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Tandem synthesis and antibacterial screening of new thieno[2,3-*b*]pyridine-fused pyrimidin-4(3*H*)-ones linked to thiazole or oxazole units

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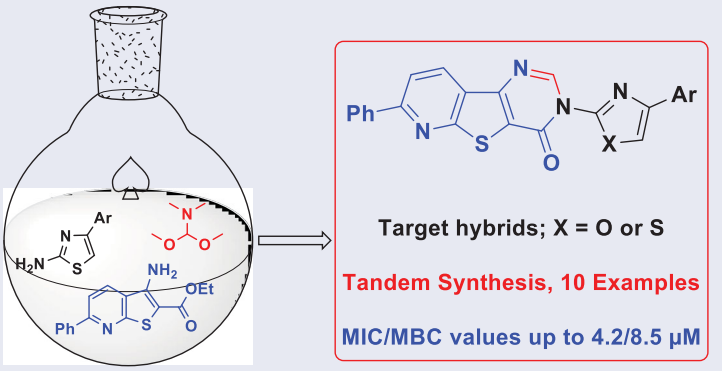
ABSTRACT

New two series of thieno[2,3-*b*]pyridine-fused pyrimidinones **1** and **2** linked to thiazole or oxazole units were prepared utilizing a three-component tandem protocol. Therefore, a mixture of 1 equiv. of 3-aminothieno[2,3-*b*]pyridine-2-carboxylate was first microwave irradiated with 1.5 equiv. of dimethylformamide-dimethylacetal in toluene was at 110 °C for 15 min. Next, the crude enamine was dissolved in dioxane and 1 equiv. of the respective 4-arylazole-based amines was added. The mixture was microwaved at 100 °C for 20–30 min, resulting in a 74–89% yield of the target pyrimidinones. The new products showed a wide spectrum of antibacterial activity. In general, oxazole-linked pyrimidinones **2** exceeded their analogs **1** attached to thiazole units in antibacterial activity. Hybrids **2d**, and **2e**, with 4-(*p*-tolyl)oxazole and 4-(4-methoxyphenyl)oxazole units, demonstrated the best antibacterial potency among the new products with MIC/MBC values of 4.4/8.8 and 4.2/8.5 µM, respectively. According to SwissADME, all new pyrimidinones could be classified as drug-like.

GRAPHICAL ABSTRACT



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In silico study; *in vitro* antibacterial activity; pyrimidinones; thieno[2,3-*b*]pyridine; three-component reactions

Introduction

The incidence of infectious diseases, especially those caused by new and emerging pathogens, has been on the rise in recent times.[1] Bacteria can develop resistance to

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antibiotics when their response to the drugs changes.[2] To combat this, more effort is being put into finding new, effective antibacterial agents to avoid resistance.[3]

Pyrimidine is a key unit that is found in many nucleic acids and nucleotides in nature, and compounds containing a pyrimidine core have a variety of potential uses in medicine, including fighting bacteria,[4,5] fungi,[6] viruses,[7] malaria,[8] and inflammation.[9] Pyrimidine derivatives have also been shown to be toxic to certain types of cancer cells in laboratory studies.[10,11] Pyrimidine-fused hybrids are promising drug candidates with a variety of pharmaceutical uses.[12] The synthesis of these structures is a rapidly expanding field in heterocyclic chemistry research,[13,14] due to their unique structures and potential applications in medicinal chemistry.[15,16]

Pyrimidine hybrids with fused thienopyridine structures are particularly important within the diverse group of pyrimidine hybrids. One example is pyrido[3′,2′:4,5]-thieno[3,2-*d*]pyrimidines, which are related to fluorene and contain 5-thia-1,3,6-triaza subunits.[17,18] Due to the various medicinal and pharmacological applications of these hybrids, there have been several published reports on their preparation.[19–21] These scaffolds have been found to inhibit mGluR1, which plays a role in the central sensitization of pain and has potential implications for neurological conditions.[22,23] In addition, pyridothienopyrimidine hybrids have also shown promise as inhibitors of phosphodiesterase IV, a target for the treatment of asthma and chronic obstructive pulmonary disease.[24] They have been found to act as potent and selective inhibitors of VEGFR-2/KDR kinase enzyme,[25] and multitarget Ser/Thr kinases.[26] These hybrids have also shown potential as antimicrobial[27,28] antifungal,[29] anticancer,[30] and antitumor agents.[31] Figure 1 illustrates some examples of potent bioactive pyridothienopyrimidine hybrids **I–VI** that have been reported in the literature.[22,25,28]

