diaminofurazan is oxidized with 30% hydrogen peroxide, ammonium persulfate in an acid medium, or a mixture of them, or with neutralized Caro's acid, a mixture of 3-amino-4-nitrofurazan and of 4,4'-diamino-3,3'-azoxyfurazan is formed in all cases [108]. The yield of the nitrofurazan (XVIII) increases with an increase in the amount of oxidant and with a rise in the acidity of the medium [108].



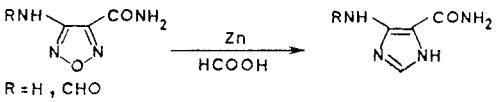
In a neutral medium, diaminofurazan is oxidized by ammonium persulfate to 4,4'-diamino-3,3'-azofurazan [108]. The oxidation of 3-amino-4-phenylazofurazan with lead tetraacetate has given 5-phenyl[1,2,3]triazolo[4,5-c]furazan (XIX) [109]. It is assumed that the reaction takes place by a nitrene mechanism. It has been shown that the triazolofurazan (XIX) is also formed when the nitrene is generated from 3-azido-4-phenylazofurazan [101]:



The furazan ring is clearly resistant to the action of reducing agents; for example, in the production of aminofurazans from aminofuroxans by the action of zinc, tin, or stannous chloride in an acid medium. Under these conditions the azo derivatives are reduced to hydrazo derivatives [39, 55, 66]:

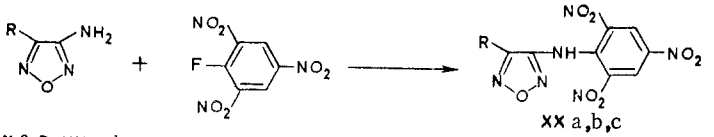


However, under more severe conditions — for example, on the reduction of 3-aminofurazan-4-carboxylic acid derivatives with zinc dust in boiling formic acid — the furazan ring opens with subsequent recyclization to imidazole derivatives [38, 110]:



2.6. Alkylation of Aminofurazans

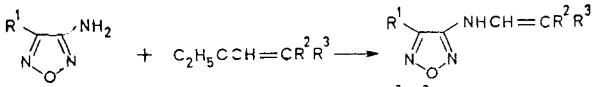
Because of their low reactivity, the amino groups of aminofurazans do not react with such typical alkylating agents as methyl iodide, dimethyl sulfate, bromoacetophenone, and trityl chloride [42]. The arylation of aminofurazans takes place under the action of picryl fluoride [35]:



XX a R=NH$_2$; b R=4-aminofurazan-3-yl ; c R= 4-(2,4,6-trinitroanilino)-furazon-3-yl

In the furazan (XXa), only one amino group is arylated, but the arylation of the furazan (XXb) with an excess of picryl fluoride forms the dipicryl derivative (XXc).

Alkylation of aminofurazans has been observed in reactions with difunctionally substituted vinyl ethers [33, 111]:

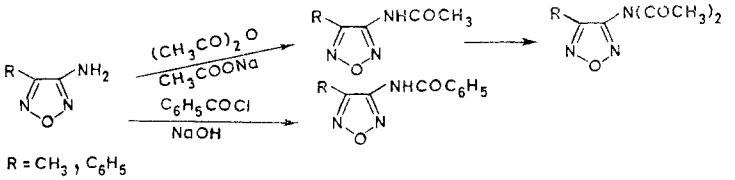


R^1=NH$_2$ or a substituted amino group ; R^2, R^3=COR, COOR, CN

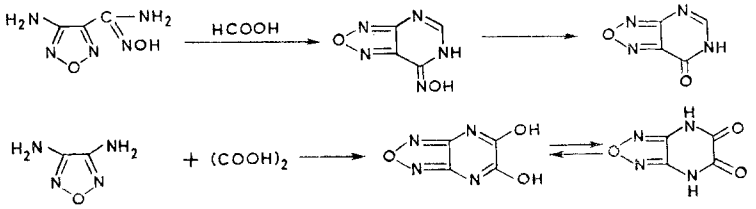
It has been established by spectroscopic investigations that some enaminofurazans of type (XXI) exist in the form of cyclic chelate complexes with a hydrogen bond between the NH proton and the oxygen atom of a carbonyl or ester group [111].

