Med Chem Res (2016) 25:292–302
DOI 10.1007/s00044-015-1481-y

MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

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

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

Received: 8 August 2015 / Accepted: 18 November 2015 / Published online: 1 December 2015

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_2 group of 5*H*-thiazolo[3,2-a]pyrimidin-5-ones afforded amide derivatives, and reduction of the NO_2 group of 5*H*-thiazolo[3,2-a]pyrimidin-5-ones gave amino derivatives. All the new compounds were confirmed by ^{1}H NMR, ^{13}C NMR, IR and HRMS spectra, and their antibacterial and antitubercular activities were screened. Some compounds showed significant antibacterial and antitubercular activities.

Keywords Thiazole · Cyclization · Thiazolopyrimidine · Antibacterial · Antitubercular

Electronic supplementary material The online version of this article (doi:10.1007/s00044-015-1481-y) contains supplementary material, which is available to authorized users.

✉ Dong Cai
Caidong0804@163.com

Zhi-Hua Zhang
Bridge1026@163.com

Yu Chen
gzweishengwu@126.com

Xin-Jia Yan
yanxinjia@yeah.net

[1] Liaoning Medical University, Jinzhou 121000, China

[2] School of Chemical and Environmental Engineering, Liaoning University of Technology, Jinzhou 121001, China

[3] School of Life Science and Biopharmaceutics, Shenyang Pharmaceutical University, Shenyang 110016, China

[4] College of Pharmacy, Harbin University of Commerce Harbin, Harbin 150076, China

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.

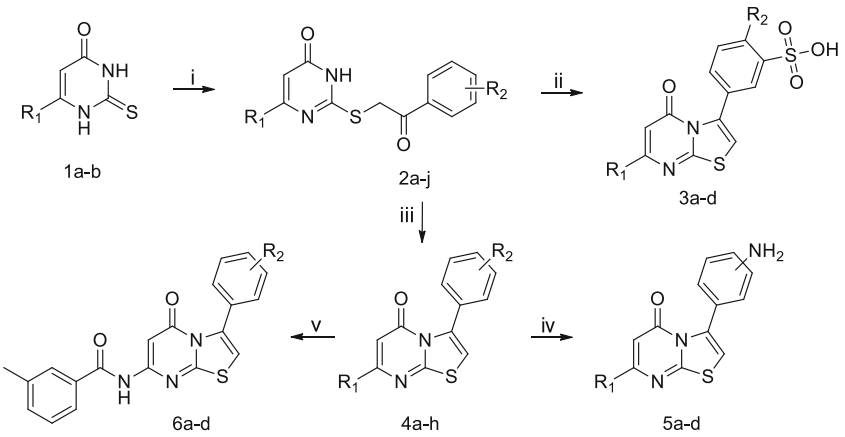
6-Substituted anilino-2-thiouracils **1a–b** were nearly quantitatively *S*-alkylated with the appropriate substituted phenacyl halides in the presence of anhydrous K_2CO_3 to give compounds **2a–j**. These intermediates **2a–j** were of sufficient purity (by TLC) to be used in subsequent reactions without 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 ^{1}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 δ 4.84 ppm. The signal of the 5-H proton of pyrimidine is observed at δ 6.04 ppm as a singlet. The signal of the N3-H proton appeared at δ 12.79 ppm as a broad singlet. Within the aromatic region, a multiplet appeared at δ 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 δ 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 δ 2.25 and δ 1.99 were all assigned to CH_3. 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 δ 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 one-pot 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: 5*H*-thiazolo[3,2-a]pyrimidin-5-ones and 7*H*-thiazolo[3,2-a]pyrimidin-7-ones. However, in practice cyclization of compounds **2a**–**j** was found to afford only the corresponding 5*H*-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_3, CH_3O). 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).



