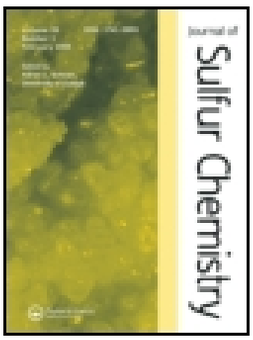

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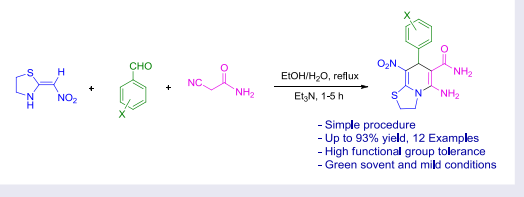
Fahimeh Sadat Hosseini, Shima Nasri and Mohammad Bayat

Department of Chemistry, Faculty of Science, Imam Khomeini International University, Qazvin, Iran

ABSTRACT

An easy, efficient, and environmentally benign synthesis of new class of thiazolopyridine carboxamide derivatives is reported *via* one-pot, multi-component reaction of 2-(nitromethylene)thiazolidine derived from the addition of cysteamine hydrochloride to nitro ketene dithioacetal with aromatic aldehydes and cyanoacetamide using catalytic amount of triethylamine (Et_3N) in ethanol/water at reflux in good to excellent yields.



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Thiazolopyridine carboxamide; multi-component reaction; 2-(nitromethylene) thiazolidine; cysteamine hydrochloride; nitro ketene dithioacetal; aromatic aldehydes; cyanoacetamide

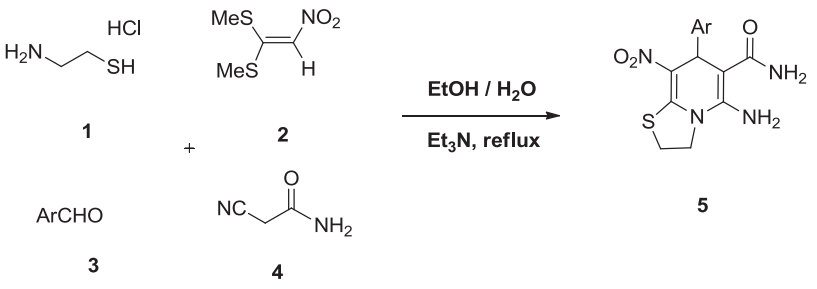
1. Introduction

Heterocycles are essential building blocks that are frequently used in the pharmaceutical [1,2]. Biologically active molecules containing various heteroatoms such as nitrogen and sulfur, always drawn the attention of chemists and pharmacologists over the years mainly because of their broad range of bioactivities [3,4]. The presence of heteroatoms results in significant changes in the cyclic molecular structure due to the availability of unshared pairs of electrons and the difference in electronegativity between heteroatoms and carbon [5,6]. Therefore, organo *S*- and *N*-heterocycles have been under investigation for a long time on account of their synthetic diversity and therapeutic relevance [7].

Among these heterocycles, derivatives of thiazolopyridines have been reported to furnish various biological activities such as anticancer [8], anti-inflammatory, antifungal [9], antimicrobial and antihypertensive [10,11].

Ketene dithioacetals are versatile intermediates in organic synthesis [12] and the enamines derived from nitro ketene dithioacetal are widely used for the synthesis of a variety of

CONTACT Mohammad Bayat m.bayat@sci.ikiu.ac.ir, bayat_mo@yahoo.com



Scheme 1. Synthetic scheme for the products **5a-l.**

S- and *N*-heterocyclic compounds in the past several years [13–24]. In continuation of our research interests regarding the development of the synthetic utility of ketene dithioacetals and cyclic *N*,*S*-ketene acetals on the basis of our previous endeavors in exploring novel and practical MCRs to synthesize useful heterocyclic compounds, herein we report a simple and efficient synthesis of a new class of thiazolopyridine carboxamide derivatives *via* a one-pot, multi-component reaction of 2-(nitromethylene)thiazolidine as a cyclic *N*,*S*-ketene acetal (derived from the addition of cysteamine hydrochloride to nitro ketene dithioacetal), aromatic aldehydes and cyanoacetamide in the presence of Et_3N in EtOH/H_2O as a green medium at reflux.

