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# Synthesis of some new thiazolo[3,2-a]pyrimidine derivatives and screening of their in vitro antibacterial and antitubercular activities

Dong Cai<sup>1</sup> · Zhi-Hua Zhang<sup>2</sup> · Yu Chen<sup>3</sup> · Xin-Jia Yan<sup>4</sup> · Shi-Ti Zhang<sup>1</sup> · Liang-Jing Zou<sup>1</sup> · Li-Hong Meng<sup>1</sup> · Fang Li<sup>1</sup> · Bing-Jie Fu<sup>1</sup>

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**Abstract** The novel 5*H*-thiazolo[3,2-a]pyrimidin-5-ones were synthesized by thiophene ring closure. The first step is the synthesis of *S*-alkylated derivatives by the reaction of 6-substituted-2-thiouracils with the appropriate substituted phenacyl halides. Upon treatment of *S*-alkylated derivatives at different temperatures, intramolecular cyclization to 3-(substituted phenyl)-5*H*-thiazolo[3,2-a]pyrimidin-5-ones or sulfonation of cyclized products to the corresponding sulfonic acid derivatives occurred. Further, acylation of the 7-NH<sub>2</sub> group of 5*H*-thiazolo[3,2-a]pyrimidin-5-ones afforded amide derivatives, and reduction of the NO<sub>2</sub> group of 5*H*-thiazolo[3,2-a]pyrimidin-5-ones gave amino derivatives. All the new compounds were confirmed by <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR and HRMS spectra, and their antibacterial and antitubercular activities were screened.

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⊠ Dong Cai Caidong0804@163.com

> Zhi-Hua Zhang Bridge1026@163.com

Yu Chen gzweishengwu@126.com

Xin-Jia Yan yanxinjia@yeah.net

- <sup>1</sup> Liaoning Medical University, Jinzhou 121000, China
- <sup>2</sup> School of Chemical and Environmental Engineering, Liaoning University of Technology, Jinzhou 121001, China
- <sup>3</sup> School of Life Science and Biopharmaceutics, Shenyang Pharmaceutical University, Shenyang 110016, China
- <sup>4</sup> College of Pharmacy, Harbin University of Commerce Harbin, Harbin 150076, China

Some compounds showed significant antibacterial and antitubercular activities.

**Keywords** Thiazole · Cyclization · Thiazolopyrimidine · Antibacterial · Antitubercular

#### Introduction

The remarkable ability of bacteria to develop resistance to antimicrobial agents is a pressing concern for public health (Boucher *et al.*, 2009). Consequently, new antimicrobial drugs to combat this problem are therefore in great demand. Over the past 50 years, only two new structural types of antimicrobial drugs, linezolid and daptomycin, have been introduced into the clinic (Simmons *et al.*, 2010). The design of new scaffolds to deal with antimicrobial resistance has become one of the most important areas of antimicrobial research today.

Thiazolo[3,2-a]pyrimidines have been consistently regarded as a structural analogs of biogenic purine bases and can be considered as potential purine antagonists (El-Bayouki and Basyouni, 2010; Nagarajaiah et al., 2012). The synthesis of thiazolo[3,2-a]pyrimidines has received considerable attention from both synthetic and medicinal chemists because of their wide range of biological activities, including antiinflammatory (Tozkoparan et al., 1998, 1999), antihypertensive (Jeanneau-Nicolle et al., 1992), antiviral (Mohamed et al., 2010), antioxidant (Maddila et al., 2012), antitumor (Flefel et al., 2007; Al-Omary et al., 2012), anti-HIV (Danel et al., 1998), calcium channel blocking (Balkan et al., 1992), acetylcholine esterase inhibitory (Liu et al., 2014), CDC25B phosphatase inhibitory (Kolb et al., 2009), Bcl-2 family proteins inhibitory (Kolb et al., 2009), glutamate receptor antagonistic (Wichmann *et al.*, 1999) and 5-HT2a receptor antagonistic activities (Awadallah, 2008). These thiazolopyrimidines have also been found to elicit antibacterial (Ghorab *et al.*, 2000), antifungal (Pan *et al.*, 2011) and antitubercular activities (Geist *et al.*, 2010).

Compounds containing sulfonic acid groups have great practical usefulness, primarily, due to a very wide spectrum of biological activities. The phosphate functional group can be replaced by sulfonic acid moieties via bioisosteric replacement. These features are functionally interchangeable due to their ability to adopt a negative charge at biological pH (Cai, 2004). Numerous compounds containing sulfonic acid group are well known as antibacterial (Khan and Rastogi, 1991; Veretennikov and Pavlov, 2013; Janietz et al., 1988; Doria et al., 1985), antifungal (Allen et al., 1959; Dhapalapur et al., 1968; Raval et al., 2012; Fujiwara and Inoi, 1992; Bondock et al., 2013) and antitubercular activities (Parekh and Maheria, 2012). Additionally, these sulfonic acids are also used as dyes (Youssef and Youssef, 2003), metal arenesulfonates complexes (El-Emary and Abdel-Mohsen, 2006).

In the light of the above facts, we have synthesized some 5*H*-thiazolo[3,2-a]pyrimidin-5-one derivatives and related compounds containing sulfonic acid active moieties with the hope to possess better antibacterial and antitubercular activities.

#### **Results and discussion**

#### Chemistry

The synthetic strategies adopted for the preparation of the intermediates and target compounds are depicted in Scheme 1.

6-Substituted anilino-2-thiouracils **1a–b** were nearly quantitatively *S*-alkylated with the appropriate substituted phenacyl halides in the presence of anhydrous  $K_2CO_3$  to give compounds **2a–j**. These intermediates **2a–j** were of sufficient purity (by TLC) to be used in subsequent reactions without further purification. The *S*-alkylated 2-thiouracils are proved to exist in solution largely in the lactam form as indicated by spectroscopic studies (Brown *et al.*, 1955; Andrew and Bradsher, 1967). The tautomeric hydrogen was found to be in position 3 (Brown *et al.*, 1955; Andrew and Bradsher, 1967; Abdel-Mohsen *et al.*, 2013; Kwiatkowski and Pullman, 1975; Mizutani *et al.*, 1985) (Scheme 2).