1a:R_1=CH_3
1b:R_1=NH_2

2a:R_1=CH_3,R_2=m-NO_2
2b:R_1=CH_3,R_2=p-NO_2
2c:R_1=CH_3,R_2=p-CH_3
2d:R_1=CH_3,R_2=p-Cl
2e:R_1=CH_3,R_2=p-CH_3O
2f:R_1=NH_2,R_2=m-NO_2
2g:R_1=NH_2,R_2=p-NO_2
2h:R_1=NH_2,R_2=p-CH_3
2i:R_1=NH_2,R_2=p-Cl
2j:R_1=NH_2,R_2=p-CH_3O

3a:R_1=CH_3,R_2=p-CH_3O
3b:R_1=CH_3,R_2=p-CH_3
3c:R_1=NH_2,R_2=p-CH_3O
3d:R_1=NH_2,R_2=p-CH_3

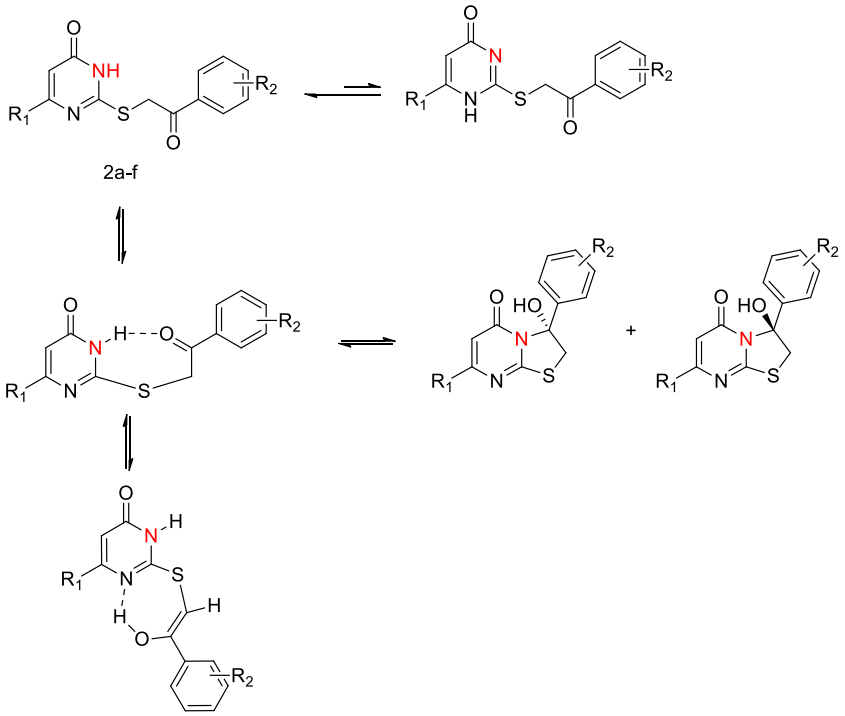
4a:R_1=CH_3,R_2=m-NO_2
4b:R_1=CH_3,R_2=p-NO_2
4c:R_1=CH_3,R_2=p-CH_3
4d:R_1=CH_3,R_2=p-Cl
4e:R_1=NH_2,R_2=m-NO_2
4f: R_1=NH_2,R_2=p-NO_2
4g:R_1=NH_2,R_2=p-CH_3
4h:R_1=NH_2,R_2=p-Cl

5a:R_1=CH_3,R_2=m-NH_2
5b:R_1=CH_3,R_2=p-NH_2
5c:R_1=NH_2,R_2=m-NH_2
5d:R_1=NH_2,R_2=p-NH_2

6a:R_2=m-NO_2
6b:R_2=p-NO_2
6c:R_2=p-CH_3
6d:,R_2=p-Cl

Scheme 1 Reagents and conditions: *i* K_2CO_3, DMF; *ii* concentrated H_2SO_4, 80 °C; *iii* concentrated H_2SO_4, 20 °C; *iv* Fe, NH_4Cl, 2:1 ethanol/water, 80 °C; *v* triethylamine, r.t., 2 h