2. Results and discussion

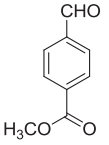
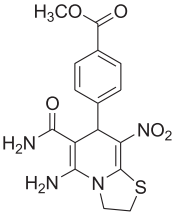
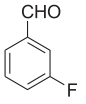
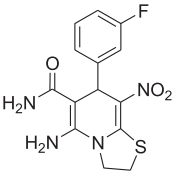
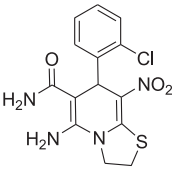
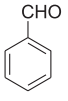
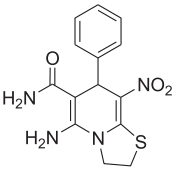
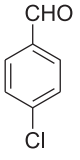
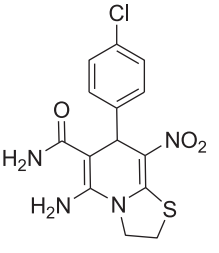
In this work, we would like to report the results of our studies involving the reaction of cysteamine hydrochloride **1** and nitro ketene dithioacetal **2** proceeds in one-pot under mild conditions, in EtOH/H_2O (1:1) at reflux to produce the 2-(nitromethylene)thiazolidine **6** in excellent yields. Next, the sequential one-pot addition of aromatic aldehydes **3**, cyanoacetamide **4**, and catalytic amounts of Et_3N, successfully gave the 5-amino-8-nitro-7-aryl-3,7-dihydro-2*H*-thiazolo[3,2-*a*]pyridine-6-carboxamide derivatives **5** in good to excellent yields (Scheme 1).

This reaction was very clean and free from side reactions in the presence of catalytic amount of Et_3N in EtOH/H_2O as a green medium at reflux. In the absence of a catalyst, the reaction did not yield any product even after long reaction times. We explored the scope of this reaction by varying the structure of the aromatic aldehydes. The reaction proceeds under the same reaction conditions to afford a series of thiazolopyridine carboxamide derivatives **5** in 74–93% yields. The results are shown in Table 1.

The structures of compounds **5a-l** (Table 1) were confirmed by IR, ^{1}H NMR, ^{13}C NMR and mass spectra. The IR spectrum of **5a** exhibit absorption bands due to two NH_2 groups (3460, 3396, 3340 and 3220 cm^{-1}) and absorption bands due to two C=O groups (1770 and 1646 cm^{-1}) and as well as 1572, 1219, 1490 and 1325 cm^{-1} due to the Ar, C–N and NO_2 groups.

^{1}H NMR spectrum (DMSO-d_6) of **5a** revealed two singlets for the NH_2 (amine) and NH_2 (amide) groups (δ 6.61, 7.90 ppm, respectively), one singlet for the methine proton (δ 5.28 ppm), one singlet for OCH_3 group (3.79 ppm), characteristic multiplets for CH_2S and CH_2N groups (.3.34–3.39, 4.15–4.36 ppm, respectively) and two doublets (δ 7.46,

Table 1. Products **5a-l**.

Entry	ArCHO	Product	Time (h)	Yield (%)
1		 **5a**	1.5	93
2		 **5b**	1.5	78
3		 **5c**	1.5	87
4		 **5d**	2.5	80
5		 **5e**	1	87

(*continued*).

Table 1. Continued.

