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Communication

Synthesis and Antimicrobial Evaluation of 2-(6-Imidazo[1,2-*a*]pyridin-2-yl-5-methyl-2,4-dioxo-3-phenyl-3,4-dihydrothieno[2,3-*d*]pyrimidin-1(2*H*)-yl)-*N*-arylacetamide Derivatives

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Abstract: 6-Heteryl-5-methylthieno[2,3-*d*]pyrimidin-2,4(1*H*,3*H*)-diones are of great interest as the promising objects for the search of antibacterials. In this communication, we obtained 6-(imidazo[1,2-*a*]pyridin-2-yl)-5-methyl-3-phenylthieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione by interaction of 6-(bromoacetyl)-5-methyl-3-phenylthieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione with 2-aminopyridine. The obtained heterocyclic hybrid was further modified by alkylation with 2-chloroarylacetamides. Antimicrobial activity studies for the synthesized compounds using the agar well diffusion method revealed their moderate activity against *S. aureus*, *E. coli* and *B. subtilis*. According to the double dilution assay MIC value results for 6-(imidazo[1,2-*a*]pyridin-2-yl)-5-methyl-3-phenylthieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dioneagainst *P. aeruginosa* was less than the value determined for the reference drug streptomycin. The docking study of the synthesized compounds to the active site of TrmD isolated from *P. aeruginosa* did not show their effective inhibitory activity.

Keywords: thieno[2,3-*d*]pyrimidine; imidazo[1,2-*a*]pyridine; alkylation; antimicrobial activity

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1. Introduction

Derivatives with 6-heteryl-5-methylthieno[2,3-*d*]pyrimidin-2,4(1*H*,3*H*)-dione structures are of great importance as biologically active substances. Such compounds were patented as A2A adenosine receptor antagonists [1], which are useful in treating mammals for various disease states. Similar compounds, patented as acetyl-KoA carboxylase inhibitors, can be used to cure diseases caused by fatty acids metabolism dysfunction [2]. The modification of the 5-methylthieno[2,3-*d*]pyrimidin-2,4(1*H*,3*H*)-dione core with 1,3-thiazol-4-yl substituent has allowed the acquisition of compounds with antimicrobial activity against *S. aureus*, *P. aeruginosa* and *B. subtilis* (I) (Figure 1) [3].

Likewise, numerous articles have been published in the last decade about the antimicrobial activity of 6-heterylthieno[2,3-*d*]pyrimidines with unsubstituted position 2 [4–7] (II-V) (Figure 1), some of them containing fused systems of heterocycles such as 1,2,4-triazolo[3,4-*b*]1,3,4-thiadiazole (III) [5] or 1,3-benzoxazole (V) [7]. One of the latest works published was devoted to the study of the antimicrobial activity of 6-heteryl-5-methyl-2-thiothieno[2,3-*d*]pyrimidines, which can possibly act as inhibitors of bacterial TrmD VI (Figure 1) [8].

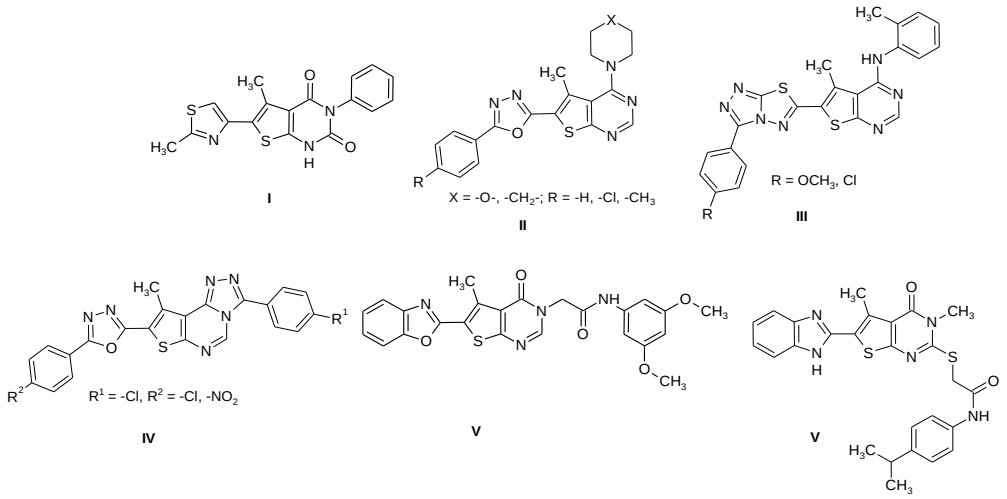


Figure 1. 6-Heteryl-5-methylthieno[2,3-*d*]pyrimidines with antimicrobial properties.