Scheme 2 Possible interconversion of *S*-alkylated derivatives



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 α,β-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 5*H*-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 ^{1}H and ^{13}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 ($^{1}H/^{13}C$) 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 ***2f***

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 ***2j***

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-3-yl)benzenesulfonic acid ***3a***

Yellow solid; yield: 88.96 %; m.p. 283.2–284.8 °C; IR (ν_{max}/cm^{-1}): 3445 (SO_3H), 1726 (C=O); ^1H NMR (400 MHz, DMSO-d_6) δ 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_2–H), 6.96 (dd, $J = 8.6$, 1.1 Hz, 1H, Ar–H), 6.05 (s, 1H, C_6–H), 3.45 (qd, $J = 7.0$, 1.2 Hz, 3H, CH_3O), 2.28 (s, 3H, 7-CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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_3O), 18.99 (CH_3); HRMS (m/z): calcd for $C_{14}H_{13}N_2O_5S_2$ (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 (ν_{max}/cm^{-1}): 3440 (SO_3H), 1721 (C=O); ^1H NMR (400 MHz, DMSO-d_6) δ 7.74 (t, $J = 1.5$ Hz, 1H, Ar–H), 7.29 (d, $J = 1.2$ Hz, 1H, C_2–H), 7.28–7.12 (m, 2H, Ar–H), 6.08 (s, 1H, C_6–H), 2.57 (s, 3H, phenyl-CH_3), 2.29 (s, 3H, 7-CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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_3), 20.34 (CH_3); HRMS (m/z): calcd for $C_{14}H_{13}N_2O_4S_2$ (neutral M + H) 337.03167; found 337.023641.

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

Yellow solid; yield: 86.46 %; m.p. (dec.) 223.7 °C; IR (ν_{max}/cm^{-1}): 3332 (SO_3H), 1659 (C=O); ^1H NMR (400 MHz, DMSO-d_6) δ 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_2–H), 6.12 (broad, s, 2H, NH_2), 5.02–4.95 (m, 1H, C_6–H), 3.80 (d, $J = 2.6$ Hz, 3H, CH_3O); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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_3); HRMS (m/z): calcd for $C_{13}H_{12}N_3O_5S_2$ (neutral M + H) 354.02184; found 354.025808.

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

Yellow solid; yield: 87.52 %; m.p. 238.1–239.2 °C; IR (ν_{max}/cm^{-1}): 3342 (SO_3H), 1660 (C=O); ^1H NMR (400 MHz, DMSO-d_6) δ 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_2–H), 6.98 (s, 1H, Ar–H), 5.73 (broad, s, 2H, NH_2), 5.01 (s, 1H, C_6–H), 2.56 (s, 3H, phenyl-CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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_3); HRMS (m/z): calcd for $C_{13}H_{12}N_3O_4S_2$ (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 (ν_{max}/cm^{-1}): 1702 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6) δ 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_2–H), 6.10 (s, 1H, C_6–H), 2.31 (s, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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_3); HRMS (m/z): calcd for $C_{13}H_{10}N_3O_3S$ (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 (ν_{max}/cm^{-1}): 1731(C=O); ^{1}H NMR (400 MHz, DMSO-d_6) δ 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_2–H), 6.11 (d, $J = 1.5$ Hz, 1H, C_6–H), 2.30 (d, $J = 1.6$ Hz, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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_3); HRMS (m/z): calcd for $C_{13}H_{10}N_3O_3S$ (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 (ν_{max}/cm^{-1}): 1649 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.30 (s, 1H, C_2–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_6–H), 2.36 (s, 3H, CH_3), 2.29 (s, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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_3), 21.34 (CH_3); HRMS (m/z): calcd for $C_{14}H_{13}N_2OS$ (neutral M + H) 257.07486; found 257.088294.

