Chemistry of Heterocyclic Compounds, Vol. 38, No. 3, 2002

SYNTHESIS AND PROPERTIES OF 6-AMINO-7-HETARYL-5-R-5H-PYRROLO-[2,3-*b*]PYRAZINE-2,3-DICARBONITRILES

Yu. M. Volovenko and G. G. Dubinina

We have established that when 5-chloro-6-[cyano(2,3-dihydro-1-R-benzo[d]azol-2-yl)methyl]-2,3-pyrazinedicarbonitriles are reacted with nucleophilic reagents (aliphatic and aromatic amines, hydrogen sulfide), annelation of the five-membered ring occurs on the [b] face of the pyrazine with formation of 6-amino-7-hetaryl-5-R-5H-pyrrolo[2,3-b]pyrazine-2,3-dicarbonitriles and 6-amino-7-(1H-benzo[d]imidazol-2-yl)thieno[2,3-b]pyrazine-2,3-dicarbonitrile respectively. Further heating with excess of acylating reagent leads to formation of a novel heterocyclic system 1H-benzo[4,5]imidazo[1,2-c]pyrazino[2',3':4,5]pyrrolo[3,2-e]pyrimidine. Reaction of vicinal dinitriles with hydrazine hydrate leads to the novel system 1H-pyrrolo[2',3':5,6]pyrazino[2,3-d]pyridazine.

Keywords: 6-aminopyrrolo[2,3-*b*]pyrazine, 1H-benzo[4,5]imidazo[1,2-*c*]pyrazino[2',3':4,5]pyrrolo-[3,2-*e*]pyrimidine, 1H-pyrrolo[2',3':5,6]pyrazino[2,3-*d*]pyridazine.

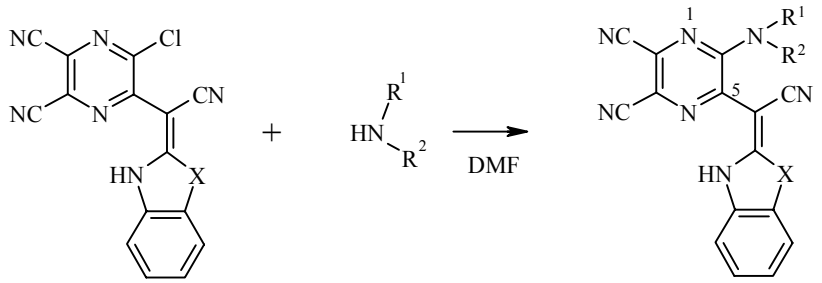
We previously [1] established that α-azahetarylacetonitriles are hetarylated by 5,6-dichloropyrazine-2,3-dicarbonitrile at the methylene group to form compounds **1a-d**. We were interested in studying the nucleophilic mobility of the chlorine atom in the 3 position of the pyrazine ring of such disubstituted acetonitriles. We know that in the structurally similar 2-(3-chloro-2-quinoxalyl)-2-hetarylacetonitriles, the chlorine atom has low nucleophilic mobility in reactions with amines [2-4]. Condensed pyrrolo[2,3-*b*]quinoxalines were obtained under rigid conditions: by heating in excess of amine at 120°C to 170°C [3,4].

In the case of derivatives of dicyanopyrazine **1a-d**, the activating effect of nitrile groups on the pyrazine ring leads to the chlorine atom being easily exchanged by nucleophilic reagents. Reaction with two equivalents of secondary amines proceeds at room temperature, and products **2a-g** are formed in high yields (Scheme 1). In the IR spectra of compounds **2a-g**, a weak vibration band for the nitrile groups of the pyrazine ring is found in the 2215-2210 cm^{-1} region (in the 2225-2215 cm^{-1} region in the starting compounds); a strong band for the nitrile group of the disubstituted acetonitrile moiety is found in the 2170-2160 cm^{-1} region (in the 2195-2185 cm^{-1} region in the starting compounds). The long-wave shift of the vibrational bands for the nitrile groups compared with the spectra of the starting compounds is probably due to conjugation of the nitrile groups with the electron pair of the amine nitrogen atom. In the 3260-3050 cm^{-1} region, we observe a broad vibrational band for the chelate N–H bond. The ^1H NMR spectra recorded in DMSO-d_6 show signals for the aliphatic protons of the amine moiety, while in the 12.58-12.76 ppm region we find signals from the exchanging protons of the NH group of the azole ring.

Kiev Taras Shevchenko National University, Kiev 01033, Ukraine; e-mail: GDubinina@ukr.net. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 372-379, March, 2002. Original article submitted June 22, 2000.