Several imidazo[1,2-*a*]pyridine derivatives were reported as compounds with antimicrobial properties which may be useful against parasites of the *Leishmania* genus (VII) (Figure 2) [9]; this heterocyclic system is the core structure of savolitinib [10], a mesenchymal epithelial transition factor (MET) inhibitor recently approved in China after the results of a pivotal phase II trial in patients with NSCLC/pulmonary sarcomatoid carcinoma [11]. This fragment is also a part of the innovative drug olprinone, which is a selective phosphodiesterase 3 (PDE3) inhibitor [12]. Imidazo[1,2-*a*]pyridines were also reported as antiproliferative agents [13], α-glucosidase inhibitors [14] and antimicrobials (VIII) (Figure 2) [15]; some of these compounds have shown promising antibacterial activity against *S. pyogenes*, *P. aeruginosa* and *S. aureus* (IX) (Figure 2) [16].

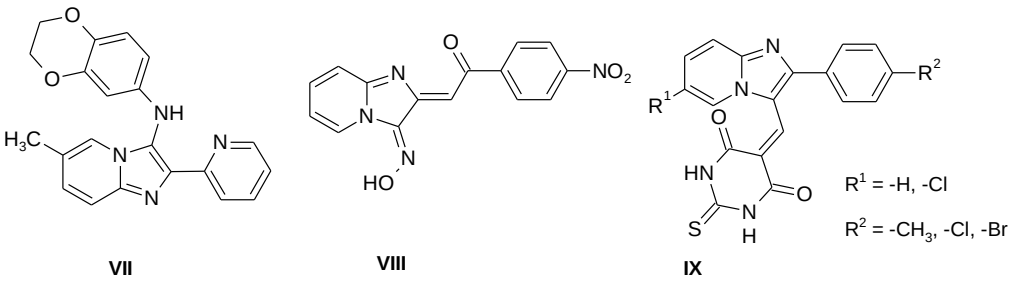


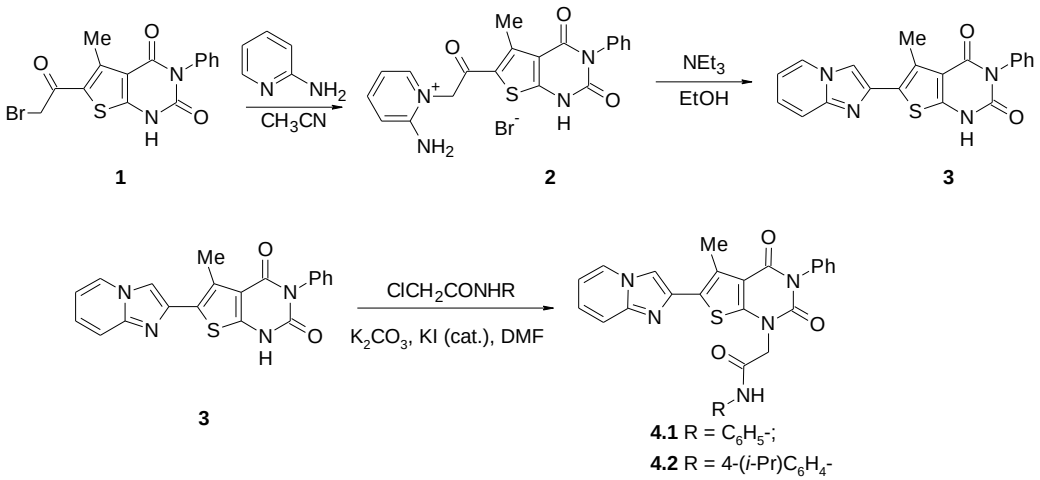
Figure 2. Antibacterial imidazo[1,2-*a*]pyridines.

In view of the published results about antimicrobial properties of 6-heterylthieno[2,3-*d*]pyrimidines as well as the promising pharmacological potential of imidazo[1,2-*a*]pyridines, we decided to modify position 6 of the 5-methylthieno[2,3-*d*]pyrimidin-2,4(1*H*,3*H*)-dione core with an imidazo[1,2-*a*]pyridine fragment as a possible approach towards active antibacterials.