2.7. Acylation of Aminofurazans

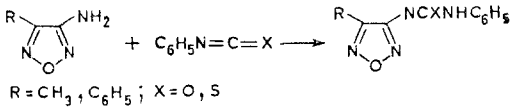
Aminofurazans are readily acylated by acid anhydrides [33, 40, 42, 55, 65, 67, 68] and acid chlorides [3, 36, 49, 65, 103, 112]. When an excess of acetic anhydride is used in the presence of sodium acetate, the introduction of two acetyl groups is possible [40, 55, 67, 68]:



Attempts to introduce two different acyl groups such as acetyl and benzoyl [55, 68] or formyl and acetyl [67], simultaneously, were unsuccessful. The mixed anhydride of acetic and formic acids has been used to formylate aminofurazans [34]. The formylation of aminofurazans was also observed when they were boiled in formic acid [38]. The reaction of carboxylic acids with aminofurazans containing functional groups in position 4 may lead to bicyclic derivatives [38, 113]:



The formation of sulfanilamide derivatives of furazan [114-118] and also of furazanoureas [42, 119] and of furazanothioureas [120] takes place smoothly.



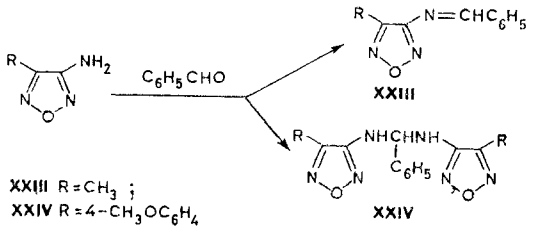
R = CH_3, C_6H_5; X = O, S

The NH proton in the amides is characterized by a high acidity (the pK_a value of 3-sulfanilamido-4-methylfurazan is 4.10 [121]). They readily dissolve in aqueous solutions of alkalis, from which they are reprecipitated by acids [49, 55, 56, 112, 113]. Silver [39] and copper [56, 65, 81] derivatives of the amides and sulfanilamides have also been described [117].

Under the action of alkalis or acids, the acylaminofurazans readily undergo hydrolysis with the formation of the initial aminofurazans [19, 26, 38, 55-57, 67, 68, 81].

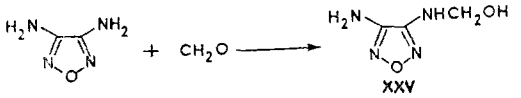
2.8. Reaction of the Aminofurazans with Carbonyl Compounds and Their Derivatives

Aminofurazans react with carbonyl compounds under fairly severe conditions, frequently on being boiled in acetic acid or in the presence of Lewis acids for several hours. In the reaction with benzaldehyde, depending on the conditions, either Schiff's bases (XXIII) [42] or amines (XXIV) [33, 66] can be formed:



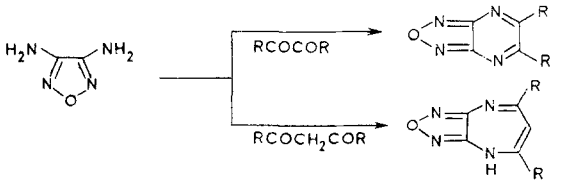
XXIII R = CH_3;
XXIV R = 4-$CH_3OC_6H_4$

Imines are also obtained on condensation with cinnamaldehyde [66]. In contrast to this, the reaction of diaminofurazans with formaldehyde at room temperature leads to the hydroxymethyl derivative (XXV) [122]:



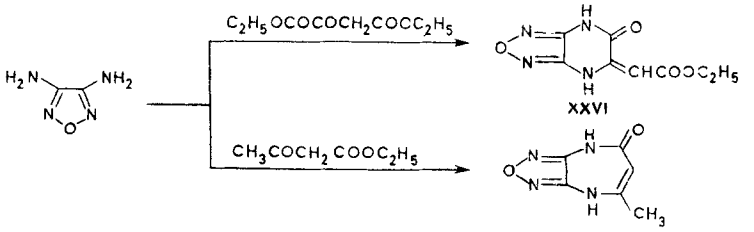
The bishydroxymethyl derivative of diaminofurazan readily polymerizes and it was impossible to isolate it in the form of the monomer [122].