Organic chemists find the rapid synthesis of bioactive heterocycles to be an intriguing task.[32,33] In recent years, multicomponent reactions have become popular methods for synthesizing diverse and complex "drug-like" scaffolds that are linked to heterocyclic units.[34,35] These reactions involve combining three or more reactants to form the target product in a single step, and they have several advantages, including simplicity,

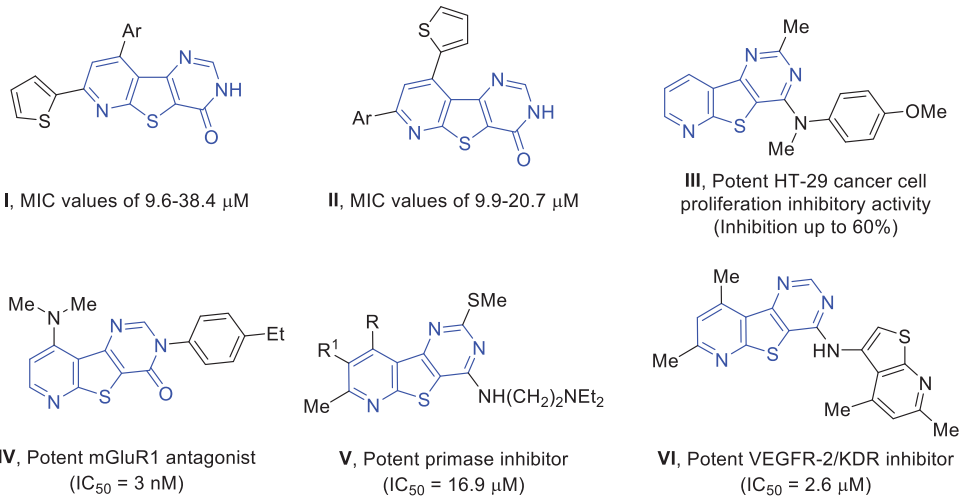


Figure 1. Structure of some potent bioactive pyrimidine-fused thieno[2,3-*b*]pyridine hybrids **I–VI**.

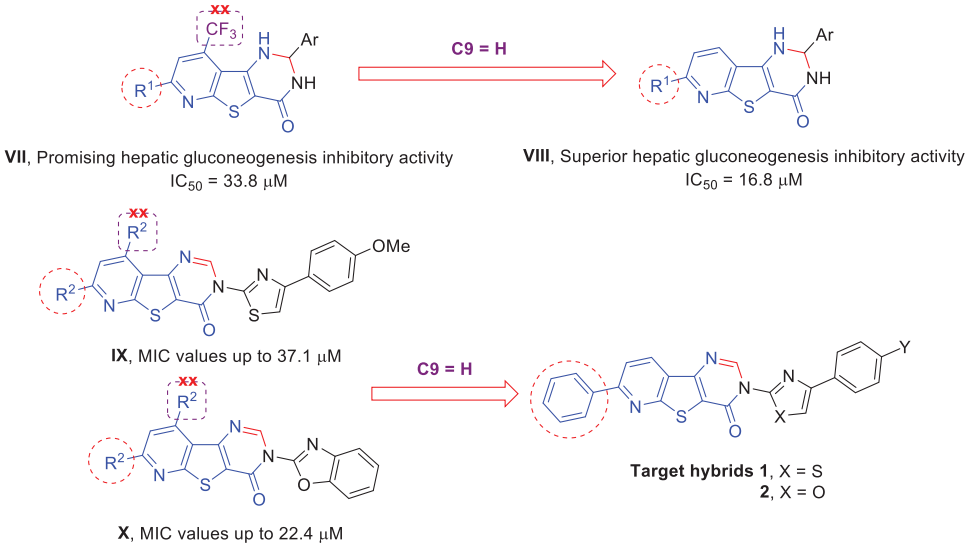


Figure 2. Structure of some azole-linked pyrimidines **VII–X** with promising antibacterial activity as well as the target hybrids **1(2)**.

shorter reaction times, higher efficiency, improved atom economy, and reduced by-product production.[36,37]

