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Synthesis of Potentially Biologically Active Fused Polyheterocycles Containing a Pyrimidine Unit

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Abstract—A number of new fused polyheterocyclic compounds were synthesized on the basis of 2-amino-6-sulfanylpyrimidin-4(3*H*)-one. In particular, reactions of 2-amino-6-sulfanylpyrimidin-4(3*H*)-one with cinnamic acids, aroyl isothiocyanate, and acetic anhydride afforded imidazo[1,2-*a*]thieno[2,3-*d*]pyrimidine, [1,3]thiazino[6′,5′:4,5]pyrimido[1,2-*a*][1,3,5]triazine, and imidazo[1,2-*a*]thieno[2,3-*d*]pyrimidine derivatives, respectively. The alkylation of 2-amino-6-sulfanylpyrimidin-4(3*H*)-one with benzyl chloride gave 3-benzyl-6-(benzylsulfanyl)-2-imino-2,5-dihydropyrimidin-4(3*H*)-one which was converted to [1,3]thiazolo[5,4-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine, imidazo[1,2-*a*]pyrimidine, dihydropyrimido[4,5-*b*]quinoline, imidazo[1,2-*a*]pyrrolo[2,3-*d*]pyrimidine, and benzo[*g*]imidazo[2,1-*b*]pteridine derivatives via reactions with nitrous acid, ethyl chloroacetate, and aniline (followed by treatment with carbon disulfide, cinnamic acid, or sodium nitrite in acetic acid). 2-Amino-3,4-dihydropyrimidin-6-sulfonic acid was obtained by oxidation of the same substrate with hydrogen peroxide in alkaline medium. Some of the synthesized compounds showed antimicrobial activity.

Keywords: pyrimidine, pyrrole, fused pyrimidines, heterocylization, acylation.

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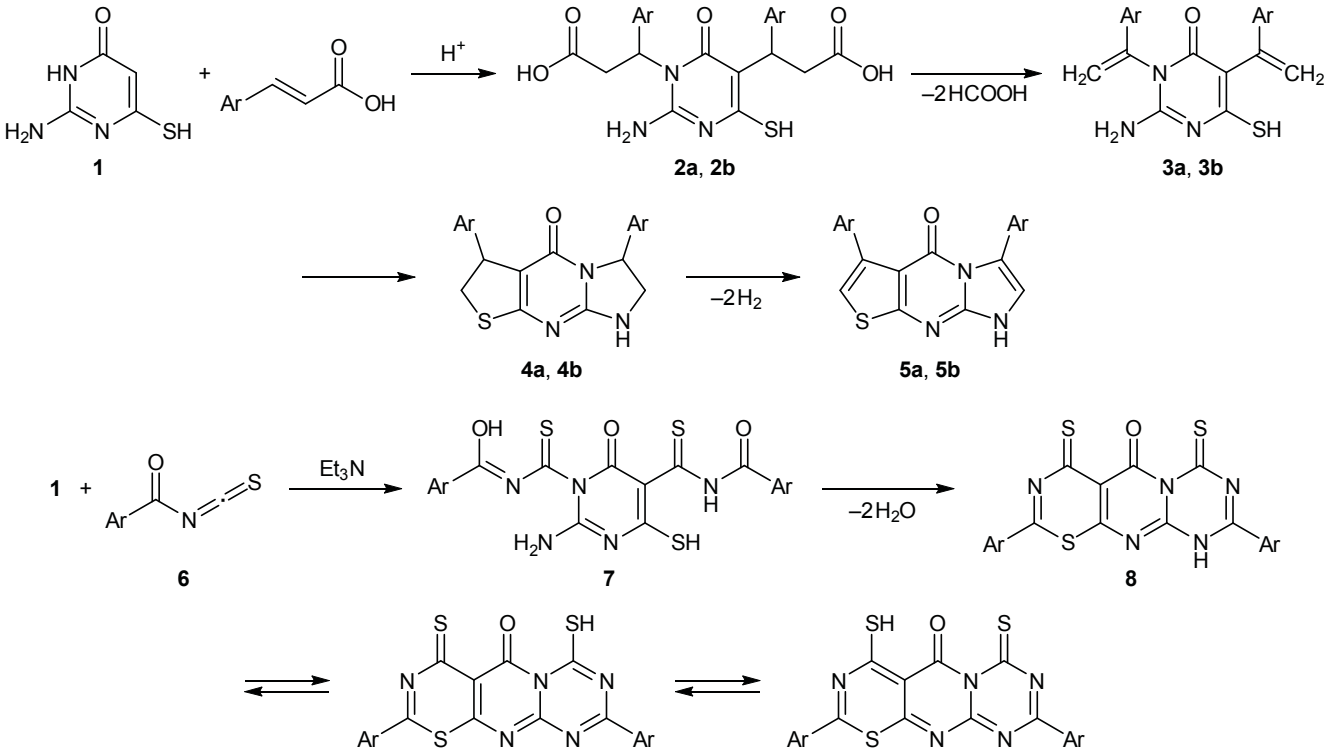
Functionalized pyrimidine building blocks are of great importance in medicinal and synthetic organic chemistry, as well as in the development of new efficient methodologies for the preparation of fused heterocyclic systems [1]. 2-Amino-6-sulfanylpyrimidin-4(3*H*)-one (**1**) [2] is the key intermediate product bearing several functional moieties that could be easily modified, and numerous derivatives have been prepared from pyrimidine **1** for evaluation as drugs and compounds with other biological functions [3–5]. Pyrimidines are also used as antibacterial [6], anticonvulsant [7], and antifungal agents [8].

