Synthesis of Pyrimidine, Dihydropyrimidinone, and Dihydroimidazole Derivatives under Free Solvent Conditions and Their Antibacterial Evaluation

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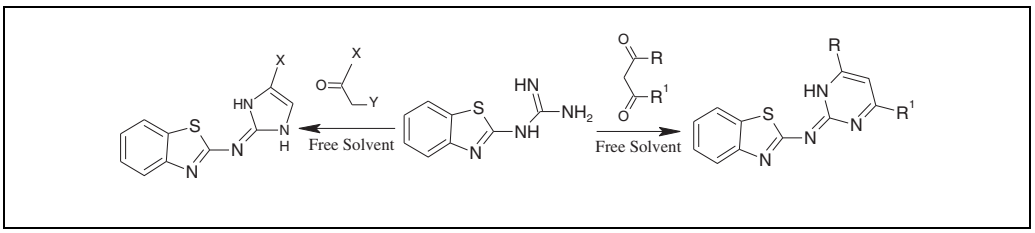

The biologically active compounds of pyrimidine, dihydropyrimidinone, and dihydroimidazole have been synthesized in excellent yield under free solvent conditions. The antibacterial evaluation of the products showed a high inhibitory effect. Reaction of 2-guanidinobenzothiazole with several active methylene compounds has revealed formation of the corresponding pyrimidine, dihydropyrimidinone, and dihydroimidazole derivatives under free solvent conditions in very good yield. All compounds have been characterized on the basis of IR, ^{1}H NMR, ^{13}C NMR, mass spectrometry, and X-ray.

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INTRODUCTION

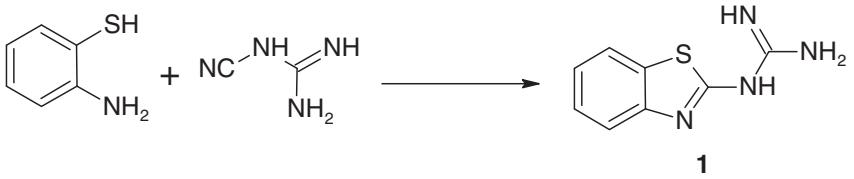
The nitrogen heterocycles in general and pyrimidines in particular are found in several biologically active natural products and depict considerable therapeutic potential [1]. In view of wide spectrum biological activities such as anti-allergic [2], antitumor [3], antipyretic, anti-inflammatory [4], and antiparasitic [5] activities exhibited by synthetic pyrimidine-based scaffolds, a number of analogues have garnered considerable attention. During a screening effort for antiviral agents, it has been found that multifunctionalized tetrahydropyrimidines derivatives bearing bulky C-2 alkyl substituents depict cytostatic activity and inhibit proliferation of murine leukemia, murine mammary carcinoma, human T-lymphocyte, and human cervix carcinoma cells [6]. The dihydropyrimidinones have recently emerged as important target molecules because of their therapeutic and pharmacological properties [7,8] such as antiviral [9], antimitotic [10], anticarcinogenic [11], and antihypertensive [12] and, noteworthy, as calcium channel modulators [13]. Additionally, their particular structure has been found in natural marine alkaloid batzelladine A and B, which are the first low-molecular-weight natural products reported in the literature to inhibit the binding of HIV gp-120 to CD4 cells, so disclosing a new field towards the development of AIDS therapy [14]. Dihydroimidazoles are reported to exhibit diverse biological and pharmacological properties. Examples of these include α-receptor stimulation, vasodepressor activity, α -adrenergic inhibition, and sympathomimetic, antihistaminic, histamine-like, and cholinomimetic activities [15,16]. Dihydroimidazoles, such as midaglizole, deriglidole, and efaroxan, have been found to be potent antihyperglycemic agents [17]. Although a large number of dihydropyrimidinone (DHPM) derivatives have been prepared in a single-pot Biginelli multi-component reaction [18] and its variants [19], very useful and convincing structural variability of these interesting heterocycles have been achieved through chemical functionalization of all the six positions around the DHPM core [20]. Recently, it was reported [6] that the C-2 amine substituted pyrimidine derivatives have inhibited *Mycobacterium tuberculosis* as well as their inhibitory effect against the proliferation of some cell cultures. In a continuation of our efforts to synthesize small molecule heterocyclic compounds from modified guanidines and active methylene compounds [21], we are reporting in this study the synthesis of C2-amino/imino benzothiazole substituted dipyrimidines, dihydropyrimidinones, and dihydroimidazoles.

RESULTS AND DISCUSSION

We have modified the reported synthesis of 2-benzothiazolylguanidine **1** in different methods A, B, and C on the basis of the reaction of cyanoguanidine with 2-aminothiophenol (Scheme 1) in excellent yield (see Experimental section). The physical and spectral data of **1** were complying with the reported data [22–24]. Moreover, we have reported its X-ray analyses (Fig. 1).