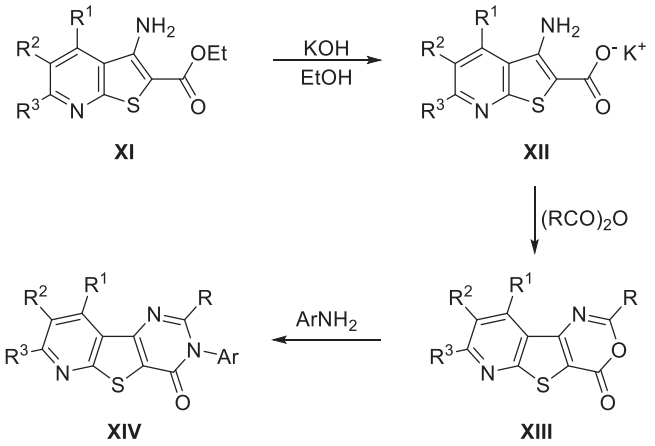
In 2017, Zhou et al.[38] reported the promising hepatic gluconeogenesis inhibitory activity of thieno[2,3-*b*]pyridine-fused pyrimidinones **VII**, which are linked to two substituents at C7 and C9. Additionally, Ma et al.[39] reported, in 2018, the superior inhibitory activity of pyrimidinone analogs **VIII**, which lack the substituent at C9. Recently, our research group reported the promising antibacterial activity of azole-linked pyrimidinones **IX** and **X**, which are linked to two methyl units at C7 and C9.[40] These findings stimulate our interest in investigating the bioactivity of new pyrimidinone derivatives linked to only one substituent at C7 (see Fig. 2).

In connection with our previous efforts in the multicomponent synthesis of biologically promising heterocyclic-based hybrids, particularly antibacterial activity,[41–46] we report herein an efficient method for the preparation of two new series of azole-linked pyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidinone hybrids **1(2)** (see Fig. 2). The antibacterial activity of the new products was screened against different ATCC bacterial strains. Additionally, SwissADME as well as drug-likeness model score were used to predict their pharmacological properties and drug-likeness.

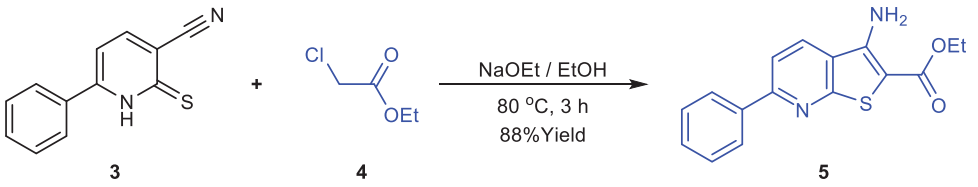
Results and discussion

Chemistry

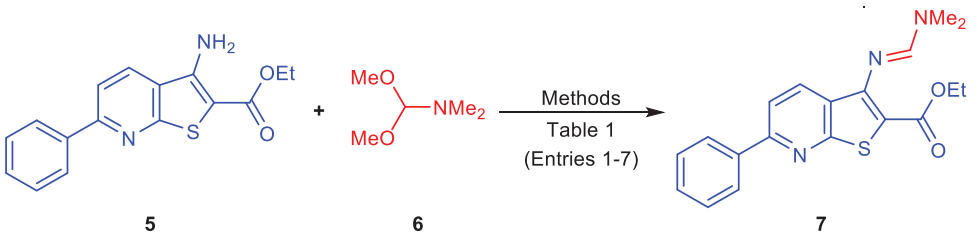
Bohm et al.[47] reported a three-step synthesis of pyrimidinone-based hybrids **XIV** using intermediate 3-aminothieno[2,3-*b*]pyridine-2-carboxylate **XI** (see Scheme 1). The process starts by heating **XI** in an alcoholic potassium hydroxide solution to form **XII**, which is then cyclocondensed with acid anhydrides to produce 2-alkyloxazinones **XIII**. The final products **XIV** are obtained by reacting **XIII** with primary amines. This study



Scheme 1. Previous preparation of pyrimidinones **XII**.



Scheme 2. Synthesis of intermediate **5**.



Scheme 3. Synthesis of enamine **7**.

describes a simple one-pot synthesis for thieno[2,3-*b*]pyridine-fused pyrimidinones using a three-component protocol.

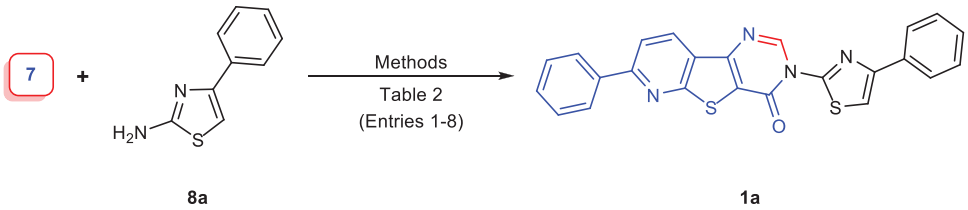
The intermediate 3-aminothieno[2,3-*b*]pyridine-2-carboxylate **5** was synthesized for the current study.[48] This synthon was produced in good yield by reacting pyridine-2(1*H*)-thione **3** with ethyl 2-chloroacetate **4** in ethanolic sodium ethoxide solution at 80 °C for 3 h (see Scheme 2).

