The synthesis of new pyrazolo[1,5-*a*]pyrimidine derivatives

Ahmad Poursattar Marjani, Jabbar Khalafy,* Fatemeh Salami, and Mahnaz Ezzati

Department of Chemistry, Faculty of Science, Urmia University, Urmia 57154, Iran
E-mail: jkhalafi@yahoo.com; j.khalafi@urmia.ac.ir

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Abstract

A simple high-yielding procedure for the synthesis of novel pyrazolo[1,5-*a*]pyrimidine analogues is reported via the condensation of 1,3-diketones or keto ester with substituted 5-aminopyrazoles in presence of H_2SO_4 using AcOH as solvent.

Keywords: 1,3-Diketones, β-ketoesters, 5-aminopyrazoles, pyrazolo[1,5-*a*]pyrimidines

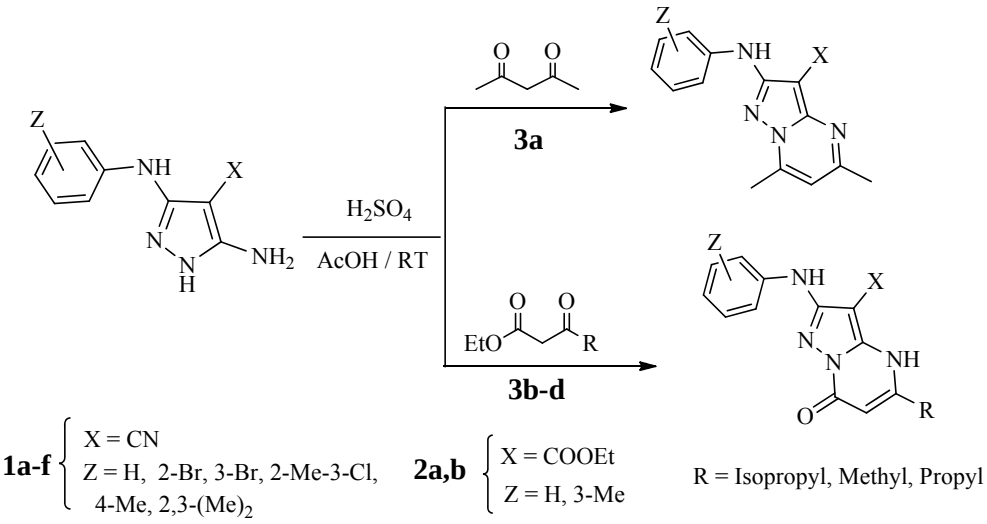
Introduction

The pyrazolopyrimidine derivatives are an important class of heterocyclic compounds with pharmacological and biological activities, such as the antibacterial,[1] antiviral,[2] cytotoxic,[3] antidepressant,[4] neuroleptic,[5] tuberculostatic,[6] antihypertensive,[7] analgesic[8] and antimicrobial activity.[9] The pyrazolo[1,5-*a*]pyrimidines as bicyclic heterocycles have an important synthetic value in the preparation of drugs with anticancer activities.[10-15] The most common methods for synthesis of pyrazolo[1,5-*a*]pyrimidine derivatives are cyclocondensations of 5-aminopyrazoles with bifunctional reagents.[16] The synthesis of 2-anilinopyrazolo[1,5-a]pyrimidine derivatives as c-Src kinase inhibitors has been reported.[17]

In continuation of our studies on the synthesis of bi-, tri- and tetracyclic heterocycles,[18-25] herein we report a convenient method for the synthesis of new pyrazolo[1,5-*a*]pyrimidine derivatives with possible pharmaceutical applications.

Result and Discussion

The reaction of 5-amino-3-arylamino-1*H*-pyrazole-4-carbonitriles (**1a-f**) and ethyl 5-amino-3-arylamino-1*H*-pyrazole-4-carboxylate (**2a,b**) with pentane-2,4-dione, ethyl acetoacetate, ethyl isobutyrylacetate and ethyl butyrylacetate (**3a-d**) afforded the corresponding pyrazolo[1,5-*a*]-pyrimidine derivatives (**4a-m**) in 87-95% yield, as shown in Scheme 1.



