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HIGHLY POLARIZED ENAMINES. 2.* SYNTHESIS AND INVESTIGATION OF THE FURTHER AMINATION OF DERIVATIVES OF α,α-DIAMINO-β-CYANO-β-NITROETHYLENE

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Highly polarized enediamines of the α,α-diamino-β-cyano-β-nitroethylene type have been obtained by the hydrolysis of 4-chloro-5-nitropyrimidines. Several chemical conversions of the enamines obtained have been studied, particularly leading to derivatives of 2-(cyanonitromethylene)imidazoline and -hexahydropyrimidine, and also to derivatives of N,N'-bisvinylpiperazine and 7-methylene-1,4-diazabicyclo[2.2.1]heptane.

As a continuation of our investigations on the synthesis and properties of highly polarized enamines [1, 2] we have now synthesized a series of new substituted α,α-diamino-β-cyano-β-niroethylenes (I). We have studied their further amination and the possibility of obtaining from them the corresponding enaminoamidine derivatives and certain chemical transformations of the latter.

Enediamines of the type of (I) were obtained by the known method of [3-5] by fission of the pyrimidine ring of the corresponding 6-RR^1-amino-4-chloro-5-nitropyrimidines (II) under acid hydrolysis conditions. Previously [2-5], 6-dialkylaminopyrimidines were generally used for this purpose. Thus on heating compound (IIa) (R = R^1 = Me) in dilute hydrochloric acid, decomposition of the pyrimidine ring occurred smoothly with the elimination of formic acid and the formation of the enediamine (Ia) [3], which was the principal starting material in the present work. We showed that this reaction also occurs for more complex amino-substituted derivatives. For example the enamine (Ib) was synthesized from the N-benzoylpiperazine derivative (IIb). In (Ib) one of the substituents is a residue of piperazine formed by debenoylation. Owing to the presence of the piperazine ring, compound (Ib) may be used in the synthesis of various substituted derivatives of this type. The synthesis of enamines containing an aminoaryl substituent in the position of the enamine was significantly more complex. Since an arylamino group at position 6 of a pyrimidine ring deactivates a chlorine atom at position 4 to a significantly lesser extent than an alkyl or alkylamino group, the reaction of 4,6-dichloro-5-nitropyrimidine (III) with aromatic amines occurs ambiguously and diarylaminonitropyrimidines (IVc-e) are formed together with the desired chlorine-containing pyrimidines (IIc-e). Compounds (IVc-e) are not capable of conversion into enediamines under the conditions indicated above. Variation of the reaction conditions, such as using amine acetates as starting materials or lower temperatures, had no significant effect on the percentage ratio of final products. Separation of the mixtures obtained was accompanied by significant losses, consequently it was convenient in several cases to use the mixture of (IIc-e) and (IVc-e) preparatively in the hydrolysis because removal of the enediamine from the unchanged diaminopyrimidine was not complicated. However it should be mentioned that fission of the chloropyrimidine (II) to the enediamine was accompanied by a side reaction, viz. formation of the corresponding 6-arylamino-5-nitropyrimid-4-one (Vc-e), which was also isolated from the reaction mixture and identified (see Table 1).

As already mentioned, α-amino-α-dimethylamino-α-cyano-α-nitroethylene (Ia) was selected as the principal starting material for studying the amination reaction.

*For Part 1, see [1].

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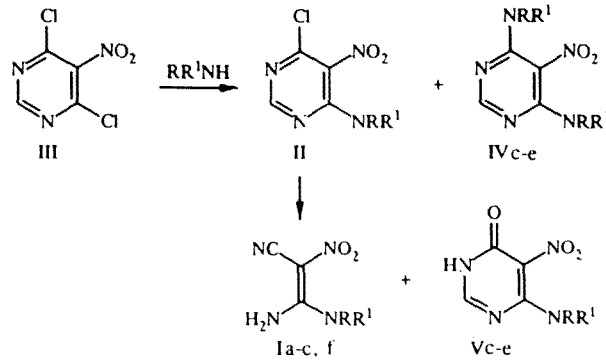
TABLE 1. Physicochemical Characteristics of the Synthesized Compounds