Regarding the 400-MHz <sup>1</sup>H NMR (in DMSO- $d_6$ ) spectra, the *S*-alkylated thiouracils **2a–j** showed similar shifts, and therefore, we discuss here the spectroscopic data only of **2b** as the representative of this series (see Supporting Information). On the basis of structure of **2b**, the methylene

group appeared as a two-proton singlet at  $\delta$  4.84 ppm. The signal of the 5-H proton of pyrimidine is observed at  $\delta$ 6.04 ppm as a singlet. The signal of the N3-H proton appeared at  $\delta$  12.79 ppm as a broad singlet. Within the aromatic region, a multiplet appeared at  $\delta$  8.30–8.37 ppm due to the substituted phenyl protons. In addition, the compound 2b seems to exist partially in the cyclic form (Danel et al., 1998), which had a pair of doublets centered at  $\delta$  3.74 and 3.65 ppm comprising an AB system (J = 12.5 Hz), but an AB quartet did not fully account for two methylene protons. Moreover, two singlets at  $\delta$  2.25 and  $\delta$  1.99 were all assigned to CH<sub>3</sub>. All these indicate that the presence of an equilibrium mixture of open-chain and cyclic forms is possible. Furthermore, the intermediate S-alkylated thiouracil exists as enol tautomeric form (Lin et al., 1979; Kaye et al., 1983; Meslin and Quiniou, 1974, 1975), and a one-proton singlet was present at  $\delta$  6.02 ppm, corresponding to the enol form of compound 2b in DMSO (Matiichuk et al., 2008) (Scheme 2).

Compounds **3a–d** can be synthesized from the *S*-alkylated thiouracils in concentrated  $H_2SO_4$  at 80 °C by a onepot procedure via an intramolecular cyclization/sulfonation sequence. The *S*-alkylated thiouracils undergo only intramolecular cyclization in concentrated  $H_2SO_4$  at room temperature to give compounds **4a–h**, which can be reduced to give the corresponding amines **5a–d**.

Theoretically, the intramolecular cyclization reactions of intermediates 2a-j may afford the two possible isomeric products: 5H-thiazolo[3,2-a]pyrimidin-5-ones and 7H-thiazolo[3,2-a]pyrimidin-7-ones. However, in practice cyclization of compounds 2a-j was found to afford only the corresponding 5H-thiazolo[3,2-a]pyrimidin-5-ones 3a-f and 4a-h. The regioselectivity of the intramolecular cyclization step was assumed to be the difference in the electron density at the N1 and N3 position of compounds 2a-j. The higher basicity of the N3 resulted in the exclusive cyclization at this position (Bakavoli et al., 2008; Dallinger et al., 2003). Moreover, the selective C2-N3 annulation has been proven by single-crystal X-ray crystallographic studies (Quan et al., 2008). Additionally, it seems that the steric hindrance at the position 6 in the S-alkylated derivatives 2a-j exerts a directive influence during this cyclization.

For products **3a–d**, all the sulfonic acid groups locate the ortho-positions relative to  $R_3$  (electron-donating groups, such as  $R_2$ =CH<sub>3</sub>, CH<sub>3</sub>O). The best explanation of this phenomenon is the influence of electronic and steric factors together determining a new substituent to the positions of the phenyl ring. Similar conclusions for the regioselectivity of sulfonation of the phenyl ring have also been reported in the studies (Schäfer *et al.*, 1984, 1991; Angioni *et al.*, 2014; Katritzky *et al.*, 1984; Coates *et al.*, 1996).





Scheme 1 Reagents and conditions: *i* K<sub>2</sub>CO<sub>3</sub>, DMF; *ii* concentrated H<sub>2</sub>SO<sub>4</sub>, 80 °C; *iii* concentrated H<sub>2</sub>SO<sub>4</sub>, 20 °C; *iv* Fe, NH<sub>4</sub>Cl, 2:1 ethanol/ water, 80 °C; *v* triethylamine, r.t., 2 h





The amines **5a–d** were prepared by reducing the nitro compounds **4a–b**, **4e–f** with iron in a mixture of  $NH_4Cl$ , ethanol and water following a literature (Dai *et al.*, 2005). However, the post-process described for the reduction was

not practical because the target compounds **5a–d** were very slightly soluble in water and slightly soluble in cool ethyl acetate and dichloromethane. The completion of the reaction was monitored by TLC. Without allowing the mixture

to cool, the iron residue is removed by filtration and washed with boiling ethanol until a clear wash was obtained. The filtrate was concentrated under reduced pressure until no more ethanol distilled, the resultant mixture was cooled to room temperature, and the solution was filtered. The crude product was recrystallized from ethanol to afford the appropriate amines.

The amino substitution of compounds **4a–h** could lead to an amino conjugation effect of the cyclic  $\alpha$ , $\beta$ -unsaturated ketone of 5*H*-thiazolo[3,2-*a*]pyrimidin-5-ones. Apparently, the negative charge density of N atom decreases, and consequently, the nucleophilicity of amino group will decrease dramatically. A mild procedure for the generation of amides **6a–d** is based on the procedure in reference Tang *et al.*, (2013). Compounds **4a–h** react with m-methylbenzoyl chloride in the presence of triethylamine to give amides **6a–d**. However, the synthesis required relatively high temperatures and/or long reaction times because of the low nucleophilicity of the amine group.

#### **Biological activity**

#### Antibacterial activity

All of the synthesized compounds were evaluated in vitro antibacterial activity against two Gram-positive bacterial strains: *Staphylococcus aureus* (*S. aureus*) and *Bacillus subtilis* (*B. subtilis*); two Gram-negative bacterial strains: *Escherichia coli* (*E. coli*) and *Pseudomonas aeruginosa* (*P. aeruginosa*), by conventional broth microdilution assay. The MIC values of antibacterial activity are given in Table 1.

The investigation of antibacterial screening data reveals that all the tested compounds showed significant activity against Gram-negative bacteria. However, most of the compounds exhibited relatively weak activity against Gram-positive bacteria. The sulfonic acid group in the phenyl ring did not seem to have a remarkable contribution to the antibacterial inhibition by compounds 3a-d; however, strong electron-withdrawing group such as nitro may have improved their effect against Gram-negative bacteria, and compounds 4e and 4f showed good activity against E. coli. Compounds 5a-d containing a primary amino substituent on phenyl group exhibited moderate potencies against P. aeruginosa. Compounds 6a-d that are having substituted benzoylamido at the C-7 position were found to be the most active compounds against the test microorganisms.