In the light of the above observations and in continuation of our previous work on developing syntheses of fused heterocyclic compounds [9–12], the present article reports heterocyclization and functionalization of polyfunctionalized aminopyrimidine **1**. Compound **1** was obtained by condensation of thiourea with ethyl cyanoacetate according to the procedure described in [2]. The acid-catalyzed reaction of **1** with 2 equiv of cinnamic or 3-ntrocinnamic acid resulted in fusion of thiophene and imidazole rings to the pyrimidine moiety, affording thienoimidazopyrimidine derivatives **5a** and **5b**, presumably via double Michael/aza-Michael addition, elimination of two formic acid molecules, intramolecular cycloaddition, and subsequent aromatization (through intermediate compounds **2**–**4**; Scheme 1). The IR spectrum of **5a** showed characteristic C=O and C=N stretching bands at 1628 and 1626 cm^{-1}, respectively. The ^1H NMR spectrum of **5a** contained a downfield signal at 12.11 ppm (D_2O-exchangeable) due to NH proton, aromatic proton signals in the region δ 7.69–7.40 ppm, and two singlets at δ 6.54 and 6.50 ppm due to protons of the imidazole and thiophene rings. The carbonyl carbon atom resonated at δ_C 167.6 ppm in the ^{13}C NMR spectrum.

The double [3+3]-cyclization of **1** with 2 equiv of 2,4-dichlorobenzoyl isothiocyanate (**6**) in the presence of triethylamine gave tricyclic compound **8**. The reaction is likely to involve conjugate addition of **6** to N^3 and C^5 of **1**, followed by intramolecular cyclization (Scheme 1). The IR spectrum of **8** displayed bands at 1651, 1585, and 1262 cm^{-1} due to C=O, C=N, and C=S stretching vibrations, respectively. The ^1H NMR spectrum of **8** showed a downfield NH (or SH) signal at δ 13.08 ppm (D_2O exchangeable) in addition to aromatic multiplet in the region δ 7.91–7.46 ppm.

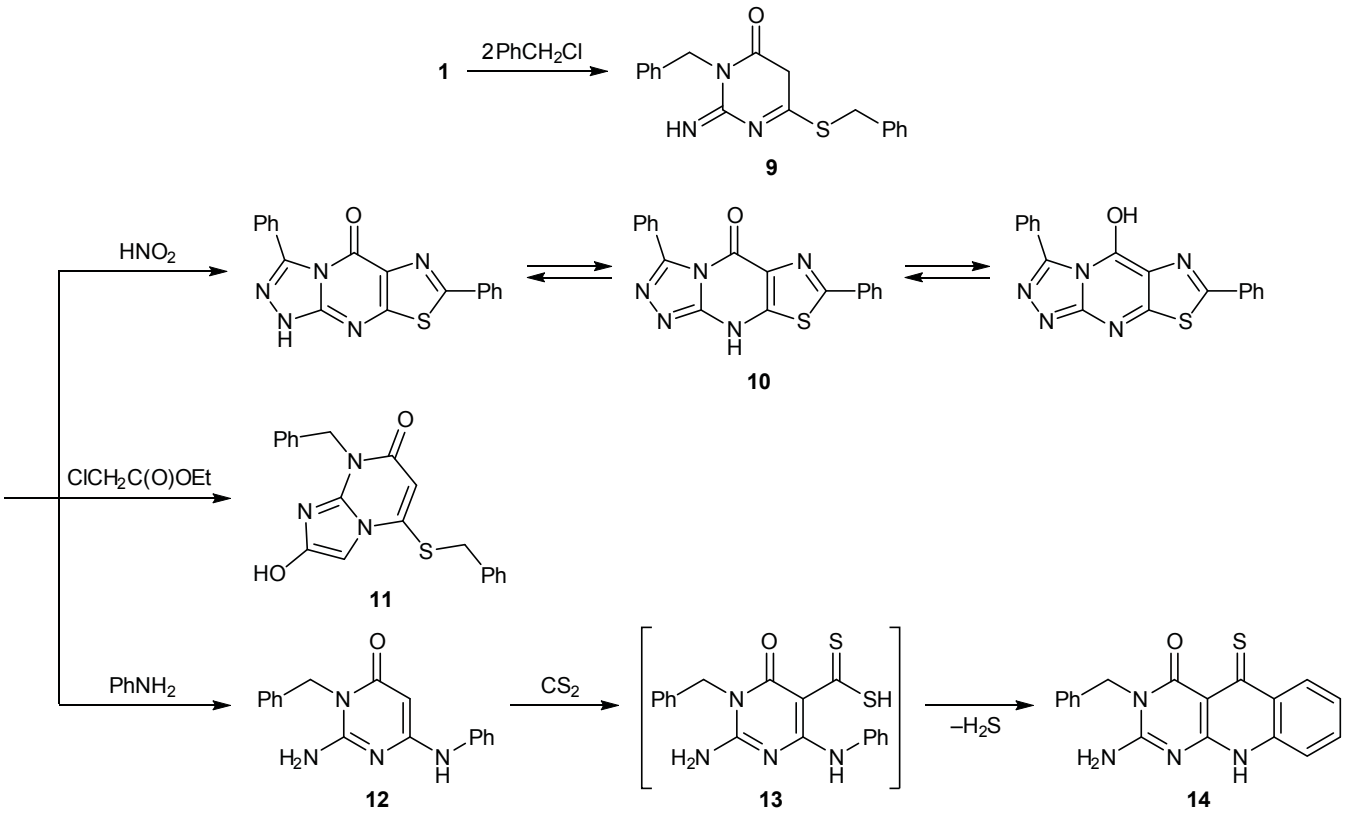
Pyrimidine **1** was alkylated with 2 equiv of benzyl chloride to obtain N^3,*S*-dibenzyl derivative **9** (Scheme 2) which showed signals at δ 11.43, 6.53, 4.94, and 4.32 ppm in the ^1H NMR spectrum; these signals were assigned to the NH, 5-H, NC$\mathbf{H}_2$Ph, and