Compound	Empirical formula	Found, %			Calculated, %			mp, °C	Crystallization solvent	IR spectrum, cm^{-1}	M^+	Yield, %
		C	H	N	C	H	N					
1	2	3	4	5	6	7	8	9	10	11	12	13
Ib	$C_7H_{11}N_5O_2 \cdot HCl$	31,23	4,11	25,87	31,11	4,01	25,93	251	MeOH/water	3356, 3212, 3178, 2206, 1656	233	72
Ic	$C_{10}H_{10}N_4O_3$	51,17	4,42	23,94	51,28	4,27	23,93	234	Water	3343, 3200, 2200, 1658, 1481	234	7
Id	$C_3H_4N_4O_2$	28,32	3,01	43,64	28,12	3,12	43,75	272	EtOH	3480, 3363, 3214, 2200, 1645	128	67
If	$C_{11}H_{12}N_4O_2$	56,67	5,16	24,28	56,89	5,17	24,14	175	EtOH	3438, 3361, 2200, 1656, 1433	232	37
Ig	$C_7H_{10}N_4O_3$	42,48	5,00	28,15	42,42	5,05	28,28	132	*i*-PrOH	3441, 3371, 2200, 1651, 1243	198	32
Ih	$C_9H_{17}N_5O_2$	47,51	7,53	31,04	47,57	7,49	30,83	220	Water	3436, 3365, 3190, 2200, 1646	227	45
Ii	$C_7H_{13}N_5O_2$	42,41	6,78	34,97	42,21	6,53	35,17	243	*i*-PrOH	3435, 3364, 3195, 2200, 1650	199	64
IIb	$C_{15}H_{14}N_5O_3Cl$	51,89	4,07	19,87	51,72	4,02	20,11	122	EtOH	1763, 1634, 1524, 1230	348	84
IIc	$C_{11}H_9N_4O_2Cl$	47,28	3,29	20,12	47,14	3,21	20,00	206	Water	3115, 1664, 1451, 1324	280	14
IId	$C_{10}H_6N_4O_2Cl_2$	42,39	2,24	19,58	42,10	2,10	19,64	249	EtOH/ water	3120, 1655, 1320, 1245	285	24
IIe	$C_{10}H_7N_4O_2Cl$	48,05	2,94	22,31	48,00	2,80	22,40	78	EtOH/ water	3122, 1660, 1331, 1255, 1178	250	45
IIf	$C_{12}H_{11}N_4O_2Cl$	51,83	3,97	19,89	51,79	3,95	20,14	120	Dioxan	1642, 1547, 1432, 1107	278	65
IVc	$C_{18}H_{17}N_5O_4$	58,75	4,52	19,33	58,85	4,63	19,07	208	EtOH	3132, 1746, 1553, 1467, 1367	367	51
IVd	$C_{16}H_{11}N_5O_2Cl$	51,13	2,98	18,52	51,06	2,92	18,61	197	EtOH	3345, 3189, 1678, 1423	376	46

TABLE 1. (Continued)

Compound	Empirical formula	Found, %			Calculated, %			mp, °C	Crystallization solvent	IR spectrum, cm^{-1}	M^+	Yield, %
		C	H	N	C	H	N					
1	2	3	4	5	6	7	8	9	10	11	12	13
IVe	$C_{16}H_{13}N_5O_3$	62,47	4,17	22,24	62,54	4,23	22,08	152	EtOH	3360, 3201, 1654, 1345, 1206	307	25
Vc	$C_{11}H_{10}N_4O_4$	50,42	3,85	21,08	50,38	3,81	21,37	239	Water	3210, 3165, 1768, 1650	262	43
Vd	$C_{10}H_7N_4O_3Cl$	45,12	2,58	21,16	45,11	2,63	21,05	254	Water	3206, 3160, 1760, 1648, 1450	266	78
Ve	$C_{10}H_8N_4O_3$	51,81	3,37	24,25	51,72	3,44	24,13	216	Water	3200, 3145, 1755, 1653, 1449	232	81
Vf	$C_{12}H_{12}N_4O_3$	55,43	4,44	21,76	55,38	4,61	21,53	251	MeOH	3150, 1759, 1657, 1437	268	65
VIa	$C_{11}H_{16}N_4O_4$	49,27	5,88	21,11	49,25	5,97	20,89	46	Water	2207, 1634, 1537, 1430, 1106	268	12
VIb	$C_7H_{12}N_4O_2$	45,71	6,60	30,61	45,65	6,52	30,43	121	*i*-PrOH	2200, 1645, 1540, 1437	184	18
VIII	$C_{10}H_{12}N_8O_4$	38,98	3,83	36,67	38,96	3,89	36,36	238	MeOH	3340, 3200, 2200, 1657, 1518	–	32
IX	$C_7H_8N_4O_2$	46,49	4,39	31,23	46,66	4,44	31,11	170	MeOH	2200, 1649, 1560, 1475	180	7
X	$C_4H_5N_3O_3$	33,67	3,60	29,45	33,56	3,49	29,37	162	Water	3210, 3167, 2215, 1650, 1489	143	66
XIIa	$C_8H_{13}N_5O_2$	45,65	6,32	33,21	45,49	6,11	33,17	176	EtOH	2195, 1643, 1505, 1383, 1290	211	98
XIIb	$C_7H_{11}N_5O_2$	42,77	5,58	35,46	42,64	5,55	35,53	174	EtOH	3230, 2203, 1641, 1597, 1362	197	97
XIIc	$C_6H_9N_5O_2$	39,67	5,02	38,41	39,34	4,91	38,25	180	EtOH	3494, 3280, 2210, 1658, 1465	183	84
XIII	$C_9H_{14}N_6O_2$	45,18	5,91	35,33	45,37	5,88	35,29	203	EtOH	2201, 1678, 1547, 1430	238	97
XIV	$C_{17}H_{16}N_4O_2$	66,34	5,23	18,45	66,23	5,19	18,18	161	EtOH	3260, 3165, 2200, 1649	308	28
XV	$C_{18}H_{17}N_5O_2$	64,41	5,01	20,97	64,47	5,07	20,89	212	*i*-PrOH	3368, 3255, 3159, 2200, 1658	335	16
XVI	$C_{11}H_{11}N_5O_2$	54,02	4,31	28,47	53,87	4,48	28,57	223	MeOH	3205, 2200, 1623, 1420, 1261	245	12



