Two approaches to a new heterocyclic system of pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine

Valery V. Mezheritsky,*[a] Vladimir I. Minkin,[a] Lyudmila G. Minyaeva,[a]
Roman G. Tyurin,[a] Valery V. Krasnikov,[a] Eugeny V. Vorobyev,[a] and Zoya A. Starikova*[b]

[a] *Institute of Physical and Organic Chemistry Rostov State University,*
194/2, Stachka Av. Rostov on Don, 344090, Russia
E-mail: mezher@ipoc.rsu.ru
[b] *A. N. Nesmeyanov Institute of Organoelement Compounds of Russian Academy of Science*
E-mail: star@xray.ineos.ac.ru

Dedicated to Prof. Alexander T. Balaban on the occasion of his 75th Birthday
in recognition of his outstanding contributions to theoretical chemistry
and chemistry of heterocyclic compounds

(received 26 May 04; accepted 13 Aug 04; published on the web 10 Dec 04)

Abstract

Derivatives of a new heterocyclic system, *viz*. pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine **5**, have been synthesized by coupling imidoesters of 1-substituted-5-aminocarbonitriles **2** with acylhydrazides. The thermal recyclization of 1-substituted-4-(2-acylhydrazin-1-yl)pyrazolo[3,4-*d*]-pyrimidines **7** is found to be an alternative approach to the heterocyclic system **5**.

Keywords: 2,7-Disubstituted pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidines, bis-heterocyclization, carboxylic acids hydrazides

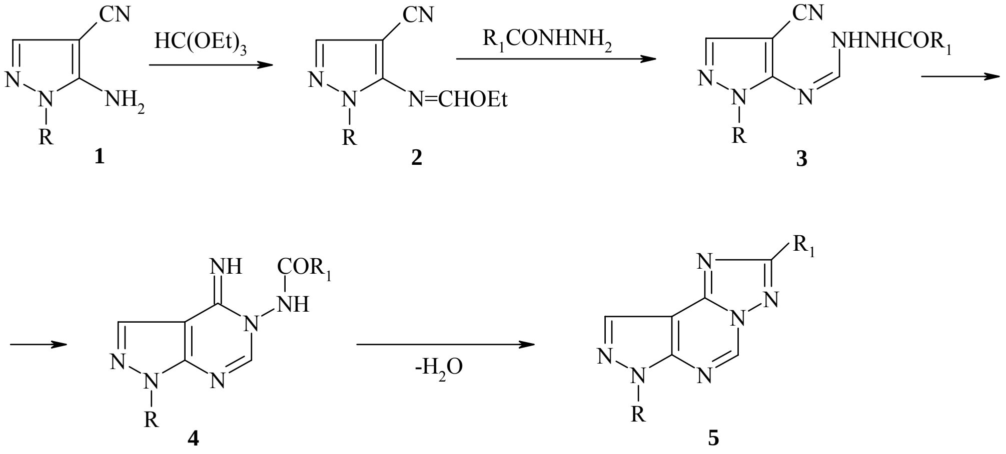
Introduction

The imidoesters **2** obtained by coupling 5-amino-1*H*-pyrazole-4-carbonitriles **1** with triethyl orthoformate react with amines to form a heterocyclic pyrazolo[3,4-*d*]pyrimidine system,[1,2] the compounds of which display interesting chemical properties[1-6] and possess a wide spectrum of biological activities.[7-11] We have presumed that by employing hydrazides as the amine components of this reaction, the cascade heterocyclization **2**→**3**→**4**→**5** may occur to afford derivatives of a new heterocyclic system of pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine **5**.[1] Indeed, it has been shown that the imidoesters **2** react with hydrazides under prolonged reflux in bromobenzene to give compounds **5** in about 50% yield. The reaction mechanism illustrated in

---

[1] A preliminary communication on this transformation has been made in the form of the conference report.[12]

Scheme 1 has been confirmed by isolation of the intermediates **3a** and **4a** in the reaction of imidoester **2** (R = H) with 4-methoxybenzoic acid hydrazide under milder conditions. Subsequent heating of a bromobenzene solution of pyrazolopyrimidine **4a** smoothly converts it to the final product **5a**.



