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

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DOI: <http://dx.doi.org/10.3998/ark.5550190.p009.062>

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 H₂SO₄ 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 analgesic⁸ 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-arylaminopyrazole-4-carbonitriles (**1a-f**) and ethyl 5-amino-3-arylaminopyrazole-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				5	89	297-299
2				7	87	330-332
3				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 = C₆H₅, 2-BrC₆H₄, 3-BrC₆H₄, 2-Me-3-ClC₆H₃, 3-MeC₆H₄, 4-MeC₆H₄, 2,3-(Me)₂C₆H₃

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 ¹H-NMR, ¹³C-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 Thermo Nicolet (Nexus 670) spectrometer using KBr discs. ¹H (300 MHz) and ¹³C (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 derivatives²⁷ (1 mmol) in acetic acid (20 mL), 1,3-diketones (2 mmol) and one drop of concentrated H₂SO₄ was added and then stirred at room temperature until the reaction was completed as monitored by TLC (CHCl₃/MeOH/CH₃CN 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 °C; IR (ν_{max}, cm⁻¹): 3314, 3156, 3061, 2959, 2817, 2231, 1670, 1635, 1596, 1560, 1459, 1379, 1220, 1153, 1087, 821, 754, 689, 610. ¹H NMR (300 MHz, DMSO-*d*₆): δ_H 0.94 (t, 3H, *J* 7.2 Hz, CH₃), 1.67 (sext, 2H, *J* 7.2 Hz, CH₂), 2.54 (t, 2H, *J* 7.2 Hz, CH₂), 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 D₂O addition, NH), 12.97 (s, 1H, exchanged by D₂O addition, NH). ¹³C 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 °C; IR ($\nu_{\max}$, cm^{-1}): 3302, 3206, 3138, 3085, 2962, 2929, 2873, 2228, 1673, 1614, 1590, 1556, 1524, 1451, 1384, 1293, 811, 501. ^1H 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 °C; IR ($\nu_{\max}$, cm^{-1}): 3387, 3166, 3085, 2961, 2214, 1681, 1629, 1588, 1543, 1512, 1476, 1442, 1385, 1302, 1199, 1093, 764. ^1H 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 °C; IR ($\nu_{\max}$, cm^{-1}): 3446, 3170, 3095, 2971, 2215, 1677, 1634, 1583, 1550, 1461, 1383, 1282, 1218, 1015, 845, 774. ^1H 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 $C_{17}H_{16}\text{ClN}_5O$: 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 °C; IR ($\nu_{\max}$, cm^{-1}): 3388, 3075, 2958, 288, 2216, 1676, 1628, 1590, 1551, 1450, 1386, 1295, 742. ^1H 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 $C_{16}H_{14}\text{BrN}_5O$: 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 °C; IR ($\nu_{\max}$, cm^{-1}): 3325, 3071, 2966, 2221, 1673, 1634, 1546, 1451, 1381, 1221, 1088, 875, 677, 553. ^1H NMR (300 MHz, $\text{DMSO}-d_6$): 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, $\text{DMSO}-d_6$): 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 $\text{C}_{16}\text{H}_{14}\text{BrN}_5\text{O}$: 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 °C; 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. ^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ_{H} 1.22 (d, 6H, J 6.9 Hz, $2\times\text{CH}_3$), 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, $\text{DMSO}-d_6$): 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 $\text{C}_{16}\text{H}_{15}\text{N}_5\text{O}$: 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 °C; 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. ^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ_{H} 1.21 (d, 6H, J 6.9 Hz, $2\times\text{CH}_3$), 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, $\text{DMSO}-d_6$): 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 $\text{C}_{18}\text{H}_{19}\text{N}_5\text{O}$: 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 °C; 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. ^1H NMR (300 MHz, $\text{DMSO}-d_6$): 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, $\text{DMSO}-d_6$): 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 $\text{C}_{15}\text{H}_{13}\text{N}_5\text{O}$: 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 °C; IR ($\nu_{\max}$, cm^{-1}): 3436, 3054, 2995, 2917, 2208, 1609, 1591, 1486, 1274, 1187, 1062, 778, 438. ^1H NMR (300 MHz, $\text{DMSO}-d_6$): 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 D₂O addition, NH). ¹³C 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 C₁₇H₁₇N₅: 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 °C; 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): δ_H 1.33 (t, 3H, J 7.2 Hz, CH₃), 2.46 (s, 3H, CH₃), 2.60 (s, 3H, CH₃), 4.31 (q, 2H, J 7.2 Hz, CH₂), 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 D₂O addition, NH). ¹³C 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 C₁₇H₁₈N₄O₂: 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 °C; 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): δ_H 1.23 (d, 6H, J 6.9 Hz, 2×CH₃), 1.37 (t, 3H, J 6.9 Hz, CH₃), 2.29 (s, 3H, CH₃), 3.20 (sep, 1H, J 6.6 Hz, CH), 4.39 (q, 2H, J 6.9 Hz, CH₂), 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 D₂O addition, NH), 10.99 (s, 1H, exchanged by D₂O addition, NH). ¹³C 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 C₁₉H₂₂N₄O₃: 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 °C; 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): δ_H 0.97 (t, 3H, J 6.6 Hz, CH₃), 1.35 (t, 3H, J 6.9 Hz, CH₃), 1.63 (tq, 2H, J 6.6 Hz, CH₂), 2.29 (s, 3H, CH₃), 2.65 (t, 2H, J 6.6 Hz, CH₂), 4.38 (q, 2H, J 6.9 Hz, CH₂), 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 D₂O addition, NH), 11.20 (s, 1H, exchanged by D₂O addition, NH). ¹³C 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 C₁₉H₂₂N₄O₃: C 64.39; H 6.26; N 15.81. Found: C 64.48; H 6.03; N 15.72%.

Acknowledgements

The authors are grateful to Urmia University for financial support.

Supplementary Information

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

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