We began our investigation using 3-aminothieno[2,3-*b*]pyridine-2-carboxylate **5** as the precursor for synthesizing related fused pyrimidinone derivatives. One equivalent of compound **5** was reacted with 1.5 equiv. of dimethylformamide-dimethylacetal (DMF-DMA) **6** (see Scheme 3).[22] To optimize the reaction, various solvents were tested with both conventional heating and microwave irradiation. In general, microwave irradiation resulted in higher yields of the desired intermediate **7** (see Table 1). The thieno[2,3-

Table 1. Synthesis of enamine **7** under either microwave irradiation or conventional method.

			[a]Thermal heating		[a,c]Microwave irradiation	
Entry	Solvent	Temp. (°C)	Time (h)	[b]Yield (%)	Time (min)	[b]Yield (%)
1	Dioxane	100	12	49	40	62
2	DMF	150	12	45	40	56
3	Benzene	80	10	69	30	86
4	Xylene	140	10	66	30	82
5	Toluene	70	12	52	30	75
6	Toluene	90	10	66	20	83
7	Toluene	110	8	74	15	97

[a]The reactions were followed up by TLC analyses.
[b]Isolated yields.
[c]The reactions were irradiated by microwaves of power 300 W.



Scheme 4. Synthesis of thiazole-linked pyrimidinone **1a**.

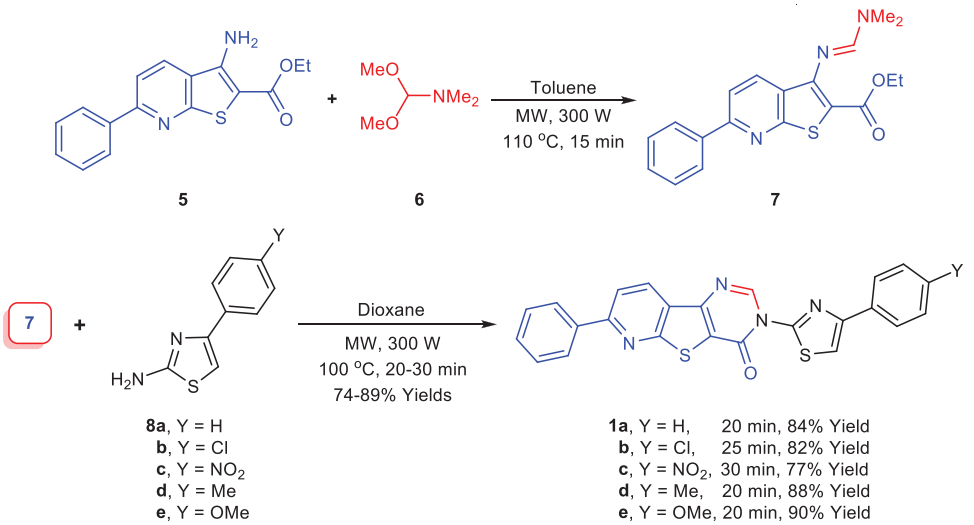
b]pyridine-based enamine intermediate **7** was obtained in yields of 45–62% by performing the reaction in polar solvents like dioxane at 100 °C or DMF at 150 °C (Table 1, Entries 1 and 2). In addition, compound **7** was obtained with yields of 66–86% by performing the reaction in non-polar solvents like benzene at 80 °C or xylene at 140 °C (Table 1, Entries 3 and 4). Moreover, the effect of toluene on the formation of **7** was studied at temperatures between 70 and 110 °C. The experiments were performed either through traditional heating for 8–12 h or through microwave exposure for 15–30 min (Table 1, Entries 5–7). The mixture of **5** and **6** was microwaved in toluene at 110 °C for 15 min, yielding **7** with a 97% yield (Table 1, Entry 7).