 0009-3122/02/3803-0336$27.00

Scheme 1



1a–c **2a–g**

1a, **2a-e** X = NH; **1b, 2f** X = NCH_3; **1c, 2g** X = S; **2a-g** $R^1 + R^2$: **a** $(CH_2)_5$, **b** $(CH_2)_2O(CH_2)_2$; **c** $(CH_2)_2NCH_3(CH_2)_2$; **d, g** $(CH_2)_2NPh(CH_2)_2$; **e** $(CH_2)_6$; **f** $(CH_2)_4$

Upon reaction of compounds **1a-d** with primary amines, N-hetarylation occurs followed by addition of the secondary amino group formed to the nitrile group, with closure of the pyrrole ring and formation of products **3a-r** (Scheme 2). Aliphatic and aromatic amines react with equal ease.

TABLE 1. Characteristics of Compounds **2a-g***

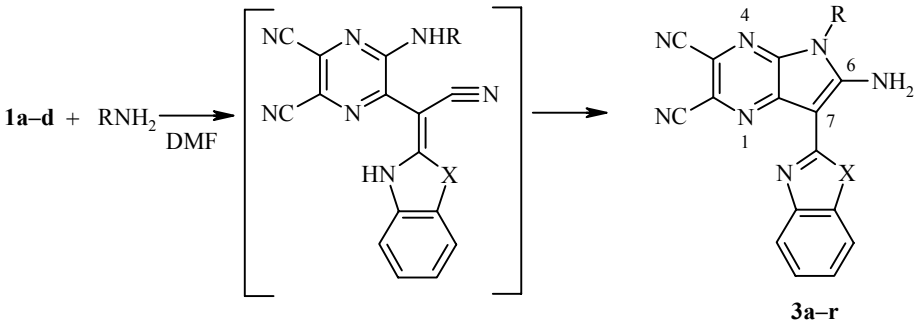
Compound	Empirical formula	Found, % / Calculated, % N	^{1}H NMR spectrum, δ, ppm, DMSO-d_6, J(Hz)*^{2}	Yield, %
2a	$C_{20}H_{16}N_8$	30.26 / 30.42	1.60-1.69 (6H, m, $3CH_2$); 3.39 (4H, m, $2NCH_2$); 7.31 (2H, m, H_{arom}); 7.56 (2H, m, H_{arom}); 12.69 (2H, s, 2NH)	88
2b	$C_{19}H_{14}N_8O$	30.53 / 30.25	3.36 (4H, m, $2NCH_2$); 3.82 (4H, m, $2OCH_2$); 7.31 (2H, m, H_{arom}); 7.58 (2H, m, H_{arom}); 12.75 (2H, s, 2NH)	72
2c	$C_{20}H_{17}N_9$	32.51 / 32.88	2.37 (3H, s, CH_3); 2.73 (4H, m, $2CH_2$); 3.43 (4H, m, CH_2); 7.25 (2H, m, H_{arom}); 7.52 (2H, m, H_{arom}); 12.67 (2H, s, NH)	67
2d	$C_{25}H_{19}N_9$	28.17 / 28.30	3.38 (4H, m, $2CH_2$); 3.54 (4H, m, $2CH_2$); 6.80 (1H, t, 4-H_{Ph}); 6.96 (2H, d, J = 8.4, 2-, 6-H_{Ph}); 7.23 (2H, t, 3-,5-H_{Ph}); 7.31 (2H, m, 5-, 6-H_{arom}); 7.59 (2H, m, 4-, 7-H_{arom}); 12.72 (2H, s, 2NH)	93
2e	$C_{21}H_{18}N_8$	29.25 / 29.30	1.47-1.68 (8H, m, $4CH_2$); 3.74 (4H, m, $2NCH_2$); 7.30 (2H, m, 5-, 6-H_{arom}); 7.51 (2H, m, 4-, 7-H_{arom}); 12.66 (2H, s, 2NH)	75
2f	$C_{20}H_{16}N_8$	30.32 / 30.42	1.80 (4H, m, $2CH_2$); 3.51 (4H, m, $2NCH_2$); 3.78 (3H, s, CH_3); 7.30-7.60 (4H, m, H_{arom}); 12.58 (1H, s, NH)	80
2g*^{3}	$C_{25}H_{18}N_8S$	24.32 / 24.23	3.38 (4H, m, $2CH_2$); 3.54 (4H, m, $2CH_2$); 6.83 (1H, t, 4-H_{Ph}); 7.01 (2H, d, J = 8, 2-, 6-H_{Ph}); 7.25 (2H, t, 3-, 5-H_{Ph}); 7.36 (1H, t, 5-H_{arom}); 7.51 (1H, t, 6-H_{arom}); 7.75 (1H, d, J = 8, 4-H_{arom}); 8.01 (1H, d, J = 8, 7-H_{arom}); 12.72 (2H, s, NH)	92

* Compounds **2a-g** melt above 300°C.