The formation of bicyclic derivatives was observed in the reaction of aminofurazan with α- and β-diketones [113, 123-125]:

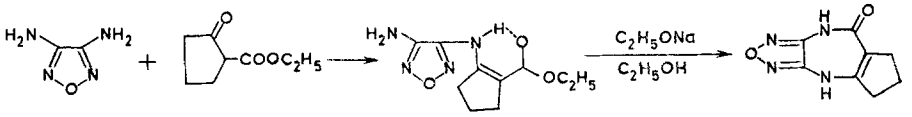


However, it has been reported that the reactions of diaminofurazan with methyl- and dimethylglyoxal do not lead to furazanopyrazines [123]. Diaminofurazan reacts with α- and β-keto esters with the formation of furazanopyrazines and of furazanodiazepinones [126] (see scheme at top of following page).

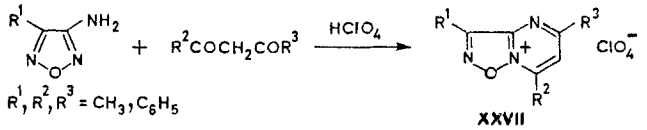
The furazanopyrazinone (XXVI) was also obtained in the reaction with diethyl acetylenedicarboxylate [125]. On reaction with diaminofurazan, cyclic β-keto esters form, in a first



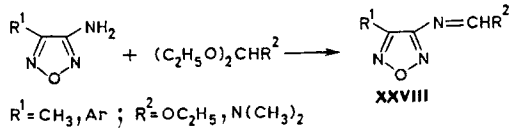
stage, enamines which, under the action of sodium ethanolate, cyclize to furazanodiazepinones [126]:



The bicyclic derivatives (XXVII), unusual for the furazan series, were obtained by the reaction of aminofurazans with β-diketones in the presence of perchloric acid [127]. This reaction is interesting by virtue of the fact that it is the first example of the synthesis of a bicyclic furazan derivative condensed in the 2,3 position.

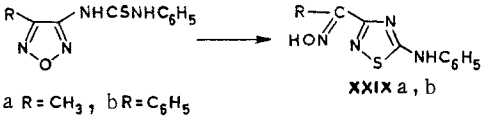


Amidines and imidic esters are formed, respectively, in the reactions of aminofurazans with dimethylformamide dimethyl acetal [42] and with orthoformic ester [119]:

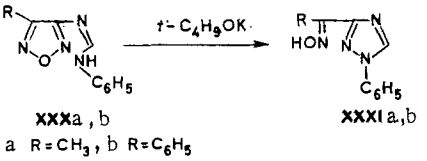


2.9. Rearrangements of Aminofurazans

Since the furazan ring in the aminofurazans is fairly stable, it is incapable of undergoing recyclization reactions. Although thioureide derivatives of furazan do in fact undergo recyclization to 1,2,4-thiadiazoles (XXIX) [120], it is impossible to perform the analogous rearrangement of the ureido derivatives [119] or of acylaminofurazans [128].



Other examples of the recylization of aminofurazans are the rearrangement of 3-amino-4-benzoylfurazans under the action of alkali into 5-benzoyl-3-carbamoyl-1,2,4-oxadiazole described above [102] and the conversion of the formamidines (XXX) into the triazoles (XXXI) [119]:



LITERATURE CITED

1. A. F. Holleman, Recl. Trav. Chim., 6, 60 (1887).
2. A. F. Holleman, Chem. Ber., 21, 2835 (1888).
3. G. Ponzio and C. Cerrina, Gaz. Chim. Ital., 58, 26 (1928).
4. R. C. Bertelson, K. D. Glanz, and D. B. McQuain, J. Heterocycl. Chem., 6, 317 (1969).