a) R=H, R_1= 4-$MeOC_6H_4$
b) R=Me, R_1= Ph
c) R=Me, R_1=4-$MeOC_6H_4$
d) R= $PhCH_2$, R_1=Ph
e) R=$PhCH_2$, R_1=4-$MeOC_6H_4$
f) R=Ph, R_1=4-$MeOC_6H_4$
g) R=Ph, R_1=4-$ClC_6H_4OCH_2$
h) R=4-MeC_6H_4, R_1=Ph
i) R=4-MeC_6H_4, R_1=4-MeC_6H_4

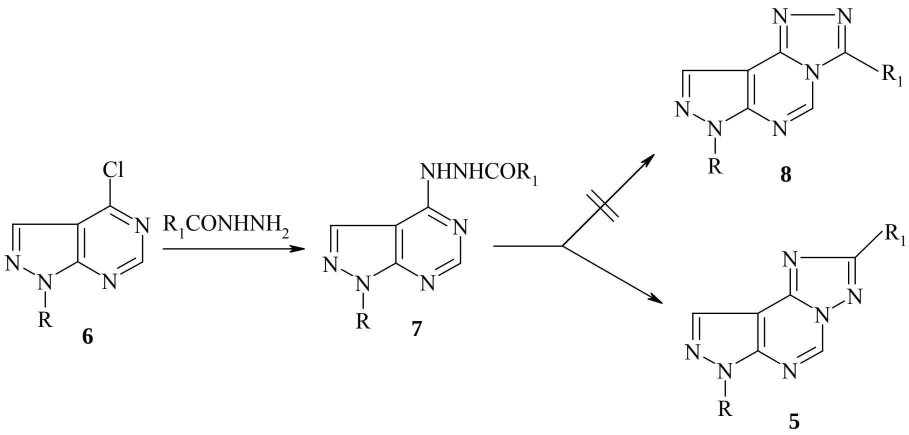
Scheme 1

Results and Discussion

The amidrazone **3a** is obtained by short-term reflux of an ethanolic solution of the imidoester **2** (R = H) and 4-methoxybenzoylhydrazine taken in equimolar amounts. The IR-spectrum of **3a** contains the bands characteristic of the stretching vibrations of nitrile (2200 cm^{-1}), carbonyl (1675 cm^{-1}), amidine (1650 cm^{-1}) and imino (3060, 3330, 3355 cm^{-1}) groups. Both the initial molecular ion peak M_1^+ (284) and that of the ion M_2^+ (266) related to the pyrazolotriazolopyrimidine **5a** formed by elimination of a molecule of water from **3a** in the gas phase appear in the mass spectrum of the amidrazone **3a**. Heating a dimethylformamide solution of the amidrazone **3a** gives rise to 4-iminopyrazolopyrimidine **4a**, the IR-spectrum of which does not contain a ν_{CN} vibration band, whereas ν_{CO} and ν_{NH} vibration bands appear at 1650 and 3115, 3200 cm^{-1}, respectively. The cyclization of **4a** to **5a**, *via* elimination of a molecule of water, proceeds upon reflux in bromobenzene for 3-4 hours. The structure of pyrazolotriazolopyrimidine **5a** was supported by its ^{1}H NMR spectrum that contained signals for a methoxy substituent (3.85 ppm), two doublets (AB-quartet *J* 8,7 Hz) for aryl protons (7.1 and

8.2 ppm) and a sharp singlet (9.5 ppm) for the H_5 proton in the pyrimidine ring. At room temperature, the signals (8.6 and 14.4 ppm, DMSO-d_6) of, respectively, CH and NH protons of the pyrazole ring, are substantially broadened, which is due to the fast prototropic exchange process associated with migration of a NH proton between the two nitrogen atoms.

With the goal of the synthesis of derivatives of another heterocyclic system of pyrazolo[4,3-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine **8** isomeric to **5** we have prepared a series of 4-acylhydrazinopyrazolo[3,4-d]pyrimidines **7** by coupling 6-chloropyrazolo[3,4-d]pyrimidines **6**[3,4] with acylhydrazines and studying their cyclization reactions. The energy preference of the amino form of the acylhydrazines **7** over the possible imino tautomer is confirmed by their ^{1}H NMR spectra (DMSO-d_6, 20°C) which exhibit broadened AB quartet signals for the vicinal NH protons appearing at 9.5 – 11.0 ppm. Dehydration of the acylhydrazines **7** occurs under severe conditions on heating their melts and gives rise not to the expected pyrazolo[4,3-*e*]-[1,2,4]triazolo[4,3-*c*]pyrimidines **8**, but to the isomeric pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]-pyrimidines **5** (Scheme 2). The identity of the products of the dehydration of acylhydrazines **7** with those obtained by cyclization of the intermediate imines **4** was confirmed by comparison of their IR and ^{1}H NMR spectra.



