NEW EXAMPLE OF THE DIMROTH REARRANGEMENT. INTRAMOLECULAR CYCLIZATION OF ACYL DERIVATIVES OF ANTHRANILIC ACID NITRILE

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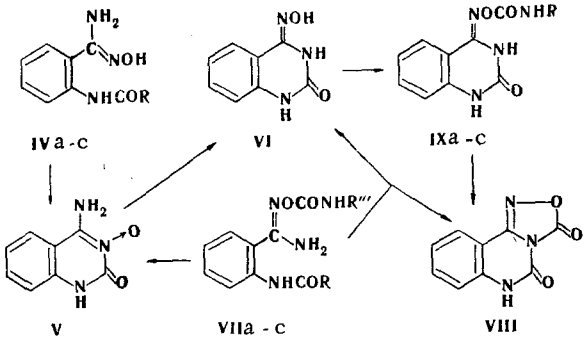
A new example of the Dimroth rearrangement in which 4-amino-1H-quinazolin-2-one 3(N)-oxide undergoes isomerization to 4-oximino-1H,3H-quinazolin-2-one was observed. It is shown that the thermal cyclization of N-(2-amidoximophenyl)ureas and carbamates leads to the production of 4-amino-1H-quinazolin-2-one 3(N)-oxides, while their O-carbamoyl derivatives give 4-oximino-1H,3H-quinazolin-2-one and 5-oxo-Δ^2-1,2,4-oxadiazolino[c:3,4]-1H,3H-quinazolin-2-one.

It has previously been shown [1] that the reaction of hydroxylamine with 2-cyanophenyl isocyanate (I) and ethyl N-(2-cyanophenyl)carbamate (II) and the thermal treatment of N-hydroxy-N'-(2-cyanophenyl)urea (III) and ethyl N-(2-amidoximophenyl)carbamate (IVa) lead only to the production of 4-amino-1H-quinazolin-2-one 3(N)-oxide (V). The second possible isomer, viz., 4-oximino-1H,3H-quinazolin-2-one (VI), was not obtained in these reactions; this may probably be associated with the greater nucleophilicity of the oxime fragment of the amidoxime radical as compared with its amide group.

However, prolonged refluxing of a solution of V in dimethylformamide (DMF) led, somewhat unexpectedly, to the production of a new compound, which, according to the results of elementary analysis, is an isomer of the starting compound. Intense absorption bands of C=O and C=N bonds at 1710 and 1680 cm^{-1} and an absorption band at 952 cm^{-1}, which corresponds to the vibrations of the covalent N–O bond, are observed in the IR spectrum of this compound. These data made it possible to assign the 4-oximino-1H,3H-quinazolin-2-one structure (VI) to the newly synthesized compound. The conversion of V to VI is a new example of the Dimroth rearrangement [2] in which the hydroxy group (or the N-oxide oxygen atom) acts as the substituent in the amidine system.

It should be noted that V and VI are stable in aqueous solutions of alkalis and are isolated from them unchanged when they are acidified. Neutralization of the hydrochlorides of V and VI, which were obtained by allowing the latter to stand in 15-20% hydrochloric acid at room temperature, also leads to the liberation of starting V and VI.



IV, VII a $R=OC_2H_5$; b $R=NHR$; c $R=NR'R''$; IX a $R=CH_3$; b $R=C_2H_5$; c $R=C_6H_5$

The acid hydrolysis of V and VI to N-hydroxyquinazoline-2,4-dione and quinazoline-2,4-dione, respectively, may serve as a confirmation of the presence of an oxygen atom attached to the endo- (V) and exo-nitrogen (VI) atoms.

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TABLE 1. N-[O-Alkyl(aryl)carbamoyl-4-oximono]-1H,3H-quinazolin-2-ones (IXa-c)

Compound	mp, °C	IR spectrum (C=O), cm^{-1}	Found, %			Empirical formula	Calculated, %			Yield, %
			C	H	N		C	H	N	
IXa	248—249	1710, 1720	51,5	4,5	23,6	$C_{10}H_{10}N_4O_3$	51,3	4,3	23,9	52
IXb	241—242	1690, 1710	53,3	4,7	22,4	$C_{11}H_{12}N_4O_3$	53,2	4,8	22,6	95
IXc	218	1710, 1730	60,7	4,0	18,7	$C_{15}H_{12}N_4O_3$	60,8	4,0	18,9	92

It should be noted that the thermal intramolecular cyclization of the previously described ureas (IVb, c), just as in the case of II, III, and IVa, leads only to V. One might have expected that the order of the nucleophilicities of the nitrogen atoms of the amidoxime fragments should change on passing from IVa, b to their corresponding O-carbamoyl derivatives (VIIa, b). In fact, VIIa, b undergo thermal cyclization to give VI mixed with 5-oxo-Δ^2-1,2,4-oxadiazolino[c:3,4]-1H,3H-quinazolin-2-one (VIII), in the IR spectrum of which three intense bands of C=O and C=N bonds at 1830, 1740, and 1640 cm^{-1}, as well as an N—O—C(O) band at 1260 cm^{-1}, are observed. The structure of VIII, which can be obtained by thermal cyclization of O-carbamoyl derivatives (IXa-c) of VI, is confirmed by its acid hydrolysis to quinazoline-2,4-dione.

However, the formation of V when VIIc is heated is evidently associated with an increase in the steric hindrance to cyclization (as compared with VIIa, b) and deacylation of VIIc to starting amidoximes IV, which also then undergo cyclization to V.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a Perkin—Elmer 457 spectrometer. The results of elementary analysis, the melting points, and the spectral characteristics of IX are presented in Table 1. The synthesis of I-IVa-c, V, and VIIb, c was described in [1].

