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REACTION OF 2-(2-AZAHETARYL)-4-CHLORO-3-OXOBUTYRONITRILES WITH SUBSTITUTED BENZALDEHYDE HYDRAZONES. UNEXPECTED FORMATION OF 4-ARYLIDENEAMINO-2-(1-R-BENZIMIDAZOL-2-YL)-3-OXOBUTYRONITRILES.

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The reaction of 2-(2-azahetaryl)-3-oxo-4-chlorobutyronitriles with substituted benzaldehyde hydrazones gives 4-arylideneamino-2-(1-R-benzimidazol-2-yl)-3-oxobutyronitriles, the structures of which were proved using spectroscopic data, the results of elemental analysis, and through their chemical reactions. It was found that the reaction course depends on the basicity of the heterocyclic fragment in the starting nitrile. A likely mechanism for the process is proposed.

Keywords: 2-(2-azahetaryl)-4-chloro-3-oxobutyronitriles, 4-arylideneamino-2-(1-R-benzimidazol-2-yl)-3-oxobutyronitriles, hydrazones, benzaldehydes.

The 2-(2-azahetaryl)- 4-chloro-3-oxobutyronitriles **1-4** [1] are convenient precursors in the preparation of pyrrole derivatives and pyrrole annelated heterocycles *via* reaction with various amines [2-5]. In this paper we present the results of a study of the reaction of compounds **1-4** with the substituted benzaldehyde hydrazones **5**.

The reaction between 2-(1-R-benzimidazol-2-yl)- 4-chloro-3-oxobutyronitriles **1, 2** and the hydrazones **5a-g** in the presence of N,N-dimethylaniline gives the 4-arylideneamino-2-(1-R-benzimidazol-2-yl)-3-oxobutyronitriles **8a-g, 9a-g** in 70-90% yields (Scheme 1) instead of the expected products of alkylation of the hydrazones at the amine nitrogen atom **6a-g, 7a-g** [6-16]. Hence, in this case we observe a rare, but none the less known alkylation at the imine nitrogen atom [17-19].

Elemental analysis of compounds **8, 9** agrees with the proposed structures (Table 1). The ^{1}H NMR spectra of these products recorded in DMSO-d_6 show a two proton singlet for the methylene group in the range 4.36-4.47 and also a one proton singlet in the range 8.99-8.47 ppm, corresponding to the azomethine fragment. The signal for the benzimidazole NH proton is seen as a singlet exchanging with D_2O (one or two protons for compounds **9** and **8** respectively) to low field 12.90-13.40 ppm and this can be explained by the presence of an intramolecular hydrogen bond. The remaining protons of the heterocyclic fragment and of the aryl substituent resonate in typical regions (Table 2). In the ^{1}H NMR spectra of compounds **8** and **9**, an absorption in the region 4.00-5.50 ppm for the proton of a secondary amino group in aldehyde alkylhydrazones [20-22] is absent. The IR spectra of the arylideneaminobutyronitriles **8, 9** have a strong absorption band for the stretching vibrations of

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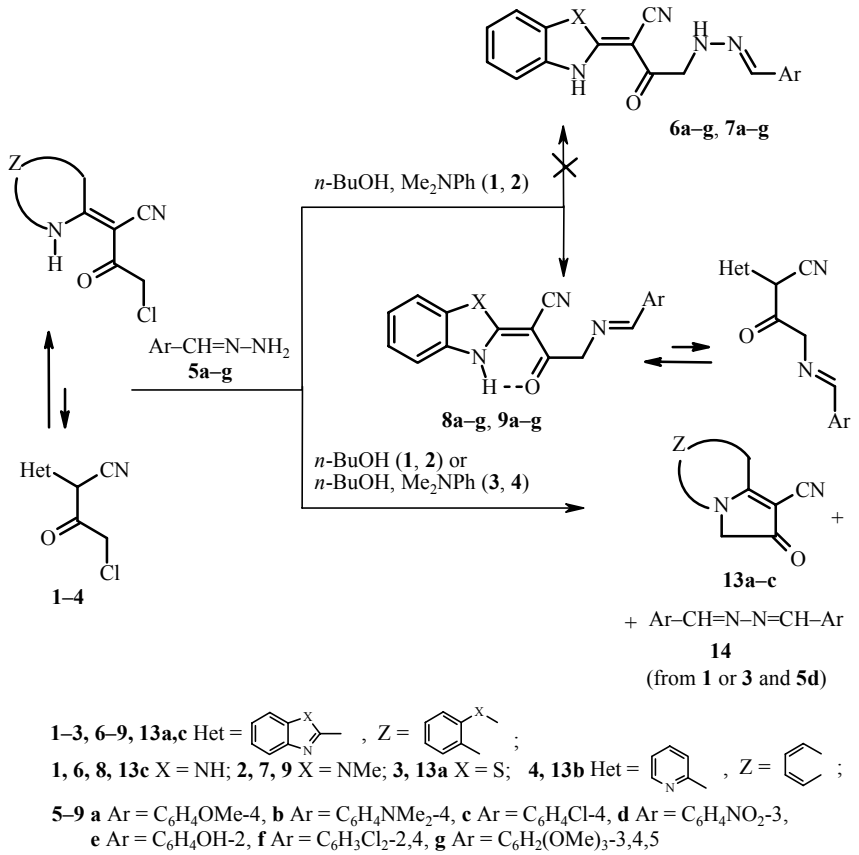
the nitrile group in the range 2170-2200 cm^{-1} and a medium sized band in the range 3140-3240 cm^{-1}, due to the N–H stretching vibrations. Hence the elemental analysis and the spectroscopic data exclude structures of type **6, 7** and are in full agreement with the structure of the corresponding compounds **8, 9**.