2. Results and Discussion

The most common route for the preparation of imidazo[1,2-a]pyridines is the reaction of 2-aminoazines with α-haloketones [15–18]. As a part of our research on the construction of 6-heteryl-5-methylthieno[2,3-*d*]pyrimidin-2,4(1*H*,3*H*)-diones, we studied the interaction of the readily synthetically available 6-(bromoacetyl)-5-methyl-3-phenylthieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione **1** [3] with 2-aminopyridine. We tried a one-step approach and heated **1** with 2-aminopyridine in 2-propanol, which gave no product of any sufficient purity. Thus, we made the decision to separate the steps and to use the solvent where it was possible to carry out the reaction homogeneously at the first step. We applied a

two-step procedure where the alkylation was carried out in acetonitrile, which was used because of the good solubility of **1** in this solvent under heating. The formation of the product **2** can be easily tracked by its precipitation. A subsequent cyclization reaction was conducted in refluxing the ethanol-triethylamine system (Scheme 1). Although the cyclization step proceeds mostly heterogeneously, it provides the sufficient yield and purity of the product **3**.



Scheme 1. Synthesis of 2-(6-imidazo[1,2-*a*]pyridin-2-yl-5-methyl-2,4-dioxo-3-phenyl-3,4-dihydrothieno[2,3-*d*]pyrimidin-1(2*H*)-yl)-*N*-arylacetamides **4**.

The ^{1}H NMR spectrum of compound **3** has the distinctive peak of the methyl group at position 5 of thieno[2,3-*d*]pyrimidine system at 2.60 ppm and the singlet of imidazole part of imidazo[1,2-*a*]pyridine at 8.23 ppm; the signal of the NH proton of pyrimidine cycle was observed at 12.38 ppm.

The next step of the synthesis was alkylation of compound **3** with arylchloroacetamides in DMF media in the presence of potassium carbonate (1 equivalent) and a catalytic amount of potassium iodide. The slight heating (50–60 °C) was found useful to increase the homogenicity of the reaction.

Similarly to compound **3**, the ^{1}H NMR spectra of compounds **4.1** and **4.2** displayed the signal of the methyl group at position 5 of thieno[2,3-*d*]pyrimidine in the range of 2.65–2.85 ppm; the signal of the imidazole proton was observed at 8.27 ppm. The signals of the methylene protons of acetamide substituents at position 1 of thieno[2,3-*d*]pyrimidine core were observed in the region 4.84–4.85 ppm. For both derivatives **4.1** and **4.2**, the ^{1}H NMR spectra also contained the signals of amide NH in the region 10.37–10.44 ppm. In comparison with the spectrum of 3 ^{13}C, the NMR spectra of compounds **4.1** and **4.2** contained additional signals in the region of aromatic carbons' resonance and the signals of methyl group carbon atoms in the region 48.4–50.7 ppm.

The results of antimicrobial activity screening show that compounds **3**, **4.1** and **4.2** have moderate inhibitory activity against *Staphylococcus aureus*, *Escherichia coli* and *Bacillus subtilis*. None of the compounds inhibited the growth of the *Candida albicans* fungal strain (Table 1). Although the results of the well diffusion method suggest compound **4.1** as the one with the best screening results, according to the double dilution assay, compound **3** showed lower MIC values. Its inhibitory activity was better than those shown by metronidazole and in the case of *P. aeruginosa*, the MIC value of **3** was even lower than the inhibitory concentration of streptomycin.

To predict the possible mechanism of antibacterial action by 6-(imidazo[1,2-*a*]pyridin-2-yl)-5-methyl-3-phenylthieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones **3**, **4.1,** and **4.2**, the docking studies of these structures were performed on selective inhibitors of tRNA—(Guanine37-N^{1})-methyltransferase (TrmD). The structure of the enzyme isolated from *P. aeruginosa* was used for the study [19]. The validation of the docking methodology using the refer-

ence ligand—the competitive TrmD inhibitor *N*-(4-((octylamino)methyl)benzyl)-4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidine-5- carboxamide—is described in the previous paper [8]. The affinity of **3**, **4.1,** and **4.2** towards the active site was estimated by binding energy in comparison with the reference ligand. Compounds **3**, **4.1,** and **4.2** have a higher affinity (8.7, −10.6, and −10.8 kcal/mol respectively) than the reference inhibitor, which has an affinity as high as −8.2 kcal/mol.