3-(4-Chlorophenyl)-7-methyl-5H-thiazolo[3,2-a]pyrimidin-5-one ***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 (ν_{max}/cm^{-1}): 1647 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.45 (d, $J = 1.1$ Hz, 4H, Ar–H), 7.39 (d, $J = 1.1$ Hz, 1H, C_2–H), 6.08 (d, $J = 0.9$ Hz, 1H, C_6–H), 2.29 (d, $J = 1.1$ Hz, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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_3); HRMS (m/z): calcd for $C_{13}H_{10}ClN_2OS$ (neutral M + H) 277.02024; found 277.022425.

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

Yellow solid; yield: 92.01 %; m.p. 256.1.1–258.0 °C; IR (ν_{max}/cm^{-1}): 3404, 3389 (NH), 1693 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6) δ 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_2–H), 6.78 (s, 2H, 7-NH_2), 4.95 (s, 1H, C_6–H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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 $C_{12}H_9N_4O_3S$ (neutral M + H) 289.03954; found 289.041969.

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

Yellow solid; yield: 91.14 %; m.p. 241.1–242.4 °C; IR (ν_{max}/cm^{-1}): 3445, 3337 (NH), 1683 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.23–8.18 (m, 2H, Ar–H), 7.70–7.63 (m, 2H, Ar–H), 7.24 (s, 1H, C_2–H), 6.79 (s, 2H, 7-NH_2), 4.95 (s, 1H, C_6–H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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 $C_{12}H_9N_4O_3S$ (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 (ν_{max}/cm^{-1}): 3380, 3341 (NH), 1721 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6) δ 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_2–H), 4.95 (s, 1H, C_6–H), 2.34 (s, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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_3); HRMS (m/z): calcd for $C_{13}H_{12}N_3OS$ (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 (ν_{max}/cm^{-1}): 3374, 3341 (NH), 1717 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6) δ 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_2–H), 5.14 (s, 1H, C_6–H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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 $C_{12}H_9ClN_3OS$ (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 (ν_{max}/cm^{-1}): 3426, 3316(N–H), 1685 (C=O), 1621 (N–H); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.21 (d, J = 1.7 Hz, 1H, C_2–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_6–H), 5.17 (s, 2H, phenyl-NH_2), 2.28 (d, J = 1.6 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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_3); HRMS (m/z): calcd for $C_{13}H_{12}N_3OS$ (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 (ν_{max}/cm^{-1}): 3419, 3318(NH), 1688 (C=O), 1623 (NH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.08–7.06 (m, 1H, C_2–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_6–H), 5.36 (s, 2H, phenyl-NH_2), 2.26 (d, J = 1.8 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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_3); HRMS (m/z): calcd for $C_{13}H_{12}N_3OS$ (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 (ν_{max}/cm^{-1}): 3464, 3304 (NH), 1671 (C=O), 1623(NH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.97 (td, J = 7.8, 1.3 Hz, 1H, Ar–H), 6.88 (d, J = 1.3 Hz, 1H, C_2–H), 6.66 (s, 2H, 7-NH_2), 6.58–6.45 (m, 3H, Ar–H), 5.12 (s, 2H, phenyl-NH_2), 4.91 (d, J = 1.3 Hz, 1H, C_6–H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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 $C_{12}H_{11}N_4OS$ (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 (ν_{max}/cm^{-1}): 3323, 3162 (NH), 1650 (C=O), 1633 (NH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.01 (dd, J = 8.3, 1.5 Hz, 2H, Ar–H), 6.74 (d, J = 1.4 Hz, 1H, C_2–H), 6.62 (s, 2H, 7-NH_2), 6.49 (dd, J = 8.3, 1.5 Hz, 2H, Ar–H), 5.29 (s, 2H, phenyl-NH_2), 4.93–4.88 (m, 1H, C_6–H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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 $C_{12}H_{11}N_4OS$ (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[3,2-a]pyrimidin-7-yl)benzamide ***6a***