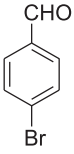
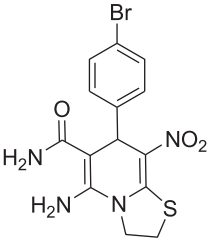
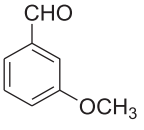
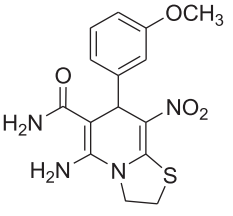
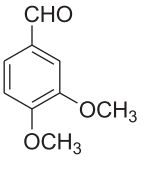
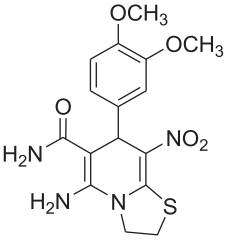
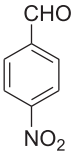
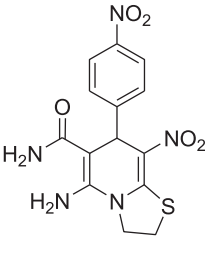
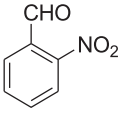
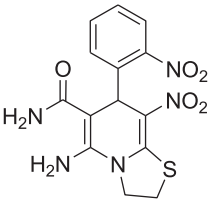
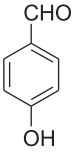
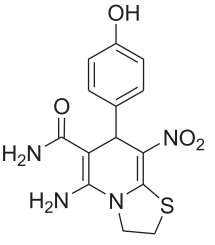
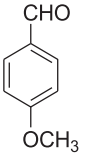
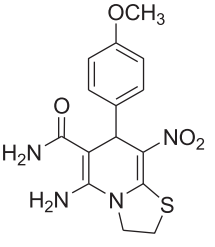
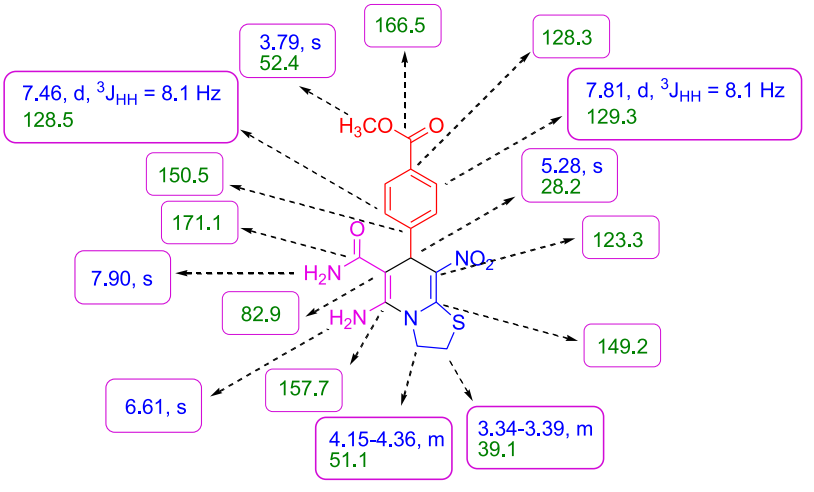
Entry	ArCHO	Product	Time (h)	Yield (%)
6		 **5f**	1	90
7		 **5g**	3	83
8		 **5h**	5	80
9		 **5i**	2	85
10			3	82

Table 1. Continued.

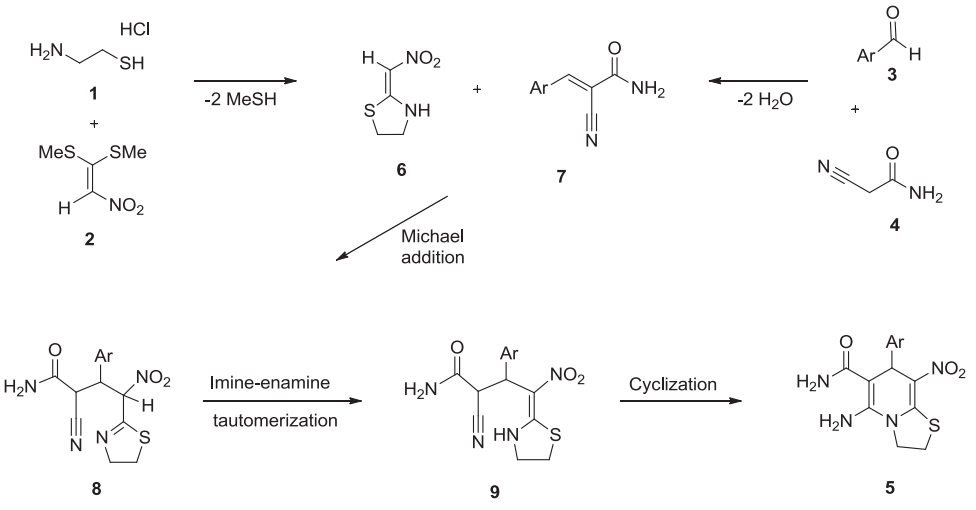
Entry	ArCHO	Product	Time (h)	Yield (%)
11		 **5k**	5	74
12		 **5l**	2.5	77

Note: Cysteamine hydrochloride (1 mmol), nitro ketene dithioacetal (1 mmol), aromatic aldehyde (1 mmol) and cyanoacetamide (1 mmol) were used.