I–V a R = R^1 = Me, c R = H, R^1 = *p*-$MeOC_6H_4$, d R = H, R^1 = *p*-ClC_6H_4, e R = H, R^1 = Ph, f R = Et, R^1 = Ph; IIb RR^1 = $-(CH_2CH_2)NCOPh$, Ib RR^1 = $-(CH_2CH_2)NH \cdot HCl$

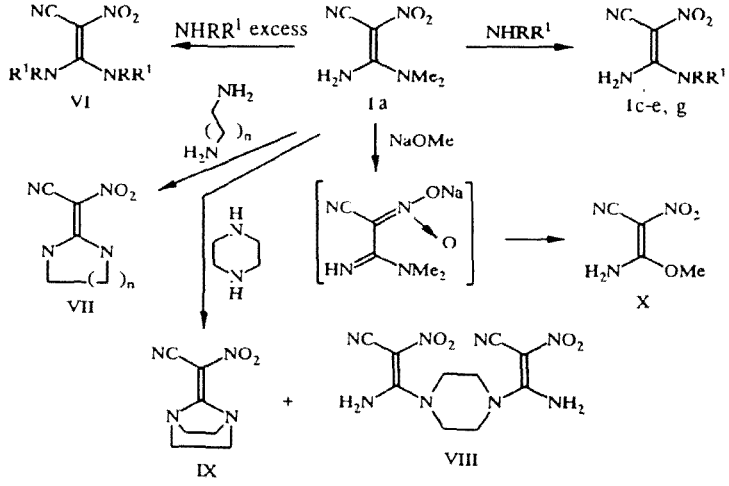
It is known that in several cases the further amination of enamines may be accelerated significantly by using acidic catalysts, since the immonium cation generated by C-protonation is capable of adding nucleophilic reagents, particularly amines, at a significantly greater rate at the α position. It is natural that such a possibility is retained only in cases when the basicity of the enamine used is adequate to generate a significant concentration of the corresponding immonium cation in the presence of acidic reagents. Since nothing was known about the basicity of highly polarized enamines of type (I) we assessed this using ^1H NMR spectroscopy. It turned out that there were no changes in the spectrum of compound (Ia) in trifluoroacetic acid characteristic of enamines protonated at the nitrogen atom or at the β-carbon atom [6]. Moreover on extended exposure of enamine (Ia) to this solution no hydrolysis was observed (within the limits of sensitivity of the method). Hence it may be concluded that the basicity of the investigated substances is extremely low and the direct addition (without catalyst) of amines to the α position of enediamines of type (I) is possible. It transpired that the result of the process is determined in many respects by the physical properties of the products formed and by the excess and basicity of the amine used. On reacting compound (Ia) with strongly basic amines in aqueous medium using a threefold excess of nucleophilic reagent (ammonia, methylamine, morpholine), monoamination products insoluble under these conditions were precipitated from the reaction mixture with only the dimethylamino group undergoing replacement. The enediamines (Ic-e, g-i) were obtained as a result of similar aminations. On carrying out the reaction with a large excess of morpholine (under these conditions the monoamination product is not precipitated and is not removed from the reaction) β-cyano-α,α-bismorpholino-β-nitroethylene (VIa) was formed. The α,α-bis dimethylamino derivative (VIb) was formed under analogous conditions. The structures of both compounds were confirmed by spectral data. For example, absorption bands characteristic of a cyano group (2200 cm^{-1}) and a nitro group (1560 cm^{-1}) were present in the IR spectrum of enamine (VIb). Absorption bands for the NH bond, present in the spectrum of the starting material, were absent. A peak was observed in the mass spectrum of enamine (VIb) for the molecular ion (M^+ · 184) and there were also peaks corresponding to the decomposition fragments of this compound (168, 154, 138, 111). In general the mass spectra of enamines (I) were characterized by intense peaks for the appropriate molecular ions, the fragmentation of which is of a single type and is caused by the breakdown of the nitro group. Peaks for $[M-O]^+$, $[M-NO]^+$, $[M-NO_2]^+$, and $[M-NO_2-HCN]^+$ ions were observed.

