# 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

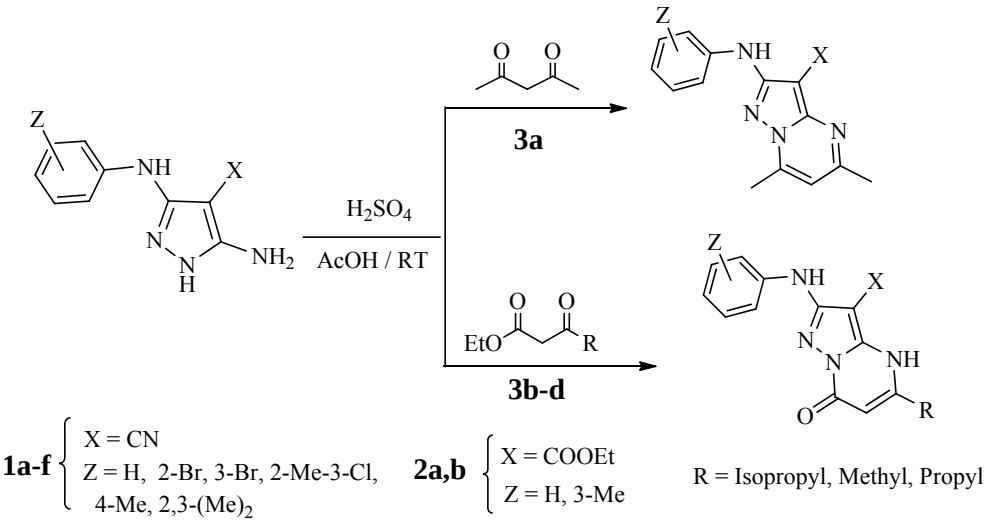
The pyrazolopyrimidine derivatives are an important class of heterocyclic compounds with pharmacological and biological activities, such as the antibacterial,[1] antiviral,[2] cytotoxic,[3] antidepressant,[4] neuroleptic,[5] tuberculostatic,[6] antihypertensive,[7] analgesic[8] and antimicrobial activity.[9] 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**

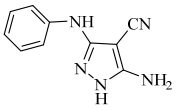
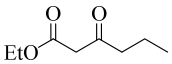
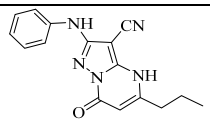
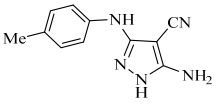
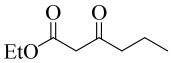
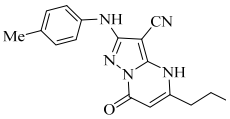
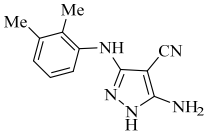
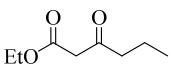
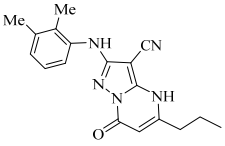
| Entry | Pyrazole derivatives (**1a-f**) / (**2a,b**) | 1,3-Diketone or keto ester (**3a-d**) | Product (**4a-m**) | Time (h) | Yield (%) | M.p. (°C) |
|---|---|---|---|---|---|---|
| 1 |  **1a** |  **3d** |  **4a** | 5 | 89 | 297-299 |
| 2 |  **1d** |  **3d** |  **4b** | 7 | 87 | 330-332 |
| 3 |  **1e**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