White solid; yield: 89.73 %; m.p. 297.1–298.4 °C. IR (ν_{max}/cm^{-1}): 3428 (NH), 1685 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6) δ 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), 7.71 (t, $J = 8.0$ Hz, 1H, Ar–H), 7.53 (d, $J = 0.9$ Hz, 1H, C_2–H), 7.48–7.35 (m, 2H, Ar–H), 7.06 (d, $J = 0.9$ Hz, 1H, C_6–H), 2.40 (s, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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_3); HRMS (m/z): calcd for $C_{20}H_{15}N_4O_4S$ (neutral M + H) 407.08140; found 407.081802.

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

White solid; yield: 84.79 %; m.p. 306.0–306.8 °C. IR (ν_{max}/cm^{-1}): 3368 (NH), 1685 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6) δ 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_2–H), 7.49–7.37 (m, 2H, Ar–H), 7.07 (s, 1H, C_6–H), 2.40 (s, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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_3); HRMS (m/z): calcd for $C_{20}H_{15}N_4O_4S$ (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 (ν_{max}/cm^{-1}): 3431 (NH), 1683 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6) δ 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_2–H), 7.20 (d, $J = 7.8$ Hz, 2H, Ar–H), 7.03 (d, $J = 1.1$ Hz, 1H, C_6–H), 2.38 (d, $J = 9.1$ Hz, 6H, two CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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_3), 21.29 (CH_3); 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 ***6d***

White solid; yield: 89.10 %; m.p. 228.1–230.6 °C. IR (ν_{max}/cm^{-1}): 3380 (NH), 1688 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6) δ 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_2–H), 7.04 (s, 1H, C_6–H), 2.40 (s, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 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_3); HRMS (m/z): calcd for $C_{20}H_{15}ClN_3O_2S$ (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 (1.5×10^7 c.f.u/mL 0.5 McFarland 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 5×10^5 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.

Acknowledgments The authors thank the Liaoning Medical University Principal Fund (No. XZJJ20130104-03) for the financial support of this research.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

References

Abdel-Mohsen HT, Conrad JR, Beifuss U (2013) Laccase-catalyzed domino reaction between catechols and 6-substituted 1, 2, 3, 4-tetrahydro-4-oxo-2-thioxo-5-pyrimidinecarbonitriles for the synthesis of pyrimidobenzothiazole derivatives. J Org Chem 78:7986–8003

Allen C, Beilfuss H, Burness D, Reynolds G, Tinker J, VanAllan J (1959) The structure of certain polyazaindenes. II. The product from ethyl acetoacetate and 3-amino-1, 2, 4-triazole. J Org Chem 24:787–793

Al-Omary FA, Hassan GS, El-Messery SM, El-Subbagh HI (2012) Substituted thiazoles V. Synthesis and antitumor activity of novel thiazolo[2, 3-b] quinazoline and pyrido [4, 3-d] thiazolo [3, 2-a] pyrimidine analogues. Eur J Med Chem 47:65–72

Andrew HF, Bradsher CK (1967) A new synthesis of thiazolo[3,2-a] pyrimidinones. J Heterocycl Chem 4:577–581

Angioni S, Villa DC, Dal Barco S, Quartarone E, Righetti PP, Tomasi C, Mustarelli P (2014) Polysulfonation of PBI-based membranes for HT-PEMFCs: a possible way to maintain high proton transport at a low H_3PO_4 doping level. J Mater Chem A 2:663–671

Awadallah FM (2008) Synthesis, pharmacophore modeling, and biological evaluation of novel 5*H*-Thiazolo[3, 2-a] pyrimidin-5-one derivatives as 5-HT2A receptor antagonists. Sci Pharm 76:415–438

Bakavoli M, Raissi H, Tajabadi J, Karimi M, Davoodnia A, Nikpour M (2008) Investigation into the regioisomeric composition of some fused pyrimidines: ^{1}H NMR and theoretical studies. J Sulphur Chem 29:25–30