After that, the reaction between 1 equiv. each of enamine **7** and 4-phenylthiazol-2-amine **8a** was studied to synthesize the desired thiazole-linked pyrimidinone **1a** (see Scheme 4).[13,16] The optimal conditions for the reaction of the target pyrimidinone **1a** were investigated by testing different solvents and heating methods. The results showed that the use of microwave irradiation resulted in higher yields of the product, regardless of the polarity of the solvent, compared to conventional heating methods. Furthermore, the use of microwave irradiation led to a shorter reaction time and higher purity of the isolated product, as determined by TLC analyses (see Table 2). Conducting the reaction in non-polar solvents like benzene at 80 °C, toluene at 110 °C, or xylene at 140 °C only results in a 24–42% yield of pyrimidinone **1a** (Table 2, Entries 1–3). Additionally, the target pyrimidinone **1a** was obtained in 49–72% yield through the reaction in polar solvents like ethanol at 80 °C or DMF at 150 °C (Table 2, Entries 4 and 5). The impact of dioxane as a mediator in producing **1a** was also examined at temperatures from 60 to 100 °C using either conventional heating for 6–12 h or microwave irradiation for 20–40 min (Table 2, Entries 6–8). Microwaving the mixture of **7** and **8a** in dioxane at 100 °C for 20 min resulted in an 86% yield of **1a** (Table 2, Entry 8). In conclusion,

Table 2. Optimizing the synthesis of thiazole-linked pyrimidinone **1a**.

			[a]Thermal heating		[a,c]Microwave irradiation	
Entry	Solvent	Temp. (°C)	Time (h)	[b]Yield (%)	Time (min)	[b]Yield (%)
1	Benzene	80	12	29	40	36
2	Toluene	110	12	35	40	42
3	Xylene	140	12	24	40	31
4	Ethanol	80	8	54	30	72
5	DMF	150	8	49	30	60
6	Dioxane	60	12	44	40	65
7	Dioxane	80	8	66	30	77
8	Dioxane	100	6	75	20	86

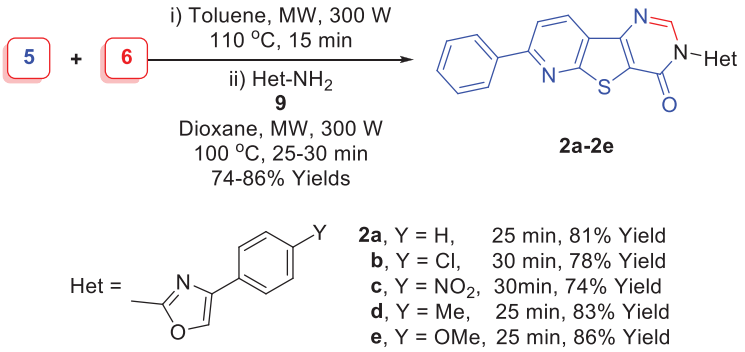
[a]The reactions were followed up by TLC analyses.
[b]Isolated yields.
[c]The reactions were irradiated by microwaves of power 300 W.



Scheme 5. Tandem synthesis of thiazole-linked pyrimidinones **1a–1e**.

microwave irradiation is a more efficient and effective method for the synthesis of the target pyrimidinone **1a**.

We aimed to synthesize target pyrimidinone **1a** using a three-step protocol, based on the above findings. We mixed 1 equiv. of intermediate **5** with 1.5 equiv. of DMF-DMA **6** in toluene and subjected the mixture to microwave irradiation at 110 °C. The TLC analysis was used to monitor the reaction. After 15 min, the enamine formation step was finished and the toluene and DMF-DMA were removed under reduced pressure. The crude enamine **7** was dissolved in dioxane without further purification and 4-phenylthiazol-2-amine **8a** was added to the mixture. The cyclocondensation step was performed using microwave irradiation at 100 °C. TLC analysis was conducted after 20 min to track the formation of pyrimidinone **1a**, yielding 84%. A new series of thiazole-linked pyrimidinones **1b–1e** was obtained with good yields by using the corresponding 4-arylthiazol-2-amines **8b–8e**. The progress of the cyclocondensation step was monitored by 20–30 min TLC analysis. The protocol resulted in the production of pyrimidinones **1b–1e** with yields of 77–90% (see Scheme 5).



Scheme 6. Tandem synthesis of oxazole-linked pyrimidinones **2a–2e**.

Table 3. MIC and MBC values in μM of new azole-linked pyrimidinones **1(2)**.