The possibility of bisamination of enediamine (Ia) established above suggested the use of bisnucleophiles in this reaction. In reality the reaction of (Ia) with ethylene- or trimethylenediamines led smoothly and in high yield to the hydrogenated imidazole (VIIa) and pyrimidine (VIIb) derivatives, which had been obtained previously by other means [7]. The reaction of compound (Ia) with piperazine is extremely interesting. In this case the diazabicycloheptane derivative (IX) was isolated in addition to the substituted N,N′-bisvinylpiperazine (VIII), which was the main reaction product. The structures of the cyclic compounds obtained were confirmed by spectral data and elemental analysis. The physicochemical characteristics of (VIIa, b) corresponded to those reported in the literature [7]. Fragmentation of the molecular ions of the cyclic compounds (VIIa, b) and (IX), as for compounds (I), were characterized in the mass spectra primarily by the elimination of the nitro group ($[M-O]^+$, $[M-NO]^+$, $[M-NO_2]^+$). Further decomposition of the $[M-NO_2]^+$ ions was linked both with elimination of HCN and with fission of bonds in the hydrogenated imidazole (VIIa), pyrimidine (VIIb), and piperazine (IX) rings. A signal was observed at 4.11 ppm (s, CH_2) in the ^1H NMR spectra (DMSO-D_6) of compounds (IX) and (VIIa) and a signal was present at 8.77 ppm (2H, s, NH) in the spectrum of (VIIa). There were no absorption bands in the IR spectrum of compound (IX)

corresponding to an amino group, but the appropriate bands were present in the spectra of products (VIIa) and (VIIb) (see Table 1).

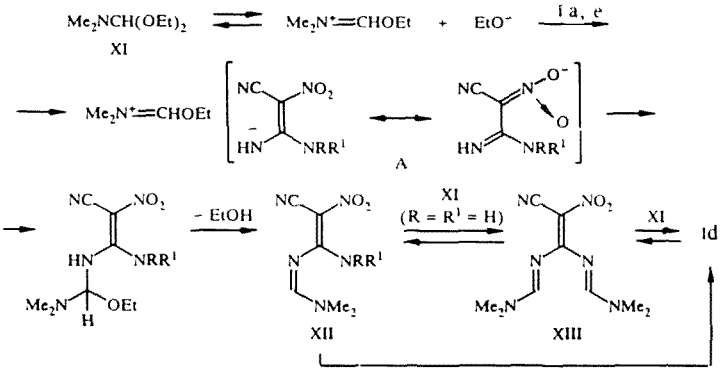
The amination reaction was significantly more difficult on using the less basic aromatic amines. Thus amination of enediamine (Ia) with p-anisidine succeeded only on extended boiling of the components in ethylene glycol. In this case α-amino-α-p-methoxyphenylamino-β-cyano-β-nitroethylene (Ic) was successfully isolated in low yield (~7%). The presence in this compound of a p-methoxyphenylamino group leads to the emergence of additional routes for decomposition under conditions of electron impact. Thus together with the usual NO_2 group elimination (see above), peaks were observed in its mass spectrum for ions of *m/z* 123 $[NH_2C_6H_4OMe]^+$ and 127 $[M-C_6H_4OMe]$.