#### Antitubercular activity

Antitubercular activity of compounds was assessed against *Mycobacterium smegmatis (M. smegmatis)* using conventional broth microdilution assay. MIC values are given in Table 2.

Table 2 shows the antitubercular activity results which depicted that compounds **6a–d** containing substituted benzoylamido at the C-7 position show good activity against *M. smegmatis*. The presence of substituted benzoylamido moiety with other groups like chloro fused to 5H-thiazolo[3,2-a]pyrimidin-5-ones may be accounted for their antitubercular activity.

#### Materials and methods

Melting points were determined in open capillary tubes with a WRS-1B melting point apparatus and are uncorrected. IR spectra (KBr) were recorded on a FTIR920 spectrophotometer. The <sup>1</sup>H and <sup>13</sup>C NMR spectra were obtained from a solution in DMSO- $d_6$  unless otherwise noted with TMS as internal standard using a 400/101 MHz (<sup>1</sup>H/<sup>13</sup>C) spectrometer. Mass spectra were acquired from a Agilent 6200 Series TOF and 6500 Series Q-TOF LC/MS System B.05.01. (B5125).

#### General procedure for preparation of compounds 2

Anhydrous potassium carbonate (1.3821 g, 10 mmol) and substituted phenacyl halides (10 mmol) were added in succession to a suspension of 6-substituted-2-thiouracils (10 mmol) in dry N,N-dimethylformamide (10 mL). After stirring for 3 h at room temperature, the mixture was quenched with water (100 mL) and filtered. The resulting solid was crystallized from a suitable solvent.

#### 6-Methyl-2-((2-(3-nitrophenyl)-2-oxoethyl)thio)pyrimidin-4(3H)-one **2a**

White solid; yield: 86.27 %; m.p. 252.2–253.7 °C. HRMS (m/z): calcd for  $C_{13}H_{12}N_3O_4S$  (neutral M + H) 306.05485; found 306.057780.

#### 6-Methyl-2-((2-(4-nitrophenyl)-2-oxoethyl)thio)pyrimidin-4(3H)-one **2b**

White solid; yield: 87.78 %; m.p. 258.1–259.5 °C (lit. (Hurst *et al.*, 1988) 71 %; m.p. > 315 °C). HRMS (m/z):

Table 1 In vitro antibacterial activity (MIC µg/mL)

Compound	Gram-positive bacteria		Gram-negative bacteria	
	S. aureus	B. subtilis	E. coli	P. aeruginosa
3a	800	800	200	200
3b	_	400	400	400
3c	400	800	200	400
3d	400	800	400	800
4a	800	400	200	200
4b	800	800	200	400
4c	800	_	800	_
4d	800	_	800	800
4e	800	800	100	400
4f	800	800	50	400
4g	800	_	400	800
4h	800	_	800	_
5a	400	800	800	200
5b	400	800	800	200
5c	_	400	400	100
5d	800	400	400	100
6a	200	200	50	50
6b	200	200	50	100
6c	100	800	200	200
6d	200	400	100	400
Ciprofloxacin	25	100	25	50

"-" indicates bacteria is resistant to the compounds at >800 µg/mL

calcd for  $C_{13}H_{12}N_3O_4S$  (neutral M + H) 306.05485; found 306.056718.

6-Methyl-2-((2-oxo-2-(p-tolyl)ethyl)thio)pyrimidin-4(3H)one **2c** 

White solid; yield: 84.56 %; m.p. 187.3–187.6 °C (lit. (Johnson *et al.*, 1913) 52 %; m.p. 191–195 °C). HRMS (m/z): calcd for  $C_{14}H_{15}N_2O_2S$  (neutral M + H) 275.0842; found 275.096403.

# 2-((2-(4-Chlorophenyl)-2-oxoethyl)thio)-6-methylpyrimidin-4(3H)-one **2d**

Yellow green solid; yield: 86.85 %; m.p. 218.7–220.0 °C (lit.(Hurst *et al.*, 1988) 80 %; m.p. 210–212 °C). HRMS (m/z): calcd for  $C_{13}H_{12}ClN_2O_2S$  (neutral M + H) 295.03080; found 295.033049.

2-((2-(4-Methoxyphenyl)-2-oxoethyl)thio)-6-methyl pyrimidin-4(3H)-one **2e** 

Yellow solid; yield: 74.05 %; m.p. 180.6–181.2 °C (lit. (Hurst *et al.*, 1988) 50 %; m.p. 186–189 °C). HRMS (m/z):

calcd for  $C_{14}H_{15}N_2O_3S$  (neutral M + H) 291.08034; found 291.088547.

6-Amino-2-((2-(3-nitrophenyl)-2-oxoethyl)thio) pyrimidin-4(3H)-one **2**f

Yellow solid; yield: 73.45 %; m.p. 217.8–218.2 °C. HRMS (m/z): calcd for  $C_{12}H_{11}N_4O_4S$  (neutral M + H) 307.05010; found 307.053381.

6-Amino-2-((2-(4-nitrophenyl)-2-oxoethyl)thio) pyrimidin-4(3H)-one **2g** 

Yellow solid; yield: 73.45 %; m.p. 222.6–223.2 °C. HRMS (m/z): calcd for  $C_{12}H_{11}N_4O_4S$  (neutral M + H) 307.05010; found 307.051107.

6-Amino-2-((2-oxo-2-(p-tolyl)ethyl)thio)pyrimidin-4(3H)one **2h** 

White solid; yield: 85.0 %; m.p. 220.0–220.4 °C (lit. (Hurst *et al.*, 1988) 68 %; m.p. 204–206 °C). HRMS (m/z): calcd for  $C_{13}H_{14}N_3O_2S$  (neutral M + H) 276.08067; found 276.090015.

Table 2 In vitro antitubercular activity (MIC µg/mL)

Compound	M. smegmatis	
3a	_	
3b	_	
3c	_	
3d	—	
4a	—	
4b	—	
4c	—	
4d	800	
4e	_	
4f	_	
4g	_	
4h	800	
5a	_	
5b	—	
5c	_	
5d	_	
6a	100	
6b	100	
6c	400	
6d	50	
Rifampicin	25	

"-" indicates bacteria is resistant to the compounds at >800 µg/mL

## 6-Amino-2-((2-(4-chlorophenyl)-2-oxoethyl)thio) pyrimidin-4(3H)-one **2i**

Yellow solid; yield: 84.53 %; m.p. 216.0–217.2 °C (lit. (Hurst *et al.*, 1988) 63 %; m.p. 220 °C (dec.)). HRMS (m/z): calcd for  $C_{12}H_{11}ClN_3O_2S$  (neutral M + H) 296.02605; found 296.028652.

