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

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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

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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**.

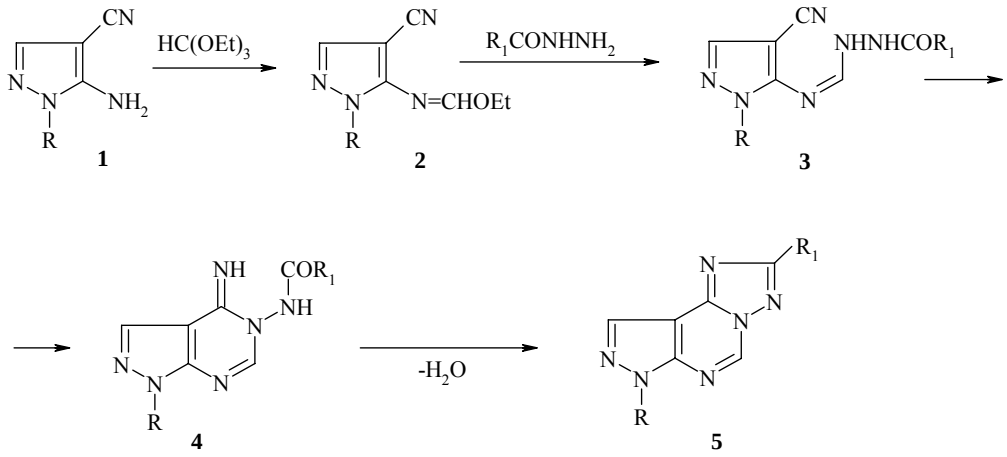
Keywords: 2,7-Disubstituted pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidines, bis-heterocyclization, carboxylic acids hydrazides

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

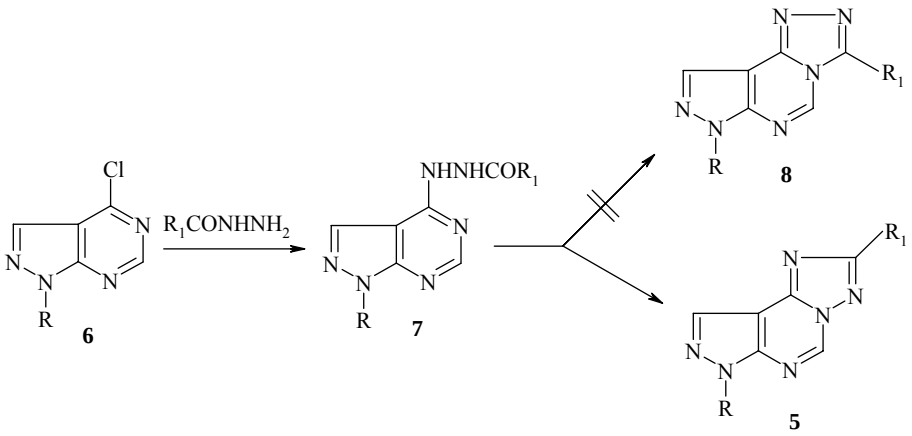
Scheme 1

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^{o}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).

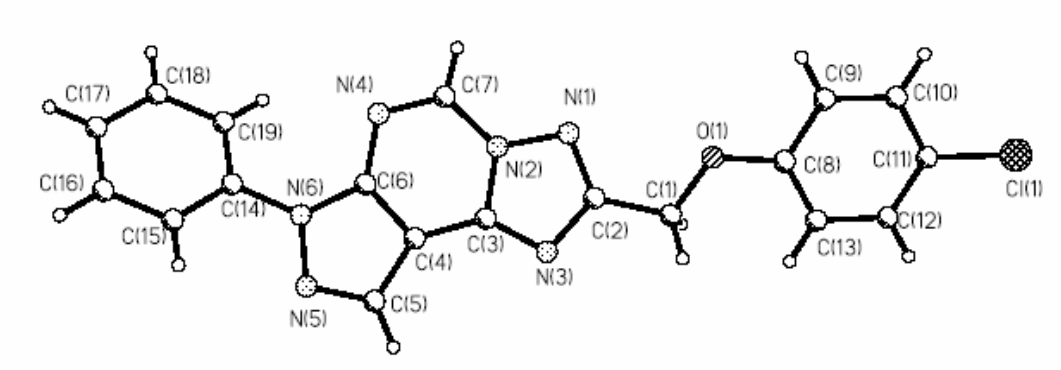


Figure 1. Perspective view and atom labeling of the X-ray crystal structure of **5g**.

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).