Attempts were made in this study to react the enediamine (Ia) with another nucleophile, viz. methoxyl anion. Enamines are not generally inclined to exchange the amino function for a methoxy group. However in the present case the reaction proceeded smoothly and in satisfactory yield. Seemingly a salt of the corresponding aci-nitro derivative is formed initially and on acidification the α-amino-α-methoxy derivative (X) was isolated in 66% yield. An intense peak was observed in the mass spectrum of this compound for the appropriate molecular ion at *m/z* 143. Replacement of an amino group by methoxy leads to the appearance in the spectrum of additional peaks caused by its decomposition. Intense peaks for $[M-NO_2-CH_3]^+$ and $[N-NO_2-OCH_3]^+$ ions were observed in the spectrum together with peaks for $[M-O]^+$, $[M-NO]^+$, and $[M-NO_2]^+$ ions. The $[M-NO_2-OCH_3]^+$ ion peak was the second most intense in the spectrum.



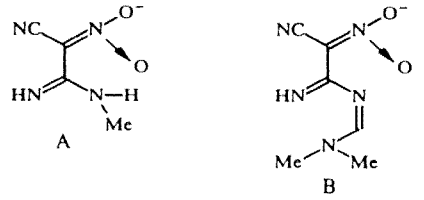
Id R = R¹ = H, e R = H, R¹ = Me, g RR¹ = -(CH₂CH₂)O, h R = H, R¹ = (CH₂)₆NH₂, i R = H, R¹ = (CH₂)₄NH₂; VIa RR¹ = -(CH₂CH₂)O, b R = R¹ = Me; VIIa n = 1, b n = 2

We also studied the reaction of the enediamines synthesized with the diethylacetal of dimethylformamide (DMF) (XI) and investigated certain properties of the enediamines obtained. Heating the enediamines (Ia, e) with acetal (XI) leads to the monoamidines (XIIa, b) in high yield. It is necessary to mention that the diamidine (XIII) was obtained under the same conditions from the diamino derivative (Id). Considering that the basicity of the initial diamines is extremely low (see above) it may be proposed that the formation of enamidines occurs in the same way as the reaction of amide acetals with sulfonamides [8]. The ethoxyl anion present in the equilibrium mixture [9] detaches the NH proton, and the resulting enediamine anion adds to the immonium cation with subsequent fission of a molecule of alcohol.



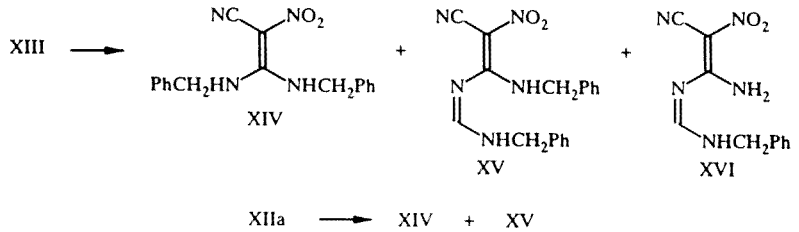
XIIa R = R¹ = Me; b R = H, R¹ = Me; c R = R¹ = H

It is extremely interesting that the rate of this reaction changes sharply depending on the group present at the α position in addition to the pri..ry amino group. Obser..ion of the reactions of enediamines (Ia) and (Ie) with the acetal (XI) showed that replacement of a dimethylamino group by a methylamino group leads to a sharp acceleration of the process. Completion of the condensation of (XI) with (Ia) requires about 4 h and of (Ie) 1 h under the same conditions. This reaction occurs particularly rapidly with the diamino derivative (Id) (~7 min) although subsequent condensation of two primary amino groups occurs in this case. This leads us to the conclusion that the main reason for the difference in reaction rates is not the steric factor (a role for which is impossible to rule out altogether) but the degree of stabilization of anions of type A due to electronic and intramolecular interactions. Since the main contribution to the resonance hybrid of anion A is made by a structure with a charge on the nitro group oxygen, the stabilization of anion A for compound (Ie) is possible with the participation of an intramolecular hydrogen bond, which is excluded for the enediamine (Ia).



A similar stabilization (more effective due to the presence of two hydrogen atoms on the primary amino group) may occur for compound (Id) in the first step of the reaction with the acetal, but another possible type of stabilization with NH and amide group participation in the second stage of the reaction with DMF acetal is illustrated by structure B. It should also be considered that the conversion of amino function into amide is accompanied by a significant reduction in electron-donating properties (polarographic data on a comparison of enamines and enamidines, see [10]). It is clear that stabilization of the intermediate anions (if the formation of anion is the limiting step of the reaction being considered) leads to an increase of their concentration in the reaction mixture and correspondingly to an increase in the rate of the process overall. It is also evident that the reports cited above require a stricter experimental basis. A similar type of fragmentation is apparent in the mass spectra of the mono- and diamidines (XIIa, b) and (XIII). Elimination of the nitro group, which is usual for these compounds, was observed and decomposition of the $[M-NO_2]^+$ ion occurs with stepwise fission of the dimethylamino group and amidine residue.