The X-ray of **1** [25] showed intermolecular N—H⁻ ⁻ ⁻N hydrogen bonds between the two independent molecules that gave rise to a hydrogen-bonded dimer. Addtional

Scheme 1



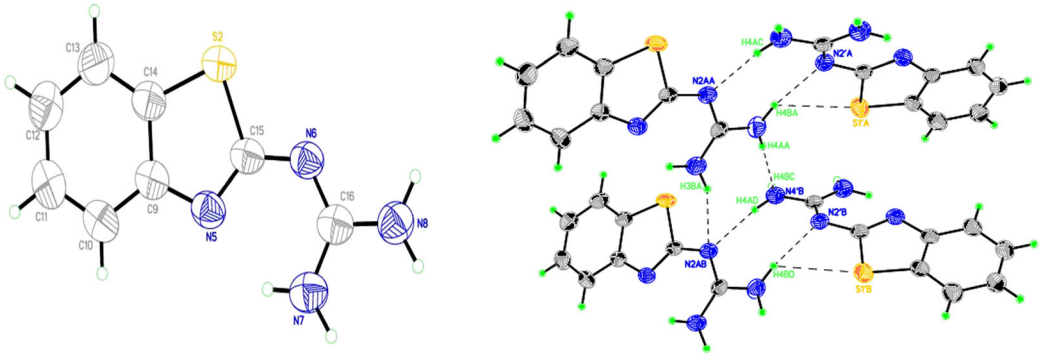


Figure 1. X-ray crystal images of compound **1**.

weak intermolecular N—H···N hydrogen bonds connect these dimers into chains along the crystal packing. An intramolecular N—H···N hydrogen bond is also observed in each independent molecule (Fig. 1).

Reaction of **1** with acetylacetone along with few drops of glacial acetic acid as a benign catalyst gave pyrimidine derivative **2** in high yield (98%) within 15 min. IR spectrum of compound **2** showed the disappearance of absorption bands corresponding to the NH and NH_2 groups. Their ^{1}H NMR spectrum showed new signals corresponding to the =CH group at 6.14 ppm, $2CH_3$ at 2.5 ppm, and NH in aromatic region, respectively. Mass spectrum of compound **2** gave molecular ion peak at *m/z* 256, the X-ray of compound **2** [26] (Fig. 2).

It has been reported that the reaction of biguanides with ethyl cyanoacetate gave triazine acetonitrile [27], whereas in our study, the same reaction afforded the product 2, 3-dihydropyrimidine-4(1*H*)-one **3** (Scheme 2). The reaction mechanism was proceeding via condensation reaction between the amino group and the ester group with elimination of