	MIC (MBC) in μM					
Compound	*S. aureus*	*S. mutans*	*E. faecalis*	*E. coli*	*P. aeruginosa*	*K. pneumonia*
1a	35.3 (70.7)	70.7 (141.5)	283.0 (>300)	35.3 (70.7)	70.7 (141.5)	283.0 (>300)
1b	65.6 (131.2)	131.2 (262.4)	>300 (>300)	65.6 (131.2)	131.2 (262.4)	>300 (>300)
1c	64.1 (128.3)	128.3 (256.7)	>300 (>300)	64.1 (128.3)	128.3 (256.7)	>300 (>300)
1d	17.1 (34.2)	34.2 (68.5)	137.1 (274.3)	17.1 (34.2)	34.2 (68.5)	137.1 (274.3)
1e	16.5 (33.1)	33.1 (66.2)	132.5 (265.0)	16.5 (33.1)	33.1 (66.2)	132.5 (265.0)
2a	9.1 (18.3)	18.3 (36.7)	73.4 (146.9)	9.1 (18.3)	18.3 (36.7)	73.4 (146.9)
2b	16.9 (33.9)	33.9 (67.9)	135.8 (271.7)	16.9 (33.9)	33.9 (67.9)	135.8 (271.7)
2c	16.6 (33.2)	33.2 (66.4)	132.8 (265.6)	16.6 (33.2)	33.2 (66.4)	132.8 (265.6)
2d	4.4 (8.8)	8.8 (17.7)	35.5 (71.1)	4.4 (8.8)	8.8 (17.7)	35.5 (71.1)
2e	4.2 (8.5)	8.5 (17.1)	34.3 (68.6)	4.2 (8.5)	8.5 (17.1)	34.3 (68.6)
Ciprofloxacin	2.9 (5.9)	2.9 (5.9)	2.9 (5.9)	2.9 (5.9)	2.9 (5.9)	2.9 (5.9)

This study also efficiently prepared another series of oxazole-linked pyrimidinones **2** using a similar protocol with slight modification. The cyclocondensation step was performed using a series of 4-aryloxazol-2-amines **9a–9e**. TLC analysis was used to monitor all reactions. Pyrimidinones **2a–2e** were produced in 74–86% yields after 25–30 min (see Scheme 6).

Biology

In vitro *antibacterial activity*

In vitro screening of the new azole-linked pyrimidinones **1(2)** was done against strains of *Staphylococcus aureus* (ATCC:6538), *Streptococcus mutans* (ATCC:25175), *Enterococcus faecalis* (ATCC:29212), *Escherichia coli* (ATCC:9637), *Pseudomonas aeruginosa* (ATCC:27953), and *Klebsiella pneumonia* (ATCC:10031). Ciprofloxacin served as a reference for the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) value determination against the selected strains (MIC/MBC values of 2.9/5.9 μM) (Table 3).[46,49–51]

Hybrids **2d** and **2e** generally displayed the highest antibacterial efficacy against all tested strains, with comparable activity to the reference ciprofloxacin on *S. aureus* and *E. coli*, with MIC/MBC values ranging from 4.4/8.8 and 4.2/8.5 μM, respectively. Additionally, they were the most effective against *S. mutans* and *P. aeruginosa*, though

they showed weaker activity than ciprofloxacin with MIC/MBC values ranging from 8.8/17.7 and 8.5/17.1 μM, respectively.

Furthermore, hybrid **2a** showed reduced efficacy against all tested strains, with MIC/MBC values of 9.1/18.3 μM against *S. aureus* and *E. coli*, and values of 18.3/36.7 μM against *S. mutans* and *P. aeruginosa*. The other hybrids displayed moderate to weak activity, with MIC and MBC values ranging from 16.6 to 65.6 and 33.2 to 131.2 μM against *S. aureus* and *E. coli*, and values ranging from 33.2 to 131.2 and 66.4 to 262.4 μM against *S. mutans* and *P. aeruginosa*. All hybrids tested showed weak to fair activity against *E. faecalis* and *K. pneumonia*, with MIC and MBC values ranging from 34.3 to over 300 μM.

Structure–activity relationship

In the present study, a new two series of thieno[2,3-*b*]pyridine-fused pyrimidinones **1** and **2** was successfully prepared. The new products **1** and **2** are linked to an azole unit at C3 that is connected to one of two heteroatoms (X). Series **1a–1e** are linked to a thiazole unit (X = S), while series **2a–2e** are linked to an oxazole unit (X = O). Additionally, each azole unit is linked to an arene unit at C4 that is attached to a para-substituent (Y) with diverse electronic properties.

Using *S. aureus* as a representative, we found that the tested series **1a–1e** (linked to thiazole, X = S) showed variable antibacterial efficacy. The potency of series **1a–1e** is linked to the electronic properties of the para-substituent (Y). As shown in Table 3, hybrid **1a** with Y = H had weak efficacy (MIC/MBC values of 35.3/70.7 μM). However, incorporating an electron withdrawing substituent (Y) in hybrids **1b** (Y = Cl) and **1c** ($Y = NO_2$) led to reduced antibacterial activity (MIC/MBC values of 65.6/131.2 and 64.1/128.3 μM, respectively). On the other hand, incorporating an electron donating substituent (Y) in hybrids **1d** (Y = Me) and **1e** (Y = OMe) resulted in 2-fold more effective antibacterial activity than **1a** (MIC/MBC values of 17.1/34.2 and 16.5/33.1 μM, respectively).