Scheme 2

The decisive evidence for the pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine structure **5** of the compounds prepared by dehydration of the acylhydrazines **7** is provided by an X-ray determination of the molecular and crystal structure of compound **5g** obtained from **7g** (Figure 1).

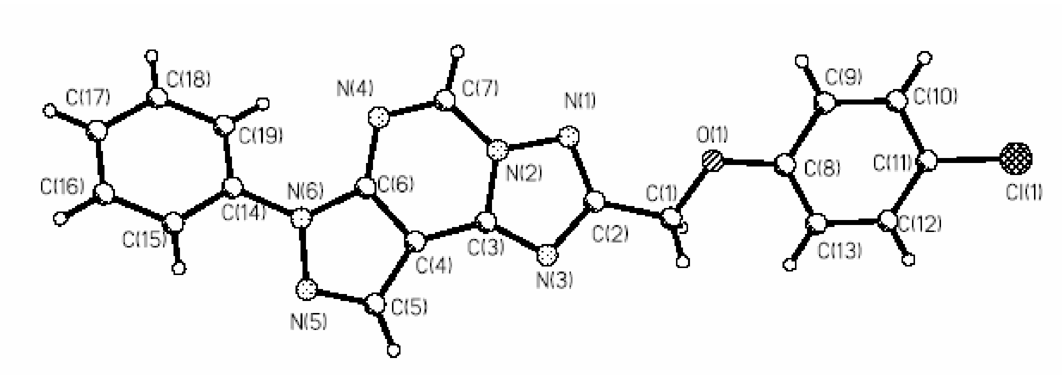


Figure 1. Perspective view and atom labeling of the X-ray crystal structure of **5g**.

The bond lengths in the tricyclic system are the following: C(2)-N(2) 1.318, C(3)-N(3) 1.322, C(5)-N(5) 1.324, C(7)-N(4) 1.301 Å), C(2)-N(3) 1.360, C(3)-N(2) 1.375, C(6)-N(4) 1.362, C(6)-N(6) 1.361, C(7)-N(2) 1.375 Å. The dihedral angles C(6)N(6)-C(14)C(19) and C(1)O(1)-C(8)C(13) are 34.9° and 20.6°, respectively.

Of certain interest is the mode of crystal packing for compound **5g**. Due to the formation of a network of C-HN bonds, the molecules of **5g** are assembled in the crystal in almost planar layers. The attractive π-π stacking interaction between the neighboring layers of the tricyclic aromatic systems of **5g** is manifested by their almost parallel (the dihedral angle between the planes is 5.5°) orientation (Figures 2 and 3).