Synthesis of the enamidines (XIIa, b) and (XIII) may be extremely helpful for obtaining various amination products since it is known that the enamidine fragment is a significantly better leaving group than amino [11]. Consequently we have investigated some properties of the enamidines described above. It turned out that the bisamidine (XIII) readily splits off one amidino fragment under various conditions. The aminoenamidine (XIIc) is formed even on recrystallization from aqueous ethanol or on treatment with primary amines in a protogenic medium.



In view of these results it was natural to try to react the enamidines obtained with amines in an aprotic medium. Reaction with benzylamine was selected as an example. It was established that the action of an excess of benzylamine on compound (XIIa) in dry toluene leads to a mixture of substances consisting of the dibenzylamino derivative (XIV) and the enamidine (XV), according to data of ^1H NMR spectroscopy and mass spectra. The enediamine (XIV) was isolated from this mixture in a pure state and was identified by spectral data and elemental analysis. It is necessary to note that the main decomposition in the mass spectrum of the dibenzylamino derivative (XIV) (M 308) was linked with the formation of benzyl cation (91) and benzylamino cation (106). An intense peak was also observed in the spectrum for the $[M-NO_2]^+$ ion. A mixture of products consisting of (XIV) and (XV), together with the enamidine (XVI) containing a primary amino group, was obtained on reacting the bisamidine (XIII) with benzylamine under the same conditions. Signals were observed in the ^1H NMR (DMSO-D_6) spectrum of this mixture which were assigned to compound (XIV) at 4.49 (4H, br s, $PhCH_2$), 7.15-7.4 (10H, m,

Ph), and 9.28 ppm (2H, br s, NH), to compound (XV) at 4.58 (2H, br s, $PhCH_2$), 4.78 (2H, d, J = 6.0 Hz, PhCH), 7.15-7.4 (10H, m, Ph), 8.03 (1H, s, CH), 9.10 (1H br s, NH), and 9.8 ppm (1H, br t, NH), and to compound (XVI, at 4.78 (2H, d, J = 6.0 Hz, $PhCH_2$), 7.15-7.4 (5H, m, Ph), 8.03 (1H, s, CH), 8.25 (1H, br s, NH), 9.28 (1H, br s, NH), and 9.28 ppm (1H, t, NH). Compounds (XV) and (XVI) were successfully isolated in a pure state from this mixture. Their mass spectra corresponded to the structures proposed. Peaks were observed for the molecular ions (335 and 245), and the benzyl cation (91), and there were intense peaks for $[M-NO_2]^+$ and $[M-NO_2-NHCHC_6H_5]$. Several other peaks were caused by the stepwise fission of the amidine grouping from the $[M-NO_2]^+$ ion. The further aminated amidines (XV) and (XVI) were formed in addition to product (XIV) arising as a result of the usual amination [11]. The attack of benzylamine was directed at the meso atom of the amidine fragment as well as to the enamine α position.

In conclusion it must be said that the investigation of further amination processes is a step towards carrying out subsequent heterocyclization since the synthesis of heterocyclic compounds from enamines is based to a significant extent on their initial reaction with primary and secondary amines. There is undoubted interest in our opinion in the study of the conformations of the compounds investigated, which will be reported in detail in subsequent work. This problem seems particularly interesting to us when it is considered that the conformation of compounds (Ia, d, e), synthesized previously in [12], was not established probably due to the inadequacy of the instruments available at that time.

EXPERIMENTAL

The IR spectra were drawn on a Perkin-Elmer instrument in Nujol suspensions and the NMR spectra were taken on an Oxford 400+ spectrometer (400 MHz). Chemical shifts are given on the δ scale, the internal standard was tetramethylsilane, and DMSO-D_6 was used as solvent in all cases. Mass spectra were obtained on a Varian 700 spectrometer with direct insertion of samples into the ion source. A check on product purity and reaction progress was effected by chromatography on Silufol UV 254 plates in the system chloroform–methanol 10:1. The physicochemical characteristics of the compounds synthesized are given in Table 1.

Compounds (Ia) and (IIa) were obtained by the procedure of [4, 5].