*^{2} H_{arom} are protons of the benzimidazole (thiazole) moiety.

*^{3} Compound **2g**: Found, S 6.74%; calculated, S 6.93%.

Scheme 2



1 d X = NCH_2Ph; **3 a-f** X = NH; **g-k** X = NMe; **l-n** X = NCH_2Ph; **o-r** X = S; **a,g,o** R = CH_2Ph; **b** R = $(CH_2)_2Ph$; **c,i,m,p** R = C_4H_3O CH_2-2; **d,h** R = $CH_2CH_2C_6H_3(OMe)_2$-3,4; **e** R = C_6H_4Me-2; **f** R = C_6H_4Cl-4; **j** R = C_6H_4OMe-3; **k** R = C_6H_4OMe-4; **l,q** R = $C_4H_7OCH_2$-2; **n** R = C_6H_4OMe-2; **r** R = $CH_2CH_2NMe_2$

In the ^{1}H NMR spectra of compounds **3a-r** recorded in DMSO-d_6, the signal for the exchanging N–H proton of the azole ring of the starting compounds **1a-d** is missing, and a singlet signal appears for the two protons of the amino group in the 8.63-9.32 ppm region (Table 2). In the IR spectra, the strong band of the stretching vibrations of the nitrile group of the dihetarylacetonitrile moiety of compounds **1a-d** is missing and a weak band for the stretching vibrations of the nitrile groups of the pyrazine ring is found in the 2220-2210 cm^{-1} region. In the 3500-3300 cm^{-1} region, we observe two bands for the stretching vibrations of the amino group; for compounds **3a-f**, these bands overlap with the stretching vibration of the N–H bond of the benzimidazole ring. The bands for scissoring bending vibrations of the amino group are observed in the 1600-1590 cm^{-1} region. The spectral data suggest intramolecular reaction between the nitrile and the amino groups, with formation of a condensed pyrrolo[2,3-*b*]pyrazine system.

When compound **1a** reacts with hydrogen sulfide in the presence of one equivalent of pyridine, the chlorine atom is substituted by a mercapto group. However, it is impossible to isolate the substitution product, since intramolecular addition of the mercapto group to the nitrile group occurs to form 6-amino-7-(1H-benzo[*d*]imidazol-2-yl)thieno[2,3-*b*]pyrazine-2,3-dicarbonitrile **4** (Scheme 3). We should note that the nitrile groups of the pyrazine ring are not affected in this case. In the ^{1}H NMR spectrum of compound **4** recorded in DMSO-d_6, the protons signal of the amino group has the form of two one-proton singlets at 10.0 ppm and 10.23 ppm, which suggests that these protons are nonequivalent due to formation of an intramolecular hydrogen bond; the signal for the benzimidazole N–H proton signal is found in the 12.06 ppm region.