**Table 1. Continued**

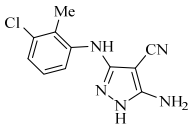
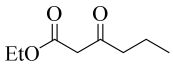
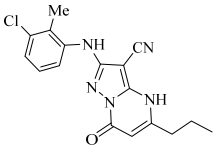
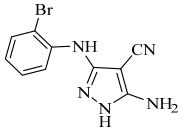
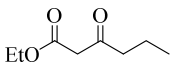
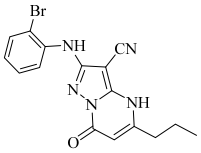
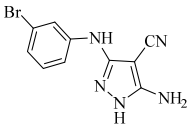
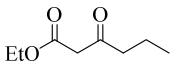
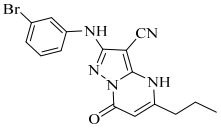
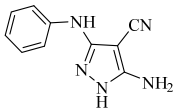
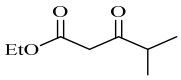
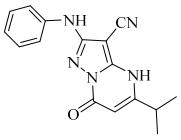
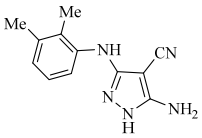
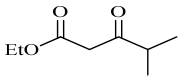
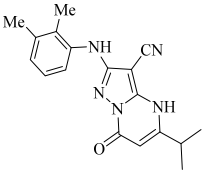
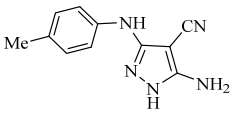
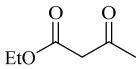
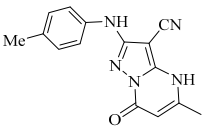
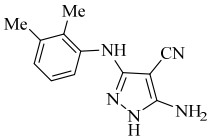
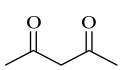
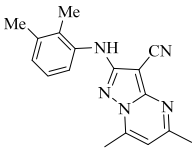
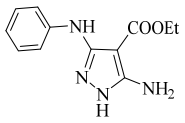
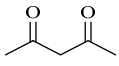
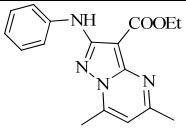
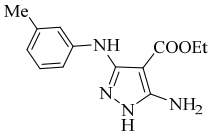
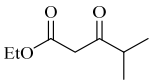
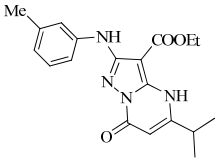
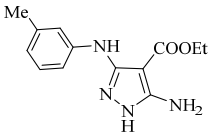
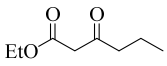
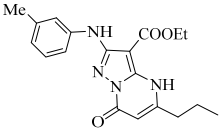
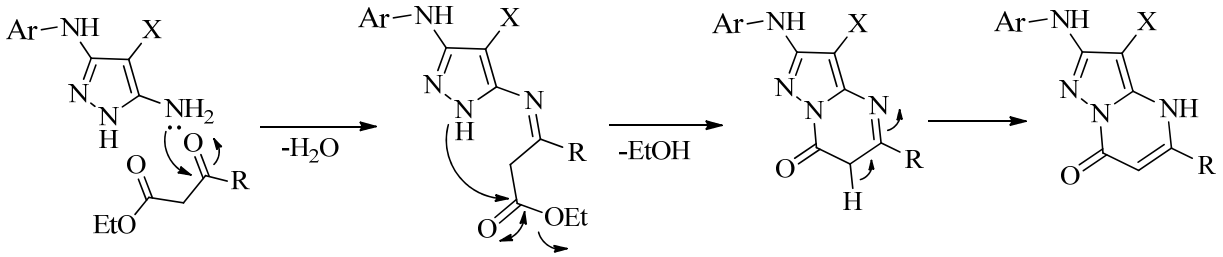
| Entry | Pyrazole derivatives (**1a-f**) / (**2a,b**) | 1,3-Diketone or keto ester (**3a-d**) | Product (**4a-m**) | Time (h) | Yield (%) | M.p. (°C) |
|---|---|---|---|---|---|---|
| 4 |  **1f** |  **3d** |  **4d** | 6 | 90 | 320-321 |
| 5 |  **1b** |  **3d** |  **4e** | 4 | 95 | 333-334 |
| 6 |  **1c** |  **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.