Scheme 1.

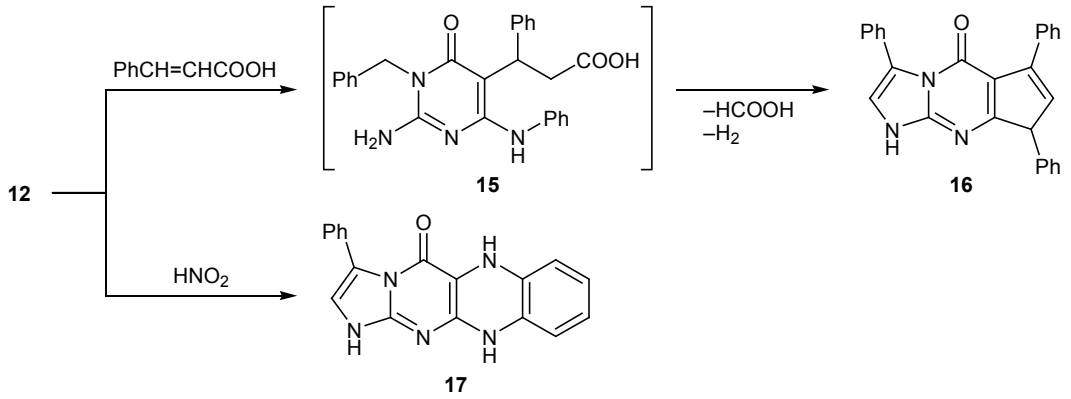


2–**5**, Ar = Ph (**a**), 4-$O_2NC_6H_4$ (**b**); **6**–**8**, Ar = 2,4-$Cl_2C_6H_3$.

Scheme 2.



Scheme 3.



SC**H**$_2$Ph protons, respectively. The nitrosation of **9** with sodium nitrite in acetic acid led to the formation of triazolothiazolopyrimidine **10** which is likely to exist as a mixture of tautomers, as followed from the presence of three downfield D_2O-exchangeable signals at δ 12.72, 11.25, and 9.15 ppm for NH (OH) proton.

The cyclic guanidine moiety of **9** was cyclized by treatment with ethyl chloroacetate. The reaction may start with alkylation of N^1, followed by intermolecular condensation of the exocyclic imino group and ester function to produce imidazopyrimidine **11** (Scheme 2). The OH proton of **11** resonated at δ 11.48 ppm (D_2O-exchangeable) in the ^{1}H NMR spectrum, and the IR spectrum of **11** displayed bands at 1735 (C=O) and 1548 cm^{-1} (C=N).

The aminolysis of **9** with aniline gave 6-anilinopyrimidine **12** as a result of substitution of the benzylsulfanyl group (Scheme 2). Compound **12** showed an IR band at 3446 cm^{-1} due to NH group in addition to the low-frequency enaminone carbonyl band at 1634 cm^{-1} (due to +*M* effect of the PhNH group). The ^{1}H NMR spectrum of **12** contained a broadened signal at δ 11.45 ppm form the PhN**H** proton.