# 6-Amino-2-((2-(4-methoxyphenyl)-2-oxoethyl)thio) pyrimidin-4(3H)-one **2**j

Yellow solid; yield: 80.32 %; m.p. 228.6–231.0 °C. HRMS (m/z): calcd for  $C_{13}H_{14}N_3O_3S$  (neutral M + H) 292.07559; found 292.085934.

#### General procedure for preparation of compounds 3

S-alkylated thiouracils 2 (1 mmol) were carefully dissolved in 3.0 mL of concentrated sulfuric acid, and the reaction mixture was stirred at 80 °C for 24 h. The progress of the reaction was monitored by TLC. After completion, the reaction mixture was cooled and poured into ethyl acetate, and the precipitate that separated was collected by filtration, washed with ethyl acetate and dried. The resulting solid was recrystallized from ethyl acetate. 2-Methoxy-5-(7-methyl-5-oxo-5H-thiazolo[3,2-a]pyrimidin-3yl)benzenesulfonic acid **3a** 

Yellow solid; yield: 88.96 %; m.p. 283.2–284.8 °C; IR ( $v_{max}/cm^{-1}$ ): 3445 (SO<sub>3</sub>H), 1726 (C=O); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ )  $\delta$  7.68 (dd, J = 2.5, 1.1 Hz, 1H, Ar–H), 7.36–7.28 (m, 1H, Ar–H), 7.22 (d, J = 1.2 Hz, 1H, C<sub>2</sub>–H), 6.96 (dd, J = 8.6, 1.1 Hz, 1H, Ar–H), 6.05 (s, 1H, C<sub>6</sub>–H), 3.45 (qd, J = 7.0, 1.2 Hz, 3H, CH<sub>3</sub>O), 2.28 (s, 3H, 7-CH<sub>3</sub>); <sup>13</sup>C NMR (101 MHz, DMSO- $d_6$ )  $\delta$  162.61 (N=C–S), 156.81 (CON, C-5), 154.41 (C-7), 146.56 (C-3), 137.71, 134.77, 131.23, 129.52, 127.87, 123.17 (Ar–C), 110.87 (C-2), 104.92 (C-6), 55.90 (CH<sub>3</sub>O), 18.99 (CH<sub>3</sub>); HRMS (m/z): calcd for C<sub>14</sub>H<sub>13</sub>N<sub>2</sub>O<sub>5</sub>S<sub>2</sub> (neutral M + H) 353.02659; found 353.029811.

# 2-Methyl-5-(7-methyl-5-oxo-5H-thiazolo[3,2-a]pyrimidin-3-yl)benzenesulfonic acid **3b**

Yellow solid; yield: 83.20 %; m.p. 245.1–247.2 °C; IR  $(v_{max}/cm^{-1})$ : 3440 (SO<sub>3</sub>H), 1721 (C=O); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ )  $\delta$  7.74 (t, J = 1.5 Hz, 1H, Ar–H), 7.29 (d, J = 1.2 Hz, 1H, C<sub>2</sub>–H), 7.28–7.12 (m, 2H, Ar–H), 6.08 (s, 1H, C<sub>6</sub>–H), 2.57 (s, 3H, phenyl-CH<sub>3</sub>), 2.29 (s, 3H, 7-CH<sub>3</sub>); <sup>13</sup>C NMR (101 MHz, DMSO- $d_6$ )  $\delta$  163.93 (N=C–S), 162.11 (CON, C-5), 158.98 (C-7), 145.36, 137.67, 136.39, 129.93, 128.89, 127.36 (Ar–C), 111.23 (C-2), 104.92 (C-6), 23.17 (CH<sub>3</sub>), 20.34 (CH<sub>3</sub>); HRMS (m/z): calcd for C<sub>14</sub>H<sub>13</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub> (neutral M + H) 337.03167; found 337.023641.

# 5-(7-Amino-5-oxo-5H-thiazolo[3,2-a]pyrimidin-3-yl)-2methoxybenzenesulfonic acid **3c**

Yellow solid; yield: 86.46 %; m.p. (dec.) 223.7 °C; IR  $(v_{max}/cm^{-1})$ : 3332 (SO<sub>3</sub>H), 1659 (C=O); <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  7.68 (q, *J* = 2.1 Hz, 1H, Ar–H), 7.32 (dq, *J* = 8.5, 2.1 Hz, 1H, Ar–H), 6.98–6.93 (m,1H, Ar–H), 6.93–6.90 (m, 1H, C<sub>2</sub>–H), 6.12 (broad, s, 2H, NH<sub>2</sub>), 5.02–4.95 (m, 1H, C<sub>6</sub>–H), 3.80 (d, *J* = 2.6 Hz, 3H, CH<sub>3</sub>O); <sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  164.74 (N=C–S), 162.75 (CON, C-5), 159.40 (C-7), 149.88 (C-3), 136.70, 131.27, 129.19, 128.47, 127.32, 111.34 (Ar–C), 108.42 (C-2), 80.10 (C-6), 54.43 (CH<sub>3</sub>); HRMS (m/z): calcd for C<sub>13</sub>H<sub>12</sub>N<sub>3</sub>O<sub>5</sub>S<sub>2</sub> (neutral M + H) 354.02184; found 354.025808.

### 5-(7-Amino-5-oxo-5H-thiazolo[3,2-a]pyrimidin-3-yl)-2methylbenzenesulfonic acid **3d**

Yellow solid; yield: 87.52 %; m.p. 238.1–239.2 °C; IR  $(v_{max}/cm^{-1})$ : 3342 (SO<sub>3</sub>H), 1660 (C=O); <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  7.71 (d, *J* = 1.9 Hz, 1H, Ar–H),

7.21 (dd, J = 7.7, 2.1 Hz, 1H, Ar–H), 7.13 (s, 1H, C<sub>2</sub>–H), 6.98 (s, 1H, Ar–H), 5.73 (broad, s, 2H, NH<sub>2</sub>), 5.01 (s, 1H, C<sub>6</sub>–H), 2.56 (s, 3H, phenyl-CH<sub>3</sub>); <sup>13</sup>C NMR (101 MHz, DMSO- $d_6$ )  $\delta$  164.89 (N=C–S), 162.65 (CON, C-5), 159.39 (C-7), 147.06 (C-3), 137.77, 136.61, 131.74, 129.83, 127.30, 124.26 (Ar–C), 109.96 (C-2), 80.33 (C-6), 20.31 (CH<sub>3</sub>); HRMS (m/z): calcd for C<sub>13</sub>H<sub>12</sub>N<sub>3</sub>O<sub>4</sub>S<sub>2</sub> (neutral M + H) 338.02692; found 338.027661.