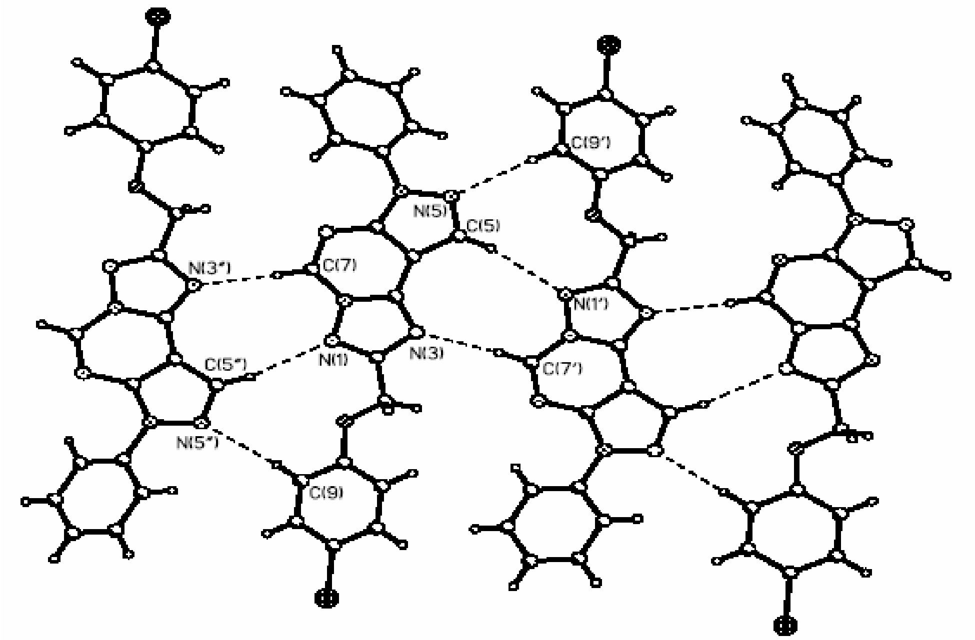


Figure 2. The layered crystal packing of molecules **5g**. The N…H distances in the C-H…N hydrogen bridges are 2.54, 2.29 and 2.55 Å for N(1)…H(5)-C(5), N(3)…H(3)-C(7) and N(5)H(9)-C(9), respectively.

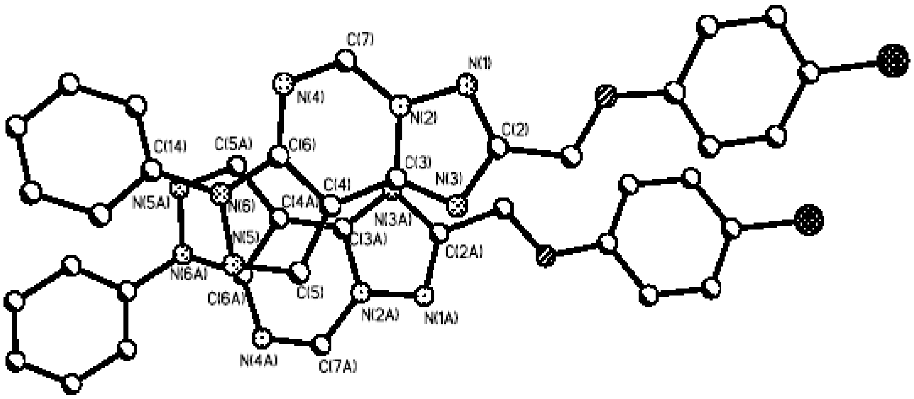
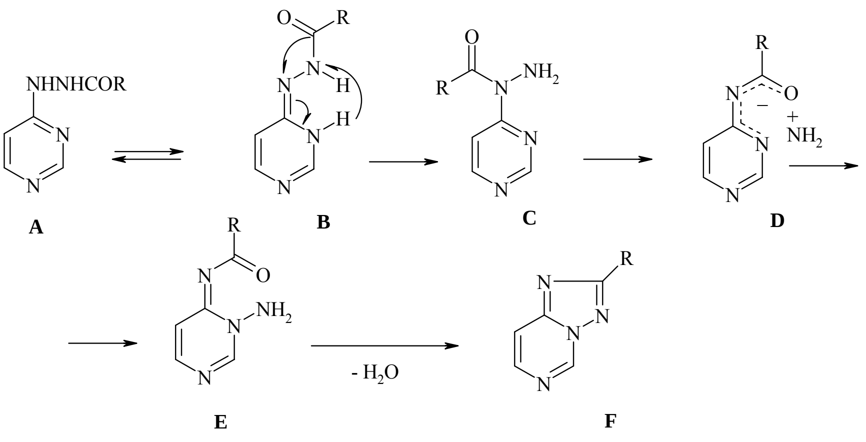


Figure 3. A fragment of the crystal structure of compound **5g**. The shortest distance between the nearly parallel layers of the molecules is that between the N(5) and C(6) atoms of the five-membered heterocyclic moiety.

Conclusions

Two new routes to the preparation of derivatives of a new fused heterocyclic system of pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine **5** have been elaborated. The heterocyclization of the acylhydrazines **7** involves a rearrangement **7→5**, the direction of which is opposite to that of the base-catalyzed Dimroth rearrangement.[1] It is suggested here that the initial step of the **7→5** rearrangement involves tandem migration of hydride and an acyl group (**B→C**). The 1-acyl-1-hetarylhydrazine (**C**) undergoes cleavage of the N-N bond with the intermediate formation of the tight ionic pair (**D**) of the resonance-stabilized anion and the aminium cation, which then quenches to the N-amine **E**. The mechanism of the last stage is similar to that operating in the N-amination of nitrogen heterocycles with hydroxylaminosulfuric acid[14]. The subsequent dehydration of **E** affords the final product (Scheme 3).