Scheme 1



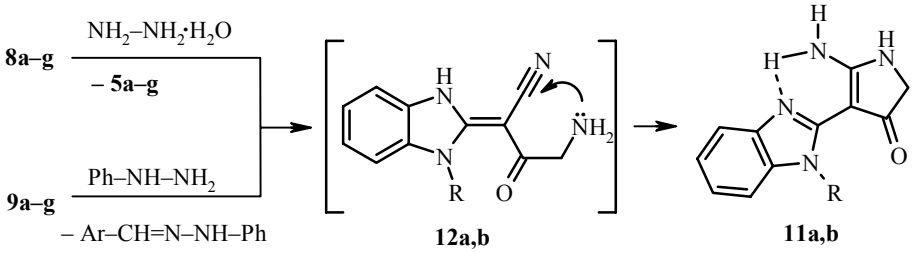
In view of the fact that this reaction of the nitriles **1, 2** with the hydrazones **5** is quite unexpected, we have obtained additional evidence for proving the structure of the products **8, 9**. It was found that the reaction of halonitriles **1, 2** with anisaldehyde methylhydrazone (**10**) gave compounds **8a** and **9a** respectively and these were identical to those synthesized from the unsubstituted aldehyde hydrazone **5a**. The results unambiguously show that the amine nitrogen atom of the hydrazones is lost during the course of the reaction and is not included in the composition of the products **8** and **9**.

The arylideneaminobutyronitriles **8, 9** are, in fact, imines formed from 4-amino-2-(2-benzimidazolyl)-3-oxobutyronitrile and variously substituted benzaldehydes. As is known, in the reaction of hydrazine derivatives, amines are readily lost from aldimines [23-26]. Short heating of compounds **8a-g** with an excess of hydrazine hydrate in dioxane gives the 2-amino-3-(2-benzimidazolyl)-4,5-dihydro-4-oxopyrrole **11a** in 50-60% yield depending on the starting azomethine **8a-g** (Scheme 2). The product **11a** is formed as a result of the heterocyclization of the intermediate amine **12** due to intramolecular addition of the amino group to the nitrile [2, 4, 5, 27, 28]. In the case of hydrazinolysis of azomethine **8a** there were isolated from the reaction mixture not only the pyrrolone **11a** but also a second product identified by comparison with a known sample which was anisaldehyde hydrazone **5a**. It was noted that the aminopyrrolone **11a** does not react with an excess of hydrazine hydrate and this is in agreement with data for derivatives of **11a** substituted at the 1 position [29].

TABLE 1. Characteristics of 4-Arylideneamino-2-(1-R-benzimidazol-2-yl)-3-oxobutyronitriles **8a-g**, **9a-g**

Compound	Empirical formula	Found N, % / Calculated N, %	mp, °C	Solvent for recrystallization	Yield, %
8a	$C_{19}H_{16}N_4O_2$	16.88 / 16.86	239	*n*-Butanol	86
8b	$C_{20}H_{19}N_5O$	20.12 / 20.29	234	*n*-Propanol	75
8c*	$C_{18}H_{13}ClN_4O$	16.58 / 16.64	253	*n*-Butanol	80
8d	$C_{18}H_{13}N_5O_3$	20.00 / 20.16	249	*i*-Propanol	96
8e	$C_{18}H_{14}N_4O_2$	17.44 / 17.60	248	*n*-Butanol	82
8f*[2]	$C_{18}H_{12}Cl_2N_4O$	15.21 / 15.09	260	Acetonitrile	74
8g	$C_{21}H_{20}N_4O_4$	14.38 / 14.29	246	Ethanol	87
9a	$C_{20}H_{18}N_4O_2$	16.26 / 16.18	204	*n*-Propanol	86
9b	$C_{21}H_{21}N_5O$	19.30 / 19.49	210	*n*-Butanol	87
9c*[3]	$C_{19}H_{15}ClN_4O$	16.15 / 15.98	222	*n*-Butanol	93
9d	$C_{19}H_{15}N_5O_3$	19.40 / 19.38	202	Ethanol	83
9e	$C_{19}H_{16}N_4O_2$	16.72 / 16.87	203	*n*-Butanol	68
9f*[4]	$C_{19}H_{14}Cl_2N_4O$	14.43 / 14.55	216	*n*-Butanol	65
9g	$C_{22}H_{22}N_4O_4$	13.58 / 13.78	199	Ethanol	86