Balkan A, Uma S, Ertan M, Wiegrebe W (1992) Thiazolo[3, 2-α]-pyrimidine derivatives as calcium antagonists. Pharmazie 47:687–688

Bondock S, El-Azab H, Kandeel E-EM, Metwally MA (2013) Efficient synthesis of new functionalized 2-(hetaryl) thiazoles. Synth Commun 43:59–71

Boucher HW, Talbot GH, Bradley JS, Edwards JE, Gilbert D, Rice LB, Scheld M, Spellberg B, Bartlett J (2009) Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. Clin Infect Dis 48:1–12

Brown D, Hoerger E, Mason S (1955) Simple pyrimidines. Part II. 1: 2-Dihydro-1-methylpyrimidines and the configuration of the *N*-methyluracils. J Chem Soc 211–217. doi:10.1039/JR9550000211

Cai J (2004) Structural chemistry and properties of metal arenesulfonates. Coord Chem Rev 248:1061–1083

Coates J, Sammes PG, West RM (1996) Enhancement of luminescence of europium (III) ions in water by use of synergistic chelation. Part 1. 1: 1 and 2: 1 complexes. J Chem Soc Perkin Trans 2:1275–1282

Dai Y, Guo Y, Frey RR (2005) Thienopyrimidine ureas as novel and potent multitargeted receptor tyrosine kinase inhibitors. J Med Chem 48:6066–6083

Dallinger D, Gorobets NY, Kappe CO (2003) High-throughput synthesis of N-3-acylated dihydropyrimidines combining microwave-assisted synthesis and scavenging techniques. Org Lett 5:1205–1208

Danel K, Pedersen EB, Nielsen C (1998) Synthesis and anti-HIV-1 activity of novel 2, 3-dihydro-7*H*-thiazolo[3, 2-a] pyrimidin-7-ones. J Med Chem 41:191–198

Dhapalapur M, Sabnis S, Deliwala C (1968) Potential anticancer agents. II. Schiff bases from benzaldehyde nitrogen mustards. J Med Chem 11:1014–1019

Doria G, Passarotti C, Sala R, Magrini R, Sberze P, Tibolla M, Ceserani R, Arcari G, Castello R, Toti D (1985) 7-trans-(2-Pyridylethenyl)-5H-thiazolo[3, 2-a] pyrimidine-5-ones: synthesis and pharmacological activity. II Farmaco 40:885–894

El-Bayouki KA, Basyouni WM (2010) Thiazolopyrimidines without bridge-head nitrogen: thiazolo [4, 5-d] pyrimidines. J Sulfur Chem 31:551–590

El-Emary T, Abdel-Mohsen SA (2006) Synthesis and antimicrobial activity of some new 1, 3-diphenylpyrazoles bearing pyrimidine, pyrimidinethione, thiazolopyrimidine, triazolopyrimidine, thio- and alkylthiotriazolop-yrimidinone moieties at the 4-position. Phosphorus Sulfur Silicon 181:2459–2474

Flefel E, Salama M, El-Shahat M, El-Hashash M, El-Farargy A (2007) A novel synthesis of some new pyrimidine and thiazolopyrimidine derivatives for anticancer evaluation. Phosphorus Sulfur Silicon 182:1739–1756

Fujiwara M, Inoi T (1992) Syntheses and anti-inflammatory activity of novel oximes and O-acyloximes. Chem Pharm Bull 40:2419–2422

Galasko GTF, Israelstam SS (1969) Reaction of aminoheterocycles with reactive esters. 2. 2-aminothiazoles. J South Afr Chem Inst 22:121–127