#### General procedure for preparation of compounds 4

S-alkylated thiouracils 2 (1 mmol) were carefully dissolved in 3.0 mL of concentrated sulfuric acid, and the reaction mixture was stirred at room temperature for 72 h. The progress of the reaction was monitored by TLC. After completion, the reaction mixture was cooled and poured into ice-cold water, and the precipitate that separated was collected by filtration, washed with ethyl acetate and dried. The resulting solid was recrystallized from ethyl acetate.

## 7-Methyl-3-(3-nitrophenyl)-5H-thiazolo[3,2-a]pyrimidin-5-one **4a**

Yellow solid; yield: 91.15 %; m.p. 260.1.1–261.7 °C; IR  $(v_{\text{max}}/\text{cm}^{-1})$ : 1702 (C=O); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ )  $\delta$  8.35–8.25 (m, 2H, Ar–H), 7.91 (d, J = 7.7 Hz, 1H, Ar–H), 7.69 (t, J = 7.9 Hz, 1H, Ar–H), 7.55 (s, 1H, C<sub>2</sub>–H), 6.10 (s, 1H, C<sub>6</sub>–H), 2.31 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (101 MHz, DMSO- $d_6$ )  $\delta$  163.70 (N=C–S), 163.14 (CON, C-5), 159.42 (C-7), 146.92 (C-3), 136.18, 135.19, 133.84, 128.93, 124.57, 123.54 (Ar–C), 113.37 (C-2), 104.96 (C-6), 23.56 (CH<sub>3</sub>); HRMS (m/z): calcd for C<sub>13</sub>H<sub>10</sub>N<sub>3</sub>O<sub>3</sub>S (neutral M + H) 288.04429; found 288.047339.

# 7-Methyl-3-(4-nitrophenyl)-5H-thiazolo[3,2-a]pyrimidin-5-one **4b**

Yellow solid; yield: 92.72 %; m.p. 215.1–216.7 °C (lit. (Hurst *et al.*, 1988) 86 %; m.p. 238–242 °C); IR ( $v_{max}/$  cm<sup>-1</sup>): 1731(C=O); <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  8.27–8.19 (m, 2H, Ar–H), 7.75–7.66 (m, 2H, Ar–H), 7.57 (d, J = 1.7 Hz, 1H, C<sub>2</sub>–H), 6.11 (d, J = 1.5 Hz, 1H, C<sub>6</sub>–H), 2.30 (d, J = 1.6 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  163.73 (N=C–S), 163.05 (CON, C-5), 159.24 (C-7), 147.44 (C-3), 138.64, 135.38, 130.90, 122.55 (Ar–C), 113.94 (C-2), 104.96 (C-6), 23.51 (CH<sub>3</sub>); HRMS (m/z): calcd for C<sub>13</sub>H<sub>10</sub>N<sub>3</sub>O<sub>3</sub>S (neutral M + H) 288.04429; found 288.048423.

# 7-Methyl-3-(p-tolyl)-5H-thiazolo[3,2-a]pyrimidin-5-one 4c

Yellow solid; yield: 92.22 %; m.p. 210.7–210.9 °C (lit. (Galasko and Israelstam, 1969) 84 %; m.p. 196–198 °C);

IR ( $v_{max}/cm^{-1}$ ): 1649 (C=O); <sup>1</sup>H NMR (400 MHz, DMSOd<sub>6</sub>)  $\delta$  7.30 (s, 1H, C<sub>2</sub>–H), 7.28 (d, J = 1.0 Hz, 2H, Ar–H), 7.18 (d, J = 7.9 Hz, 2H, Ar–H), 6.06 (t, J = 0.9 Hz, 1H, C<sub>6</sub>–H), 2.36 (s, 3H, CH<sub>3</sub>), 2.29 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (101 MHz, DMSO-d<sub>6</sub>)  $\delta$  163.96 (N=C–S), 162.30 (CON, C-5), 159.12 (C-7), 138.23 (C-3), 137.95, 129.54, 129.46, 128.08 (Ar–C), 111.00 (C-2), 104.96 (C-6), 23.28 (CH<sub>3</sub>), 21.34 (CH<sub>3</sub>); HRMS (m/z): calcd for C<sub>14</sub>H<sub>13</sub>N<sub>2</sub>OS (neutral M + H) 257.07486; found 257.088294.

#### 3-(4-Chlorophenyl)-7-methyl-5H-thiazolo[3,2-a]pyrimidin-5one 4d

Yellow solid; yield: 92.91 %; m.p. 210.9–211.5 °C (lit. (Galasko and Israelstam, 1969) 80 %; m.p. 210–212 °C); IR ( $v_{max}/cm^{-1}$ ): 1647 (C=O); <sup>1</sup>H NMR (400 MHz, DMSOd<sub>6</sub>)  $\delta$  7.45 (d, J = 1.1 Hz, 4H, Ar–H), 7.39 (d, J = 1.1 Hz, 1H, C<sub>2</sub>–H), 6.08 (d, J = 0.9 Hz, 1H, C<sub>6</sub>–H), 2.29 (d, J = 1.1 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (101 MHz, DMSOd<sub>6</sub>)  $\delta$  163.83 (N=C–S), 162.73 (CON, C-5), 159.23 (C-7), 136.46 (C-3), 133.59, 131.49, 131.21, 127.48 (Ar–C), 112.03 (C-2), 104.96 (C-6), 23.42 (CH<sub>3</sub>); HRMS (m/z): calcd for C<sub>13</sub>H<sub>10</sub>ClN<sub>2</sub>OS (neutral M + H) 277.02024; found 277.022425.