6-N-Benzoylpiperazino-4-chloro-5-nitropyrimidine (IIb). A solution of N-benzoylpiperazine (2.33 g, 10.3 mmole) in water (5 ml) was added to a solution of 4,6-dichloro-5-nitropyrimidine (III) (2.0 g, 10.3 mmole) and then potassium hydroxide (0.58 g, 10.3 mmole) in water (5 ml) was added. After 1 h the reaction mixture was diluted with water and the product (IIb) (2.90 g) filtered off.

4-Chloro-6-(p-methoxyphenyl)-5-nitropyrimidine (IIc). A solution of p-anisidine (1.26 g, 10.3 mmole) in dioxan (10 ml) and acetic acid (0.6 ml, 10.3 mmole) was added slowly dropwise with vigorous stirring to prevent the reaction mixture becoming warm to a solution of (III) (2 g, 10.3 mmole) in dioxan (40 ml). The reaction mixture was left for 2 h, the precipitated solid filtered off, and immediately crystallized from water. The orange–red crystalline diaminopyrimidine (IVc) (2.7 g) remained on the filter and was afterwards crystallized from alcohol. The yellow solid product (IIc) (0.4 g) precipitated from the filtrate.

6-Anilino-4-chloro-5-nitropyrimidine (IIe). The reaction was carried out analogously to the synthesis of (IIc). However the bright yellow solid disubstituted 5-nitropyrimidine (IVe) precipitated from the reaction mixture, after which the filtrate was poured into water and the yellow product (IIe) obtained.

4-Chloro-6-(p-chloroanilino)-5-nitropyrimidine (IId). The synthetic procedure was similar to that used to obtain the above pyrimidine but without adding acetic acid to the solution of p-chloroaniline in dioxan. After dilution of the reaction mixture with water, the yellow solid was filtered off and crystallized from aqueous alcohol. The disubstituted compound (IVe) (24%) remained on the filter. The product (IIe) (56%) was isolated from the filtrate.

4-Chloro-6-(N-ethylanilino)-5-nitropyrimidine (IIf). N-Ethylaniline (2 ml: 15.4 mmole) was added slowly dropwise to a solution of 4,6-dichloro-5-nitropyrimidine (3 g, 15.4 mmole) in dioxan (40 ml). After 2 h the reaction mixture was diluted with water and the product (IIf) (2.8 g) filtered off.

Hydrolysis of 6-RR^1-amino-4-chloro-5-nitropyrimidines (IIb-e). A solution of compound (II) (1 g) in 1 N HCl was boiled for 4 h. The reaction mixture was cooled and 4-oxopyrimidine (V) was filtered off. The filtrate was evaporated, the solid triturated with alcohol, and the corresponding enediamine (I) obtained.

β-Cyano-β-nitro-α-piperazinoenamine Hydrochloride (Ib). The general procedure for the hydrolysis of compound (II) was used. After cooling the reaction mixture, the precipitate of benzoic acid was filtered off, the filtrate evaporated, and the residue triturated with methanol. Enamine hydrochloride (Ib) was obtained.

α-Amino-β-cyano-α-(p-methoxyphenyl)-β-nitroethylene (Ic). A mixture of enediamine (Ia) (1 g, 6.4 mmole) and p-anisidine (2 g, 12.8 mmole) in ethylene glycol (40 ml) was boiled for 5 h. The reaction mixture was cooled and poured into water (200 ml), the precipitated brown solid was filtered off, dissolved in ethyl acetate, and decolorized with activated carbon. The solution obtained was evaporated and the residue (0.3 g) of product (Ic) crystallized from isopropyl alcohol.

Enediamines (Id, e, g-i) and (VII). A. A solution of amine (18 mmole) in water or methanol was added to enediamine (Ia) (1 g, 6.4 mmole) and the mixture boiled until the initial enamine had completely disappeared on checking the progress of the reaction by TLC. The reaction mixture was cooled and the amination product filtered off. Compounds (VIII) and (IX) were separated by crystallization from methanol, (VIII) remained on the filter, and white (IX) precipitated from the filtrate.

B. Enaminoamidines (XIIa, b) or (XIII) (5 mmole) were boiled with 5% aqueous ammonia solution (10 ml) or dimethylamine for 30 min and the resulting white solid (Ia d, e) filtered off in quantitative yield.