Scheme 1. Synthesis of pyrazolo[1,5-*a*]pyrimidine derivatives (**4a-i, 4l-m 4j,k**).

Thirteen examples of the conversion of 5-amino-3-arylamino-1*H*-pyrazole-4-carbonitriles (**1a-f**) and ethyl 5-amino-3-arylamino-1*H*-pyrazole-4-carboxylate (**2a,b**) to the corresponding 4,7-dihydropyrazolo[1,5-*a*]pyrimidine derivatives (**4a-m**) along with reaction time, melting points and yields are listed in Table 1.

Table 1. The physical properties, yields and reaction condition for compounds **4a-m**

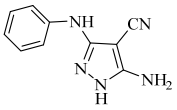
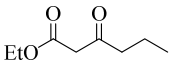
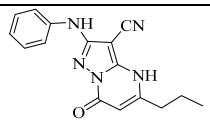
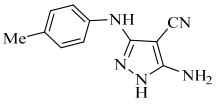
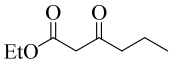
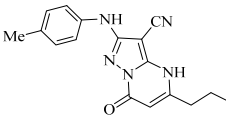
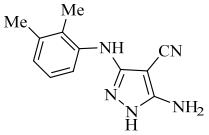
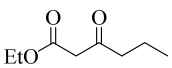
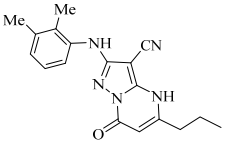
Entry	Pyrazole derivatives (**1a-f**) / (**2a,b**)	1,3-Diketone or keto ester (**3a-d**)	Product (**4a-m**)	Time (h)	Yield (%)	M.p. (°C)
1	 **1a**	 **3d**	 **4a**	5	89	297-299
2	 **1d**	 **3d**	 **4b**	7	87	330-332
3	 **1e**	 **3d**	 **4c**	8	90	244-246