Scheme 2



11, **12 a** R = H, **b** R = Me

The IR spectrum of compound **11a** shows the absence of the absorption band for the nitrile group and the presence of a strong absorption in the range 3080-3360 cm^{-1} due to the N–H bond stretching vibrations. The ^1H NMR spectrum of pyrrolone **11a**, recorded in DMSO-d_6, shows a two proton methylene group singlet at 3.87 and a one proton 1-H pyrrole ring singlet which exchanges in D_2O. It was of interest that the signals for the primary amino group protons were seen as two singlets, each of one proton, at 8.30 and 7.80 ppm and this non-equivalence is due to the intramolecular hydrogen bond. All of the spectroscopic parameters for compound **11a** agree well with known data for its 1-substituted derivatives [4, 5, 27, 28] and allow one to propose that, as in the latter, it exists in the amino ketone tautomeric form.

TABLE 2. Spectroscopic Characteristics of Compounds **8a-g**, **9a-g**

Compound	IR spectrum, cm^{-1}	^1H NMR spectrum (DMSO-d_6), δ, ppm, spin-spin coupling (*J*), Hz
8a	2200 (CN), 3240 (NH)	12.98 (2H, s, 2NH); 8.62 (1H, s, –N=CH–); 7.82 (2H, d, *J* = 9.0, 2'- and 6'-H_{Ar}); 7.54 (2H, m, H_{Bi}); 7.28 (2H, m, H_{Bi}); 7.05 (2H, d, *J* = 9.0, 3'- and 5'-H_{Ar}); 4.40 (2H, s, CH_2); 3.82 (3H, s, OCH_3)
8b	2180 (CN), 3220 (NH)	12.87 (2H, s, 2NH); 8.47 (1H, s, –N=CH–); 7.67 (2H, d, *J* = 9.0, 2'- and 6'-H_{Ar}); 7.54 (2H, m, H_{Bi}); 7.28 (2H, m, H_{Bi}); 6.77 (2H, d, *J* = 9.0, 3'- and 5'-H_{Ar}); 4.37 (2H, s, CH_2); 3.00 (6H, s, $N(CH_3)_2$)
8c	2185 (CN), 3220 (NH)	12.92 (2H, s, 2NH); 8.68 (1H, s, –N=CH–); 7.91 (2H, d, *J* = 8.5, 2'- and 6'-H_{Ar}); 7.56 (4H, m and d, *J* = 8.5, 3'- and 5'-H_{Ar} and H_{Bi}); 7.28 (2H, m, H_{Bi}); 4.37 (2H, s, CH_2)
8d	2185 (CN); 3225 (NH); 1520, 1335 (NO_2)	12.92 (2H, s, 2NH); 8.88 (1H, s, –N=CH–); 8.72 (1H, t, *J* = 1.5, 2'-H_{Ar}); 8.35 (2H, m, *J* = 8.0, *J* = 1.5, 4'- and 6'-H_{Ar}); 7.83 (1H, t, *J* = 8.0, 5'-H_{Ar}); 7.56 (2H, m, H_{Bi}); 7.28 (2H, m, H_{Bi}); 4.38 (2H, s, CH_2)
8e	2180 (CN); 3080-3220 (OH, NH)	12.93 (2H, s, 2NH); 11.07 (1H, s, OH); 8.97 (1H, s, –N=CH–); 7.69 (1H, d, *J* = 8.5, 6'-H_{Ar}); 7.55 (2H, m, H_{Bi}); 7.40 (1H, t, *J* = 7.5, 4'-H_{Ar}); 7.21 (2H, m, H_{Bi}); 6.97 (2H, d and dd, *J* = 7.5, *J* = 8.5, 3'- and 5'-H_{Ar}); 4.38 (2H, s, CH_2)
8f	2180 (CN), 3200 (NH)	12.80 (2H, s, 2NH); 8.87 (1H, s, –N=CH–); 8.13 (1H, d, *J* = 8.5, 6'-H_{Ar}); 7.47-7.74 (4H, m, 3'-, 5'-H_{Ar} and H_{Bi}); 7.27 (2H, m, H_{Bi}); 4.36 (2H, s, CH_2)