Scheme 3

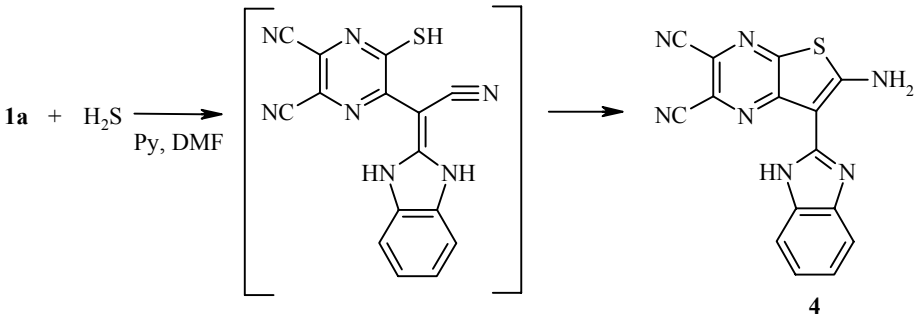


TABLE 2. Characteristics of Compounds **3a-r, 4, 5***

Com-pound	Empirical formula	Found, %*[2] / Calculated, %		^{1}H NMR spectrum (DMSO-d_6), δ, ppm, *J* (Hz)*[3]	Yield, %
		N	S		
1	2	3	4	5	6
3a	$C_{22}H_{14}N_8$	28.47 / 28.70		5.52 (2H, s, CH_2); 7.2-7.7 (9H, m, 4-H_{arom}, 5-H_{Ph}); 9.19 (2H, s, NH_2); 11.83 (1H, s, NH)	96
3b	$C_{23}H_{16}N_8$	27.63 / 27.71		3.08 (2H, t, CH_2); 4.45 (2H, t, NCH_2); 7.27-7.30 (7H, m, 5-H_{Ph}, 5-, 6-H_{arom}); 7.60-7.64 (2H, m, 4-, 7-H_{arom}); 9.32 (2H, s, NH_2); 12.20 (1H, s, NH)	95
3c	$C_{20}H_{12}N_8O$	29.14 / 29.46		5.54 (2H, s, CH_2); 6.50 (2H, m, 3-,4-H_{Het}); 7.18-7.20 (2H, m, 5-, 6-H_{arom}); 7.60-7.62 (3H, m, 4-, 7-H_{arom}, 5-H_{Het}); 9.30 (2H, s, NH_2); 11.92 (1H, s, NH)	86
3d	$C_{25}H_{20}N_8O_2$	23.88 / 24.12		3.00 (2H, t, CH_2); 3.66 (6H, s, OCH_3); 4.50 (2H, t, NCH_2); 6.60-6.80 (3H, m, H_{Ph}); 7.15-7.25 (2H, m, 5-, 6-H_{arom}); 7.60-7.62 (2H, m, 4-, 7-H_{arom}); 9.17 (2H, s, NH_2); 11.86 (1H, s, NH)	81
3e	$C_{22}H_{14}N_8$	28.90 / 28.70		2.47 (3H, s, CH_3); 7.20-7.75 (8H, m, 4-H_{arom}, 4-H_{Ph}); 8.85 (2H, s, NH_2); 12.00 (1H, s, NH)	81
3f*[3]	$C_{21}H_{11}ClN_8$	27.34 / 27.28		7.20-7.80 (8H, m, 4-H_{arom}, 4-H_{Ph}); 9.03 (2H, s, NH_2); 12.30 (1H, s, NH)	74
3g	$C_{23}H_{16}N_8$	27.87 / 27.71		4.04 (3H, s, CH_3); 5.57 (2H, s, CH_2); 7.2-7.8 (9H, m, 4-H_{arom}, 5-H_{Ph}); 8.98 (2H, s, NH_2)	96
3h	$C_{26}H_{22}N_8O_2$	23.62 / 23.42		3.00 (2H, t, CH_2); 3.70 (6H, s, 2OCH_3); 4.04 (3H, s, NCH_3); 4.54 (2H, t, NCH_2); 6.65-6.85 (3H, m, H_{Ph}); 7.25-7.32 (2H, m, 5-, 6-H_{arom}); 7.55-7.75 (2H, m, 4-, 7'-H_{arom}); 8.97 (2H, s, NH_2)	89
3i	$C_{21}H_{14}N_8O$	28.52 / 28.41		4.02 (3H, s, CH_3); 5.55 (2H, s, CH_2); 6.47 (2H, m, 3-, 4-H_{Het}); 7.25-7.58 (5H, m, 4-H_{arom}, 5-H_{Het}); 9.00 (2H, s, NH_2)	77
3j	$C_{23}H_{16}N_8O$	26.62 / 26.65		3.84 (3H, s, OCH_3); 4.08 (3H, s, NCH_3); 7.20-7.60 (8H, m, 4-H_{arom}, 4-H_{Ph}); 8.63 (2H, s, NH_2)	65
3k	$C_{23}H_{16}N_8O$	26.47 / 26.65		3.83 (3H, s, OCH_3); 4.10 (3H, s, NCH_3); 7.20-7.70 (8H, m, 4-H_{arom}+ 4-H_{Ph}); 8.70 (2H, s, NH_2)	83
3l	$C_{27}H_{22}N_8O$	23.57 / 23.61		1.65-2.00 (4H, m, 3-,4-CH_2 in THF*[4]); 3.64-3.77 (2H, m, 5-CH_2 in THF); 4.28-4.33 (3H, m, NCH_2+2-CH in THF); 6.02 (2H, s, N$\underline{CH_2}$Ph); 6.98 (2H, d, *J* = 6.6, 2-,6-H_{Ph}); 7.16-7.24 (5H, m, 3-, 4-, 5-H_{Ph}, 5-,6-H_{arom}); 7.48 (1H, d, *J* = 7.5, 7-H_{arom}); 7.67 (1H, d, *J* = 7.5, 4-H_{arom}); 9.07 (2H, s, NH_2)	91
3m	$C_{27}H_{18}N_8O$	23.49 / 23.82		5.54 (2H, s, NCH_2); 5.97 (2H, s, N$\underline{CH_2}$Ph); 6.43 (1H, dd, 4-H_{Het}); 6.46 (1H, d, *J* = 3.5, 3-H_{Het}); 6.98 (2H, d, *J* = 6.6, 2-, 6-H_{Ph}); 7.15-7.23 (5H, m, 3-, 4-, 5-H_{Ph}, 5-,6-H_{arom}); 7.49 (1H, d, *J* = 7.5, 7-H_{arom}); 7.63 (1H, d, *J* = 1.8, 5-H_{Het}); 7.68 (1H, d, *J* = 7.5, 4-H_{arom}); 9.18 (2H, s, NH_2)	88