5. C. Lehmann, E. Renk, and A. Gagneux, Swiss Patent, No. 498,137.
6. C. Lehmann, E. Renk, and A. Gagneux, Swiss Patent, No. 498,857.
7. C. Lehmann, E. Renk, and A. Gagneux, Czechoslovakian Patent No. 140,464.
8. C. Lehmann, E. Renk, and A. Gagneux, Swiss Patent, No. 498,135.
9. C. Lehmann, E. Renk, and A. Gagneux, Swiss Patent, No. 498,854.
10. C. Lehmann, E. Renk, and A. Gagneux, Swiss Patent, No. 498,134.
11. C. Lehmann, E. Renk, and A. Gagneux, GFR Patent No. 1,903,569; Chem. Abstr., 71, No. 128,725 (1969).
12. C. Lehmann, E. Renk, and A. Gagneux, Swiss Patent, No. 498,136.
13. C. Lehmann, E. Renk, and A. Gagneux, Swiss Patent, No. 498,856.
14. C. Lehmann, E. Renk, and A. Gagneux, Swiss Patent, No. 498,855.
15. C. Lehmann, E. Renk, and A. Gagneux, South African Patent, No. 6,800,799; Chem. Abstr., 70, No. 57,855 (1969).
16. C. Lehmann and E. Renk, Swiss Patent, No. 479,605.
17. C. Lehmann and E. Renk, Swiss Patent, No. 479,606.
18. C. Lehmann and E. Renk, US Patent, No. 3,711,609.
19. C. Lehmann, E. Renk, and A. Gagneux, South African Patent No. 6,800,778; Chem. Abstr., 71, 3387 (1969).
20. C. Lehmann and E. Renk, Swiss Patent, No. 480,352.
21. C. Lehmann and E. Renk, Swiss Patent, No. 481,126.
22. C. Lehmann, E. Renk, and A. Gagneux, Swiss Patent, No. 502,365.
23. A. Fundaro, Boll. Soc. It. Biol. Sper., 50, 1650 (1974).
24. R. Calvino and A. Fundaro, Farmaco, Ed. Sci., 32, 789 (1977).
25. C. Lehmann, E. Renk, and A. Gagneux, Swiss Patent, No. 508,650.
26. C. Lehmann, E. Renk, and A. Gagneux, Czechoslovakian Patent, No. 140,460.
27. C. Lehmann and E. Renk, Swiss Patent, No. 478,825.
28. J. Boyer, in: Heterocyclic Compounds, R. C. Elderfield (ed.), Wiley, New York, Vol. 7 (1961), p. 462.
29. L. C. Behr, in: Five- and Six-Membered Compounds with Nitrogen and Oxygen, R. H. Wiley (ed.), Interscience, New York (1962), p. 283.
30. K. L. Stuart, Heterocycles, 3, 651 (1975).
31. T. Ichikawa, T. Kato, and T. Takenishi, Japanese Patent No. 20,710; Chem. Abstr., 64, 2101 (1966).
32. C. Grundmann, V. Mini, J. M. Dean, and H.-D. Frommeld, Ann. Chem., 687, 191 (1965).
33. S. Cusmano, Gazz. Chim. Ital., 81, 106 (1951).
34. A. R. Gagneux and R. Meier, Helv. Chim. Acta, 53, 1883 (1970).
35. M. D. Coburn, J. Heterocycl. Chem., 5, 83 (1968).
36. A. P. Komin, R. W. Street, and M. Carmack, J. Org. Chem., 40, 2749 (1975).
37. I. V. Vigalok and A. V. Ostrovskaya, in: The Chemistry and Technology of Organometallic Compounds and Polymers [in Russian], Kazan', No. 7 (1978), p. 48.
38. T. Ichikawa, T. Kato, and T. Takenishi, J. Heterocycl. Chem., 2, 253 (1965).
39. E. Durio and S. Dugone, Gazz. Chim. Ital., 66, 139 (1936).
40. F. Angelico and S. Cusmano, Gazz. Chim. Ital., 66, 3 (1936).
41. M. Iwao and T. Kuraishi, J. Heterocycl. Chem., 16, 689 (1979).
42. G. Westphal and R. Schmidt, J. Prakt. Chem., 315, 791 (1973).
43. T. E. Ivanova, S. N. Vergizov, S. F. Mel'nikova, and I. V. Tselinskii, USSR Inventors Certificate, No. 2,629,465; Byull. Izobret., No. 6, 75 (1980).
44. A. Russanov, Chem. Ber., 24, 3497 (1891).
45. G. Ponzio, Gazz. Chim. Ital., 62, 854 (1932).
46. E. Durio and A. Sburlati, Gazz. Chim. Ital., 62, 1035 (1932).
47. W. Zinkeisen, Chem. Ber., 22, 2946 (1889).
48. G. Longo, Gazz. Chim. Ital., 62, 873 (1932).
49. G. Ponzio and G. Bertini, Gazz. Chim. Ital., 61, 51 (1931).
50. G. Longo, Gazz. Chim. Ital., 61, 575 (1931).
51. H. Wieland and H. Hess, Chem. Ber., 42, 1346 (1909).
52. I. Paolini, Gazz. Chim. Ital., 58, 196 (1928).
53. I. Paolini and A. Castiglioni, Gazz. Chim. Ital., 59, 723 (1929).
54. G. Ponzio, Gazz. Chim. Ital., 60, 886 (1930).
55. G. Ponzio and L. Avogadro, Gazz. Chim. Ital., 53, 318 (1923).
56. G. Ponzio, Gazz. Chim. Ital., 61, 704 (1931).
57. A. Vianello, Gazz. Chim. Ital., 58, 326 (1928).
58. G. Ponzio and E. Durio, Gazz. Chim. Ital., 60, 436 (1930).