Table 1. Antimicrobial activity of 6-(imidazo[1,2-*a*]pyridin-2-yl)-5-methyl-3-phenylthieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones **3, 4.1** and **4.2.**

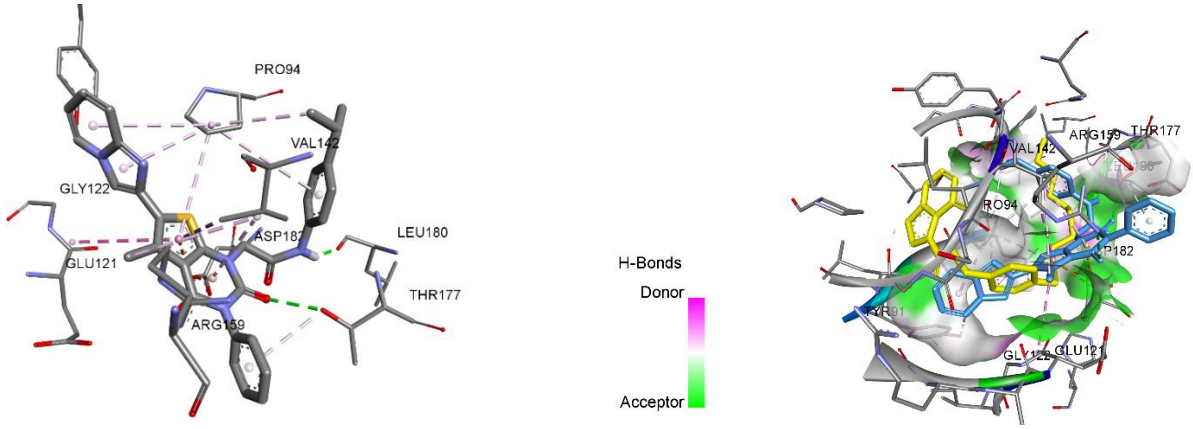
Compound	Diameters (mm) of Growth Inhibition Zone, Number of Test Repetitions *n* = 3 MIC mg/mL					
	Staphylococcus aureus ATCC 25923	*Escherichia coli ATCC 25922*	*Proteus vulgaris ATCC 4636*	*Pseudomonas aeruginosa ATCC 27853*	*Bacillus subtilis ATCC 6633*	*Candida albicans ATCC 653/885*
3	15, 14, 15 0.4	14, 13, 14 0.8	growth 0.8	growth 0.8	15, 14, 15 0.8	growth >10
4.1	18, 17, 18 0.8	16, 15, 16 3.2	15, 15, 15 3.2	15, 14, 14 3.2	17, 18, 17 0.8	growth >10
4.2	16, 15, 16 0.8	14, 15, 14 3.2	growth 3.2	growth 3.2	17, 17, 16 0.8	growth >10
Metronidazole	14, 15, 14 0.8	14, 13, 14 0.8	growth 6.4	growth 6.4	16, 15, 16 0.8	14, 14, 14 >10
Streptomycin	15, 16, 15 0.1	15, 16, 17 0.8	growth 0.8	growth 1.6	17, 16, 17 0.2	growth 3.2

The docking study predicts a possible stable conformation due to hydrophobic interactions that is additionally stabilized with hydrogen bonds (Figure 3a). Among the amino acids that influence the conformation of the ligand, only proline (PRO94), glutamic (GLU121) and aspartic acids residues (ASP182) belong to the active site (Table 2). Interaction of tyrosine residues (Tyr141, and 120) with TrmD inhibitors is known to be crucial for TrmD inhibition, but it was not observed in the case of compounds **3**, **4.1**, and **4.2**. 6-(Imidazo[1,2-*a*]pyridin-2-yl)-5-methyl-3-phenylthieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones **3**, **4.1** and **4.2** do not interact with residues of glutamine (Gln95) and glycines (Gly 118, 145,146), which bind the methionine fragment of SAM [19]. This predicts absence of the interaction with the hydrophobic pocket of the active site. Comparative conformations of **3**, **4.1** and **4.2** with the reference inhibitor evidently show their inability to enter the hydrophobic pocket and to reach the place of thienopyrimidine pharmacophore fixing. Hence, despite good calculated values of scoring functions, the ligands' pose analysis shows the low probability for the compounds **3**, **4.1** and **4.2** to be the inhibitors of bacterial TrmD.