Geist JG, Lauw S, Illarionova V, Illarionov B, Fischer M, Gräwert T, Rohdich F, Eisenreich W, Kaiser J, Groll M (2010) Thiazolopyrimidine inhibitors of 2-methylerythritol 2, 4-cyclodiphosphate synthase (IspF) from mycobacterium tuberculosis and plasmodium falciparum. ChemMedChem 5:1092–1101

Ghorab M, Abdel-Gawad S, El-Gaby M (2000) Synthesis and evaluation of some new fluorinated hydroquinazoline derivatives as antifungal agents. II Farmaco 55:249–255

Hurst D, Beaumont C, Jones D, Kingsley D, Patridge J, Rutherford T (1988) The chemistry of pyrimidinethiols. II. The preparation and reactions of some 2-arenecarbonylmethylthiopyrimidines. Aust J Chem 41:1209–1219

Janietz D, Goldmann B, Rudorf WD (1988) Chlormethyl-substituierte heterocyclen aus chlortetrolsäuremethylester. J Prakt Chem 330:607–616

Jeanneau-Nicolle E, Benoit-Guyod M, Namil A, Leclerc G (1992) New thiazolo[3, 2-a] pyrimidine derivatives, synthesis and structure–activity relationships. Eur J Med Chem 27:115–120

Johnson TB, Moran RC, Kohmann EF (1913) 1, 4-Dithienes. I. J Am Chem Soc 35:447–452

Katritzky AR, Yang Y-K, Gabrielsen B, Marquet J (1984) Pyrylium-mediated transformations of natural products. Part 3. Synthesis of water-soluble pyrylium salts and their preparative reactions with amines. J Chem Soc Perkin Trans 2:857–866

Kaye PT, Meakin GD, Smith AK, Tirel MD (1983) *N*, *N*-disubstituted 2-aminothiazole-5-carboxylates: preparation and rotation of functional groups. J Chem Soc Perkin Trans 1:1677–1680

Khan RH, Rastogi RC (1991) Condensed heterocycles: synthesis and antifungal activity of π-deficient pyrimidines linked with π-rich heterocycles. J Agric Food Chem 39:2300–2303

Kolb S, Mondésert O, Goddard ML, Jullien D, Villoutreix BO, Ducommun B, Garbay C, Braud E (2009) Development of novel thiazolopyrimidines as CDC25B phosphatase inhibitors. ChemMedChem 4:633–648

Kwiatkowski J, Pullman B (1975) Taulomerism and electronic structure of biological pyrimidines. Adv Heterocycl Chem 18:199–335

Lin Y, Seifert C, Kang S, Dusza J, Lang S (1979) The synthesis of substituted 2-aminothiazoles. J Heterocycl Chem 16:1377–1383

Liu SJ, Shang R, Shi L, Wan DC-C, Lin H (2014) Synthesis and biological evaluation of 7*H*-thiazolo[3,2-b]-1,2,4-triazin-7-one derivatives as dual binding site acetylcholinesterase inhibitors. Eur J Med Chem 81:237–244

Maddila S, Damu G, Oseghe E, Abafe O, Rao CV, Lavanya P (2012) Synthesis and biological studies of novel biphenyl-3,5-dihydro-2*H*-thiazolopyrimidines derivatives. J Korean Chem Soc 56:334–340

Matiichuk V, Potopnyk M, Obushak N (2008) Molecular design of pyrazolo[3, 4-d] pyridazines. Russ J Org Chem 44:1352–1361

Meslin J-C, Quiniou H (1974) The syntheses of 6-oxo-(and 6-thioxo)-6*H*-1, 3-thiazines and 5-aroylthiazoles from *N*′-thioaroyl *N*, *N*-dimethylformamidines. Synthesis 1974:298–300

Meslin J, Quiniou H (1975) Enchainements heteroatomiques et leurs produits de cyclisation—II: *N*, *N*-dimethyl N′-thioaroylformamidines, aroyl-5 thiazoles et 6H-thiazine-1, 3 ones (thiones)-6 substitues. Tetrahedron 31:3055–3058