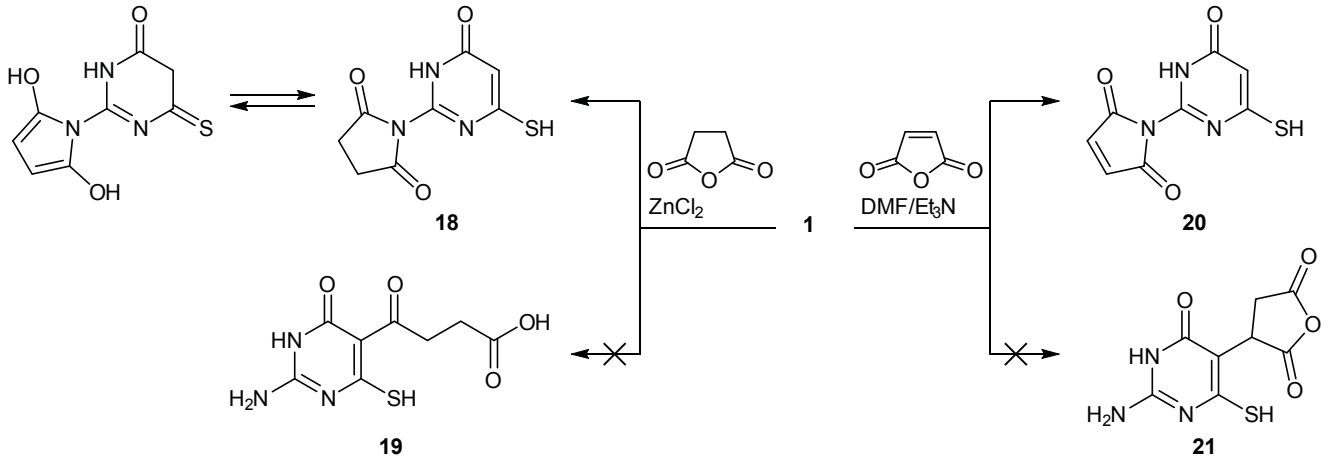
Nucleophilic addition of the C^5 enamine carbon atom of **12** to electrophilic carbon of carbon disulfide, followed by cyclization involving the *ortho* position of the anilino group with elimination of hydrogen sulfide, afforded pyrimidoquinoline **14** (Scheme 2). The IR spectrum of **14** displayed a broadened medium-intensity peak at 3294 cm^{-1} (N–H), a sharp carbonyl peak at 1686 cm^{-1}, and a band at 1286 cm^{-1} due to C=S group. The NH proton of **14** resonated as a broadened signal at δ 11.73 ppm.

Treatment of anilinopyrimidine **12** with 2 equiv of cinnamic acid resulted in pyrrole ring closure with the formation of pyrrolopyrimidine derivative **16**, presumably through intermediate **15** (Scheme 3). Compound **16** was characterized by IR bands at 3427, 1683, and 1628 cm^{-1} assigned to the N–H, C=O, and C=N stretchings, respectively. The ^{1}H NMR spectrum of **16** showed a downfield D_2O-exchangeable signal at δ 12.33 for the NH proton. The reaction of **12** with nitrous acid ($NaNO_2$/AcOH) afforded fused tetracyclic pteridine **17** (Scheme 3). The NH and C=O groups of **17** gave rise to IR absorption bands at 3437 and 1684 cm^{-1}, respectively, and the NH signals of **17** were located at δ 12.72, 11.25, and 9.16 ppm.

The reaction of **1** with succinic anhydride involved the exocyclic amino group to give N-substituted succinimide **18**, whereas no acylation product at C^5 was detected (Scheme 4). The NMR spectra of **18** displayed downfield D_2O-exchangeable proton signals at δ 11.60 and 11.51 ppm (OH, NH), C=S carbon signal at δ_C 174.59 ppm, and C^4=O signal at δ_C 161.64 ppm. Likewise, compound **1** reacted with maleic anhydride in DMF in the presence of triethylamine to produce maleimide **20** but no adduct **21**. The ^{1}H NMR spectrum of **20** showed D_2O-exchangeable signals at δ 12.74 (SH) and 11.77 ppm (NH), and the carbonyl carbon resonated in the ^{13}C NMR spectrum at δ_C 176.88 ppm.

The acylation of **1** with acetic anhydride in the presence of zinc chloride afforded imidazothienopyrimidine **25**, presumably via enolization of intermediate 3,5-diacetyl derivative **22**, followed by cyclization and dehydration (Scheme 5). The ^{1}H NMR spectrum of **25** contained a D_2O-exchangeable signal at δ 12.00 ppm (NH) and signals in the region δ 8.55–7.95 ppm due to protons of the thiophene and imidazole rings. Treatment of **1** with hydrogen peroxide under alkaline conditions led to the oxidation of the 6-sulfanyl group to sulfonic acid moiety (**26**), but no expected 6-hydroxy derivative **27** was formed (Scheme 5). The IR spectrum of **26** displayed an O–H peak at 3426 cm^{-1} and a C=O band at 1630 cm^{-1}, and signals at δ 11.60,11.50, and

Scheme 4.