TABLE 2 (continued)

1	2	3	4	5	6
3n	$C_{29}H_{20}N_8O$	22.45 / 22.57		3.75 (3H, s, OCH_3); 6.15 (2H, s, CH_2); 7.10-7.70 (13H, m, $9H_{Ph}$, $4H_{arom}$); 8.83 (2H, s, NH_2)	82
3o	$C_{22}H_{13}N_7S$	23.80 / 24.06	8.01 / 7.87	5.53 (2H, s, CH_2); 7.23-7.40 (6H, m, 5-H_{Ph}, 5-H_{arom}); 7.49 (1H, t, 6-H_{arom}); 7.93 (1H, d, J = 8, 4-H_{arom}); 8.16 (1H, d, J = 8, 7-H_{arom}); 9.23 (2H, s, NH_2)	87
3p	$C_{20}H_{11}N_7OS$	24.90 / 24.67	8.08 / 8.07	5.50 (2H, s, CH_2); 6.48 (1H, dd, 4'-H_{Het}); 6.65 (1H, d, J = 3.5, 3-H_{Het}); 7.35 (1H, t, 5-H_{arom}); 7.48 (1H, t, 6-H_{arom}); 7.65 (1H, d, J = 1.8, 5-H_{Het}); 7.83 (1H, d, J = 8, 4-H_{arom}); 7.96 (1H, d, J = 8, 7-H_{arom}); 9.25 (2H, s, NH_2)	93
3q	$C_{20}H_{15}N_7OS$	24.47 / 24.42	8.16 / 7.99	1.65-2.00 (4H, m, 3-, 4-CH_2 in THF); 3.70-3.81 (2H, m, 5-CH_2 in THF); 4.31-4.33 (3H, m, NCH_2+2-CH in THF); 7.48-7.52 (2H, m, 5-, 6-H_{arom}); 7.90 (1H, d, J = 8, 4-H_{arom}); 8.03 (1H, d, J = 8, 7-H_{arom}); 9.03 (2H, s, NH_2)	94
3r	$C_{19}H_{16}N_8S$	28.96 / 28.85	8.37 / 8.25	2.25 (6H, s, CH_3); 2.70 (2H, t, CH_2); 4.35 (2H, t, CH_2); 7.34 (1H, t, 5-H_{arom}); 7.48 (1H, t, 6-H_{arom}); 7.88 (1H, d, J = 8, 4-H_{arom}); 8.03 (1H, d, J = 8, 7-H_{arom}); 9.20 (2H, s, NH_2)	85
4	$C_{15}H_7N_7S$	31.08 / 30.90	9.91 / 10.10	7.24 (2H, m, 5-, 6-H_{arom}); 7.69 (2H, m, 4-, 7-H_{arom}); 10.0 (1H, s, NH_2); 10.23 (1H, s, NH_2); 12.06 (1H, s, NH_{arom})	85
5	$C_{27}H_{22}N_{10}O$	28.02 / 27.87		5.34 (2H, s, NH_2); 5.67 (2H, s, CH_2); 5.85 (2H, s, NH_2); 6.29 (2H, s, $\underline{CH_2}$Ph); 6.42 (1H, dd, 4-H_{Het}); 6.52 (1H, d, J = 3.5, 3-H_{Het}); 7.06 (2H, d, J = 6.9, 2-, 6-H_{Ph}); 7.15-7.25 (5H, m, 3-, 4-, 5-H_{Ph}+5-, 6-H_{arom}); 7.37 (1H, d, J = 7.3, 7-H_{arom}); 7.61 (1H, d , J = 1.7, 5-H_{Het}); 7.67 (1H, d, J = 7.3, 4-H_{arom}); 9.11 (2H, s, NH_2)	67

* Compounds **3a-r, 4, 5** melt above 300°C.

*[2] Compound **3f**: Found, Cl 8.79%; calculated, Cl 8.63%. H_{Het} are protons of the furan ring.