α,α-Di-RR^1-Amino-β-cyano-β-Nitroethylenes (VI). A 30% aqueous solution (20 ml) of the amine was added to the enediamine (I) (1 g, 6.4 mmole) and the mixture boiled under reflux for 8 h. The reaction mixture was evaporated, the residual oil triturated with a mixture of methanol and ether (1:1) and compound (VI) filtered off.

β-Cyano-α-methoxy-β-nitroenamine (X). A solution (25 ml) of sodium methylate, prepared from sodium (0.88 g, 20 mmole), was added to a suspension of enediamine (Ia) (1.5 g, 9.6 mmole) in methanol (40 ml). The mixture was boiled for 8 h, evaporated, and titrated with 1 N HCl to pH ~7. The white solid product (X) (0.9 g, 66%) was precipitated.

Enaminoamidines (XII) and (XIII). The enediamines (Ia, d, e) or enaminoamidine (XIIc) in dimethylformamide acetal as solvent were boiled for 4 h, 1 h, 7 min, or 10 min respectively. The reaction mixture was evaporated to 2-3 ml and diluted with isopropyl alcohol. The resulting enaminoamidine (XII) or (XIII) was filtered off. PMR spectrum of enaminoamidine (XIIa) (DMSO-D_6): 3.11 (3H, s, NCH_3 enamine), 3.17 (3H, s, NCH_3 enamine), 3.14 (3H, s, NCH_3 amidine), 3.24 (3H, s, NCH_3 amidine), and 8.22 ppm (1H, s, CH).

β-Cyano-α-dimethylaminomethyleneamino-β-nitroenamine (XIIc). Compound (XIIc) (1 g, 5.4 mmole) was boiled in aqueous alcohol for 30 min. The reaction mixture was cooled and product (XIIc) (0.75 g, quantitative) was filtered off.

Amination of Amidines (XIIa) and (XIII). Benzylamine (40 mmole) was added with vigorous stirring to a suspension of amidine (10 mmole) in toluene (40 ml) and the mixture boiled for 6 h. The reaction mixture was evaporated and the residue triturated with isopropyl alcohol. In the case of amidine (XIIa) the solid product formed was filtered off, washed with ether, and crystallized from ethanol. Enediamine (XIV) crystals of enaminoamidine (XV) (0.6 g, 24%) were filtered off. The filtrate was evaporated to dryness and treated with an alcohol–ether (1:1) mixture to yield enaminoamidine (XVIc) (0.5 g, 15%).

REFERENCES

1. V. A. Makarov, A. L. Sedov, M. P. Nemeryuk, N. P. Solov'eva, and T. S. Safonova, Khim. Geterotsikl. Soedin., No. 7, 976 (1994).
2. M. P. Nemeryuk, A. L. Sedov, V. A. Makarov, N. P. Solov'eva, and T. S. Safonova, Khim. Geterotsikl. Soedin., No. 7, 999 (1991).
3. J. Clark, I. Gelling, and G. Noath, J. Chem. Soc., Chem. Commun., No. 17, 859 (1967).
4. J. Clark, I. Gelling, I. W. Southon, and M. S. Morton, J. Chem. Soc. C, No. 3, 494 (1970).
5. J. Clark, M. Curphey, and I. W. Southon, J. Chem. Soc., Perkin Trans. 1, No. 14, 1611 (1974).
6. V. G. Granik, S. S. Kiselev, N. P. Solov'eva, I. V. Persianova, M. K. Polievktov, and Yu. N. Sheinker, Khim. Geterotsikl. Soedin., No. 3, 344 (1980).
7. S. Rajappa and B. G. Advani, Indian. J. Chem., **15**, 890 (1977).
8. V. G. Granik, A. M. Zhidkova, R. G. Glushkov, I. V. Persianova, E. M. Peresleni, A. R. Engoyan, and Yu. N. Sheinker, Khim. Geterotsikl. Soedin., No. 9, 1220 (1974).
9. V. G. Granik, A. M. Zhidkova, and R. G. Glushkov, Usp. Khim., **46**, 685 (1977).
10. V. G. Granik, N. B. Marchenko, E. O. Sochneva, T. F. Vlasova, A. B. Grigor'ev, M. K. Polievktov, and R. G. Glushkov, Khim. Geterotsikl. Soedin., No. 11, 1506 (1976).

11. V. G. Granik, E. N. Dozorova, N. B. Marchenko, L. I. Budanova, V. A. Kuzovkin, and R. G. Glushkov, Khim.-farm. Zh., No. 10, 1249 (1987).
12. J. Clark, B. Parvizi, and I. W. Southon, J. Chem. Soc. Perkin Trans. 1, 125 (1976).