6.35 ppm due to SO_3H, NH, and NH_2 group were observed in the ^1H NMR spectrum of **26**.

Some of the newly synthesized compounds were screened for their *in vitro* antibacterial activities against gram-positive (*Staphylococcus aureus* ATCC 6538) and gram-negative bacteria (*E. coli* ATCC 8739) at a concentration of 100 μg/mL. Also, their antifungal activity against *Candida albicans* ATCC 10231 was evaluated. Table 1 shows the results of antimicrobial studies. Compounds **12** and **14** showed excellent activity against *C. albicans*, which was comparable with the activity of Fluconazole used as reference. Compounds **20** and **25** demonstrated high antimicrobial activity in comparison to Ciprofloxacin. The other compounds showed good to moderate activity or were inactive against the tested microorganisms.

EXPERIMENTAL

The IR spectra were recorded on a Perkin Elmer FT/IR-400 spectrometer from samples prepared as KBr discs. The ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker-400 spectrometer at 400 and 100 MHz, respectively, from solutions in DMSO-d_6. Elemental analyses and antibacterial assays were carried out at the Micro Analytical Center, Cairo University. Compound **1** was prepared as reported in [2]. The melting points are uncorrected.

3,6-Diphenylimidazo[1,2-*a*]thieno[2,3-*d*]pyrimidin-5(1*H*)-one (5a). Sulfuric acid (2 mL) was added to a solution of pyrimidine **1** (0.01 mol) and cinnamic acid derivative (0.02 mol) in anhydrous 1,4-dioxane (30 mL), and the mixture was refluxed for

Scheme 5.

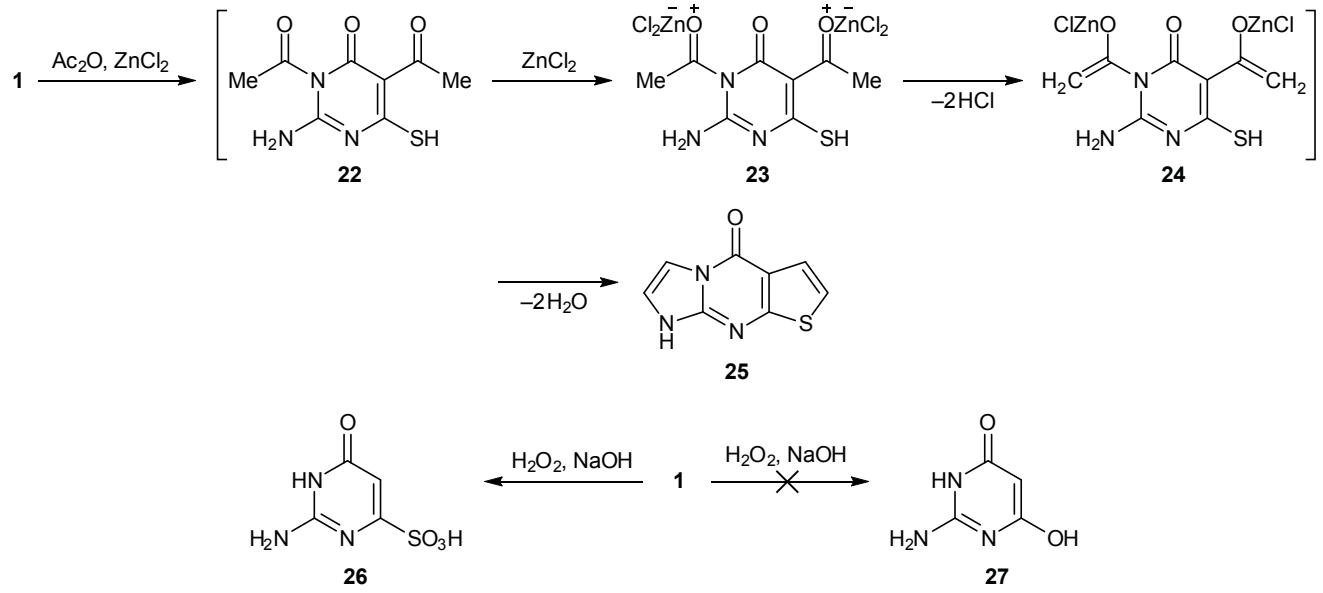


Table 1. *In vitro* antimicrobial activity (inhibition zone diameter, mm)[a] of compounds **5a**, **8**, **10**–**12**, **14**, **17**, **18**, **20**, and **25**

Compound no.	*S. aureus*	*E. coli*	*C. albicans*
5a	N/A	20.1	N/A
8	N/A	20	N/A
10	13.3	N/A	N/A
11	N/A	22	N/A
12	N/A	22	21
14	N/A	22	18
17	12.04	16.10	N/A
18	19.3	N/A	N/A
20	N/A	33	N/A
25	N/A	28	N/A
Ciprofloxacin	42	41.4	N/A
Fluconazole	N/A	N/A	25.5

[a] Mean values from three replicates are given; N/A stands for no activity.