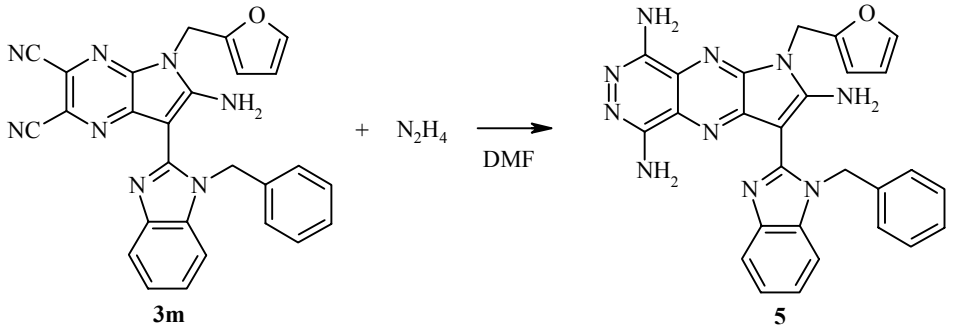
*[3] H_{arom} are protons of the benzimidazole (thiazole) moiety; H_{Ph} are protons of the unsubstituted and substituted benzene ring.

*[4] Protons of the THF residue.

In the IR spectrum of compound **4**, in the 3400-3320 cm^{-1} region, vibration bands of the amino group and the N–H bond of benzimidazole are overlaped, the vibration band for the nitrile groups of the pyrazine ring is found in the 2220 cm^{-1} region, the band for scissoring bending vibrations of the amino group is found in the 1590 cm^{-1} region. A similar intramolecular reaction between mercapto and nitrile groups is known for dichloroquinoxaline derivatives: sodium hydrosulfide in the presence of triethylamine was used as the reagent, cyanoacetic ester and malonodinitrile hetarylated by dichloroquinoxaline served as the nitrile component [5].

Compounds **3** have one more reaction moiety: vicinal nitrile groups of the pyrazine ring. We have found that when pyrazinedicarbonitrile **3m** is reacted with excess of hydrazine hydrate in DMF, its addition at the nitrile groups occurs with formation of a novel heterocyclic system 1H-pyrrolo[2',3':5,6]pyrazino[2,3-*d*]-pyridazine **5** (Scheme 4).

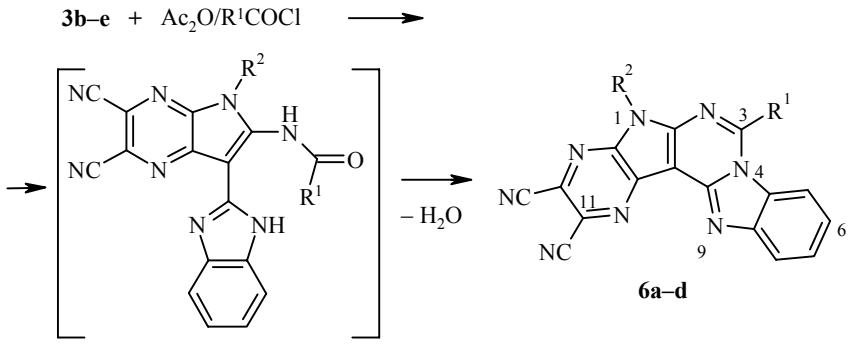
Scheme 4



A similar conversion was carried out previously with 5,6-diaminopyrazine-2,3-dicarbonitriles [6]. In the IR spectrum of compound **5**, the band for vibrations of the nitrile groups of the starting material is missing, the bands for the stretching vibrations of the amino groups are observed in the 3470-3360 cm^{-1} region, and the bands for scissoring bending vibrations of the amino groups are found in the 1610-1600 cm^{-1} region. In the ^1H NMR spectrum of pyridazine **5** recorded in DMSO-d_6, compared with the spectrum of the starting compound the signals from all the protons are slightly shifted downfield, and at 5.34 and 5.85 ppm, we observe two two-proton singlets for the amino groups that disappear when D_2O is added.

Acylation of compounds **3b-e** is completed by formation of polycycles **6** (Scheme 5). Compounds **6a,b** were obtained by refluxing the corresponding starting compounds **3c,d** with excess of acetic anhydride.