Mizutani M, Sanemitsu Y, Tamaru Y, Yoshida Z (1985) Palladium-catalyzed polyhetero-Claisen rearrangement of 2-(allylthio) pyrimidin-4 (3*H*)-ones. J Org Chem 50:764–768

Mohamed SF, Flefel EM, Amr AE-GE, El-Shafy DNA (2010) Anti-HSV-1 activity and mechanism of action of some new synthesized substituted pyrimidine, thiopyrimidine and thiazolopyrimidine derivatives. Eur J Med Chem 45:1494–1501

Nagarajaiah H, Khazi I, Begum NS (2012) Synthesis, characterization and biological evaluation of thiazolopyrimidine derivatives. J Chem Sci 124:847–855

Pan B, Huang R, Zheng L, Chen C, Han S, Qu D, Zhu M, Wei P (2011) Thiazolidione derivatives as novel antibiofilm agents: Design, synthesis, biological evaluation, and structure–activity relationships. Eur J Med Chem 46:819–824

Parekh NM, Maheria KC (2012) Antituberculosis and antibacterial evaluations of some novel phenyl pyrazolone-substituted 1*H*-benzo[g]pyrazolo[3, 4-b] quinoline-3-ylamine derivatives. Med Chem Res 21:4168–4176

Quan ZJ, Zhang Z, Wang JK, Wang XC, Liu YJ, Ji PY (2008) Efficient synthesis of 5*H*-thiazolo [3, 2-a] pyrimidines from reactions of 3, 4-dihydropyrimidine-thiones with α-bromoacetone in aqueous media. Heteroat Chem 19:149–153

Raval JP, Naik BN, Desai KR (2012) A convenient, rapid microwave-assisted synthesis of 2-substituted phenyl-2, 3-dihydrobenzo [B][1, 4] thiazepine-3-carboxamide derivatives and its antimicrobial activity. Phosphorus Sulfur Silicon Relat Elem 187:255–267

Schäfer H, Jablokoff H, Hentschel M, Gewald K (1984) 2-Arylaminothiophen-3-carbonsäurederivate. J Prakt Chem 326:917–923

Schäfer H, Gewald K, Bellmann P, Gruner M (1991) Synthese und reaktionen von 2-arylhydrazono-2-cyan-*N*, *N*-dialkyl-acetamidinen. Monatsh Chem 122:195–207

Simmons KJ, Chopra I, Fishwick CW (2010) Structure-based discovery of antibacterial drugs. Nat Rev Microbiol 8:501–510

Tang J, Lackey KE, Dickerson SH (2013) The discovery of potent and selective 4-aminothienopyridines as B-Raf kinase inhibitors. Bioorg Med Chem Lett 23:66–70

Tozkoparan B, Ertan M, Krebs B, Läge M, Kelicen P, Demirdamar R (1998) Condensed heterocyclic compounds: synthesis and anti-inflammatory activity of novel thiazolo [3, 2-a] pyrimidines. Arch Pharm 331:201–206

Tozkoparan B, Ertan M, Kelicen P, Demirdamar R (1999) Synthesis and anti-inflammatory activities of some thiazolo [3, 2-a] pyrimidine derivatives. II Farmaco 54:588–593

Veretennikov E, Pavlov A (2013) Synthesis of 5*H*-[1,3] thiazolo [3, 2-a] pyrimidin-5-one derivatives. Russ J Org Chem 49:575–579

Wichmann J, Adam G, Kolczewski S, Mutel V, Woltering T (1999) Structure–activity relationships of substituted 5*H*-thiazolo[3, 2-a] pyrimidines as group 2 metabotropic glutamate receptor antagonists. Bioorg Med Chem Lett 9:1573–1576

Youssef MM, Youssef AMS (2003) Reactions with 2-thiothymine; selective cyclization of S-substituted-2-thiothymine. Phosphorus Sulfur Silicon Relat Elem 178:67–81