Table 1. Continued

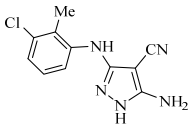
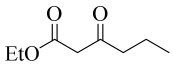
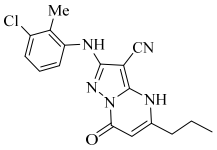
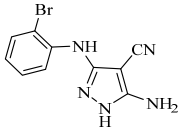
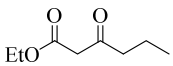
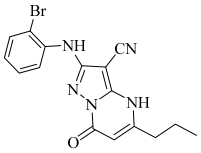
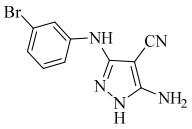
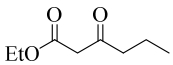
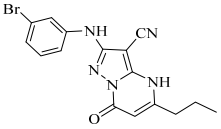
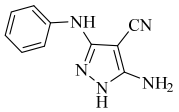
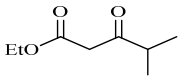
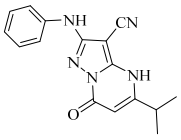
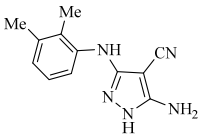
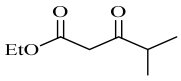
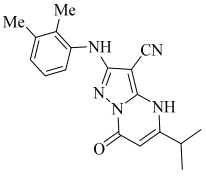
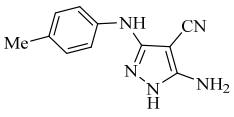
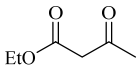
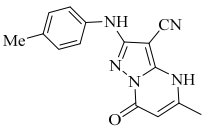
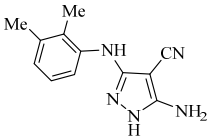
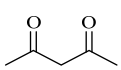
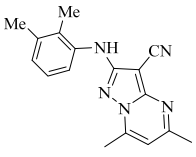
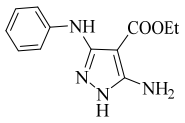
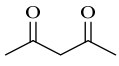
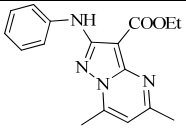
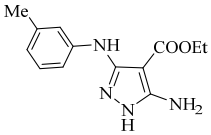
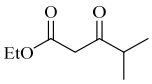
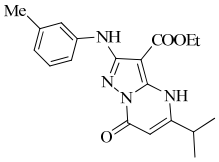
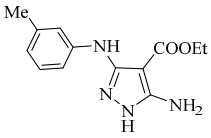
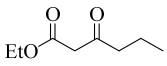
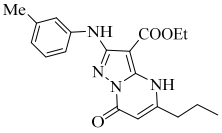
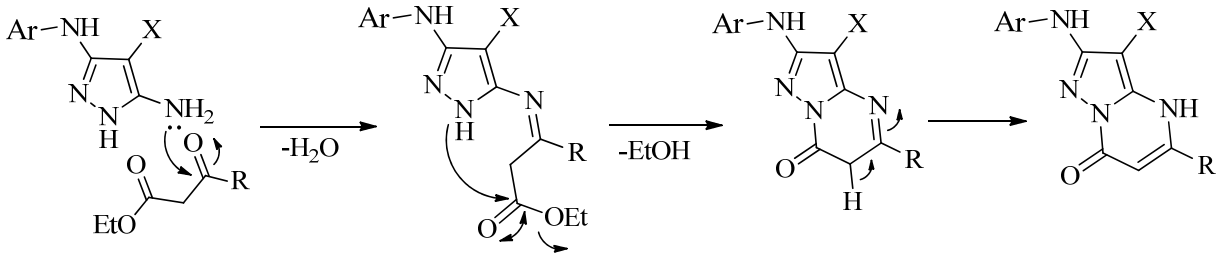
Entry	Pyrazole derivatives (**1a-f**) / (**2a,b**)	1,3-Diketone or keto ester (**3a-d**)	Product (**4a-m**)	Time (h)	Yield (%)	M.p. (°C)
4	 **1f**	 **3d**	 **4d**	6	90	320-321
5	 **1b**	 **3d**	 **4e**	4	95	333-334
6	 **1c**	 **3d**	 **4f**	4	93	288-289
7	 **1a**	 **3c**	 **4g**	5	92	326-328
8	 **1e**	 **3c**	 **4h**	8	88	370-372
9	 **1d**	 **3b**	 **4i**	6	89	360-361
10	 **1e**	 **3a**	 **4j**	5	88	288-290

Table 1. Continued

Entry	Pyrazole derivatives (**1a-f**) / (**2a,b**)	1,3-Diketone or keto ester (**3a-d**)	Product (**4a-m**)	Time (h)	Yield (%)	M.p. (°C)
11	 **2a**	 **3a**	 **4k**	4	92	159-160
12	 **2b**	 **3c**	 **4l**	4.5	91	205-206
13	 **2b**	 **3d**	 **4m**	4	94	209-210

The proposed mechanism for the formation of the fused pyrimidinones may be explained by Scheme 2.



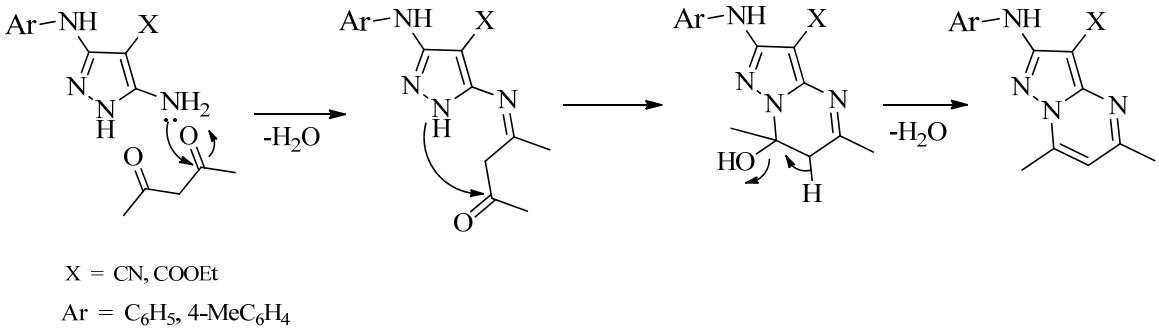
X = CN, COOEt

R = Isopropyl, Methyl, Propyl

Ar = C_6H_5, 2-BrC_6H_4, 3-BrC_6H_4, 2-Me-3-ClC_6H_3, 3-MeC_6H_4, 4-MeC_6H_4, 2,3-$(Me)_2C_6H_3$