Scheme 2. ^{1}H and ^{13}C NMR chemical shift of **5a.**

7.81 ppm) for the aromatic region which completely in accord with the assigned structure. The ^{1}H-decoupled ^{13}C NMR spectrum (DMSO-d_6) of **5a** showed 14 distinct resonances which was consistent with proposed structure (Scheme 2). The characteristic signal due to the methane carbon was discernible (at δ 28.2 ppm). There are two signals for CH_2S and CH_2N groups (at δ = 39.1 and 51.1 ppm, respectively) and two signals at δ 82.9, 157.7 ppm



Scheme 3. Plausible mechanism for the formation of product **5**.

for two olefinic carbons (NH_2CO-**C9C**-NH_2). The ^1H and ^{13}C NMR spectra of **5b-l** are similar to that of **5a**, except for the signals of aryl moieties.

The EI-MS of **5a** displayed the molecular ion peak at *m/z* 376.5, which was in agreement with the proposed structure.

The acceptable mechanism for this reaction is designated in Scheme 3. It is possible that initially the formation of 2-(nitromethylene)thiazolidine **6** occurs through addition of cysteamine hydrochloride **1** to nitro ketene dithioacetal **2**, while Knoevenagel condensation between the aromatic aldehyde **3** and cyanoacetamide **4** would give intermediate **7**. The 2-(nitromethylene)thiazolidine **6** then adds to the Knoevenagel adduct **7** to give intermediate **8**, which undergoes successive imine–enamine tautomerization, followed by *N*-cyclization *via* attack of the secondary amino group to the cyano group, leading to the formation of **5**.

3. Conclusion

In summary, we have developed a convenient, efficient, one-pot and multi-component synthesis of thiazolopyridine carboxamide frameworks by the reaction of cysteamine hydrochloride, nitro ketene dithioacetal, aromatic aldehydes and cyanoacetamide in the presence of Et_3N in $EtOH/H_2O$ at reflux. This strategy includes some advantages, such as green methodoloy, simple experimental procedures, easy accessibility of reactants, high atom economy, compatibility with various functional groups and good to excellent product yields.

4. Experimental

4.1. General

All research chemicals (cysteamine hydrochloride, nitro ketene dithioacetal, aromatic aldehydes, cyanoacetamide and triethylamine) and solvents were purchased from Merck and

Aldrich and were used without further purification. The melting points were taken in an open capillary tube using an electrotherma1 9100 apparatus. NMR spectra were recorded with a Bruker DRX-300 Avance instrument (300 MHz for ^{1}H and 75.4 MHz for ^{13}C) with DMSO as solvent. Chemical shifts are expressed in parts per million (ppm), and coupling constant (*J*) are reported in hertz (Hz). IR spectra were recorded on a Bruker Tensor 27 spectrometer. Mass spectra were recorded with an Agilent 5975C VL MSD with Triple-Axis Detector operating at an ionization potential of 70 eV. Elemental analyses for C, H and N were performed using a PerkinElmer 2004 series [II] CHN elemental analyzer.

4.2. General procedure for the synthesis of product 5

The stoichiometric mixtures of cysteamine hydrochloride (0.113 g, 1 mmol), nitro ketene dithioacetal (0.165 g, 1 mmol) and Et_3N (140 µL, 1 mmol) in 10 mL of H_2O/EtOH (1:1), in 50 mL flask, was stirred under reflux for 5 h. Next, aromatic aldehyde (1 mmol), cyanoacetamide (0.084 g, 1 mmol) and one drop Et_3N as a catalyst were added at once, respectively, and the solution was heated at reflux for the time given in Table 1. Upon completion as monitored by TLC, the reaction mixture was cooled to room temperature and resulting solid product was filtered, washed with a small amount of H_2O/EtOH (1:1) to give product **5**.