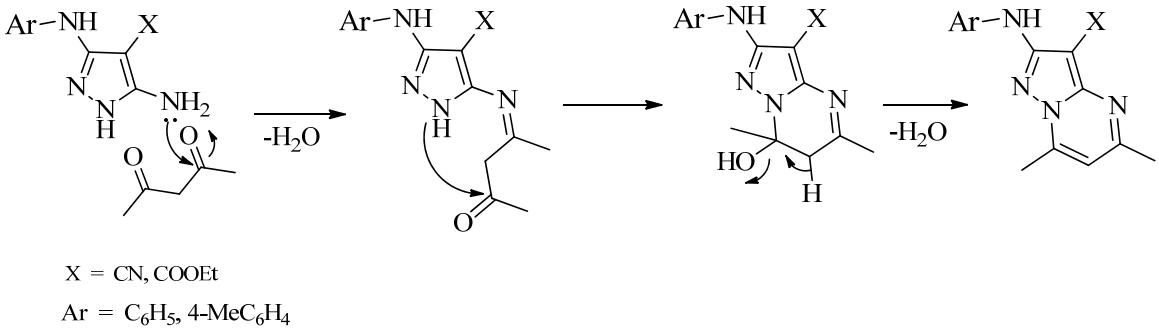

X = CN, COOEt

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 ($\nu_{max}$, 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-$d_6$): $\delta_H$ 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-$d_6$): $\delta_c$ 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 ($\nu_{max}$, $cm^{-1}$): 3302, 3206, 3138, 3085, 2962, 2929, 2873, 2228, 1673, 1614, 1590, 1556, 1524, 1451, 1384, 1293, 811, 501. $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta_H$ 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-$d_6$): $\delta_c$ 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 ($\nu_{max}$, $cm^{-1}$): 3387, 3166, 3085, 2961, 2214, 1681, 1629, 1588, 1543, 1512, 1476, 1442, 1385, 1302, 1199, 1093, 764. $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta_H$ 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-$d_6$): $\delta_c$ 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 ($\nu_{max}$, $cm^{-1}$): 3446, 3170, 3095, 2971, 2215, 1677, 1634, 1583, 1550, 1461, 1383, 1282, 1218, 1015, 845, 774. $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta_H$ 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-$d_6$): $\delta_c$ 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 ($\nu_{max}$, $cm^{-1}$): 3388, 3075, 2958, 288, 2216, 1676, 1628, 1590, 1551, 1450, 1386, 1295, 742. $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta_H$ 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-$d_6$): $\delta_c$ 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 ($\nu_{max}$, $cm^{-1}$): 3325, 3071, 2966, 2221, 1673, 1634, 1546, 1451, 1381, 1221, 1088, 875, 677, 553. $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta_H$ 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-$d_6$): $\delta_c$ 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 ($\nu_{max}$, $cm^{-1}$): 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-$d_6$): $\delta_H$ 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-$d_6$): $\delta_c$ 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 ($\nu_{max}$, $cm^{-1}$): 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-$d_6$): $\delta_H$ 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-$d_6$): $\delta_c$ 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 ($\nu_{max}$, $cm^{-1}$): 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-$d_6$): $\delta_H$ 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-$d_6$): $\delta_c$ 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 ($\nu_{max}$, $cm^{-1}$): 3436, 3054, 2995, 2917, 2208, 1609, 1591, 1486, 1274, 1187, 1062, 778, 438. $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta_H$ 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-$d_6$): $\delta_c$ 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 ($\nu_{max}$, $cm^{-1}$): 3319, 2971, 2927, 1656, 1597, 1563, 1497, 1428, 1388, 1295, 1238, 1203, 1154, 1099, 1028, 892, 791, 691. $^1H$ NMR (300 MHz, DMSO-$d_6$): $\delta_H$ 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-$d_6$): $\delta_c$ 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 ($\nu_{max}$, $cm^{-1}$): 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-$d_6$): $\delta_H$ 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-$d_6$): $\delta_c$ 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 ($\nu_{max}$, $cm^{-1}$): 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-$d_6$): $\delta_H$ 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-$d_6$): $\delta_c$ 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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