Scheme 3

Experimental Section

General Procedures. NMR spectra were recorded on a Varian Unity-300 spectrometer (300 MHz) using DMSO and $CDCl_3$ as solvents. IR spectra were recorded on a Specord 71 spectrophotometer in nujol or KBr tablets. Mass spectra were obtained on a Kratos instrument using an ionization energy of 71 eV and a directing voltage of 1.75 kV. Single-crystal X-ray diffraction experiments were carried out with a Bruker SMART 1000 CCD area detector using graphite monochromated Mo-Kα radiation (λ = 0.71073 Å), ω-scans with a 0.3° step in w and 10s per frame exposure, $2\theta < 58^o$) at 120 K. A total of 12416 reflections were measured, 4436 (R_{int} = 0.0531). The structures were solved by direct method and refined by the full-matrix least-squares against F^2 in anisotropic (for no-hydrogen atoms) approximation. The hydrogen atom positions were calculated and were refined isotropically in riding model approximation. The final refinements were converged to R1 = 0.0576 (from 3549 unique reflections with $I > 2\sigma(I)$) and wR2 = 0.1693 (from all 4436 unique reflections; the number of the refined parameters is 244. All calculations were performed on an IBM PC/AT using the SHELXTL software[13].
Crystal data for 5g. Colorless plate $C_{19}H_{13}ClN_6O$ (M = 376.80), monoclinic, space group *P2₁/c* (no. 14), a = 19.047(7)Å, b = 12.206(5)Å, c = 7.226(3)Å, β = 93.292(8)°, V = 1677(1)Å^3, Z = 4, d_{calc} = 1.492 g cm^{-3}, μ = 0.252 mm^{-1}, F(000) = , crystal size 0.07 × 0.40 × 0.50 mm.

5-Amino-1*H*-pyrazole-4-carbonitriles (1) were prepared by coupling ethoxymethylene-malodinitrile with hydrazine hydrate and the corresponding monosubstituted hydrazines according to the previously described procedure.[4] By treatment of 5-amino-1*H*-pyrazole-4-carbonitriles **1** with ethyl orthoformate, imidoesters **2** were prepared following a literature method.[2] Chloropyrazolopyrimidines **6** were obtained by the method described by Robins.[3,4]
5-[2-(4-methoxyphenyl)-1-hydrazinomethylidenamino]-1*H*-4-pyrazolecarbonitrile (3a). To a solution of imidoester **2a** (0.082 g, 0.5 mmol) in 2 ml of ethanol a solution 4-methoxybenzoyl hydrazine (0.083 g, 0.5 mmol) in 1 ml of ethanol was added and the reaction mixture was allowed to stand at room temperature for 1 h. The precipitate formed was filtered off, washed with ethanol and water and dried (0.060 g, 0.21 mmol, 42.3 %): m.p. 304 – 306 °C, molecular ion *m/e* 284; IR (ν, cm^{-1}): 3555, 3330, 3060, 2200, 1673, 1650. Anal. Calcd. for $C_{13}H_{12}N_6O_2$: C, 54.92; H, 4.23; N, 29.58. Found: C, 54.71; H, 4.35; N, 29.63.
4-Amino-5-(4-methoxyphenylcarboxamido)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidine (4a). A suspension of carbonitrile **3a** (0.060 g, 0.21 mmol) in 2 ml of DMF was heated to reflux for 10 min. The precipitate formed was filtered off, washed with hexane and dried (0.050 g, 0.17 mmol, 92 %): m.p. 345 – 346 °C; IR (ν, cm^{-1}): 3200, 3115, 1650. Anal. Calcd. for $C_{13}H_{12}N_6O_2$: C, 54.92; H, 4.23; N, 29.58. Found: C, 55.12; H, 4.35; N, 29.71.
2-(4-Methoxyphenyl)-7*H*-pyrazolo[4,3-*e*]triazolo[1,5-*c*]pyrimidine (5a). A suspension of pyrimidine 4a (0.100 g, 0.35 mmol) in 2 ml of bromobenzene was refluxed for 10 h, then cooled to room temperature and the formed colorless precipitate was filtered off, washed with ethanol, and dried (0.060 g, 0.225 mmol, 64 %): m. p. 274 – 275 °C; IR (ν, cm^{-1}): 3167, 3100, 1650; ^{1}H

NMR (δ, ppm, DMSO): 3.85 (s, 3H), 7.1 (d, 2H), 8.2 (d, 2H), 8.6 (s, 1H), 14,4 (s, 1H). Molecular ion *m/e* 266. Anal. Calcd. for $C_{13}H_{10}N_6O$: C, 58.65; H, 3.76; N, 31.58. Found: C, 58.78; H, 3.83; N, 31.46.