Scheme 2. The proposed mechanism for the formation of compounds (**4a-i, 4l and 4m**).

The proposed mechanism for the formation of pyrazolo[1,5-*a*]pyrimidine derivatives **4j,k** is shown in Scheme 3.



Scheme 3. The proposed reaction mechanism for the formation of compounds **4j,k**.

The structure of all products were confirmed by their ^{1}H-NMR, ^{13}C-NMR and FT-IR spectral data and by elemental analysis.

Experimental Section

General. The chemicals used in this work were purchased from Acros and Merck companies and were used without purification. Freshly distilled solvents are used throughout; anhydrous solvents are dried according to Perrin and Armarego.[26] Melting Points were measured on an Electrothermal 9200 apparatus and are uncorrected. FT-IR spectra were recorded via a Thermonicolet (Nexus 670) spectrometer using KBr discs. ^{1}H (300 MHz) and ^{13}C (75.5 MHz) NMR spectra were recorded on a Bruker DRX-300 Avance spectrometer in DMSO-d_6 using TMS as the internal reference. Microanalyses are performed on Leco Analyzer 932**.**

General procedure for the Synthesis of 4,7-dihydropyrazolo[1,5-*a*]pyrimidine (4a-i, 4l, 4m) and pyrazolo[1,5-*a*]pyrimidine derivatives (4j, 4k). To a solution of pyrazole derivatives[27] (1 mmol) in acetic acid (20 mL), 1,3-diketones (2 mmol) and one drop of concentrated H_2SO_4 was added and then stirred at room temperature until the reaction was completed as monitored by TLC **(**$CHCl_3$/MeOH/CH_3CN v/v, 30: 3: 1). Ice-water (10 mL) was added to the reaction mixture. The precipitate was filtered, washed with cold water and dried to give the corresponding 4,7-dihydropyrazolo[1,5-*a*]pyrimidine or pyrazolo[1,5-*a*]pyrimidine derivatives in 87-95% yields.
7-Oxo-2-phenylamino-5-propyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (4a). White crystals; 89%; mp 297-299 ºC; IR (ν_{max}, cm^{-1}): 3314, 3156, 3061, 2959, 2817, 2231, 1670, 1635, 1596, 1560, 1459, 1379, 1220, 1153, 1087, 821, 754, 689, 610. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 0.94 (t, 3H, *J* 7.2 Hz, CH_3), 1.67 (sext, 2H, *J* 7.2 Hz, CH_2), 2.54 (t, 2H, *J* 7.2 Hz, CH_2), 5.80 (s, 1H, CH), 6.93 (t, 1H, *J* 7.4 Hz, ArH), 7.29 (t, 2H, *J* 7.4 Hz, ArH), 7.72 (d, 2H, *J* 8.4 Hz, ArH), 9.16 (s, 1H, exchanged by D_2O addition, NH), 12.97 (s, 1H, exchanged by D_2O addition, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ_c 13.74, 21.78, 34.29, 64.95, 98.89, 112.97,

118.11, 121.42, 129.07, 141.41, 145.96, 153.82, 154.20, 155.03; Anal. Calc. for $C_{16}H_{15}N_5O$: C 65.52; H 5.15; N 23.88. Found: C 65.44; H 5.23; N 23.98%.