# 7-Amino-3-(3-nitrophenyl)-5H-thiazolo[3,2-a]pyrimidin-5one **4e**

Yellow solid; yield: 92.01 %; m.p. 256.1.1–258.0 °C; IR  $(v_{max}/cm^{-1})$ : 3404, 3389 (NH), 1693 (C=O); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ )  $\delta$  8.28–8.20 (m, 2H, Ar–H), 7.86 (dt, J = 7.6, 1.3 Hz, 1H, Ar–H), 7.70–7.60 (m, 1H, Ar–H), 7.23 (s, 1H, C<sub>2</sub>–H), 6.78 (s, 2H, 7-NH<sub>2</sub>), 4.95 (s, 1H, C<sub>6</sub>–H); <sup>13</sup>C NMR (101 MHz, DMSO- $d_6$ )  $\delta$  164.64 (N=C–S), 162.91 (CON, C-5), 159.50 (C-7), 146.85 (C-3), 135.98, 135.47, 134.38, 128.77, 124.30, 123.23 (Ar–C), 109.76 (C-2), 80.05 (C-6); HRMS (m/z): calcd for C<sub>12</sub>H<sub>9</sub>N<sub>4</sub>O<sub>3</sub>S (neutral M + H) 289.03954; found 289.041969.

## 7-Amino-3-(4-nitrophenyl)-5H-thiazolo[3,2-a]pyrimidin-5one **4f**

Yellow solid; yield: 91.14 %; m.p. 241.1–242.4 °C; IR  $(v_{max}/cm^{-1})$ : 3445, 3337 (NH), 1683 (C=O); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ )  $\delta$  8.23–8.18 (m, 2H, Ar–H), 7.70–7.63 (m, 2H, Ar–H), 7.24 (s, 1H, C<sub>2</sub>–H), 6.79 (s, 2H, 7-NH<sub>2</sub>), 4.95 (s, 1H, C<sub>6</sub>–H); <sup>13</sup>C NMR (101 MHz, DMSO- $d_6$ )  $\delta$  164.65 (N=C–S), 162.91 (CON, C-5), 159.34 (C-7), 147.21 (C-3), 139.29, 135.69, 130.63, 122.42 (Ar–C), 110.31 (C-2), 79.97 (C-6); HRMS (m/z): calcd for C<sub>12</sub>H<sub>9</sub>N<sub>4</sub>O<sub>3</sub>S (neutral M + H) 289.03954; found 289.041732.

7-Amino-3-(p-tolyl)-5H-thiazolo[3,2-a]pyrimidin-5-one 4g

Yellow solid; yield: 90.71 %; m.p. 201.5–202.3 °C; IR ( $v_{max}/cm^{-1}$ ): 3380, 3341 (NH), 1721 (C=O); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ )  $\delta$  7.25 (d, J = 7.8 Hz, 2H, Ar–H), 7.15 (d, J = 7.9 Hz, 2H, Ar–H), 6.96 (d, J = 1.1 Hz, 1H, C<sub>2</sub>–H), 4.95 (s, 1H, C<sub>6</sub>–H), 2.34 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (101 MHz, DMSO- $d_6$ )  $\delta$  162.61 (N=C–S), 159.41 (CON, C-5), 157.37 (C-7), 137.82 (C-3), 129.78, 129.34, 127.93, 126.56 (Ar–C), 107.43 (C-2), 80.22 (C-6), 21.30 (CH<sub>3</sub>); HRMS (m/z): calcd for C<sub>13</sub>H<sub>12</sub>N<sub>3</sub>OS (neutral M + H) 258.07011; found 258.081756.

# 7-Amino-3-(4-chlorophenyl)-5H-thiazolo[3,2-a]pyrimidin-5-one **4h**

Yellow solid; yield: 90.66 %; m.p. 175.0–177.4 °C(lit. (Hurst *et al.*, 1988) 75 %; m.p. 186–188 °C); IR ( $\nu_{max}$ / cm<sup>-1</sup>): 3374, 3341 (NH), 1717 (C=O); <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  8.19 (s, 1H, Ar–H), 7.66 (s, 2H, Ar–H), 7.31 (s, 1H, Ar–H), 7.00–6.92 (m, 1H, C<sub>2</sub>–H), 5.14 (s, 1H, C<sub>6</sub>–H); <sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  164.65 (N=C–S), 159.81 (CON, C-5), 159.36 (C-7), 147.27 (C-3), 139.07, 130.69, 124.67, 122.47 (Ar–C), 112.99 (C-2), 80.21 (C-6); HRMS (m/z): calcd for C<sub>12</sub>H<sub>9</sub>ClN<sub>3</sub>OS (neutral M + H) 278.01549; found 278.017832.

#### General procedure for preparation of compounds 5

A suspension of nitro compounds 4 (3.53 mmol) in ethanol (60 mL) and water (30 mL) was treated with ammonium chloride (0.1888 g, 3.53 mmol) and iron powder (0.9857 g, 17.65 mmol). After being stirred at 80 °C for 2 h, the mixture was filtered while hot. The filtrate was washed with hot ethanol and concentrated. The resulting concentrate was allowed to in an ice bath, and the precipitate was filtered.

# 3-(3-Aminophenyl)-7-methyl-5H-thiazolo[3,2-a]pyrimidin-5-one **5a**

Yellow solid; yield: 78.84 %; m.p. 231.6–237.3 °C; IR ( $v_{max}/cm^{-1}$ ): 3426, 3316(N–H), 1685 (C=O), 1621 (N–H); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ )  $\delta$  7.21 (d, J = 1.7 Hz, 1H, C<sub>2</sub>–H), 7.01 (td, J = 7.8, 1.6 Hz, 1H, Ar–H), 6.59 (dd, J = 7.5, 1.8 Hz, 1H, Ar–H), 6.60–6.47 (m, 2H, Ar–H), 6.05 (d, J = 1.6 Hz, 1H, C<sub>6</sub>–H), 5.17 (s, 2H, phenyl-NH<sub>2</sub>), 2.28 (d, J = 1.6 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (101 MHz, DMSO- $d_6$ )  $\delta$  163.97 (N=C–S), 162.69 (CON, C-5), 158.98 (C-7), 148.02 (C-3), 138.57, 132.89, 128.09, 117.30, 115.01, 114.32 (Ar–C), 110.40 (C-2), 104.91 (C-6), 23.49 (CH<sub>3</sub>); HRMS (m/z): calcd for C<sub>13</sub>H<sub>12</sub>N<sub>3</sub>OS (neutral M + H) 258.07011; found 258.071755. 3-(4-Aminophenyl)-7-methyl-5H-thiazolo[3,2-a]pyrimidin-5-one **5b** 