3 h. The mixture was cooled and poured onto crushed ice, and the solid product was filtered off, dried, and recrystallized from ethanol. Yield 90%, yellowish crystals, mp 150–152°C. IR spectrum, ν, cm^{-1}: 3204 (NH), 1628 (C=O), 1626 (C=N). ^1H NMR spectrum, δ, ppm: 6.54–6.50 s (2H, 2-H, 7-H), 7.40–7.69 m (10H, H_{arom}), 12.11 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 110.25, 119.24, 128.22, 128.93, 129.25, 130.25, 131.25, 131.6, 132.4, 134.25, 138.6, 143.96, 154.22, 162.5, 167.6. Found, %: C 69.90; H 3.80; N 12.20. $C_{20}H_{13}N_3OS$. Calculated, %: C 69.95; H 3.82; N 12.24.

3,6-Bis(3-nitrophenyl)imidazo[1,2-*a*]thieno-[2,3-*d*]pyrimidin-5(1*H*)-one (5b) was synthesized in a similar way. Yield 90%, rose crystals, mp 250–251°C (from EtOH). IR spectrum, ν, cm^{-1}: 3437 (NH), 1698 (C=O), 1525, 1353 (NO_2). ^1H NMR spectrum, δ, ppm: 6.71 s and 6.75 s (2H, 2-H, 7-H), 7.68–8.24 m (8H, H_{arom}), 12.11 s (1H, NH). Found, %: C 55.40; H 2.50; N 16.10; $C_{20}H_{11}N_5O_5S$. Calculated, %: C 55.43; H 2.56; N 16.16.

2,9-Bis(3,4-dichlorophenyl)-4-sulfanyl-7-sulfanylidene-11,11a-dihydro-6*H*,7*H*-[1,3]thiazino[6′,5′:4,5]pyrimido[1,2-*a*][1,3,5]triazin-6-one (8). A mixture of compound **1** (0.01 mol) and 2,4-dichlorobenzoyl isothiocyanate (0.021 mol) [13] in anhydrous dioxane (30 mL) containing a few drops of triethylamine was refluxed for 6 h. The mixture was poured onto crushed ice and acidified with aqueous HCl, and the product was filtered off and recrystallized from DMF. Yield 85%, brownish crystals, mp >360°C. IR spectrum, ν, cm^{-1}: 1651 (C=O), 1585 (C=N), 1262 (C=S). ^1H NMR spectrum, δ, ppm: 7.46–7.91 m (6H, H_{arom}), 13.08 s (1H, NH), 13.60 s (1H, SH). Found, %: C 41.70; H 1.50; N 12.10. $C_{20}H_9Cl_4N_5OS_3$ Calculated, %: C 41.90; H 1.58; N, 12.22.

3-Benzyl-6-(benzylsulfanyl)-2-imino-2,5-dihydropyrimidin-4(3*H*)-one (9). Compound **1** (0.01 mol) was dissolved in a solution of Na_2CO_3 (0.01 mol) in water (50 mL), benzyl chloride (0.02 mol) was added, and the mixture was stirred for 12 h. The precipitate was filtered off, washed several times with water, dried, and recrystallized from ethanol. Yield 80%, white powder, mp 270–272°C. IR spectrum, ν, cm^{-1} 3446 (NH), 1638 (C=O). ^1H NMR spectrum, δ, ppm: 4.32 s (2H, SCH_2), 4.94 s (2H, NCH_2), 6.53 s (2H, 5-H), 7.23–7.43 m (10H, H_{arom}), 11.43 s (1H, NH). Found, %: C 66.80; H 5.29; N 12.90. $C_{18}H_{17}N_3OS$. Calculated, %: C 66.85; H 5.30; N 12.99.

3,7-Diphenyl[1,3]thiazolo[5,4-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one (10). A cold solution of sodium nitrite (0.01 mol) in 10 mL of water was added with stirring to a cold solution of compound **9** (0.01 mol) in acetic acid. The mixture was stirred for 1 h, and the solid product was filtered off and recrystallized from dilute ethanol. Yield 95%, blue crystals, mp 220−221°C. IR spectrum, ν, cm^{-1}: 3426 (OH), 3156 (NH), 3058 (NH), 1677 (C=O), 1613 (C=N). ^1H NMR spectrum, δ, ppm: 7.24–7.49 m (10H, H_{arom}); 9.15 s, 11.25 s, and 12.72 s (1H, NH, OH). ^{13}C NMR spectrum, δ_C, ppm: 127.50, 128.52, 128.67, 128.73, 129.30, 131.25, 132.04, 136.84, 143.04, 146.69, 148.25, 150.52, 161.19, 167.13. Found, %: C 2.59; H 3.20; N 20.20. $C_{18}H_{11}N_5OS$. Calculated, %: C 62.60; H 3.21; N 20.28.