General procedure for the preparation of 2,7-disubstituted 7*H*-pyrazolo[4,3-*e*][1,2,3]-triazolo[1,5-*c*]pyrimidine 7b-i

A suspension of equimolar amounts of 1-substituted 4- chloro-pyrazolopyrimidines **6** and the corresponding acylhydrazine in ethanol was refluxed for 0.5 – 1.0 h. On heating, the suspension passes into solution and a precipitate of 2,7- disubstituted 7H-pyrazolo[4,3-*e*][1,2,3]-triazolo[1,5-*c*]pyrimidine **7b-i** is gradually formed. It was filtered off, washed with ethanol and water and crystallized from DMF.

1-(1-Methyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl)-2-(4-phenylcarboxamido)hydrazine (7b). Yield 69%; m. p. 245–246 °C; ^{1}H NMR (δ, ppm, DMSO-d_6): 3.95 (s, 1H), 7.4 – 8.2 (m, 6H), 9.8 – 11.0 (m, 2H). Anal. Calcd. for $C_{13}H_{12}N_6O$: C, 58.21; H, 4.48; N, 31.34. Found: C, 58.42; H, 4.54; N, 31.26.

1-(1-Methyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl)-2-(4-methoxyphenylcarboxamido)hydrazine (7c). Yield 78%, m. p. 228–230 °C; ^{1}H NMR (δ, ppm, DMSO-d_6): 3.80 (s, 3H), 3.90 (s, 3H), 7.0 – 8.5 (m, 6H), 11.0 – 11.2 (d, 1H), 12.2 (s, 1H). Anal. Calc. for $C_{14}H_{14}N_6O$: C, 56.37; H, 4.70; N, 28.19. Found: C, 56.48; H, 4.91; N, 28.31.

1-(1-Benzyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl)-2-(4-phenylcarboxamido)hydrazine (7d). Yield 73%; m. p. 230–232 °C; ^{1}H NMR (δ, ppm, DMSO-d_6): 5.50 (s, 1H), 7.2 – 8.0 (m, 10H), 8.12 (s, 1H), 8.38 (s, 1H), 11.5 (d, 1H), 12.5 (s, 1H). Anal. Calc. for $C_{19}H_{16}N_6O$: C, 66.28; H, 4.65; N, 24.42. Found: C, 66.41; H, 4.72; N, 24.36.

1-(1-Benzyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl)-2-(4-*p*-methoxyhenylcarboxamido)hydrazine (7e). Yield 73%; m. p. 217–219 °C; ^{1}H NMR (δ, ppm, DMSO-d_6): 3.80 (s, 3H), 5.6 (d, 2H), 7.1 – 8.5 (m, 12H), 11.1 (s, 1H). Anal. Calcd. for $C_{20}H_{18}N_6O_2$: C, 64.17; H, 4.81; N, 22.46. Found: C, 64.53; H, 4.68; N, 22.72.

1-(1-Phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl)-2-(4-methoxyphenylcarboxamido)hydrazine (7f). Yield 69%; m. p. 233–235 °C; ^{1}H NMR (δ, ppm, DMSO-d_6): 3.90 (s, 3H), 3.90 (s, 3H), 7.0 – 8.6 (m, 11H), 9.8 – 11.6 (m, 2H). Anal. Calcd. for $C_{19}H_{16}N_6O_2$: C, 63.34; H, 4.45; N, 23.33. Found: C, 63.27; H, 4.51; N, 23.15.

1-(1-Phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl)-2-(4-chlorophenyloxyacetylcarboxamido) hydrazine (7g). Yield 86%; m. p. 218–220 °C; ^{1}H NMR (δ, ppm, DMSO-d_6): 5.50 (s, 2H), 3.90 (s, 3H), 7.0 – 8.6 (m, 11H), 9.8 – 11.6 (m, 2H). Anal. Calcd. for $C_{19}H_{16}N_6O_2$: C, 63.34; H, 4.45; N, 23.33. Found: C, 63.27; H, 4.51; N, 23.15.