The antibacterial activity of series **2**, linked to oxazole units, was tested and found to be superior to series **1** linked to thiazole units. As shown in Table 3, the obtained antibacterial activity of series **2a–2e** and the electronic properties of the substituent (Y) have the same relationship. Hybrid **2a** with X = O and Y = H was found to have 4 times higher potency than analog **1a** with X = S and Y = H, with MIC/MBC values of 9.1/18.3 μM. However, the addition of electron withdrawal substituents (Y) to hybrids **2b** and **2c** reduced the activity. Hybrids **2b** (Y = Cl) and **2c** ($Y = NO_2$) had MIC/MBC values of 16.9/33.9 and 16.6/33.2 μM, respectively. On the other hand, adding electron donating substituents (Y) to hybrids **2d** (Y = Me), and **2e** (Y = OMe) led to a nearly 2-fold increase in antibacterial activity compared to **2a**, resulting in the best antibacterial potency among the new products with MIC/MBC values of 4.4/8.8 and 4.2/8.5 μM, respectively.

As a result, the pattern of antibacterial activity for azole-linked pyrimidinones was X = O>S. The antibacterial potency improves with electron-releasing substituent (Y). These conclusions are summarized in Figure 3.

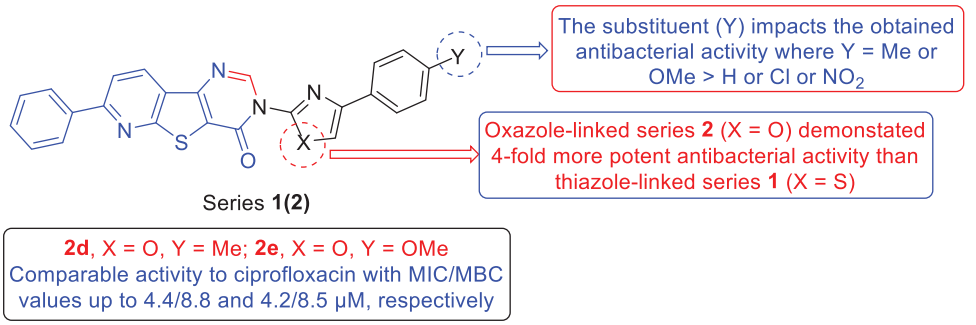


Figure 3. Structure-activity relationships of the target azole-linked pyrimidinones **1(2)**.

In silico *study: SwissADME predictions of new pyrimidinones 1(2)*

Table S1 in the Electronic Supplemental File shows the predicted values for various characteristics, including physicochemical properties, lipophilicity, solubility, pharmacokinetics, drug-likeness, and medicinal chemistry, of new pyrimidinones **1(2)** as determined by SwissADME (http://www.swissadme.ch).[52] The molecular weights for series **1** of compounds fall between 438.52 and 483.52 g/mol, with a range of rotatable bonds from 3 to 4, and H-bond acceptors from 4 to 6, with no H-bond donor. Their topological polar surface area (TPSA) varies from 117.15 to 162.97 Å^2. On the other hand, series **2** of compounds have molecular weights ranging from 422.46 to 467.46 g/mol, with a range of rotatable bonds from 3 to 4, and H-bond acceptors from 5 to 7, with no H-bond donor. Their TPSA ranges from 102.05 to 147.87 Å^2.

The ability of a drug to dissolve in fats and oils, known as lipophilicity, is a key descriptor in determining its pharmacokinetics and is measured by the partition coefficient between octanol and water (log $P_{o/w}$).[53] The SwissADME website provides several predictive models, including XLOGP3,[54] WLOGP,[55] and MLOGP,[56] which were used to evaluate the lipophilicity of tested drug hybrids. The lipophilicity of the hybrids in series **1**, as measured by XLOGP3, WLOGP, and MLOGP, falls within the ranges of 5.58–6.38, 5.79–6.44, and 2.57–4.02, respectively. Meanwhile, the lipophilicity of the hybrids in series **2**, as measured by the same models, falls within the ranges of 4.96–5.76, 5.32–5.97, and 2.19–3.61, respectively.