8g	2190 (CN), 3220 (NH)	12.90 (2H, s, 2NH); 8.62 (1H, s, –N=CH–); 7.55 (2H, m, H_{Bi}); 7.27 and 7.21 (4H, m and s, H_{Bi} and 2'-,6'-H_{Ar}); 4.37 (2H, s, CH_2); 3.85 (6H, s, 3'- and 5'-OCH_3); 3.75 (3H, s, 4'-OCH_3)
9a	2170 (CN), 3140 (NH)	13.35 (1H, s, NH); 8.61 (1H, s, –N=CH–); 7.82 (2H, d, *J* = 9.5, 2'- and 6'-H_{Ar}); 7.67 (2H, m, H_{Bi}); 7.36 (2H, m, H_{Bi}); 7.06 (2H, d, *J* = 9.5, 3'- and 5'-H_{Ar}); 4.46 (2H, s, CH_2); 3.96 (3H, s, NCH_3); 3.82 (3H, s, OCH_3)
9b	2170 (CN), 3150 (NH)	13.40 (1H, s, NH); 8.49 (1H, s, –N=CH–); 7.72 and 7.65 (4H, m and d, *J* = 9.0, H_{Bi} and 2'-, 6'-H_{Ar}); 7.37 (2H, m, H_{Bi}); 6.77 (2H, d, *J* = 9.0, 3'- and 5'-H_{Ar}); 4.46 (2H, s, CH_2); 3.97 (3H, s, NCH_3); 3.00 (6H, s, $N(CH_3)_2$)
9c	2180 (CN), 3140 (NH)	13.28 (1H, s, NH); 8.67 (1H, s, –N=CH–); 7.88 (2H, d, *J* = 8.5, 2'- and 6'-H_{Ar}); 7.65 (2H, m, H_{Bi}); 7.54 (2H, d, *J* = 8.5, 3'- and 5'-H_{Ar}); 7.31 (2H, m, H_{Bi}); 4.43 (2H, s, CH_2); 3.92 (3H, s, NCH_3)
9d	2180 (CN); 3145 (NH); 1515, 1350 (NO_2)	13.30 (1H, s, NH); 8.92 (1H, s, –N=CH–); 8.71 (1H, t, *J* = 2.0, 2'-H_{Ar}); 8.38 (2H, m, *J* = 8.0, *J* = 2.0, 4'- and 6'-H_{Ar}); 7.84 (1H, t, *J* = 8.0, 5'-H_{Ar}); 7.70 (2H, m, H_{Bi}); 7.36 (2H, m, H_{Bi}); 4.47 (2H, s, CH_2); 3.98 (3H, s, NCH_3)
9e	3220-3060 (OH, NH); 2190 (CN)	13.30 (1H, s, NH); 11.08 (1H, s, OH); 8.99 (1H, s, –N=CH–); 7.70 and 7.55 (3H, dd and m, *J* = 8.0, *J* = 2.0, 6'-H_{Ar} and H_{Bi}); 7.41 (1H, dt, *J* = 8.0, *J* = 2.0, 4'-H_{Ar}); 7.19 (2H, m, H_{Bi}); 6.96 and 6.94 (2H, t and d, *J* = 8.0, 3'- and 5'-H_{Ar}); 4.45 (2H, s, CH_2); 3.97 (3H, s, NCH_3)
9f	3150 (NH), 2180 (CN)	13.31 (1H, s, NH); 8.88 (1H, s, –N=CH–); 8.14 (1H, d, *J* = 8.5, 6'-H_{Ar}); 7.75, 7.67 and 7.56 (4H, d, *J* = 2.0, m and dd, *J* = 8.5, *J* = 2.0, 3'-H_{Ar}, H_{Bi} and 5'-H_{Ar}); 7.34 (2H, m, H_{Bi}); 4.44 (2H, s, CH_2); 3.97 (3H, s, NCH_3)
9g	2175 (CN), 3150 (NH)	13.30 (1H, s, NH); 8.61 (1H, s, –N=CH–); 7.63 (2H, m, H_{Bi}); 7.37 (2H, m, H_{Bi}); 7.21 (2H, s, 2'- and 6'-H_{Ar}); 4.44 (2H, s, CH_2); 3.97 (3H, s, NCH_3); 3.86 (6H, s, 3'- and 5'-OCH_3); 3.77 (3H, s, 4'-OCH_3)

Reaction of the azomethines **9a-g** with phenylhydrazine occurs through the amino nitrile **12b** to the aminooxopyrrole **11b** in 50-55% yields (Scheme 2). The spectroscopic characteristics of the product **11b** are similar to those of the product **11a**. In the case of compound **9a**, also anisaldehyde phenylhydrazone was separated from the reaction mixture.