8-Benzyl-5-(benzylsulfanyl)-2-hydroxyimidazo[1,2-*a*]pyrimidin-7(8*H*)-one (11). A mixture of compound **9** (0.01 mol), ethyl chloroacetate (0.01 mol), and triethylamine (3 drops) in DMF (20 mL) was refluxed for 6 h. The mixture was cooled, poured into cold water, and acidified with aqueous HCl, and the solid product was filtered off, dried, and recrystallized from DMF. Yield 90%, yellow crystals, mp 230–231°C. IR spectrum, ν, cm^{-1}: 3446 (OH), 1735 (C=O), 1584 (C=N). ^1H NMR spectrum, δ, ppm: 4.32 s (2H, SCH_2), 4.93 s (2H, NCH_2), 6.52 s (1H, 6-H), 7.23–7.43 m (11H, H_{arom}, 3-H), 11.48 s (1H, OH). Found, %: C 66.90; H 4.70; N 11.50. $C_{20}H_{17}N_3O_2S$. Calculated, %: C 66.10; H 4.72; N 11.5.

2-Amino-6-anilino-3-benzylpyrimidin-4(3*H*)-one (12). A mixture of compound **9** (0.01 mol) and aniline (0.01 mol) in ethanol (30 mL) was refluxed for 8 h. After cooling, the solid product was filtered off, dried, and recrystallized from ethanol. Yield 90%, colorless crystals, mp 250–251°C. IR spectrum, ν, cm^{-1}: 3446 (NH), 3294, 3151 (NH_2), 1634 (C=O). ^1H NMR spectrum, δ, ppm: 4.94 s (2H, NCH_2), 6.53 s (2H, NH_2), 7.23–7.43 m (11H, H_{arom}, 5-H), 11.45 s (1H, NH). Found, %: C 69.80; H 5.50; N 19.10. $C_{17}H_{16}N_4O$. Calculated, %: C 69.85; H 5.52; N 19.17.

2-Amino-3-benzyl-5-sulfanylidene-5,10-dihydropyrimido[4,5-*b*]quinolin-4(3*H*)-one (14). A mixture of compound **12** (0.01 mol), carbon disulfide (0.02 mol), and sodium acetate (0.02 mol, 1.64 mg) in acetic acid (20 mL) was heated under reflux for 8 h. The mixture was cooled and poured into ice water, and the solid product was filtered off, dried, and recrystallized from ethanol. Yield 90%, yellow crystals, mp 280–281°C. IR spectrum, ν, cm^{-1}: 3474 (NH), 3294, 3183 (NH_2) 1686 (C=O), 1614 (C=N), 1286 (C=S). ^1H NMR spectrum, δ, ppm: 4.95 s (2H, NCH_2), 6.54 s (2H, NH_2), 7.23–7.43 m (9H, H_{arom}), 11.75 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 33.32, 111.5, 116.2, 121.5, 126.5, 127.19, 128.46, 129.18, 130.5, 137.98, 148.5, 162.16, 163.67, 164.66, 172.14. Found, %: C 64.60; H 4.20; N 16.70. $C_{18}H_{14}N_4OS$. Calculated, %: C 64.65; H 4.22; N 16.75.

3,6,8-Triphenyl-1,8-dihydro-5*H*-imidazo[1,2-*a*]-pyrrolo[2,3-*d*]pyrimidin-5-one (16). Sulfuric acid (2 mL) was added to a solution of **12** (0.01 mol) and cinnamic acid (0.02 mol) in anhydrous dioxane (20 mL), and the mixture was refluxed for 3 h. The mixture was cooled and poured onto crushed ice, and the product was filtered off, dried, and recrystallized from ethanol. Yield 90%, yellowish crystals, mp 100–101°C. IR spectrum, ν, cm^{-1}: 3427 (NH), 1683 (C=O), 1628 (C=N). ^1H NMR spectrum, δ, ppm: 6.50 s (1H, 2-H), 6.54 s (1H, 7-H), 7.39–7.69 m (15H, Ph), 12.33 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 110.12, 112.5, 116.20, 119.20, 122.5, 126.80, 127.25, 128.18, 128.22, 128.89, 129.2, 129.4, 130.21, 130.5, 134.2, 136.69, 137.3, 143.91, 154.60, 167.54. Found, %: C 77.53; H 4.50; N 13.80. $C_{26}H_{18}N_4O$. Calculated, %: C 77.59; H 4.51; N 13.92.

3-Phenyl-6,11-dihydrobenzo[*g*]imidazo[2,1-*b*]-pteridin-5(1*H*)-one (17). A cold solution of sodium nitrite (0.01 mol) in 20 mL of water was added to a cold solution of compound **12** (0.01 mol) in acetic acid. The mixture was stirred for 1 h, and the precipitate was filtered off and recrystallized from dilute ethanol. Yield 95%, violet crystals, mp 220–221°C. IR spectrum, ν, cm^{-1}: 3437 (NH), 1684 (C=O). ^1H NMR spectrum, δ, ppm: 7.24–7.49 m (10H, H_{arom}); 9.16 s, 11.25 s, and 12.72 s (3H, NH). Found, %: C 68.50; H 4.10; N 22.20. $C_{18}H_{13}N_5O$. Calculated, %: C 68.56; H 4.16; N 22.21.