Table 2. The results of the docking studies of 3, 4.1 and 4.2 and the native inhibitor to the active site of *P. aeruginosa* TrmD.

Ligand	Binding Energy Kcal/Mol	Hydrophobic Interaction	Hydrogen Interaction	Other Interaction
Reference Inhibitor	−8.2	TYR141, SER93 (2) [#], PRO94 (4), PRO149 (2), ILE138, LEU143, GLY 145, GLY146	LEU143, GLN95, GLU121, Gly139, ASP182	-
3	−8.7	VAL142 (3) *, GLU121, GLY122 *, PRO94 (3)	ARG159 *, THR177 *, TYR91 *	ASP182 (Pi-Anion)
4.1	−10.6	VAL142 (3) *, GLU121,GLY122 *, PRO94 (3)	ARG159 *, THR177(3) *, TYR91 *, GLU121	ASP182 (Pi-Anion)
4.2	−10.8	VAL142 (3) *, GLU121, GLY122*, PRO94 (5)	ARG159 *, THR177(3) *, LEU180 *, TYR91 *	ASP159 * (Pi-Anion)

[#] The number of bonds is given in brackets. * The amino acids that do not interact with the native ligand in the experiment.



(**a**) (**b**)

Figure 3. 3-D visualization: (**a**) interaction of the ligand **4.2** with amino acids of the active site of TrmD; (**b**) conformational pose of the reference inhibitor (yellow molecule) [19] and the ligand **4.2** (blue molecule) in the active site of *P. aeruginosa* TrmD.

3. Materials and Methods

3.1. Materials and Instrumentation

All solvents and reagents were obtained from commercial sources or prepared by previously reported methods. Melting points were determined in a capillary using an electrothermal IA9100X1 (Bibby Scientific Limited, Staffordshire, UK) digital melting point apparatus. Elemental analyses were performed on a Euro Vector EA-3000 (Eurovector SPA, Redavalle, Italy) microanalyzer and were within 0.4% of the theoretical values. ^{1}H NMR spectra for compound **3** were recorded with a Varian Mercury (200 MHz) in DMSO-d_6. In all other cases, they were acquired with a Bruker Avance drx 500 (500 MHz) in DMSO-d_6; the latter was also used for measurement of the ^{13}C NMR (125 MHz) in CF_3COOD for compound **3** and in DMSO-d_6 for the compounds **4.1** and **4.2**. TMS was used as an internal standard.

Mass-spectral analyses for the compound **3** were obtained on a PE SCIEX API 150EX-MS spectrometer (SCIEX, Singapore, The Republic of Singapore) with turbo ion spray sources device (API+); for compounds **4**, LC-MS analysis was performed on an Agilent 1100 HPLC apparatus with diode array and mass-selective detectors (Agilent, Santa Clara, CA, USA), Zorbax SB-C18 column (4.6 × 150 mm) with chemical ionization at atmospheric pressure (APCI) (Please see the supplementary materials).

3.2. Chemical Part

The starting 6-(bromoacetyl)-5-methyl-3-phenylthieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione **1** was obtained using a previously reported procedure [3].

Procedure for synthesis of 6-(imidazo[1,2-a]pyridin-2-yl)-5-methyl-3-phenylthieno[2,3-d] pyrimidine-2,4(1H,3H)-dione **3**

To 3.0 g (0.008 mol) of 6-(bromoacetyl)-5-methyl-3-phenylthieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione **1** in 20 mL of acetonitrile, 0.75 g (0.008 mol) of 2-aminopyridine was added and the reaction mixture was heated at reflux until the formation of the first crystals of the product and then additionally for 1–2 h. The precipitate formed was filtered off and dried. The product was used for the next step without additional purification. To 2.8 g of the product isolated in previous step, 0.82 mL (0.006 mol) of trimethylamine in 50 mL ethanol was added and the mixture was refluxed for 8–10 h. The reaction mixture was cooled and the precipitate was filtered off and washed with ethanol (10 mL × 3).