7-Oxo-5-propyl-2-(*p*-tolylamino)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (4b). White crystals; 87%; mp 330-332 ºC; IR (ν_{max}, cm^{-1}): 3302, 3206, 3138, 3085, 2962, 2929, 2873, 2228, 1673, 1614, 1590, 1556, 1524, 1451, 1384, 1293, 811, 501. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 0.92 (t, 3H, *J* 7.2 Hz, CH_3), 1.65 (sext, 2H, *J* 7.5 Hz, CH_2), 2.24 (s, 3H, CH_3), 2.52 (t, 2H, *J* 7.5 Hz, CH_2), 5.77 (s, 1H, CH), 7.08 (d, 2H, *J* 8.1 Hz, ArH), 7.59 (d, 2H, *J* 8.1 Hz, ArH), 9.02 (s, 1H, exchanged by D_2O addition, NH), 12.93 (s, 1H, exchanged by D_2O addition, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ_c 13.75, 20.79, 21.77, 34.21, 64.73, 98.88, 113.03, 118.28, 129.46, 130.19, 138.93, 145.95, 153.97, 154.03, 155.01; Anal. Calc. for $C_{17}H_{17}N_5O$: C 66.43; H 5.58; N 22.79. Found: C 66.58; H 5.41; N 22.67%.

2-[(2,3-Dimethylphenyl)amino]-7-oxo-5-propyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (4c). White crystals; 90%; mp 244-246 ºC; IR (ν_{max}, cm^{-1}): 3387, 3166, 3085, 2961, 2214, 1681, 1629, 1588, 1543, 1512, 1476, 1442, 1385, 1302, 1199, 1093, 764. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 0.90 (t, 3H, *J* 6.9 Hz, CH_3), 1.61 (sext, 2H, *J* 6.9 Hz, CH_2), 2.09 (s, 3H, CH_3), 2.23 (s, 3H, CH_3), 2.50 (t, 2H, *J* 6.9 Hz, CH_2), 5.71 (s, 1H, CH), 6.95 (d, 1H, *J* 6.6 Hz, ArH), 6.99-7.05 (m, 1H, ArH), 7.16 (bd, 1H, *J* 7.5 Hz, ArH), 8.37 (s, 1H, exchanged by D_2O addition, NH), 12.90 (s, 1H, exchanged by D_2O addition, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ_c 13.73, 14.40, 20.67, 21.78, 34.17, 64.59, 98.68, 113.04, 122.44, 125.85, 126.52, 131.14, 137.40, 139.05, 146.17, 153.87, 155.06, 156.21; Anal. Calc. for $C_{18}H_{19}N_5O$: C 67.27; H 5.96; N 21.79. Found: C 67.16; H 6.02; N 21.81%.

2-[(3-Chloro-2-methylphenyl)amino]-7-oxo-5-propyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (4d). White crystals; 90%; mp 320-321 ºC; IR (ν_{max}, cm^{-1}): 3446, 3170, 3095, 2971, 2215, 1677, 1634, 1583, 1550, 1461, 1383, 1282, 1218, 1015, 845, 774. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 0.91 (t, 3H, *J* 7.2 Hz, CH_3), 1.63 (sext, 2H, *J* 7.5 Hz, CH_2), 2.23 (s, 3H, CH_3), 2.53 (t, 2H, *J* 7.5 Hz, CH_2), 5.74 (s, 1H, CH), 7.14-7.21 (m, 2H, ArH), 7.34 (d, 1H, *J* 6.9 Hz, ArH), 8.64 (s, 1H, exchanged by D_2O addition, NH), 12.96 (s, 1H, exchanged by D_2O addition, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ_c 13.73, 15.53, 21.79, 34.20, 65.08, 98.77, 112.93, 122.77, 125.20, 127.48, 129.97, 134.33, 141.08, 146.13, 154.10, 155.03, 155.53; Anal. Calc. for $C_{17}H_{16}ClN_5O$: C 59.74; H 4.72; N 20.49. Found: C 59.85; H 4.62; N 20.33%.