2-Cyanophenyl Isocyanate (I).* This compound was obtained by phosgenation of anthranilic acid nitrile by the method in [3].

4-Oximino-1H,3H-quinazolin-2-one (IV). This compound was obtained by the method in [4].

Ethyl N-(O-Methylcarbamoyl-2-amidoximophenyl)carbamate (VIIa). A 0.01-mole sample of methylisocyanate was added to a solution of 0.01 mole of IVa in 30 ml of tetrahydrofuran (THF), and the resulting solution was maintained at 30°C for 8 h. The solvent was then removed by vacuum distillation, and the residue was recrystallized from alcohol to give a product with mp 161°C in 80% yield. IR spectrum: 930 (N—O), 1640 (C=N), and 1720 cm^{-1} (C=O). Found: C 51.1; H 5.6; N 19.9%. $C_{12}H_{16}N_4O_4$. Calculated: C 51.4; H 5.7; N 20.0%.

5-Oxo-Δ^2-1,2,4-oxadiazolino[c:3,4]-1H,3H-quinazolin-2-one (VIII). Compounds VIIa, b or IXa-c were gradually heated to their melting points, after which the resulting melts were heated until they began to crystallize. Compound VIII was isolated by fractional crystallization from alcohol and had mp 268°C. Found: C 53.1; H 2.6; N 20.6%. $C_9H_5N_3O_3$. Calculated: C 53.2; H 2.5; N 20.7%.

N-[O-Alkyl(aryl)carbamoyl-4-oximino]-1H,3H-quinazolin-2-one (IX). An equimolar amount of the corresponding isocyanate was added to a suspension of 0.01 mole of VI in 50 ml of acetone, and the reaction mixture was refluxed for 5 h. The precipitate was separated and recrystallized from alcohol (see Table 1).

LITERATURE CITED

1. N. V. Abbakumova, Yu. A. Baskakov, Yu. G. Putsykin, and L. D. Tomina, Paper deposited at VINITI, No. 239/74; Ref. Zh. Khim., 19N670 (1974).
2. K. V. Vatsuro and G. A. Mishchenko, Name Reactions in Organic Chemistry [in Russian], Khimiya, Moscow (1976), p. 180.
3. W. Borsche and W. Sander, Ber., 47, 2815 (1914).

*A method for the preparation of I from isatin β-oxime was described in [1].

4. N. V. Abbakumova, A. F. Vasil'ev, and E. B. Nazarova, Khim. Geterotsikl. Soedin., No. 7, 968 (1981).

HETEROCYCLIC DERIVATIVES OF PURINES.

4.* REACTIONS OF THIAZOLO[3,2-f]XANTHINES

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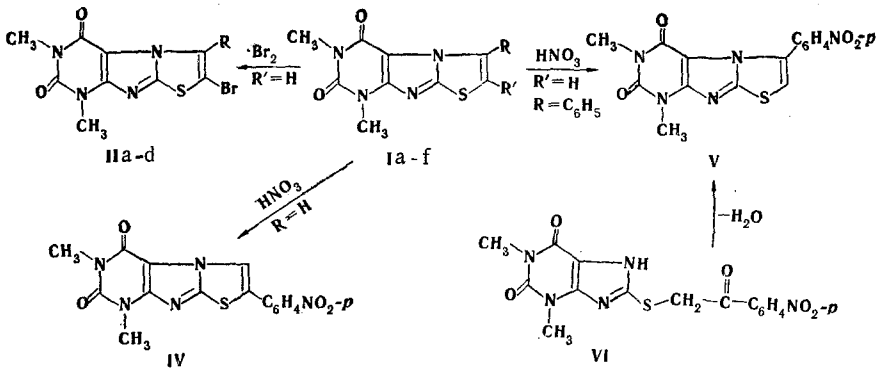
The chemical transformations of 2- and 3-substituted thiazolo[3,2-f]xanthines with electrophilic reagents were studied, and it was established that the 2 position of the thiazole ring is active in bromination, while the para position of the aryl substituent is active in nitration. The structures of the substances obtained were established from the IR, PMR, and mass-spectral data.

We have previously observed [2] that imidazo[1,2-f]xanthines readily undergo electrophilic substitution, as a result of which derivatives that have physiological activity are formed. The synthesis of these substances by other methods is either extremely complex or is completely impossible. In a continuation of our research on condensed heterocyclic derivatives of purine we verified the possibility of the direct replacement of the hydrogen atoms by electrophilic reagents in the case of 2- or 3-substituted thiazolo[3,2-f]xanthines, the chemical properties of which have not been investigated up until now. We attempted to determine the conditions for carrying out the bromination, nitration, acylation, formylation, and hydroxy-, amino-, and chloromethylation of 2- or 3-substituted thiazolo[3,2-f]xanthines (Ia-f).

In contrast to imidazo[1,2-f]xanthines [2], the bromination of Ia-f with molecular bromine or N-bromosuccinimide under various conditions takes place only in the 2 position of the thiazole ring to give 2-bromo derivatives (IIa-d). We were unable to realize the bromination of 2-substituted thiazolo[3,2-f]xanthines in the free 3 position.



Ia R=R′=H; Ib R=CH$_3$, R′=H; Ic R=C$_6$H$_5$, R′=H; Id R=C$_6$H$_4$Br-*p*, R′=H; Ie R=H, R′=CH$_3$; If R=H, R′=C$_6$H$_5$; IIa R=H; IIb R=CH$_3$; IIc R=C$_6$H$_5$; IId R=C$_6$H$_4$Br-*p*; V R′=H; IV R=H

The bromine atoms in IIa-d are inactive in nucleophilic substitution reactions and do not undergo exchange in the case of interaction of these compounds with ammonia and various amines.

*See [1] for Communication 3.

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