Lipinski's rule of five is a guideline for determining the oral bioavailability of a drug, which states that drugs should have a molecular weight of <500, no more than five hydrogen bond donors, no more than 10 hydrogen bond acceptors, and a log $P_{o/w}$ of <5.[57] All hybrids in series **1** or **2** had no violations., so they could be classified as drug-like. However, none of these hybrids met the criteria for lead-likeness, as they all had an XLOGP3 > 3.5 and a molecular weight >350.[58]

Conclusions

New series of thieno[2,3-*b*]pyridine-fused pyrimidinones were made using a three-step process. The process involved mixing 3-aminothieno[2,3-*b*]pyridine-2-carboxylate with DMF-DMA and microwaving, then adding the respective 4-arylazole-based amine and microwaving again to get the target pyrimidinones. The new products showed wide

spectrum antibacterial activity, with oxazole-linked pyrimidinones showing better activity than their thiazole-linked counterparts. All new pyrimidinones were considered drug-like by SwissADME.

Experimental

Materials

All solvents were acquired from commercial sources and used as received unless otherwise stated. All other chemicals were acquired from Merck or Aldrich. These chemicals were used without further purification. Microwave experiments were performed using CEM Discover apparatus (300 W), utilizing 35 mL capped glass reaction vessels Automated power control based on temperature feedback. The melting points were measured on a Stuart melting point apparatus and are uncorrected. IR spectra were recorded on a Smart iTR, which is an ultra-high-performance, versatile attenuated total reflectance (ATR) sampling accessory on the Nicolet iS10 FT-IR spectrometer manufactured. NMR spectra were recorded on a Bruker Avance III 400 spectrometer (400 MHz for ^{1}H-NMR and 100 MHz for ^{13}C-NMR) using TMS as an internal standard and DMSO-d_6 as solvent and chemical shifts were expressed as δ ppm units. Mass spectra were recorded on a GC-MS-QP1000EX spectrometer using inlet type at 70 eV. Elemental analyses were carried out on a EuroVector instrument C, H, N analyzer EA3000 Series. For the characterization and spectral data of all new products, see the Electronic Supplementary File.

General procedure for the tandem synthesis of thieno[2,3-b]pyridine-fused pyrimidinone hybrids 1(2)

A mixture of 3-aminothieno[2,3-*b*]pyridine-2-carboxylate **5** (1 mmol) and dimethylformamide-dimethylacetal (DMF-DMA) **6** (1.5 mmol) in toluene (5 mL) was irradiated by microwaves with a power of 300 W to reach a reaction temperature of 110 °C under autogenerated pressure for 15 min. After the enamine formation-step was completed (monitored by TLC), the solvent and the excess DMF-DMA was evaporated under reduced pressure to give the crude enamine **7**, which was then re-dissolved in dioxane (10 mL) and each of the respective 4-arylthiazol-2-amines **8a–8e** or 4-aryloxazol-2-amines **9a–9e** (1 mmol) was added. The previous mixture was irradiated by microwaves with a power of 300 W to reach a reaction temperature of 100 °C under autogenerated pressure for 20–30 min. After the cyclocondensation-step was completed (monitored by TLC), the mixture was reduced under reduced pressure and then 2 mL of ethanol was added. The obtained product was collected by filtration, washed with cold ethanol, dried, and recrystallized from the appropriate solvent.

7-Phenyl-3-(4-phenylthiazol-2-yl)pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidin-4(3H)-one (1a)

Pale yellow solid (dioxane, 84%); m.p. 230–233 °C; IR (υ cm^{-1}): 1652 (CO); ^{1}H-NMR (DMSO-d_6): δ 7.40–7.48 (m, 3H, ArH), 7.52 (s, 1H, thiazole-H), 7.55–7.61 (m, 3H,

ArH), 7.89 (d, $J = 7.6$ Hz, 2H, ArH), 8.13 (s, 1H, H2), 8.18–8.21 (m, 3H, 2 ArH and H8), 8.49 (d, $J = 5.6$ Hz, 1H, H9); ^{13}C-NMR (DMSO-d_6): δ 112.7, 114.3, 123.8, 126.5, 127.6, 128.0, 128.5, 128.8, 129.1, 129.3, 130.4, 133.0, 135.2, 141.0, 144.3, 150.5, 152.4, 152.6, 157.6, 164.7; MS *m/z* (%): 438 (M^+, 36.2); Anal. calcd. for $C_{24}H_{14}N_4OS_2$: C, 65.74; H, 3.22; N, 12.78; found: C, 65.98; H, 3.07; N, 12.55%.

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