2-[(2-Bromophenyl)amino]-7-oxo-5-propyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (4e). White crystals; 95%; mp 333-334 ºC; IR (ν_{max}, cm^{-1}): 3388, 3075, 2958, 288, 2216, 1676, 1628, 1590, 1551, 1450, 1386, 1295, 742. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 0.91 (t, 3H, *J* 6.9 Hz, CH_3), 1.63 (sext, 2H, *J* 6.9 Hz, CH_2), 2.51 (t, 2H, *J* 6.9 Hz, CH_2), 5.77 (s, 1H, CH), 7.00-7.04 (m, 1H, ArH), 7.34-39 (m, 1H, ArH), 7.62 (bd, 1H, *J* 7.8 Hz, ArH), 7.83 (d, 1H, *J* 7.8 Hz, ArH), 8.19 (s, 1H, exchanged by D_2O addition, NH), 13.01 (s, 1H, exchanged by D_2O addition, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ_c 13.73, 21.74, 34.25, 65.66, 98.88, 112.69, 116.07, 123.32, 125.21, 128.85, 133.17, 138.71, 145.68, 154.27, 154.57, 155.04; Anal. Calc. for $C_{16}H_{14}BrN_5O$: C 51.63; H 3.79; N 18.82. Found: C 51.51; H 3.85; N 18.94%.

2-[(3-Bromophenyl)amino]-7-oxo-5-propyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (**4f**)**.** White crystals; 93%; mp 288-289 ºC; IR (ν_{max}, cm^{-1}): 3325, 3071, 2966, 2221, 1673, 1634, 1546, 1451, 1381, 1221, 1088, 875, 677, 553. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 0.92 (t, 3H, *J* 7.2 Hz, CH_3), 1.64 (sext, 2H, *J* 7.2 Hz, CH_2), 2.52 (t, 2H, *J* 7.5 Hz, CH_2), 5.80 (s, 1H, CH), 7.08 (d, 1H, *J* 7.8 Hz, ArH), 7.24 (t, 1H, *J* 8.1 Hz, ArH), 7.67 (d, 1H, *J* 8.1 Hz, ArH), 8.0 (s, 1H, ArH), 9.40 (s, 1H, exchanged by D_2O addition, NH), 13.03 (s, 1H, exchanged by D_2O addition, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ_c 13.74, 21.77, 34.22, 65.15, 98.97, 112.77, 116.82, 120.10, 122.11, 123.85, 131.04, 143.01, 145.94, 153.30, 154.33, 154.98; Anal. Calc. for $C_{16}H_{14}BrN_5O$: C 51.63; H 3.79; N 18.82. Found: C 51.79; H 3.68; N 18.73%.

5-Isopropyl-7-oxo-2-phenylamino-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (**4g**)**.**[28] White crystals; 92%, mp 326-328 ºC; IR (ν_{max}, cm^{-1}): 3395, 3152, 3060, 2976, 2825, 2219, 1672, 1629, 1592, 1551, 1498, 1460, 1392, 1314, 1234, 1173, 1080, 842, 754, 692, 560, 522, 469. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 1.22 (d, 6H, *J* 6.9 Hz, 2×CH_3), 2.86 (sep, 1H, *J* 6.9 Hz, CH), 5.84 (s, 1H, CH), 6.90 (t, 1H, *J* 7.2 Hz, ArH), 7.29-7.34 (m, 2H, *J* 7.8 Hz, ArH), 7.72 (d, 2H, *J* 7.5 Hz, ArH), 8.31 (s, 1H, exchanged by D_2O addition, NH), 12.90 (s, 1H, exchanged by D_2O addition, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ_c 21.79, 31.90, 64.93, 96.71, 113.39, 117.84, 121.53, 129.33, 140.64, 143.38, 153.17, 155.44, 159.89; Anal. Calc. for $C_{16}H_{15}N_5O$: C 65.52; H 5.15; N 23.88. Found: C 65.66; H 5.01; N 23.75%.