Yield: 52%, m.p. >300 °C, beige solid. ^{1}H NMR (200 MHz, DMSO-d_6): δ: 2.60 (s, 3H, CH_3), 6.91 (t, 1H, *J* = 6.9 Hz, Ar-H), 7.19–7.61 (m, 7H, Ar-H), 8.23 (s, 1H, Ar-H), 8.51 (d, 1H, *J* = 6.9 Hz, Ar-H), 12.38 (s, 1H, NH). ^{13}C NMR (125 MHz, CF_3COOD): δ 12.3, 110.1, 110.8,

111.8, 112.3, 112.9, 114.6, 116.8, 117.6, 127.1, 127.4, 129.3, 129.6, 131.6, 134.5, 138.3, 139.4, 152.4. LC-MS *m*/*z* (ES+) 375.2 (MH^+). Anal. calcd. for $C_{20}H_{14}N_4O_2S$ (374.42): C, 64.16; H, 3.77; N, 14.96. Found: C, 64.22; H, 3.83; N, 15.02.

General procedure for synthesis of 2-(6-imidazo[1,2-a]pyridin-2-yl-5-methyl-2,4-dioxo-3-phenyl-3,4-dihydrothieno[2,3-d]pyrimidin-1(2H)-yl)-N-arylacetamides **4.1**, **4.2**

To the suspension of 0.15 g (0.0004 mol) of 6-(imidazo[1,2-*a*]pyridin-2-yl)-5-methyl-3-phenylthieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione **3** and 0.056 g (0.4 mmol) in 5 mL of dimethylformamide, 0.4 mmol of corresponding phenyl chloroacetamide and catalytic amount of potassium iodide was added. The reaction mixture was stirred and heated (40–50 °C) for 5–6 h. Then the reaction mixture was cooled and quenched with water (20 mL). The resulting precipitate was filtered off and dried. The products were additionally crystallized from an ethanol-DMF mixture.

2-[6-(Imidazo[1,2-a]pyridin-2-yl)-5-methyl-2,4-dioxo-3-phenyl-3,4-dihydrothieno[2,3-d] pyrimidin-1(2H)-yl]-N-phenylacetamide **4.1**

Yield: 83%, m.p. >300 °C, beige solid. ^{1}H NMR (500 MHz, DMSO-d_6): δ: 2.65 (s, 3H, CH_3), 4.85 (s, 2H, CH_2), 6.91 (t, 1H, *J* = 5.8 Hz, Ar-H), 7,07 (t, 1H, *J* = 5.8 Hz, Ar-H), 7.20–7.64 (m, 11H, Ar-H), 8,27 (s, 1H, Ar-H), 8.52 (d, 1H, *J* = 5.8 Hz, Ar-H), 10.44 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 14.7, 50.7, 109.9, 113.0, 114.8, 116.5, 119.7, 123.9, 124.2, 124.5, 126.2, 127.4, 128.7, 129.3, 129.4, 131.0, 136.3, 137.9, 138.8, 144.2, 150.5, 154.4, 159.0, 164.5. LC-MS *m*/*z* (ES+) 508.0 (MH^+). Anal. calcd. for $C_{28}H_{21}N_5O_3S$ (507.58): C, 66.26; H, 4.17; N, 13.80. Found: C, 66.30; H, 4.20; N, 13.84.

2-[6-(Imidazo[1,2-a]pyridin-2-yl)-5-methyl-2,4-dioxo-3-phenyl-3,4-dihydrothieno[2,3-d] pyrimidin-1(2H)-yl]-N-[4-(propan-2-yl)phenyl]acetamide **4.2**

Yield: 74%, m.p. >300 °C, white solid. ^{1}H NMR (500 MHz, DMSO-d_6): δ: 1.15 (d, 6H, *J* = 6.9 Hz, $2CH_3$); 2.65 (s, 3H, CH_3), 2.81 (sep, 1H, *J* = 6.9 Hz, CH), 4.84 (s, 2H, CH_2), 6.91 (t, 1H, *J* = 6.4 Hz, Ar-H), 7.18 (d, 2H, *J* = 8.1 Hz, Ar-H), 7.22–7.32 (m, 3H, Ar-H), 7.38–7.55 (m, 6H, Ar-H), 8,27 (s, 1H, Ar-H), 8.51 (d, 1H, J = 6.4 Hz, Ar-H), 10.37 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 12.4, 22.1, 31.0, 48.4, 107.7, 110.8, 112.6, 114.2, 117.5, 122.2, 123.9, 124.8, 125.1, 126.4, 127.1 (two peaks 127.16 and 127.17), 128.7, 134.1, 134.3, 135.7, 142.0 (two peaks 142,02 and 142.08), 148.3, 152.2, 156.7, 162.0. LC-MS *m*/*z* (ES+) 550.2 (MH^+). Anal. calcd. for $C_{31}H_{27}N_5O_3S$ (549.66): C, 67.74; H, 4.95; N, 12.74. Found: C, 67.83; H, 5.04; N, 12.79.