59. R. A. Olofson and J. S. Michelman, J. Org. Chem., 30, 1854 (1965).
60. G. Ponzio, Gazz. Chim. Ital., 61, 561 (1931).
61. G. Longo and G. Randone, Gazz. Chim. Ital., 66, 145 (1936).
62. G. Ponzio and L. Avogadro, Gazz. Chim. Ital., 53, 305 (1923).
63. G. Longo, Gazz. Chim. Ital., 62, 139 (1932).
64. P. Gramantieri, Gazz. Chim. Ital., 65, 102 (1935).
65. G. Ponzio, Gazz. Chim. Ital., 61, 138 (1931).
66. G. Ponzio and G. Ruggeru, Gazz. Chim. Ital., 53, 297 (1923).
67. S. Gusmano and M. Ruccia, Gazz. Chim. Ital., 88, 463 (1958).
68. S. Gusmano and M. Ruccia, Gazz. Chim. Ital., 86, 187 (1956).
69. A. F. Holleman, Recl. Trav. Chim., 11, 258 (1892).
70. J. Boeseken and D. P. Ross van Lennep, Recl. Trav. Chim., 31, 196 (1912).
71. A. F. Holleman, Recl. Trav. Chim., 10, 211 (1891).
72. J. Boeseken, Recl. Trav. Chim., 16, 297 (1897).
73. J. Boeseken, Recl. Trav. Chim., 29, 275 (1910).
74. H. Wieland and E. Gmelin, Ann. Chem., 375, 297 (1910).
75. A. V. Eremeev, V. G. Andrianov, and I. P. Piskunova, Khim. Geterotsikl. Soedin., No. 5, 616 (1978).
76. C. Ulpiani, Gazz. Chim. Ital., II, 35, 7 (1905).
77. C. Ulpiani, Gazz. Chim. Ital., I, 42, 375 (1912).
78. H. Wieland, Z. Kitasato, and S. Utzino, Ann. Chem., 478, 43 (1930).
79. C. Grundmann, G. W. Nickel, and R. K. Bansal, Ann. Chem., No. 6, 1029 (1975).
80. G. Ponzio, Gazz. Chim. Ital., 66, 114 (1936).
81. G. Ponzio, Gazz. Chim. Ital., 66, 119 (1936).
82. G. Ponzio, Gazz. Chim. Ital., 66, 127 (1936).
83. A. Gasco, V. Mortarini, G. Rua, and A. Serafino, J. Heterocycl. Chem., 10, 587 (1973).
84. J. E. Oliver, S. C. Chang, R. T. Brown, J. B. Stokes, and A. B. Borkovec, J. Med. Chem., 15, 315 (1972).
85. J. M. Tedder and D. J. Woodcock, J. Chem. Res. (s), No. 9, 356 (1978).
86. A. Gasco, G. Rua, E. Menziani, V. Mortarini, and A. Fundaro, Farmaco, Ed. Sci., 26, 241 (1971).
87. E. C. Taylor, G. P. Beardsley, and Y. Maki, J. Org. Chem., 36, 3211 (1971).
88. P. Fernandes-Resa, P. Goya Laza, C. Ochoade Ocariz, and M. S. Schueter, Spanish Patent, No. 497,899; Chem. Abstr., 97, No. 23,790 (1982).
89. P. C. Guha and M. N. Chakladar, Proceedings of the 15th Indian Science Congress (1928), p. 157; Chem. Abstr., 25, 2999 (1931).
90. D. Viterbo and A. Serafino, Acta Crystallogr., B34, 3444 (1978).
91. M. A. Shokhen, V. G. Andrianov, and A. V. Eremeev, Khim. Geterotsikl. Soedin., No. 10, 1355 (1979).
92. I. V. Tselinskii, S. F. Mel'nikova, and S. N. Vergizov, Khim. Geterotsikl. Soedin., No. 3, 321 (1981).
93. R. Kraft, P. Helklein, G. Etzold, and H. Zopfl., J. Org. Mass. Spectrom., 11, 304 (1976).
94. E. Borello, A. Zecchina, and E. Guglielminotti, Gazz. Chim. Ital., 95, 1465 (1965).
95. E. Borello, A. Zecchina, and E. Guglielminotti, Gazz. Chim. Ital., 96, 532 (1966).
96. M. Milone and E. Borello, Gazz. Chim. Ital., 81, 386 (1951).
97. M. Milone and S. Allavena, Gazz. Chim. Ital., 61, 75 (1931).
98. V. V. Zverev, I. Sh. Saifullin, and G. P. Sharnin, Izv. Akad. Nauk SSSR, Ser. Khim., No. 2, 313 (1978).
99. V. G. Prokudin, G. M. Nazin, and G. B. Manelis, Dokl. Akad. Nauk SSSR, 255, 917 (1980).
100. I. V. Tselinskii, S. F. Mel'nikova, S. N. Vergizov, and G. M. Frolova, Khim. Geterotsikl. Soedin., No. 1, 35 (1981).
101. I. V. Tselinskii, S. F. Mel'nikova, and S. N. Vergizov, Zh. Org. Khim., 17, 1123 (1981).
102. G. Ponzio, Gazz. Chem. Ital., 62, 415 (1932).
103. G. Ponzio, Gazz. Chim. Ital., 62, 860 (1932).
104. D. Viterbo, R. Calvino, and A. Serafino, J. Chem. Soc., Perkin. Trans. II, No. 7, 1096 (1980).
105. R. Calvino, V. Mortarini, and A. Gasco, Eur. J. Med. Chem.-Chim. Ter., 15, 485 (1980).
106. R. Calvino, A. Gasco, A. Serafino, and D. Viterbo, J. Chem. Soc., Perkin Trans. II, No. 9, 1240 (1981).
107. M. N. Makhova, I. V. Ovchinnikov, B. N. Khasanov, and L. I. Khmel'nitskii, Izv. Akad. Nauk SSSR, Ser. Khim., No. 3, 646 (1982).
108. G. D. Solodyuk, M. D. Bold'rev, B. V. Gidaspov, and V. D. Nikolaev, Zh. Org. Khim., 17, 861 (1981).