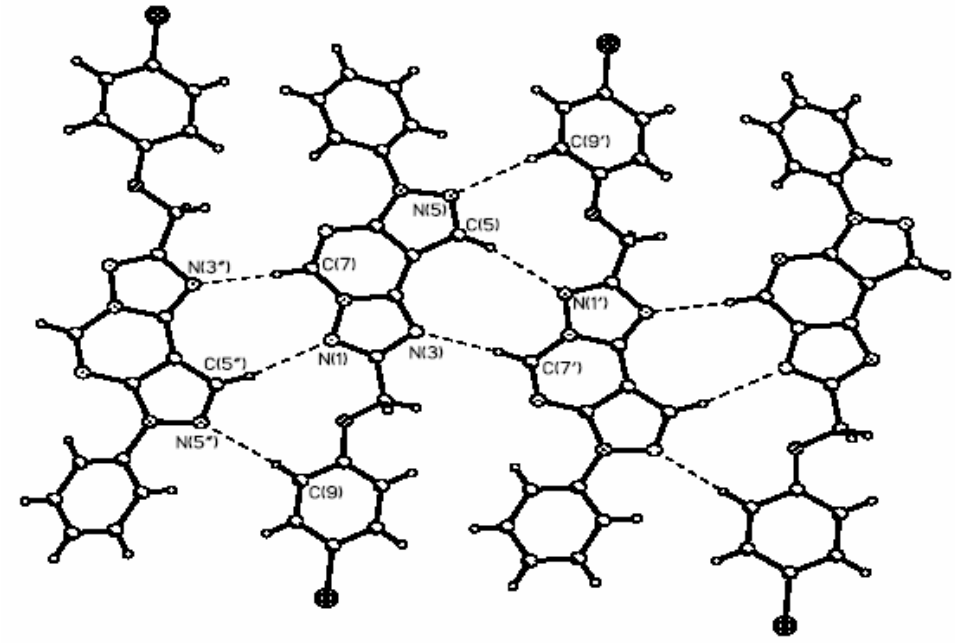


Figure 2. The layered crystal packing of molecules **5g**. The N…H distances in the C-H…N hydrogen bridges are 2.54, 2.29 and 2.55 Å for N(1)…H(5)-C(5), N(3)…H(3)-C(7) and N(5)H(9)-C(9), respectively.

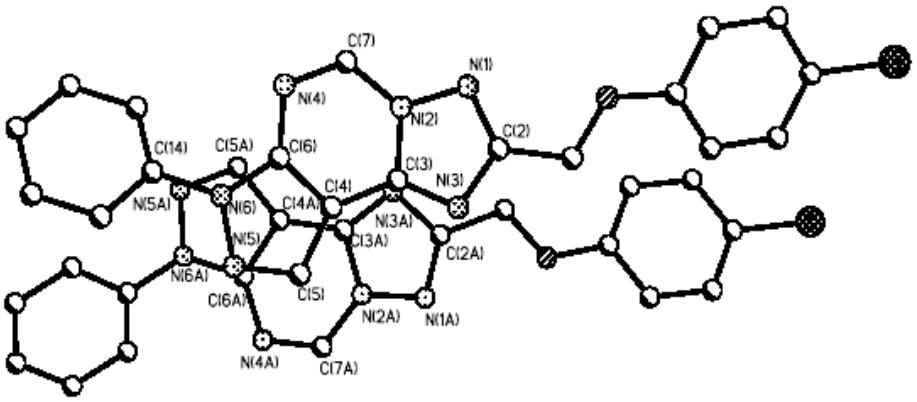
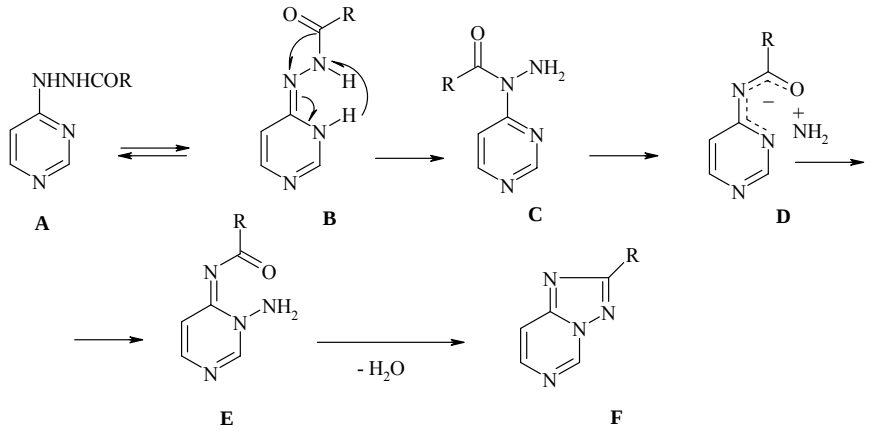


Figure 3. A fragment of the crystal structure of compound **5g**. The shortest distance between the nearly parallel layers of the molecules is that between the N(5) and C(6) atoms of the five-membered heterocyclic moiety.

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, 2θ <58°) 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 $P2_1/c$ (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

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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. He terocycl. 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.*