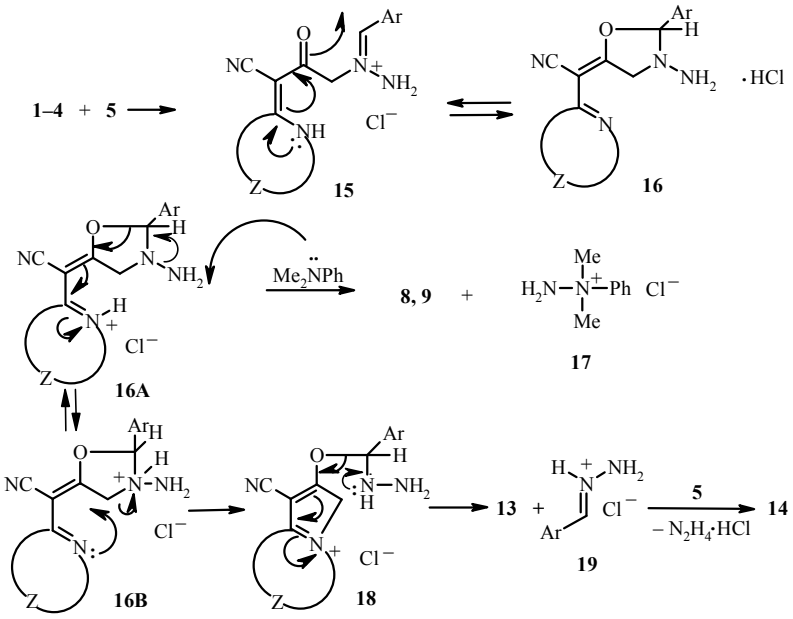
In order to explain the mechanism of formation of compounds **8, 9** we first examined the effect of the basicity of the heterocyclic substituent in the halonitriles **1-4** on the course of the reaction. It was found that the 2-benzothiazolyl- and also the 2-pyridyl derivatives **3, 4** and the hydrazones **5** did not form the corresponding hetero analogs of compounds **8, 9** under the same conditions. Instead, there were isolated from the reaction mixture only the products of intramolecular alkylation of the starting halo nitriles **3** and **4** which are the known

compounds **13a** and **13b** respectively [1, 4] (Scheme 1). Hence the nature of the reaction of the halo nitriles **1-4** with the hydrazones **5** depends on the basicity of the heterocycle in compounds **1-4** and occurs at the imine nitrogen atom to give the products **8, 9** only in the case of the highly basic benzimidazolyl derivatives **1, 2**.

The reaction of the benzothiazolyl derivative **3** with *m*-nitrobenzaldehyde hydrazone **5d** gave a reaction mixture which contained both compound **13a** and also 3,3'-dinitrobenzaldazine **14**, i.e. the formation of the products of intramolecular alkylation **13** is accompanied by the symmetrization of hydrazone **5** to the corresponding azine **14** (Scheme 1). We therefore propose that compounds **13a,b** are formed with the direct participation of hydrazones **5**.

It was of no less interest that the absence of N,N-dimethylaniline in the reaction mixture influences the reaction course in a basic way. Hence reaction of the halo nitrile **1** with hydrazone **5d** in *n*-butanol in the absence of N,N-dimethylaniline leads to the formation of the corresponding intramolecular alkylation product **13c** and 3,3'-dinitrobenzaldazine **14** while, in the presence of N,N-dimethylaniline, compound **8d** is formed. This means that, on the one hand, N,N-dimethylaniline takes part in the formation of compounds **8, 9** directly as reagent. On the other hand, the possibility of forming compound **13c** along with the azine **14** in the absence of N,N-dimethylaniline confirms the proposal regarding formation of the products **13** *via* direct participation of the hydrazones **5**. It appears likely that the formation of the arylideneaminobutyronitriles **8, 9** and oxonitriles **13** along with the aldazines **14** occurs *via* a single, general intermediate, and the pathway depends both on the basicity of the heterocyclic fragment and the presence or absence in the reaction mixture of N,N-dimethylaniline. On this basis we propose the following mechanism for the formation of compounds **8, 9** (Scheme 3).