109. A. Matsumoto, M. Yoshida, and O. Simamura, Bull. Chem. Soc. Jpn., 47, 1493 (1974).
110. T. Takenisu, T. Kato, and T. Itikawa, Japanese Patent, No. 15,577 (66).
111. A. V. Eremeev, V. G. Andrianov, and I. P. Poshunova, Khim. Geterotsikl. Soedin., No. 3, 319 (1979).
112. A. Gasco, G. Rua, E. Menziani, and V. Mortarini, Farmaco, Ed. Sci., 26, 233 (1971).
113. A. Gasco, G. Rua, E. Menziani, G. M. Nano, and G. Tappi, J. Heterocycl. Chem., 6, 769 (1969).
114. G. Tappi and C. Migliardi, Arch. Sci. Biol., 27, 170 (1941).
115. G. Tappi and C. Migliardi, Arch. Sci. Biol., 28, 472 (1942).
116. G. Tappi, Recl. Trav. Chim., 62, 207 (1943).
117. R. O. Roblin and G. W. Anderson, US Patent, No. 2,367,057; Chem. Abstr., 39, 2383 (1945).
118. G. W. Anderson, H. E. Faith, H. W. Marson, P. S. Winnek, and R. O. Roblin, J. Am. Chem. Soc., 64, 2902 (1942).
119. M. Ruccia, N. Vivona, G. Cusmano, and G. Macaluso, J. Chem. Soc., Perkin Trans. I, No. 6, 589 (1977).
120. N. Vivona, G. Cusmano, and G. Macaluso, J. Chem. Soc., Perkin Trans. I, No. 14, 1616 (1977).
121. P. H. Bell and R. O. Roblin, J. Am. Chem. Soc., 64, 2905 (1942).
122. A. V. Ostrovskaya, I. V. Vigalok, and N. V. Svetlakov, USSR Inventors' Certificate, No. 771,117; Byull. Izobret., No. 38, 142 (1980).
123. N. Sato and J. Adachi, J. Org. Chem., 43, 341 (1978).
124. A. Gasco, G. Rua, E. Menziani, G. M. Nano, and G. Tappi, J. Heterocycl. Chem., 7, 131 (1970).
125. A. V. Eremeev, V. G. Andrianov, and I. P. Piskunova, Khim. Geterotsikl. Soedin., No. 5, 613 (1978).
126. A. V. Eremeev, V. G. Andrianov, and I. P. Piskunova, Khim. Geterotsikl. Soedin., No. 9, 1196 (1978).
127. I. P. Bachkovskii, A. P. Mikhailovskii, and V. A. Chuiguk, Ukr. Khim. Zh., 46, 637 (1980).
128. A. J. Boulton, A. R. Katritzky, and A. M. Hamid, J. Chem. Soc., No. 20, 2005 (1967).