4.2.1. Methyl 4-(5-amino-6-carbamoyl-3,7-dihydro-8-nitro-2H-thiazolo[3,2-a]pyridin-7-yl)benzoate (5a)

Red solid; yield: 0.350 g (93%); m.p. 253–255°C. ^{1}H NMR (300 MHz, DMSO): δ 3.34–3.39 (m, 2H, CH_2S), 3.79 (s, 3H, OCH_3), 4.15–4.36 (m, 2H, CH_2N), 5.28 (s, 1H, CH), 6.61 (s, 2H, NH_2), 7.46 (d, $^{3}J_{HH}$ = 8.1 Hz, 2H, Ar), 7.81 (d, $^{3}J_{HH}$ = 8.1 Hz, 2H, Ar), 7.90 (s, 2H, NH_2). ^{13}C NMR (75.4 MHz, DMSO): δ 28.2 (CH), 39.1 (CH_2S), 51.1 (CH_2N), 52.4 (OCH_3), 82.9, 123.3, 128.3, 128.5, 129.3, 149.2, 150.5, 157.7, 166.5 (C=O), 171.1 (C=O). IR (KBr) (ν_{max}/cm^{-1}): 3460, 3396, 3340 and 3220 (NH_2), 1717 (C=O), 1646 (C=O), 1572 (Ar), 1490 and 1325 (NO_2), 1219 (C–N). MS (EI, 70 eV): *m/z* (%) = 376.5 (M^+, 1.1), 316 (100), 285 (69), 229 (32), 199 (59), 171 (31), 129 (32), 101 (25), 60 (76). Anal. Calc. for $C_{16}H_{16}N_4O_5S$ (376.39): C, 51.06; H, 4.28; N, 14.89. Found: C, 51.5; H, 4.7; N, 14.6.

4.2.2. 5-Amino-7-(3-fluorophenyl)-3,7-dihydro-8-nitro-2H-thiazolo[3,2-a]pyridine-6-carboxamide (5b)

Orange solid; yield: 0.262 g (78%); m.p. 256–258°C. ^{1}H NMR (300 MHz, DMSO): δ 3.36–3.47 (m, 2H, CH_2S), 4.13–4.37 (m, 2H, CH_2N), 5.21 (s, 1H, CH), 6.62 (s, 2H, NH_2), 6.93–7.29 (m, 4H, Ar), 7.91 (s, 2H, NH_2). ^{13}C NMR (75.4 MHz, DMSO): δ 28.2 (CH), 38.9 (CH_2S), 51.1 (CH_2N), 83.0, 113.6 (d, $^{2}J_{CF}$ = 21 Hz), 115.1 (d, $^{2}J_{CF}$ = 21 Hz), 123.4, 124.1, 130.3, 148.1, 149.2, 157.6, 161.0 (d, $^{1}J_{CF}$ = 243 Hz), 171.1 (C=O). IR (KBr) (ν_{max}/cm^{-1}): 3439, 3346 and 3196 (NH_2), 1636 (C=O), 1562 (Ar), 1482 and 1329 (NO_2), 1236 (C–N). MS (EI, 70 eV): *m/z* (%) = 336.5 (M^+, 9.3), 292 (100), 241 (93), 189 (24), 146 (31), 95 (13), 61 (32). Anal. Calc. for $C_{14}H_{13}FN_4O_3S$ (336.34): C, 49.99; H, 3.90; N, 16.66. Found: C, 49.9; H, 4.2; N, 16.5.

4.2.3. 5-Amino-7-(2-chlorophenyl)-3,7-dihydro-8-nitro-2H-thiazolo[3,2-a]pyridine-6-carboxamide (5c)

Orange solid; yield: 0.306 g (87%); m.p. 249–251°C. ^{1}H NMR (300 MHz, DMSO): δ 3.37–3.42 (m, 2H, CH_2S), 4.22–4.36 (m, 2H, CH_2N), 5.39 (s, 1H, CH), 6.37 (s, 2H, NH_2), 7.13–7.46 (m, 4H, Ar), 7.90 (s, 2H, NH_2). ^{13}C NMR (75.4 MHz, DMSO): δ 28.0 (CH), 38.9 (CH_2S), 50.9 (CH_2N), 82.1, 122.6, 127.5, 128.7, 130.0, 132.3, 132.5, 141.6, 149.3, 158.0, 171.3 (C=O). Anal. Calc. for $C_{14}H_{13}ClN_4O_3S$ (352.80): C, 47.66; H, 3.71; N, 15.88. Found: C, 76.3; H, 4.2; N, 15.5.