Scheme 3



The first stage involves alkylation of the hydrazone **5** by the halo nitrile **1-4** at the imine nitrogen atom to give the immonium intermediates **15**. The oxygen atom of the latter occurs within a β-enamino ketone fragment. An oxygen of this type has a significant excess of electron density due to conjugation with the unshared electron pair of the nitrogen atom of the β-amino group and, as a consequence, a marked nucleophilicity [30]. On the other hand, there is also present an electrophilic center in the intermediates **15** which is the azomethine carbon

atom of the immonium fragment. Hence there is the possibility of an intramolecular O-aminoalkylation, as a result of which there are formed intermediate oxazolidines **16** which are the general intermediates referred to above. In the oxazolidines **16** there exist two basic centers which are the nitrogen atoms of the heterocyclic substituent and the hydrazine fragment. Hence for the intermediates **16** there are two possible protonated forms **16A** and **16B**, between which there can be established an acid-base equilibrium, the position of which is determined only by the basicity of the heterocyclic substituent, since the basicity of the second center is virtually the same for all of the oxazolidines **16** with different Ar. Hence for the highly basic benzimidazolyl derivatives the equilibrium must be shifted towards protonation at the heterocyclic substituent form **16A**, while for the less basic pyridyl- and benzothiazolyl derivatives the alternative form **16B** predominates. The different protonated forms of intermediate **16** subsequently undergo different reactions. Hence the heterocyclic substituent proves to have an effect on the equilibrium position for the protonated forms **A** and **B,** thus influencing the whole reaction course.

The strong polarization and hence lability of the 1–2 bond must serve as a strong driving force in the subsequent reactions of the intermediates **16A**. The latter results from the opportunity for conjugation of the *p*-electrons of the oxygen atom with the two strong acceptors, i.e. the nitrile group and the nitrogen atom of the heterocyclic substituent which bears the positive charge. Because of this, such an oxygen atom is an excellent nucleofuge. In itself, fission of the O–CHAr bond would lead only to the initial immonium intermediate **15** which implies a likely reversible formation of the oxazolidines **16**. However in the presence of a nucleophile such as, in this case, N,N-dimethylaniline, fission of the O–CHAr bond becomes possible with its help. In addition, the direct nucleophilic attack of N,N-dimethylaniline at position 2 of the oxazolidine ring of the intermediate **16A** is significantly sterically hindered. The primary amino group at position 3 in the indicated intermediates is sterically fully available and, along with the moderate energy of the N–N bond, this makes possible its fission via nucleophilic attack of N,N-dimethylaniline. As a result of such a process, accompanied by the redistribution of electron density (Scheme 3), there are formed the arylideneaminobutyronitriles **8, 9** and N,N-dimethyl-N-phenylhydrazinium chloride **17**. The given process can be considered as a nucleophilic substitution at the primary amino group nitrogen atom in which the N,N-dimethylaniline takes the part of the nucleophile and the leaving group is the whole remaining oxazolidine fragment **16A**. A similar formation of a N,N-dimethyl-N-phenylhydrazinium salt **17** from N,N-dimethylaniline and a compound of the type H_2NX where X is a leaving group has been reported in the literature [31, 32]. In the light of the proposal presented, experiments were undertaken to separate from the reaction mixture salts of the type **17** with different anions. Unfortunately no kind of identifiable products were obtained other than compounds **8, 9**. According to literature data [31, 32], salts of type **17B** are prepared under mild conditions and data concerning their thermal stability is not available. Since, in our case, the reaction occurs under quite forcing conditions (117°C, 10-15 h), further reactions of the indicated salts **17** are quite possible.

The oxazolidine forms **16B** protonated at the hydrazine nitrogen (Scheme 3) undergo a standard intramolecular, nucleophilic substitution at a carbon center. The heterocyclic substituent nitrogen atom takes the part of the nucleophile, having an unshared electron pair, and the leaving group is the quaternary nitrogen atom which bears the overall positive charge. As a result, the intermediates **18** are formed. These are effectively O-substituted polyaminals which are labile intermediates in the preparation and hydrolysis of imines and related compounds (hydrazones, oximes etc.) and decompose with the formation of carbonyl compounds or imines, depending on the reaction route. Of course, the O-substituted polyaminals can decompose only in the direction of formation of imines. Thus the standard reaction of the polyaminal intermediates **18** leads to formation of the products **13** and of the protonated hydrazones **19**. In turn, the protonated molecules of the hydrazone are the first stage of a known acid catalyzed symmetrization reaction of N-unsubstituted hydrazones to azines [33, 34] and the reaction of the salts **19** with a molecule of the hydrazone **5** present in the reaction mixture can give the azines **14**. The direct formation of the latter from the hydrazones **5** without participation of the halo nitriles **1-4** cannot be ruled out.