1-[1-(4-Methylphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl]-2-(4-phenylcarboxamido) hydrazine (7h). Yield 89 %, M. p. 263–265 °C. ^{1}H NMR (δ, ppm, DMSO-d_6): 2.50 (s, 3H), 7.2 – 8.2 (m, 11H), 10.0 – 11.1 (m, 2H). Anal. Calcd. for $C_{19}H_{16}N_6O$: C, 66.28; H, 4.65; N, 24.42. Found: C, 66.41; H, 4.70; N, 24.65.

1-[1-(4-Methylphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl]-2-[4-(4-methylphenyl)

carboxamido] hydrazine (7i). Yield 89 %, M. p. 263–265 °C. ^{1}H NMR (δ, ppm, DMSO-d_6): 2.50 (s, 3H), 7.2 – 8.2 (m, 11H), 10.0 – 11.1 (m, 2H). Anal. Calc. for $C_{19}H_{16}N_6O$: C, 66.28; H, 4.65; N, 24.42. Found: C, 66.41; H, 4.70; N, 24.65.

General procedure for the preparation of 2,7-disubstituted-7*H*-pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidines 5b-i

Method (a). A bromobenzene solution of equimolar amounts of imidoester **2** (R = Me, CH_2Ph, Ph, C_6H_4Me-*p*) and the corresponding acylhydrazine was refluxed for 5 – 10 h, allowed to reach room temperature and the precipitate formed was filtered off, washed with ethanol, dried and crystallized from DMF.

Method (b). 4-Acylhydrazino derivatives of pyrazolo[3,4-d]pyrimidines **7b-i** were melted in an open vessel until evaporation of the eliminated water ceased. The remaining solid was crystallized from DMF. The melting points and yields of compounds **5a-i** obtained by the methods **(a)** and **(b)** are given in **Table 1**.

Table 1. Melting points and yields of derivatives of 7*H*-pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]-pyrimidine **5** synthesized by the methods **(a)** and **(b)**

Compound	M. p., °C	Yield by method **(a)**	Yield by method **(b)**
5a	274-275	64	-
5b	247-249	45	75
5c	242-243	39	65
5d	278-280	42	65
5e	208-209	54	76
5f	233-235	43	72
5g	190-192	58	70
5h	282-283	38	66
5i	310-311	56	71

2-Phenyl-7-methyl-7*H*-pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (5b). ^{1}H NMR (δ, ppm, DMSO-d_6): 4.20 (s, 3H), 7.5 – 8.3 (m, 5H), 8.40 (s, 1H). Anal. Calc. for $C_{13}H_{10}N_6$: C, 62.40; H, 4.01; N, 33.60 Found: C, 62.30; H, 4.00; N, 33.75

2-(4-Methoxyphenyl-7-methyl-7*H*-pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (**5c).**
^{1}H NMR (δ, ppm, DMSO-d_6): 3.9 (s, 3H), 4.2 (s, 3H), 7.0 – 8.0 (m, 4H), 8.40 (s, 1H), 9.1 (s, 1H). Anal. Calc. for $C_{14}H_{12}N_6O$: C, 60.04; H, 4.30; N, 30.00. Found: C, 60.30; H, 4.10; N, 29.91.

2-Phenyl-7-benzyl-7*H*-pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (5d). NMR ^{1}H (δ, ppm, DMSO-d_6): 5.70 (s, 2H), 7.3 – 8.3 (m, 10H), 8.40 (s, 1H), 9.11 (s, 1H). Anal. Calc. for $C_{19}H_{14}N_6$: C, 69.94; H, 4.30; N, 25.77 Found: C, 69.50; H, 4.15; N, 25.80.

2-(4-Methoxyphenyl-7-benzyl-7*H*-pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (**5e).**
^{1}H NMR (δ, ppm, DMSO-d_6): 3.90 (s, 3H), 5.70 (s, 2H), 7.0 – 7.4 (m, 9H), 8.40 (s, 1H), 9.20 (s, 1H). Anal. Calc. for $C_{20}H_{16}N_6O$: C, 67.42; H, 4.49; N, 23.60. Found: C, 67.50; H, 4.20; N, 23.59.