Scheme 5



6 a R = Me, R^1 = 2-$CH_2C_4H_3O$; **b** R^1 = Me, R^2 = $CH_2CH_2C_6H_3(OMe)_2$-3,4; **c** R^1 = CH_2Me, R^2 = CH_2CH_2Ph; **d** R^1 = C_3H_7-*i*, R^2 = $C_6H_4CH_2$-2

In synthesis of compounds **6c,d**, the best yields are obtained when the reaction is conducted in DMF with a three-fold excess of the corresponding acid chloride and pyridine. In the ^1H NMR spectra of compounds **6a-d**, the proton signals of the amino group and the signal from the N–H of the benzimidazole disappear; the signals from the remaining protons are slightly shifted downfield. Signals also appear from the corresponding alkyl groups (Table 3). In the IR spectra, the bands for the stretching and bending vibrations of the amino group disappear, the bands for the stretching vibrations of the nitrile groups are observed in the same region as in the spectra of the starting compounds, 2220 cm^{-1}, but their intensity is reduced.

The spectral data suggest that intramolecular condensation has occurred and as a result, a novel heterocyclic system is obtained: 1H-benzo[4,5]imidazo[1,2-*c*]pyrazino[2',3':4,5]pyrrolo[3,2-*e*]pyrimidine.

TABLE 3. Characteristics of Compounds **6a-d***

Compound	Empirical formula	Found N, % / Calculated N, %	^{1}H NMR spectrum, δ, ppm, DMSO-d_6, *J*(Hz)	Yield, %
6a	$C_{22}H_{12}N_8O$	27.49 / 27.71	3.37 (3H, s, CH_3); 5.81 (2H, s, CH_2); 6.42 (1H, dd, 4-H_{Het}); 6,55 (1H, d, *J* = 3.5, 3-H_{Het}); 7.47-7.56 (3H, m, 6-, 7-H, 5-H_{Het}); 7.88 (1H, d, *J* = 8, 8-H); 8.23 (1H, d, *J* = 8, 5-H)	87
6b	$C_{27}H_{20}N_8O_2$	23.14 / 22.94	3.08 (2H, t, CH_2); 3.32 (3H, s, CH_3); 3.64 (6H, s, OCH_3); 4.83 (2H, t, NCH_2); 6.60-6.75 (3H, m, H_{Ar}); 7.63 (2H, m, 6-,7-H); 7.95 (1H, d, *J* = 8, 8-H); 8.29 (1H, d, *J* = 8, 5-H)	88
6c	$C_{26}H_{18}N_8$	25.04 / 25.32	1.58 (3H, t, $CH_2\underline{CH_3}$); 3.25 (2H, q, $\underline{CH_2}CH_3$); 3.67 (2H, t, CH_2); 4.87 (2H, t, NCH_2); 7.18-7.22 (5H, m, H_{Ph}); 7.55 (1H, t, 7-H); 7.65 (1H, t, 6-H); 7.96 (1H, d, *J* = 8, 8-H); 8.30 (1H, d, *J* = 8, 5-H)	72
6d	$C_{26}H_{18}N_8$	25.18 / 25.32	1.55 (6H, d, $2CH_3$); 2.48 (3H, s, $C_6H_4\underline{CH_3}$); 4.20 (1H, m, CH); 7.45-7.75 (6H, m, 4-H_{Ar}, 6-, 7-H); 8.05 (1H, d, *J* = 8, 8-H); 8.30 (1H, d, *J* = 8, 5-H)	75

* Compounds **6a-d** melt above 300°C.

EXPERIMENTAL

The reaction and the purity of the synthesized compounds were monitored chromatographically on Silufol UV-254 plates with 9:1 chloroform–methanol as the eluent. The IR spectra were recorded in KBr tablets on a UR-20, a Specord IR-75, and a Pye Unicam in the 4000-400 cm^{-1} region. The ^{1}H NMR spectra were obtained for solutions in DMSO-d_6 on a Varian spectrometer, operating frequency 300 MHz, internal standard TMS.

The starting chloropyrazines **1a-d** were synthesized by the familiar procedure described in [1]. The characteristics of the newly synthesized compounds **2a-g** are given in Table 1; for **3a-r, 4, 5**, in Table 2; for **6a-d**, in Table 3.

5-[(2,3-Dihydrobenzazol-2-ylidene)cyanomethyl)]-6-NR^{1}R^2-2,3-pyrazinedicarbonitriles (2a-g). The corresponding secondary aliphatic amine (10 mmol) was added to a solution of chloropyrazine **1a-c** (5 mmol) in DMF (8 ml) and then stirred for 2 h at a temperature of 30-40°C. The precipitate of the product **2a-g** was filtered off and then washed with a small amount of DMF and water. The compounds obtained were chromatographically pure; they were crystallized from DMF as needed.

6-Amino-7-(2,3-dihydrobenzazol-2-ylidene)-5-R-5H-pyrrolo[2,3-*b*]pyrazine-2,3-dicarbonitriles (3a-r). The corresponding primary aliphatic amine (10 mmol) was added to a solution of chloropyrazine **1a-d** (5 mmol) in DMF (8 ml) and the mixture was stirred at 50-60°C for 5 h. The precipitate of the product **3a-r** was filtered off, washed with a small amount of DMF and then water, and then recrystallized from DMF.