It is likely that, with the N,N-dimethylaniline absent from the reaction mixture, the benzimidazolyl derivatives **1, 2** are converted to the corresponding pyrrolo[1,2-*a*] heterocycles **13** via the protonated forms of the oxazolidine intermediates of type **16B**. Although the latter, in this case, are present in the equilibrium mixture with the protonated forms **16A** only in very small amount, the possibility of their irreversible conversion to compound **13** promotes this reaction. With the N,N-dimethylaniline present in the reaction mixture the basic process becomes the formation of the arylideneaminobutyronitriles **8, 9**.

Thus as a result of studying the reaction of the 2-(2-azahetaryl)- 4-chloro-3-oxobutyronitriles **1-4** with substituted benzaldehyde hydrazones **5** we have found an extremely unusual reaction which forms the 4-arylideneamino-2-(1-R-benzimidazol-2-yl)-3-oxobutyronitriles **8, 9**. To our knowledge this is the first example of a unique reaction between N- unsubstituted hydrazones and α-halo ketones which has led to the separation of identifiable products. Additionally, the hydrazones are converted to imines in the given reaction. Within the scope of many examples of reversible reactions there was known only one case of a reaction of the type hydrazone → azomethine which was observed for N-arylsulfonyl substituted hydrazones [35]. For a series of N-unsubstituted hydrazones an analogous reaction is reported for the first time. Evidently, these results are obtained thanks to the extremely specific structure of the α-halo ketones **1, 2**. We should mention that, in the course of establishing the structure of the products **8, 9**, there were synthesized the previously unknown 2-amino-3-(1-R-benzimidazol-2-yl)-4,5-dihydro-4-oxopyrroles **11a,b**. It was noted that all of the developed methods for the synthesis of 2-amino-3-hetaryl-4-oxopyrroles do not allow the preparation of those which are substituted at the 1 position in this series [4, 5, 27, 28].

EXPERIMENTAL

Monitoring of the course of the reaction and the purity of the compounds obtained was carried out using TLC on Silufol UV-254 plates in the systems chloroform-methanol (9: 1) and benzene-ethanol (9: 1). IR spectra were recorded on a Pye Unicam SP3-300 instrument for KBr tablets. ^{1}H NMR spectra were recorded for DMSO-d_6 solutions on a Bruker WP-100 instrument with a working frequency of 100 MHz.

The yields and analytical parameters for compounds **8a-g, 9a-g** are given in Table 1 and the spectroscopic characteristics in Table 2.

The 2-(2-azahetaryl)-4-chloro-3-oxobutyronitriles **1-4** were synthesized by a known method [1, 4]. Hydrazones **5a-g** were prepared as reported previously [33, 36-40].

4-(Arylideneamino)-2-(2-benzimidazolyl)-3-oxobutyronitrile (8a-g). N,N-Dimethylaniline (1 ml) was added to a suspension of the nitrile **1** (1.2 g, 0.005 mol) and the hydrazone **5a-g** (0.0055 mol) in *n*-butanol (40 ml). The mixture obtained was refluxed for 10-15 h until compound **1** had disappeared on TLC. The precipitate obtained on cooling the reaction product was filtered off, washed successively with *n*-butanol, water, and methanol and then dried in air and recrystallized from the appropriate solvent (see Table 1).

4-(Arylideneamino)-2-(1-methylbenzimidazol-2-yl)-3-oxobutyronitriles (9a-g). N,N-Dimethylaniline (0.8 ml) was added to a suspension of nitrile **2** (1.0 g, 0.004 mol) and the hydrazone **5a-g** (0.0045 mol) in *n*-butanol (25 ml) and then worked up as described in the previous method.

Reaction of 2-(1-R-Benzimidazol-2-yl)-4-chloro-3-oxobutyronitriles 1, 2 with Anisaldehyde Methylhydrazone (10). N,N-Dimethylaniline (1.0 ml) was added to a suspension of the nitrile **1** or **2** (0.005 mol) and the methylhydrazone **10** (0.9 g, 0.0055 mol) in *n*-butanol (35-40 ml). The reaction mixture was refluxed for 10-15 h until halo nitriles **1, 2** had disappeared on TLC. The precipitate obtained on cooling the reaction product was filtered off, washed successively with *n*-butanol, water, and methanol and then dried and recrystallized from *n*-butanol. The nitriles **8a** (0.8 g, 46%) or **9a** (1.3 g, 75%) obtained were identical to products synthesized from the nitriles **1, 2** and the hydrazone **5a** respectively (no depression in melting point in either case being found for mixed samples).