2-(4-Methoxyphenyl-7-phenyl-7*H*-pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (5f). ^{1}H NMR (δ, ppm, DMSO-d_6): 7.4 – 8.4 (m, 12H), 8.60 (s, 1H), 9.20 (s, 1H). Anal. Calc. for $C_{19}H_{14}N_6O$: C, 66.66; H, 4.03; N, 24.56. Found: C, 66.50; H, 4.10; N, 24.60.

2-(4-Chlorophenoxymethyl-7-phenyl-7*H*-pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*] pyrimidine (5g). ^{1}H NMR (δ, ppm, DMSO-d_6): 5.4 (s, 2H), 7.0 – 8.2 (m, 9H), 8.50 (s, 1H), 9.20 (s, 1H). Anal. Calc. for $C_{19}H_{13}N_6OCl$: C, 60.56; H, 3.45; N, 22.31; Cl, 9.43. Found: C, 60.72; H, 3.56; N, 22.46; Cl, 9.62.

2-Phenyl-7-(4-methylphenyl)-7*H*-pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (5h). ^{1}H NMR (δ, ppm, DMSO-d_6): 2.40 (s, 3H), 7.4 – 8.4 (m, 9H), 8.60 (s, 1H), 9.20 (s, 1H). Anal. Calc. for $C_{19}H_{14}N_6$: C, 69.94; H, 4.30; N, 25.77 Found: C, 70.15; H, 4.16; N, 25.91.

2-(4-Methylphenyl)-7-(4-methylphenyl)-7*H*-pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (5i). ^{1}H NMR (δ, ppm, DMSO-d_6): 2.40 (s, 6H), 7.3 – 8.2 (m, 8H), 8.60 (s, 1H), 9.20 (s, 1H). Anal. Calc. for $C_{20}H_{16}N_6$: C, 70.59; H, 4.71; N, 24.71 Found: C, 70.72; H, 4.83; N, 24.93.

Acknowledgments

This work was supported by Grants N. Sh. 945. 03. 2003 from Ministry of Education and Science RF and REC-004 from CRDF and Ministry of Education and Science RF.

References

1. Taylor, E. C.; Mc Killop, A. *The Chemistry of Cyclic Enaminonitriles and o-Aminonitriles in Adv. in Org. Chem*., J. Wiley-Interscience: New York, 1970; Vol. 7, p 415.
2. Taylor, E. C.; Loeffler, R. K. *J. Am. Chem. Soc.* **1960**, *82*, 3147.
3. Robins, R. K. *J. Am. Chem. Soc.* **1956**, *78*, 784.
4. Cheng, C. C.; Robins, R. K. *J. Org. Chem.*1956, *21*, 1240.
5. Cheng, C. C.; Robins, R. K. *J. Org. Chem.* **1958**, *23*, 191.
6. Cheng, C. C.; Robins, R. K. *J. Org. Chem.* **1958**, *23*, 852
7. Bhat, G. A.; Montero, J. G.; Panzica, R. P.; Warting, L. L.; Towsend, L. B. *J. Med. Chem.* **1981**, *24*, 1165.
8. Petrie, C. R.; Cottam, H. B.; Mc Kernan, P. A.; Robins, R. K.; Revankar, G. R. *J. Med. Chem.* **1985**, *28*, 1010.
9. Avila, J. L.; Polegre, M. A.; Avila, A. R.; Robins, R. K. *Comp. Biochem. Physiol.* **1986**, *83 C*, 285.
10. Anderson, J. D.; Cottam, H. B.; Larson, S. B.; Nord, L. D.; Revankar, G. R.; Robins, R. K. *J. Heterocycl. Chem.* **1990**, *27*, 439.
11. Zaharie, C. B.; Connolly, T. P.; Rej, R.; Attardo, G.; Penney, C. L. *Tetrahedron* **1996**, *52*, 2271.
12. Krasnikov, V. V.; Milgizina, G. R.; Tyurin, R. V.; Minyaeva, L. G.; Mezheritskii, V. V. In: *Abstracts of reports at the 1st International Conference "Chemistry and Biological Activity of Nitrogen-Containing Heterocycles and Alkaloids"* Moscow, 2001; Vol. 1, p 356.
13. Sheldrick, G. M. *SHELXTL-97, Version 5.10, Bruker AXS Inc., Madison, WI-53719, USA.*
14. Rees, C. W.; Storr, R. C. *Chem. Commun.* **1965**, *193.*