2-[(2,3-Dimethylphenyl)amino]-5-isopropyl-7-oxo-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (**4h**)**.** White crystals; 88%; mp 370-372 ºC; IR (ν_{max}, cm^{-1}): 3376, 3168, 3085, 2970, 2216, 1682, 1629, 1587, 1536, 1513, 1468, 1388, 1323, 1228, 1172, 1120, 1083, 918, 825, 768. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 1.21 (d, 6H, *J* 6.9 Hz, 2×CH_3), 2.09 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 2.84 (sep, 1H, *J* 6.9 Hz, CH), 5.71 (s, 1H, CH), 6.93 (d, 1H, *J* 7.2 Hz, ArH), 7.01 (t, 1H, *J* 7.5 Hz, ArH), 7.16 (d, 1H, *J* 7.5 Hz, ArH), 8.35 (s, 1H, exchanged by D_2O addition, NH), 12.82 (s, 1H, exchanged by D_2O addition, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ_c 14.39, 20.65, 21.42, 31.45, 64.70, 95.95, 113.06, 122.47, 125.82, 126.52, 131.15, 137.39, 139.03, 145.89, 155.40, 156.38, 159.43; Anal. Calc. for $C_{18}H_{19}N_5O$: C 67.27; H 5.96; N 21.79. Found: C 67.11; H 6.08; N 21.66%.

5-Methyl-7-oxo-2-(*p*-tolylamino)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (**4i**). White crystals; 89%; mp 360-361 ºC; IR (ν_{max}, cm^{-1}): 3384, 3167, 3077, 2975, 2833, 2216, 1678, 1634, 1591, 1550, 1450, 1396, 1308, 1221, 1169, 1021, 840, 739, 663, 562, 472. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 2.23 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 5.74 (s, 1H, CH), 7.07 (d, 2H, *J* 8.1 Hz, ArH), 7.59 (d, 2H, *J* 8.1 Hz, ArH), 9.04 (s, 1H, exchanged by D_2O addition, NH), 13.01 (s, 1H, exchanged by D_2O addition, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ_c 18.53, 20.79, 64.55, 99.52, 113.00, 118.24, 129.47, 130.18, 138.91, 145.84, 150.50, 153.86, 154.91; Anal. Calc. for $C_{15}H_{13}N_5O$: C 64.51; H 4.69; N 25.07. Found: C 64.40; H 4.78; N 25.19%.

2-[(2,3-Dimethylphenyl)amino]-5,7-dimethylpyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (**4j**)**.** White crystals; 88%; mp 288-290 ºC; IR (ν_{max}, cm^{-1}): 3436, 3054, 2995, 2917, 2208, 1609, 1591, 1486, 1274, 1187, 1062, 778, 438. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 2.13 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 2.53 (s, 3H, CH_3), 6.94 (s, 1H, ArH), 6.98 (d, 1H, *J* 7.2 Hz,

ArH), 7.05 (t, 1H, *J* 7.5 Hz, ArH), 7.21 (d, 1H, *J* 7.8 Hz, ArH), 8.74 (s, 1H, exchanged by D_2O addition, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ_c 14.57, 17.02, 20.70, 24.40, 66.90, 110.40, 114.20, 122.68, 125.86, 126.84, 131.52, 137.54, 138.59, 146.41, 151.41, 158.69, 161.66; Anal. Calc. for $C_{17}H_{17}N_5$: C 70.08; H 5.88; N 24.04. Found: C 69.97; H 5.76; N 24.20%.

Ethyl 5,7-dimethyl-2-(phenylamino)pyrazolo[1,5-*a*]pyrimidine-3-carboxylate (**4k**)**.** White crystals; 92%; mp 159-160 ºC; IR (ν_{max}, cm^{-1}): 3319, 2971, 2927, 1656, 1597, 1563, 1497, 1428, 1388, 1295, 1238, 1203, 1154, 1099, 1028, 892, 791, 691. ^1H NMR (300 MHz, DMSO-d_6): δ_H 1.33 (t, 3H, *J* 7.2 Hz, CH_3), 2.46 (s, 3H, CH_3), 2.60 (s, 3H, CH_3), 4.31 (q, 2H, *J* 7.2 Hz, CH_2), 6.87 (s, 1H, ArH), 6.95 (t, 1H, *J* 7.2 Hz, ArH), 7.32 (t, 2H, *J* 7.2 Hz, ArH), 7.70 (d, 2H, *J* 7.8 Hz, ArH), 8.97 (s, 1H, exchanged by D_2O addition, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ_c 14.92, 17.17, 24.85, 59.95, 110.28, 117.86, 121.57, 129.44, 140.56, 146.22, 147.27, 156.92, 162.01, 165.05; Anal. Calc. for $C_{17}H_{18}N_4O_2$: C 65.79; H 5.85; N 18.05. Found: C 65.83; H 5.76; N 17.88%.