RING-CHAIN TAUTOMERISM OF VINYLOGS OF 2(3)-AMINO DERIVATIVES OF HETEROCYCLIC o-HYDROXY ALDEHYDES

A. D. Dubonosov, L. M. Sitkina, V. A. Bren',
A. Ya. Bushkov, and V. I. Minkin

UDC 547.728'735'751:541.623:
543.422.25'4'

Previously unknown vinylogs of 2(3)-aminomethylene-substituted benzo[b]thiophene-3-one, 1-methyloxindole, 1-methylindoxyl, benzo[b]furan-3-one, and indan-1,3-dione have been synthesized. Their tautomeric transformations have been studied by methods of UV, IR, and PMR spectroscopy. It has been shown that the introduction of a substituent into the β position of a dienic chain favors the appearance of the cyclic form.

We have previously [1] established the existence of the ring-chain tautomerism of derivatives of 2-(γ-dimethylaminopropenylidene)benzo[b]thiophene-3(2H)-one. In the present investigation we have studied the possibility of solvato-, photo-, and thermochromic transformations of vinylogs of 2(3)-aminomethylene-substituted derivatives of benzo[b]thiophene-3-one (I), 1-methyloxindole (II), 1-methylindoxyl (III), benzo[b]furan-3-one (IV), and indan-1,3-dione (V) and their acylated derivatives, and the influence of structural factors on the position of the ring-chain tautomeric equilibrium A ⇄ B.

Scientific-Research Institute of Physical Organic Chemistry, M. A. Suslov Rostov State University, Rostov-on-Don. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1171-1176, September, 1984. Original article submitted August 31, 1983.

0009-3122/84/2009- 0951$08.50