4.2.4. 5-Amino-3,7-dihydro-8-nitro-7-phenyl-2H-thiazolo[3,2-a]pyridine-6-carboxamide (5d)

Orange solid; yield: 0.254 g (80%); m.p. 262–264°C. ^{1}H NMR (300 MHz, DMSO): δ 3.32–3.38 (m, 2H, CH_2S), 4.14–4.30 (m, 2H, CH_2N), 5.16 (s, 1H, CH), 6.56 (s, 2H, NH_2), 7.12–7.32 (m, 5H, Ar), 7.84 (s, 2H, NH_2). ^{13}C NMR (75.4 MHz, DMSO): δ 28.2 (CH), 39.1 (CH_2S), 51.0 (CH_2N), 83.6, 124.0, 126.9, 128.1, 128.3, 145.2, 149.1, 157.3, 171.3 (C=O). IR (KBr) (ν_{max}/cm^{-1}): 3433, 3344 and 3203 (NH_2), 1636 (C=O), 1563 (Ar), 1482 and 1325 (NO_2), 1237 (C–N). MS (EI, 70 eV): *m/z* (%) = 318.5 (M^+, 9.9), 274 (100), 241 (90), 198 (10), 171 (31), 128 (25), 102 (20), 61 (25). Anal. Calc. for $C_{14}H_{14}N_4O_3S$ (318.35): C, 52.82; H, 4.43; N, 17.60. Found: C, 53.3; H, 4.9; N, 17.4.

4.2.5. 5-Amino-7-(4-chlorophenyl)-3,7-dihydro-8-nitro-2H-thiazolo[3,2-a]pyridine-6-carboxamide (5e)

Orange solid; yield: 0.306 g (87%); m.p. 245–247°C. ^{1}H NMR (300 MHz, DMSO): δ 3.37–3.40 (m, 2H, CH_2S), 4.13–4.34 (m, 2H, CH_2N), 5.19 (s, 1H, CH), 6.60 (s, 2H, NH_2), 7.26 (d, $^{3}J_{HH}$ = 8.4 Hz, 2H, Ar), 7.33 (d, $^{3}J_{HH}$ = 8.4 Hz, 2H, Ar), 7.89 (s, 2H, NH_2). ^{13}C NMR (75.4 MHz, DMSO): δ 28.2 (CH), 38.7 (CH_2S), 51.1 (CH_2N), 83.1, 123.5, 128.2, 130.0, 131.4, 144.2, 149.1, 157.5, 171.1 (C9 O). IR (KBr) (ν_{max}/cm^{-1}): 3466, 3360 and 3191 (NH_2), 1631 (C=O), 1561 (Ar), 1482 and 1332 (NO_2), 1226 (C–N). Anal. Calc. for $C_{14}H_{13}ClN_4O_3S$ (352.80): C, 47.66; H, 3.71; N, 15.88. Found: C, 48.1; H, 4.0; N, 15.5.

4.2.6. 5-Amino-7-(4-bromophenyl)-3,7-dihydro-8-nitro-2H-thiazolo[3,2-a]pyridine-6-carboxamide (5f)

Orange solid; yield: 0.357 g (90%); m.p. 250–252°C. ^{1}H NMR (300 MHz, DMSO): δ 3.35–3.40 (m, 2H, CH_2S), 4.13–4.32 (m, 2H, CH_2N), 5.18 (s, 1H, CH), 6.60 (s, 2H, NH_2), 7.27 (d, $^{3}J_{HH}$ = 8.4 Hz, 2H, Ar), 7.40 (d, $^{3}J_{HH}$ = 8.4 Hz, 2H, Ar), 7.89 (s, 2H, NH_2). ^{13}C NMR (75.4 MHz, DMSO): δ 28.2 (CH), 38.8 (CH_2S), 51.1 (CH_2N), 83.0, 120.0, 123.5, 130.4, 131.1, 144.6, 149.1, 157.5, 171.1 (C=O). Anal. Calc. for $C_{14}H_{13}BrN_4O_3S$ (397.25): C, 42.33; H, 3.30; N, 14.10. Found: C, 42.8; H, 3.7; N, 13.8.