Yellow solid; yield: 80.16 %; m.p. 205.3–206.2 °C; IR ( $v_{max}$ /cm<sup>-1</sup>): 3419, 3318(NH), 1688 (C=O), 1623 (NH); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ )  $\delta$  7.08–7.06 (m, 1H, C<sub>2</sub>–H), 7.04 (dd, J = 8.4, 1.8 Hz, 2H, Ar–H), 6.52 (dt, J = 8.3, 1.6 Hz, 2H, Ar–H), 6.02 (d, J = 1.8 Hz, 1H, C<sub>6</sub>–H), 5.36 (s, 2H, phenyl-NH<sub>2</sub>), 2.26 (d, J = 1.8 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (101 MHz, DMSO- $d_6$ )  $\delta$  164.06 (N=C–S), 162.47 (CON, C-5), 159.41 (C-7), 149.49 (C-3), 139.19, 130.56, 119.42, 112.52 (Ar–C), 108.56 (C-2), 104.93 (C-6), 23.43 (CH<sub>3</sub>); HRMS (m/z): calcd for C<sub>13</sub>H<sub>12</sub>N<sub>3</sub>OS (neutral M + H) 258.07011; found 258.070469.

# 7-Amino-3-(3-aminophenyl)-5H-thiazolo[3,2-a]pyrimidin-5-one **5c**

Yellow solid; yield: 75.23 %; m.p. 198.0–199.1 °C; IR ( $\nu_{max}$ /cm<sup>-1</sup>): 3464, 3304 (NH), 1671 (C=O), 1623(NH); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ )  $\delta$  6.97 (td, J = 7.8, 1.3 Hz, 1H, Ar–H), 6.88 (d, J = 1.3 Hz, 1H, C<sub>2</sub>–H), 6.66 (s, 2H, 7-NH<sub>2</sub>), 6.58–6.45 (m, 3H, Ar–H), 5.12 (s, 2H, phenyl-NH<sub>2</sub>), 4.91 (d, J = 1.3 Hz, 1H, C<sub>6</sub>–H); <sup>13</sup>C NMR (101 MHz, DMSO- $d_6$ )  $\delta$  164.91 (N=C–S), 162.66 (CON, C-5), 159.21 (C-7), 147.89 (C-3), 138.94, 133.53, 127.94, 117.20, 114.98, 114.07 (Ar–C), 106.81 (C-2), 80.14 (C-6); HRMS (m/z): calcd for C<sub>12</sub>H<sub>11</sub>N<sub>4</sub>OS (neutral M + H) 259.06536; found 259.065181.

7-Amino-3-(4-aminophenyl)-5H-thiazolo[3,2-a]pyrimidin-5-one **5d** 

Yellow solid; yield: 75.0 %; m.p. 201.3–202.8 °C; IR  $(v_{max}/cm^{-1})$ : 3323, 3162 (NH), 1650 (C=O), 1633 (NH); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ )  $\delta$  7.01 (dd, J = 8.3, 1.5 Hz, 2H, Ar–H), 6.74 (d, J = 1.4 Hz, 1H, C<sub>2</sub>–H), 6.62 (s, 2H, 7-NH<sub>2</sub>), 6.49 (dd, J = 8.3, 1.5 Hz, 2H, Ar–H), 5.29 (s, 2H, phenyl-NH<sub>2</sub>), 4.93–4.88 (m, 1H, C<sub>6</sub>–H); <sup>13</sup>C NMR (101 MHz, DMSO- $d_6$ )  $\delta$  165.03 (N=C–S), 162.54 (CON, C-5), 159.64 (C-7), 149.22 (C-3), 139.51, 130.38, 120.18, 112.46 (Ar–C), 105.01 (C-2), 80.29 (C-6); HRMS (m/z): calcd for C<sub>12</sub>H<sub>11</sub>N<sub>4</sub>OS (neutral M + H) 259.06536; found 259.064633.

#### General procedure for preparation of compounds 6

A mixture of compounds 4 (1.0 mmoL), 3-methylbenzoyl chloride (0. 1855 g, 1.2 equiv., 1.2 mmol) and triethylamine (0.2024 g, 2 equiv., 2.0 mmol) was refluxed at 80 °C for 2 h. After the completion of reaction, the reaction was quenched with water and extracted with dichloromethane. Finally, the combined organic layer was washed with brine and dried over anhydrous  $Na_2SO_4$ . After removal of the solvent in vacuum, the residue was purified by recrystallization.

# 3-Methyl-N-(3-(3-nitrophenyl)-5-oxo-5H-thiazolo[3,2a]pyrimidin-7-yl)benzamide **6a**

White solid; yield: 89.73 %; m.p. 297.1–298.4 °C. IR  $(v_{max}/cm^{-1})$ : 3428 (NH), 1685 (C=O); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ )  $\delta$  10.91 (s, 1H, CONH), 8.35 (t, J = 2.0 Hz, 1H, Ar–H), 8.30 (ddd, J = 8.2, 2.4, 1.1 Hz, 1H, Ar–H), 7.94 (dt, J = 7.7, 1.3 Hz, 1H, Ar–H), 7.87 (s, 1H, Ar–H), 7.82 (d, J = 7.4 Hz, 1H, Ar–H), 7.87 (s, 1H, Ar–H), 7.82 (d, J = 7.4 Hz, 1H, Ar–H), 7.71 (t, J = 8.0 Hz, 1H, Ar–H), 7.53 (d, J = 0.9 Hz, 1H, C<sub>2</sub>–H), 7.48–7.35 (m, 2H, Ar–H), 7.06 (d, J = 0.9 Hz, 1H, C<sub>6</sub>–H), 2.40 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (101 MHz, DMSO- $d_6$ )  $\delta$  167.17 (CONH), 163.68 (N=C–S), 160.45 (CON, C-5), 155.42 (C-7), 146.98 (C-3), 138.26, 136.25, 135.48, 133.81, 133.75, 133.47, 129.20, 129.00, 128.80, 125.77, 124.64, 123.63 (Ar–C), 112.65 (C-2), 91.85 (C-6), 21.34 (CH<sub>3</sub>); HRMS (m/z): calcd for C<sub>20</sub>H<sub>15</sub>N<sub>4</sub>O<sub>4</sub>S (neutral M + H) 407.08140; found 407.081802.