6-Amino-7-(1H-benzo[*d*]imidazol-2-yl)-5-(2-methylphenyl)-5H-pyrrolo[2,3-*b*]pyrazine-2,3-dicarbonitrile (3e); 6-Amino-7-(1H-benzo[*d*]imidazol-2-yl)-5-(4-chlorophenyl)-5H-pyrrolo[2,3-*b*]pyrazine-2,3-dicarbonitrile (3f); 6-Amino-5-(3-methoxyphenyl)-7-(1-methyl-1H-benzo[*d*]imidazol-2-yl)-5H-pyrrolo-[2,3-*b*]pyrazine-2,3-dicarbonitrile (3j); 6-Amino-5-(4-methoxyphenyl)-7-(1-methyl-1H-benzo[*d*]imidazol-2-yl)-5H-pyrrolo[2,3-*b*]pyrazine-2,3-dicarbonitrile (3k); 6-Amino-7-(1-benzyl-1H-benzo[*d*]imidazol-2-yl)-5-(2-methoxyphenyl)-5H-pyrrolo[2,3-*b*]pyrazine-2,3-dicarbonitrile (3n). The corresponding primary

aromatic amine (15 mmol) was added to a solution of chloropyrazine **1a,b,d** (5 mmol) in DMF (8 ml), and the reaction mass was stirred at 80-90°C for 5 h. The product **3e,f,j,k,n** was isolated as described above.

6-Amino-7-(1H-benzo[*d*]imidazol-2-yl)thieno[2,3-*b*]pyrazine-2,3-dicarbonitrile (4). A stream of hydrogen sulfide (2 equivalents) was passed through a solution of chloropyrazine **1a** (1.6 g, 5 mmol) and pyridine (0.4 g, 5 mmol) in DMF (10 ml) at 70-80°C with stirring for 30 min. The product **4** that precipitated out of solution on cooling was filtered out, washed with water, and recrystallized from DMF.

3-(1-Benzyl-1-benzo[*d*]imidazol-2-yl)-1-(2-furylmethyl)-1H-pyrrolo[2',3':5,6]pyrazino-[2,3-*d*]-pyridazine-2,5,8-triamine (5). $N_2H_4 \cdot H_2O$ (3 g, 60 mmol) was added to a solution of pyrazinedicarbonitrile **3m** (1.41 g, 3 mmol) in DMF (10 ml) and this was refluxed for 2 h. The precipitate of product **5** that precipitated out of solution on cooling was filtered out, washed with water, and recrystallized from DMF.

1-R^2-3-R^3-1H-Benzo[4,5]imidazo[1,2-*c*]pyrazino[2',3':4,5]pyrrolo[3,2-*e*]pyrimidine-11,12-dicarbonitriles (6a-d). A. **Compounds 6a,b**. Compound **3c,d** (5 mmol) was refluxed for 8 h in Ac_2O (30 ml). The product was cooled, filtered off, washed with water, and recrystallized from DMF.

B. **Compounds 6c,d.** The corresponding acid chloride (5 mmol) and pyridine (0.4 g, 5 mmol) were added to a solution of compound **3b,e** (5 mmol) in DMF (15 ml). This was refluxed for 1 h, then 10 more mmol each of the acid chloride and pyridine were added, it was refluxed for 5 h and cooled. The product **6b,c** was filtered off, washed with water, and recrystallized from DMF.

REFERENCES

1. Yu. M. Volovenko and G. G. Dubinina, *Khim. Geterotsikl. Soedin.*, 1234 (1999).
2. Yu. M. Volovenko, S. V. Litvinenko, T. V. Tabeleva, and F. S. Babichev, *Dokl. Akad. Nauk UkrSSR*, No. 6, 33 (1989).
3. A. P. Kozynchenko, Yu. M. Volovenko, F. S. Babichev, and V. K. Promonenkov, *Ukr. Khim. Zh.*, **55**, 737 (1989).
4. A. P. Kozynchenko, Yu. M. Volovenko, V. K. Promonenkov, A. V. Turov, and F. S. Babichev, *Khim. Geterotsikl. Soedin.*, 1119 (1988).
5. A. P. Kozynchenko, F. S. Babichev, V. K. Promonenkov, A. I. Zubenko, and L. I. Savranskii, *Ukr. Khim. Zh.*, **53**, 401 (1987).
6. W. Reid and G. Tsiotis, *Liebigs Ann. Chem.*, **12**, 1197 (1988).