4.2.7. 5-Amino-3,7-dihydro-7-(3-methoxyphenyl)-8-nitro-2H-thiazolo[3,2-a]pyridine-6-carboxamide (5 g)

Red solid; yield: 0.289 g (83%); m.p. 247–249°C. ^{1}H NMR (300 MHz, DMSO): δ 3.34–3.40 (m, 2H, CH_2S), 3.67 (s, 3H, OCH_3), 4.13–4.34 (m, 2H, CH_2N), 5.14 (s, 1H, CH), 6.58 (s, 2H, NH_2), 6.71 (d, $^{3}J_{HH}$ = 8.1 Hz, 1H, Ar), 6.83 (d, $^{3}J_{HH}$ = 7.8 Hz, 1H, Ar), 6.91 (s, 1H, Ar), 7.13 (*t*, $^{3}J_{HH}$ = 8.1 Hz, 1H, Ar), 7.85 (s, 2H, NH_2). ^{13}C NMR (75.4 MHz, DMSO): δ 28.2 (CH), 39.1 (CH_2S), 51.1 (CH_2N), 55.3 (OCH_3), 83.5, 111.5, 114.9, 120.2,

123.8, 129.5, 146.7, 149.1, 157.3, 159.2, 171.2 (C=O). IR (KBr) (ν_{max}/cm^{-1}): 3438, 3346 and 3196 (NH_2), 1633 (C=O), 1557 (Ar), 1484 and 1337 (NO_2), 1237 (C–N). MS (EI, 70 eV): *m/z* (%) = 348.5 (M^+, 11.8), 304 (75), 241 (100), 201 (22), 44 (20). Anal. Calc. for $C_{15}H_{16}N_4O_4S$ (348.38): C, 51.71; H, 4.63; N, 16.08. Found: C, 51.3; H, 4.9; N, 15.7.

4.2.8. 5-Amino-3,7-dihydro-7-(3,4-dimethoxyphenyl)-8-nitro-2H-thiazolo[3,2-a]pyridine-6-carboxamide (5 h)

Red solid; yield: 0.302 g (80%); m.p. 223–225°C. ^{1}H NMR (300 MHz, DMSO): δ 3.36–3.43 (m, 2H, CH_2S), 3.66 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 4.15–4.32 (m, 2H, CH_2N), 5.09 (s, 1H, CH), 6.53 (s, 2H, NH_2), 6.71–6.80 (m, 2H, Ar), 7.00 (s, 1H, Ar), 7.83 (s, 2H, NH_2). ^{13}C NMR (75.4 MHz, DMSO): δ 28.2 (CH), 38.7 (CH_2S), 51.0 (CH_2N), 55.9 (OCH_3), 83.7, 112.2, 112.8, 119.9, 124.2, 137.8, 147.9, 148.4, 149.1, 156.9, 171.3 (C=O). Anal. Calc. for $C_{16}H_{18}N_4O_5S$ (378.40): C, 50.78; H, 4.79; N, 14.81. Found: C, 50.4; H, 5.2; N, 14.6.

4.2.9. 5-Amino-3,7-dihydro-8-nitro-7-(4-nitrophenyl)-2H-thiazolo[3,2-a]pyridine-6-carboxamide (5i)

Orange solid; yield: 0.308 g (85%); m.p. 235–237°C. ^{1}H NMR (300 MHz, DMSO): δ 3.33–3.40 (m, 2H, CH_2S), 4.16–4.37 (m, 2H, CH_2N), 5.37 (s, 1H, CH), 6.68 (s, 2H, NH_2), 7.60 (d, $^3J_{HH}$ = 8.7 Hz, 2H, Ar), 7.97 (s, 2H, NH_2), 8.09 (d, $^3J_{HH}$ = 8.7 Hz, 2H, Ar). ^{13}C NMR (75.4 MHz, DMSO): δ 28.2 (CH), 39.1 (CH_2S), 51.1 (CH_2N), 82.4, 122.9, 123.6, 129.4, 146.5, 149.2, 152.7, 158.1, 171.0 (C=O). Anal. Calc. for $C_{14}H_{13}N_4O_5S$ (363.35): C, 46.28; H, 3.61; N, 19.27. Found: C, 46.0; H, 3.8; N, 18.9.