Reaction of 2-(2-Benzimidazolyl)-4-(*p*-methoxybenzylideneamino)-3-oxobutyronitrile 8a with Hydrazine Hydrate. Hydrazine hydrate (1.2 ml, 0.024 mol) was added rapidly to a hot suspension of the nitrile **8a** (2.0 g, 0.006 mol) in dioxane (40 ml). Due to an exothermic reaction a solution was formed which was refluxed for a further 40 min, cooled, and the white crystals obtained were filtered off, dried, and recrystallized from dioxane to give 2-amino-3-(2-benzimidazolyl)-4,5-dihydro-4-oxopyrrole **11a** (0.8 g, 63%); mp 273°C. Found, %: N 26.32. $C_{11}H_{10}N_4O$. Calculated, %: N 26.15. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 11.50 (1H, s, NH···O); 8.30 (1H, s, HN<u>H</u>···N); 7.80 (1H, s, <u>H</u>NH···N); 7.44 (2H, m, H_{Bi}); 7.01 (2H, m, H_{Bi}); 4.83 (1H, s, 1-H); 3.87 (2H, s, CH_2).

Treatment of the nitriles **8b-g** with hydrazine hydrate under analogous conditions also gave compound **11a**. The filtrate after removal of pyrrolone **11a** was evaporated to dryness *in vacuo*. The dry residue was triturated with water, filtered, and recrystallized from ethanol using carbon to give the hydrazone **5a** (0.8 g, 89%) which was identical to an independently prepared sample [36].

Reaction of 4-(*p*-Methoxybenzylideneamino)-2-(1-methylbenzimidazol-2-yl)-3-oxobutyronitrile 9a with Phenylhydrazine. Phenylhydrazine (1 ml, 0.01 mol) was added to a hot suspension of the nitrile **9a** (1.7 g, 0.005 mol) in 2-propanol (40 ml) and the mixture was refluxed for 2.5 h. The yellowish-white precipitate formed on cooling was filtered off, dried in air, and recrystallized from 2-propanol to give 2-amino-3-(1-methylbenzimidazol-2-yl)-4,5-dihydro-4-oxopyrrole **11b** (0.6 g, 53%); mp 261°C. Found, %: N 24.44. $C_{12}H_{12}N_4O$. Calculated, %: N 24.55. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.60 (2H, s, NH_2); 7.37 (2H, m, H_{Bi}); 7.00 (2H, m, H_{Bi}); 4.23 (1H, s, 1-H); 3.96 (3H, s, CH_3); 3.74 (2H, s, CH_2).

The reaction of the nitriles **9b-g** with hydrazine hydrate under similar conditions gave compound **11b**. The filtrate after removal of pyrrolone **11b** from the reaction mixture was evaporated to dryness *in vacuo*. The dry residue was triturated with methanol (10 ml), filtered, dried, and recrystallized from *n*-hexane to give pinkish-white crystals with mp 120°C and these were identified as anisaldehyde phenylhydrazone (lit. mp 122°C [41]) by comparison with an independently prepared sample.

Reaction of 2-(2-Benzothiazolyl)- and 4-Chloro-3-oxo-2-(2-pyridyl)butyronitriles 3, 4 with *m*-Nitrobenzaldehyde Hydrazone 5d. N,N-Dimethylaniline (0.8 ml) was added to a suspension of the halonitrile **3** or **4** (0.004 mol) and the hydrazone **5d** (0.75 g, 0.0045 mol) in *n*-butanol (35 ml). The mixture obtained was refluxed for 10-15 h until the starting nitrile had disappeared on TLC. The precipitate formed on cooling was filtered off, washed successively with n-butanol, water, and methanol, dried in air, refluxed with dioxane (35-40 ml), and filtered while hot. Compounds **13a** (0.6 g, 70%, from nitrile **3**) or **13b** (0.5 g, 79%, from nitrile **4**) were obtained and were identified by comparison with previously synthesized samples [4]. In the case of nitrile **3**, the white crystals formed on cooling the filtrate and after drying in air were identified as compound **14** (0.5 g, 42%); mp 193°C (lit. mp 194°C [33]).

Reaction of 2-(2-Benzimidazolyl)-4-chloro-3-oxobutyronitrile 1 with *m*-Nitrobenzaldehyde Hydrazone in the Absence of N,N-Dimethylaniline. A mixture of nitrile **1** (1.2 g, 0.005 mol), hydrazone **5d** (0.85 g, 0.0055 mol), and *n*-butanol (40 ml) was refluxed for 10-15 h. After the standard work up (see the synthesis of compounds **13a,b, 14**) 2-oxo-3-cyano-1H,4H-pyrrolo[1,2-*a*]benzimidazole **13c** [4] (0.7 g, 71%) and 3,3'-dinitrobenzaldazine **14** (0.5 g) were obtained.

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