## 3-Methyl-N-(3-(4-nitrophenyl)-5-oxo-5H-thiazolo[3,2a]pyrimidin-7-yl)benzamide **6b**

White solid; yield: 84.79 %; m.p. 306.0–306.8 °C. IR ( $\nu_{max}/cm^{-1}$ ): 3368 (NH), 1685 (C=O); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ )  $\delta$  10.92 (s, 1H, CONH), 8.31–8.22 (m, 2H, Ar–H), 7.90–7.78 (m, 2H, Ar–H), 7.83–7.71 (m, 2H, Ar–H), 7.55 (s, 1H, C<sub>2</sub>–H), 7.49–7.37 (m, 2H, Ar–H), 7.07 (s, 1H, C<sub>6</sub>–H), 2.40 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (101 MHz, DMSO- $d_6$ )  $\delta$  167.14 (CONH), 163.68 (N=C–S), 160.26 (CON, C-5), 155.38 (C-7), 147.49 (C-3), 138.56, 138.22, 135.65, 133.77, 133.44, 130.94, 129.16, 128.77, 125.73, 122.57 (Ar–C), 113.11 (C-2), 91.76 (C-6), 21.29 (CH<sub>3</sub>); HRMS (m/z): calcd for C<sub>20</sub>H<sub>15</sub>N<sub>4</sub>O<sub>4</sub>S (neutral M + H) 407.08140; found 407.081674.

# 3-Methyl-N-(5-oxo-3-(p-tolyl)-5H-thiazolo[3,2-a]pyrimidin-7-yl)benzamide **6c**

White solid; yield: 85.84 %; m.p. 231.8–232.9 °C. IR ( $v_{max}/$  cm<sup>-1</sup>): 3431 (NH), 1683 (C=O); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ )  $\delta$  10.86 (s, 1H, CONH), 7.86 (s, 1H, Ar–H), 7.81 (dt, J = 7.6, 1.7 Hz, 1H, Ar–H), 7.47–7.37 (m, 2H, Ar–H), 7.33 (d, J = 7.8 Hz, 2H, Ar–H), 7.25 (s, 1H, C<sub>2</sub>–H), 7.20 (d, J = 7.8 Hz, 2H, Ar–H), 7.03 (d, J = 1.1 Hz, 1H, C<sub>6</sub>–H), 2.38 (d, J = 9.1 Hz, 6H, two CH<sub>3</sub>); <sup>13</sup>C NMR (101 MHz, DMSO- $d_6$ )  $\delta$  167.09 (CONH), 163.87 (N=C–S), 160.21 (CON, C-5), 155.13 (C-7), 138.23 (C-3), 138.20, 138.16, 133.83, 133.38, 129.56, 129.41, 129.15, 128.74, 128.08, 125.71 (Ar–C), 110.11 (C-2), 91.83 (C-6), 21.33 (CH<sub>3</sub>),

21.29 (CH<sub>3</sub>); HRMS (m/z): calcd for  $C_{21}H_{18}N_3O_2S$  (neutral M + H) 376.11197; found 376.112952.

# *N-(3-(4-Chlorophenyl)-5-oxo-5H-thiazolo[3,2-a]pyrimidin-7-yl)-3-methylbenzamide* **6***d*

White solid; yield: 89.10 %; m.p. 228.1–230.6 °C. IR  $(v_{max}/cm^{-1})$ : 3380 (NH), 1688 (C=O); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ )  $\delta$  10.88 (s, 1H, CONH), 7.89–7.75 (m, 2H, Ar–H), 7.51–7.38 (m, 6H, Ar–H), 7.36 (s, 1H, C<sub>2</sub>–H), 7.04 (s, 1H, C<sub>6</sub>–H), 2.40 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (101 MHz, DMSO- $d_6$ )  $\delta$  167.12 (CONH), 163.76 (N=C–S), 160.28 (CON, C-5), 155.26 (C-7), 138.22 (C-3), 136.71, 133.80, 133.64, 133.41, 131.53, 131.12, 129.16, 128.76, 127.51, 125.73 (Ar–C), 111.21 (C-2), 91.82 (C-6), 21.31 (CH<sub>3</sub>); HRMS (m/z): calcd for C<sub>20</sub>H<sub>15</sub>ClN<sub>3</sub>O<sub>2</sub>S (neutral M + H) 396.05735; found 396.057856.

#### **Biological activity**

The standard strains were obtained from National Center for Medical Culture Collection. The antibacterial activity of the synthesized compounds was performed by conventional broth microdilution method against two Gram-positive bacterial strains: *Staphylococcus aureus* [CMCC (B) 26003] and *Bacillus subtilis* [CMCC(B) 63501]; two Gram-negative bacterial strains: *Escherichia coli* [CMCC (B) 44102] and *Pseudomonas aeruginosa* [CMCC (B) 10104].

A standard inoculum  $(1.5 \times 10^7 \text{ c.f.u/mL } 0.5 \text{ McFar-}$ land standards) was introduced onto the surface of sterile agar plates. The tested compounds and reference drugs were dissolved in MeOH to get a solution of 2 mg/mL concentration. The series diluted compounds in Mueller-Hinton Broth were dispensed into 96-well microtiter plates (200 µL/well), and then, an aliquot of  $5 \times 10^5$  c.f.u/mL of bacterial culture was added to each well to final concentrations in a range of 1–800 µg/mL. After incubating at 37 °C for 24 h, the lowest concentration required to arrest the growth of bacteria was recorded as the MIC value. MeOH showed no inhibition effect. Ciprofloxacin was used as reference antibacterial agent.

*Mycobacterium smegmatis* [CGMCC (B) 1.2621] was obtained from China General Microbiological Culture Collection Center. MIC of compounds was determined against *Mycobacterium smegmatis* strain by using broth microdilution assay. Rifampicin was used as a reference drug.

## Conclusion

The present research study reports the successful synthetic method leading to 7-substituted-5*H*-thiazolo[3,2-a]pyrimidin-5-ones or corresponding sulfonic acid derivatives at

different temperature in high yield and purity. The structures are fully supported by spectroscopic data. All the synthesised compounds were tested for their antibacterial and antitubercular activities. These compounds showed significant activity against Gram-negative bacteria, and the sulfonic acid group in the phenyl ring did not seem to have a remarkable contribution to the antibacterial activity. The presence of substituted benzoylamido moiety at the C-7 position of 5*H*-thiazolo[3,2-a]pyrimidin-5-ones showed enhanced their antibacterial and antitubercular activities.

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#### Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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