4.2.10. 5-Amino-3,7-dihydro-8-nitro-7-(2-nitrophenyl)-2H-thiazolo[3,2-a]pyridine-6-carboxamide (5j)

Yellow solid; yield: 0.297 g (82%); m.p. 245–247°C. ^{1}H NMR (300 MHz, DMSO): δ 3.34–3.39 (m, 2H, CH_2S), 4.18–4.39 (m, 2H, CH_2N), 5.64 (s, 1H, CH), 6.65 (s, 2H, NH_2), 7.41–7.78 (m, 4H, Ar), 8.27 (s, 2H, NH_2). ^{13}C NMR (75.4 MHz, DMSO): δ 28.1 (CH), 34.9 (CH_2S), 51.2 (CH_2N), 80.9, 122.9, 124.0, 128.8, 131.3, 134.5, 138.4, 149.0, 150.4, 158.4, 170.9 (C=O). Anal. Calc. for $C_{14}H_{13}N_4O_5S$ (363.35): C, 46.28; H, 3.61; N, 19.27. Found: C, 46.8; H, 3.9; N, 19.0.

4.2.11. 5-Amino-3,7-dihydro-7-(4-hydroxyphenyl)-8-nitro-2H-thiazolo[3,2-a]pyridine-6-carboxamide (5k)

Yellow solid; yield: 0.247 g (74%); m.p. 246–248°C. ^{1}H NMR (300 MHz, DMSO): δ 3.35–3.41 (m, 2H, CH_2S), 4.15–4.29 (m, 2H, CH_2N), 5.02 (s, 1H, CH), 6.47 (s, 2H, NH_2), 6.58 (d, $^3J_{HH}$ = 7.8 Hz, 2H, Ar), 7.08 (d, $^3J_{HH}$ = 7.8 Hz, 2H, Ar), 7.78 (s, 2H, NH_2), 9.17 (s, 1H, OH). ^{13}C NMR (75.4 MHz, DMSO): δ 28.1 (CH), 38.4 (CH_2S), 51.0 (CH_2N), 84.0, 115.0, 124.4, 129.1, 135.6, 148.9, 156.3, 156.8, 171.3 (C=O). Anal. Calc. for $C_{14}H_{14}N_4O_4S$ (334.35): C, 50.29; H, 4.22; N, 16.76. Found: C, 50.8; H, 4.8; N, 16.5.

4.2.12. 5-Amino-3,7-dihydro-7-(4-methoxyphenyl)-8-nitro-2H-thiazolo[3,2-a]pyridine-6-carboxamide (5 l)

Red solid; yield: 0.268 g (77%); m.p. 245–247°C. ^{1}H NMR (300 MHz, DMSO): δ 3.36–3.46 (m, 2H, CH_2S), 3.84 (s, 3H, OCH_3), 4.13–4.33 (m, 2H, CH_2N), 5.09 (s, 1H, CH), 6.53 (s, 2H, NH_2), 6.76 (d, $^3J_{HH}$ = 8.7 Hz, 2H, Ar), 7.21 (d, $^3J_{HH}$ = 8.4 Hz, 2H, Ar), 7.86

(s, 2H, NH_2). ^{13}C NMR (75.4 MHz, DMSO): δ 28.2 (CH), 38.3 (CH_2S), 51.1 (CH_2N), 55.4 (OCH_3), 81.8, 108.5, 113.4, 129.1, 138.1, 149.1, 152.1, 157.9, 171.3 (C=O). IR (KBr) (ν_{max}/cm^{-1}): 3432, 3341, 3257 and 3198 (NH_2), 1638 (C=O), 1561 (Ar), 1487 and 1336 (NO_2), 1237 (C–N). MS (EI, 70 eV): *m/z* (%) = 348.5 (M^+, 4.4), 305 (46), 288 (100), 257 (77), 218 (23), 201 (76), 171 (19), 146 (29), 60 (28). Anal. Calc. for $C_{15}H_{16}N_4O_4S$ (348.38): C, 51.71; H, 4.63; N, 16.08. Found: C, 51.4; H, 4.9; N, 16.3.

Disclosure statement

No potential conflict of interest was reported by the authors.

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