Ethyl 5-isopropyl-7-oxo-2-(*m*-tolylamino)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-3-carboxylate (**4l**)**.** White crystals; 91%; mp 205-206 ºC; IR (ν_{max}, cm^{-1}): 3338, 3193, 3097, 2964, 2878, 1691, 1616, 1599, 1560, 1487, 1460, 1401, 1259, 1155, 1101, 1017, 885, 781, 690, 611, 585. ^1H NMR (300 MHz, DMSO-d_6): δ_H 1.23 (d, 6H, *J* 6.9 Hz, 2×CH_3), 1.37 (t, 3H, *J* 6.9 Hz, CH_3), 2.29 (s, 3H, CH_3), 3.20 (sep, 1H, *J* 6.6 Hz, CH), 4.39 (q, 2H, *J* 6.9 Hz, CH_2), 5.83 (s, 1H, CH), 6.77 (d, 1H, *J* 7.5 Hz, ArH), 7.20 (t, 1H, *J* 7.8 Hz, ArH), 7.44 (s, 1H, ArH), 7.61 (d, 1H, *J* 7.8 Hz, ArH), 8.23 (s, 1H, exchanged by D_2O addition, NH), 10.99 (s, 1H, exchanged by D_2O addition, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ_c 14.89, 21.74, 21.80, 30.80, 60.63, 84.42, 96.75, 115.03, 118.31, 122.32, 129.21, 138.51, 140.59, 143.41, 153.14, 155.36, 159.77, 163.17; Anal. Calc. for $C_{19}H_{22}N_4O_3$: C 64.39; H 6.26; N 15.81. Found: C 64.42; H 6.17; N 15.68%.

Ethyl 7-oxo-5-propyl-2-(*m*-tolylamino)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-3-carboxylate (**4m**)**.** White crystals; 94%; mp 209-210 ºC; IR (ν_{max}, cm^{-1}): 3394, 3060, 2954, 1699, 1668, 1602, 1563, 1498, 1444, 1355, 1276, 1557, 1122, 1025, 855, 785, 745, 690, 647, 523; ^1H NMR (300 MHz, DMSO-d_6): δ_H 0.97 (t, 3H, *J* 6.6 Hz, CH_3), 1.35 (t, 3H, *J* 6.9 Hz, CH_3), 1.63 (tq, 2H, *J* 6.6 Hz, CH_2), 2.29 (s, 3H, CH_3), 2.65 (t, 2H, *J* 6.6 Hz, CH_2), 4.38 (q, 2H, *J* 6.9 Hz, CH_2), 5.80 (s, 1H, CH), 6.76 (bd, 1H, *J* 6.6 Hz, ArH), 7.19 (bt, 1H, *J* 6.9 Hz, ArH), 7.42 (bs, 1H, ArH), 7.60 (bd, 1H, *J* 7.2 Hz, ArH), 8.23 (s, 1H, exchanged by D_2O addition, NH), 11.20 (s, 1H, exchanged by D_2O addition, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ_c 13.75, 14.90, 21.71, 21.88, 34.11, 60.61, 84.41, 99.48, 114.99, 118.27, 122.31, 129.20, 138.52, 140.57, 143.52, 153.09, 154.19, 155.11, 163.17; Anal. Calc. for $C_{19}H_{22}N_4O_3$: C 64.39; H 6.26; N 15.81. Found: C 64.48; H 6.03; N 15.72%.

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Supplementary Information

^{1}H-NMR, ^{13}C-NMR and FT-IR spectral data for compounds **4a-m** are available as supplementary information.

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