3.3. Microbiological Studies

The antimicrobial activity study was performed at Mechnikov Institute of Microbiology and Immunology of the NAMS of Ukraine, Kharkiv, Ukraine, the Laboratory of Biochemistry and Biotechnology (headed by Dr. Tetyana P. Osolodchenko).

According to the international and national recommendations [20–22], the following strains of micro-organisms were used as the test strains *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Proteus vulgaris* ATCC 4636, *Bacillus subtilis* ATCC 6633 and *Candida albicans* ATCC653/885.

The microbial suspension of microorganisms was prepared using a Densi-La-Meter device (manufactured by PLIVA-Lachema, Czech Republic; wavelength 540 nm). The microbial load was 10^7 microbial cells per 1 mL of medium and was established according to the MacFarland standard. An 18–24-h microorganism culture was used for the test. Muller–Hinton (HIMedia Laboratorles Pvt. Ltd., Mumbai, India) and Sabouraud agars (HIMedia Laboratorles Pvt. Ltd., Mumbai, India) were used in the studies. The studied compounds were administered in the form of DMSO solutions (concentration 100 μg/mL) in 0.3-mL aliquots; streptomycin and metronidazole were used as standards in the form of a solution in DMSO (30 μg/mL). The measurement for each sample was repeated three times. The antibacterial activity was assessed by measuring the growth inhibition zones of the corresponding microorganism.

The susceptibility of the microorganism strain to the tested compounds was estimated using the following criteria: inhibitory zone diameter less than 10 mm—no susceptibility

or low concentration of the compound; inhibitory zone diameter 10–15 mm—low susceptibility of the microorganism to the compound in the particular concentration; inhibitory zone diameter 15–25 mm—susceptibility of the microorganism to the compound in the particular concentration; inhibitory zone diameter more than 25 mm—high susceptibility of the microorganism to the compound in the particular concentration.

The minimal inhibitory concentrations (MICs) were determined by the broth double dilution method. The test was performed using 1 mL of each dilution with the concentration 5×10^5 CFU/mL. After the inoculation for 24 h (bacterial strains) and 48–72 h (C. albicans), test tubes were examined for growth of microorganisms. The minimal inhibitory concentration (MIC) was determined as the lowest concentration of a tested compound that inhibited the visible growth of a microorganism.

3.4. Molecular Docking Study

The molecular docking study was performed using AutoDock Vina and AutoDockTools 1.5.6 computer programs [23]. The target enzyme was acquired from Protein Data Bank [24]: TrmD *Pseudomonas aeruginosa* PDB ID—5ZHN. BIOVIADraw 2017R2 was used for drawing of the ligands, and mol format was used to store the structures. Optimization of structures was performed using Chem3D (MM2 algorithm) and the results were stored as pdb. AutoDockTools-1.5.6. was used for pdbqt format transformation. To the macromolecule, polar hydrogen atoms were added with Discovery Studio Visualizer 2017/R2 and AutoDockTools-1.5.6. The size and the center of the Grid box were aligned according to the center coordinates of the native ligand complex with A subunit of TrmD (PDB ID 5ZHN): x = 40.04, y = 107.23, z = −3.40; size x = 18, y = 22, z = 20. The results were visualized using Discovery Studio V17.2.0.16349.

4. Conclusions

Simple procedures for preparation of novel 6-(imidazo[1,2-*a*]pyridin-2-yl)-5-methyl-3-phenylthieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione derivatives were developed. The structures of the target molecules were confirmed using ^{1}H, ^{13}C NMR and LC-MS methods. These compounds, which are the derivatives of 6-heterylthieno[2,3-*d*]pyrimidines, are of great interest as possible antibacterials and were screened using both the agar well diffusion method and the double dilution method. Antimicrobial activity studies for the synthesized compounds using the agar well diffusion method revealed their moderate activity against *S. aureus*, *E. coli* and *B. subtilis*. According to the double dilution assay, the MIC value for 6-(imidazo[1,2-*a*]pyridin-2-yl)-5-methyl-3-phenylthieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione against *P. aeruginosa* was less than the value determined for the reference drug streptomycin.

Supplementary Materials: The following are available online: copies of LC-MS, ^{1}H, ^{13}C NMR, spectra for compounds **3** and **4**.

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