2-(2,5-Dihydroxy-1*H*-pyrrol-1-yl)-6-sulfanylidene-5,6-dihydropyrimidin-4(3*H*)-one (18). A mixture of compound **1** (0.01 mol), succinic anhydride (0.01 mol), and zinc chloride (0.01 mol) in DMF (30 mL) was refluxed for 12 h. The mixture was cooled and poured into ice water, and the solid product was filtered off, dried, and recrystallized from DMF. Yield 90%, yellow crystals, mp >360°C. IR spectrum, ν, cm^{-1}: 3426, 3325 (OH, NH), 1630 (C=O). ^1H NMR spectrum, δ, ppm: 4.69 s (2H, 5-H), 6.35 s (2H, 3′-H, 4′-H), 11.51 s (1H, NH), 11.60 s (2H, OH). ^{13}C NMR spectrum, δ_C, ppm: 43.81, 78.18, 145.60, 154.33, 161.64, 174.59. Found, %: C 42.60; H 3.10; N 18.60. $C_8H_7N_3O_3S$. Calculated, %: C 42.66; H 3.13; N 18.66.

1-(6-Oxo-4-sulfanyl-1,6-dihydropyrimidin-2-yl)-1*H*-pyrrole-2,5-dione (20). A mixture of compound **1** (0.01 mol), maleic anhydride (0.01 mol), and triethylamine (3 drops) in DMF (30 mL) was refluxed for 12 h. The mixture was cooled and poured into an ice–aqueous HCl mixture, and the precipitate was filtered off, dried, and recrystallized from DMF. Yield 90%, yellow crystals, mp 290–291°C. IR spectrum: ν 1622 cm^{-1} (C=O). ^1H NMR spectrum, δ, ppm: 7.94 s (2H, 3′-H, 4′-H), 8.51 s (1H, 5-H), 11.77 s (1H, NH), 12.74 s (1H, SH). ^{13}C NMR spectrum, δ_C, ppm: 109.14, 137.01, 152.89, 154.38, 163.42, 176.88. Found, %: C 43.04; H 2.20; N 18.80. $C_8H_5N_3O_3S$. Calculated, %: C 43.05; H 2.26; N 18.83.

Imidazo[1,2-*a*]thieno[2,3-*d*]pyrimidin-5(1*H*)-one (25). A mixture of compound **1** (0.01 mol), acetic anhydride (0.01 mol), and zinc chloride (0.01 mol) in DMF (30 mL) was refluxed for 12 h. The mixture was cooled and poured into ice water, and the solid was filtered off and recrystallized from DMF. Yield 90%, yellow crystals, mp >360°C. IR spectrum, ν, cm^{-1}: 3441 (NH), 1614 (C=O). ^1H NMR spectrum, δ, ppm: 7.95–8.55 m (4H, 2-H, 3-H, 6-H, 7-H), 12.00 s (1H, NH). Found, %: C 50.20; H 2.60; N 21.90. $C_8H_5N_3OS$. Calculated, %: C 50.25; H 2.64; N 21.98.

2-Amino-6-oxo-1,6-dihydropyrimidine-4-sulfonic acid (26). Hydrogen peroxide (60 mL, 30%) was added to a solution of compound **1** (0.01 mol) in aqueous sodium hydroxide (0.01 mol, 20 mL), and the mixture was stirred for 10 min and allowed to stand at

room temperature for 12 h. The mixture was then acidified with aqueous HCl, and the white precipitate was filtered off and recrystallized from acetic acid. Yield 90%, mp >360°C. IR spectrum, ν, cm^{-1}: 3426, 3321, 3320 (OH, NH, NH_2), 1630 (C=O), 1294, 1185 (SO_2). ^1H NMR spectrum, δ, ppm: 6.35 s (2H, NH_2), 7.94 s (1H, 5-H), 11.50 s (1H, NH), 11.60 s (1H, SO_3H). Found, %: C 25.10; H 2.60; N 21.90. $C_4H_5N_3O_4S$. Calculated, %: C 25.13; H 2.64; N 21.98.

The antimicrobial activity of compounds **5a**, **8**, **10**–**12**, **14**, **17**, **18**, **20**, and **25** was evaluated by the agar diffusion technique [14]. The compounds were tested as solutions in dimethyl sulfoxide with a concentration of 100 μg/mL. Pure dimethyl sulfoxide was used as a negative control, and Ciprofloxacin and Fluconazole at a concentration of 100 μg/mL in dimethyl sulfoxide were used as reference drugs for bacteria and fungi, respectively.

CONFLICT OF INTEREST

No conflict of interest is declared by the authors.

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