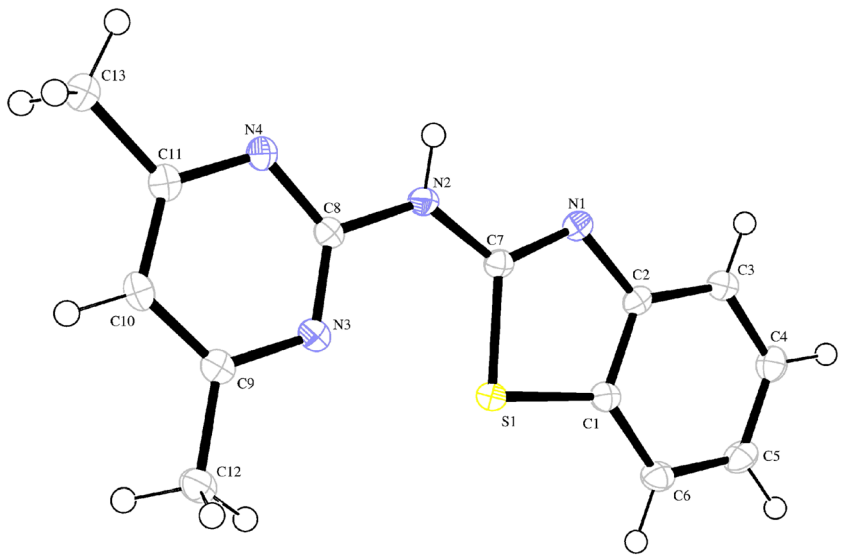
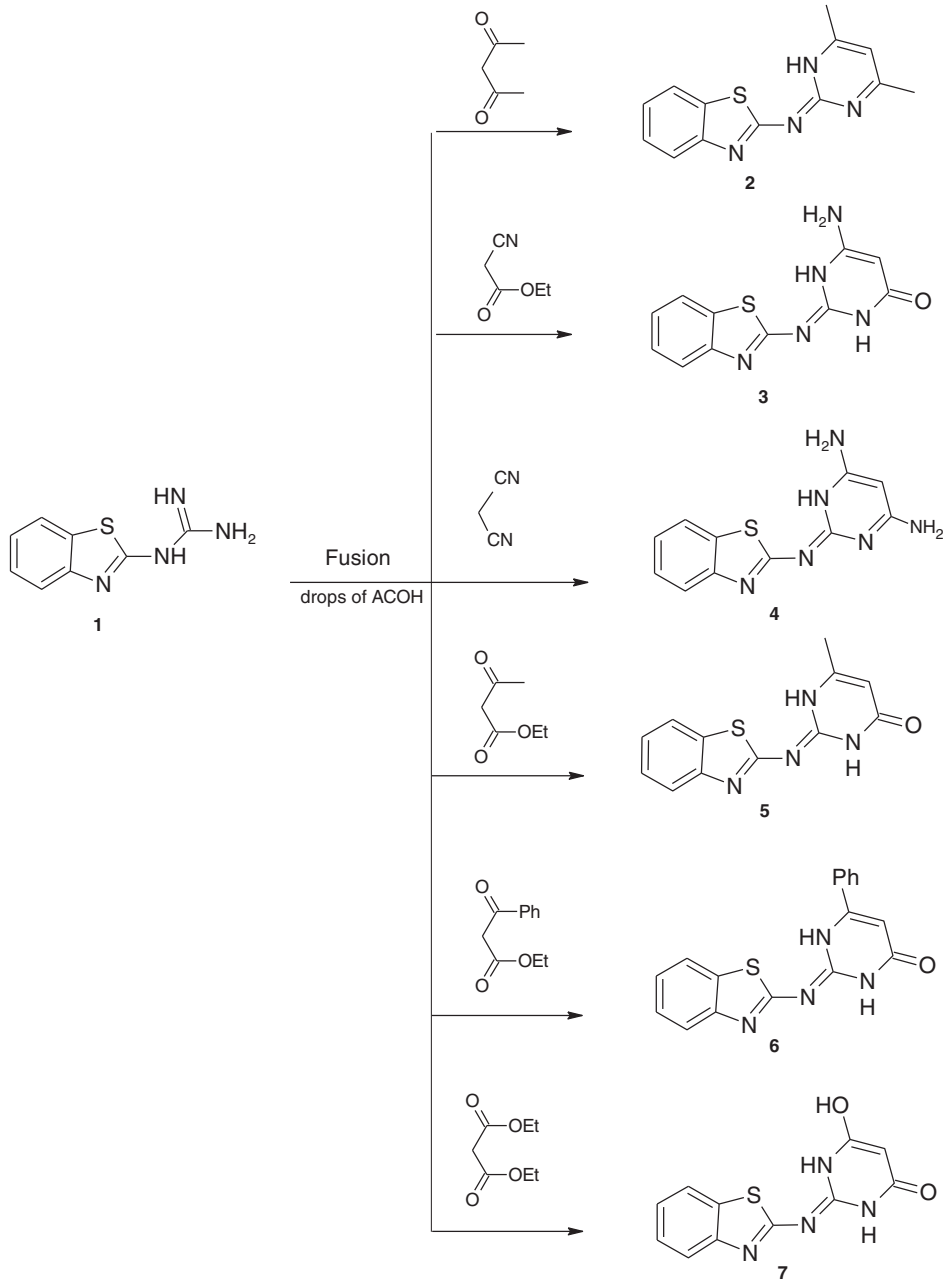


Figure 2. X-ray crystal images of compound **2**.

Scheme 2



ethanol molecule followed by an addition of the amino group to the cyano group. IR spectrum of compound **3** showed no peak for the CN group; instead absorption band corresponding to the NH_2 group at 3383–3290 cm^{-1} was observed. Meanwhile, a molecular ion peak at *m*/*z* 259 in mass spectrum was recorded. Similarly, a nucleophilic addition of the two amino groups in **1** to the two cyano groups in malononitrile afforded the corresponding hydropyrimidine **4**. IR spectra for the latter showed new absorption bands corresponding to the NH_2 groups at 3213–3321 cm^{-1}, a signal at 5.45 ppm in ^1H NMR for 2-NH_2; and the molecular ion (M^+) in mass spectrum was observed to be sharp at *m*/*z* 258.

6-Methyl-, 6-phenyl, and 6-hydroxy-2,3-dihydropyrimidine-4(1*H*)-ones **5–7** were synthesized via the reaction of compound **1** with ethyl acetoacetate, ethyl benzoylacetate, or diethyl malonate, respectively (Scheme 2). IR absorption bands between 1661 and 1691 cm^{-1} for the carbonyl groups and a slightly broad peak at 3155–3303 cm^{-1} for stretch vibration of the NH groups in addition to a broad peak at 3431 cm^{-1} for the OH group were observed in compound **7**. Mass spectra of compounds **5** and **6** showed molecular

Scheme 3

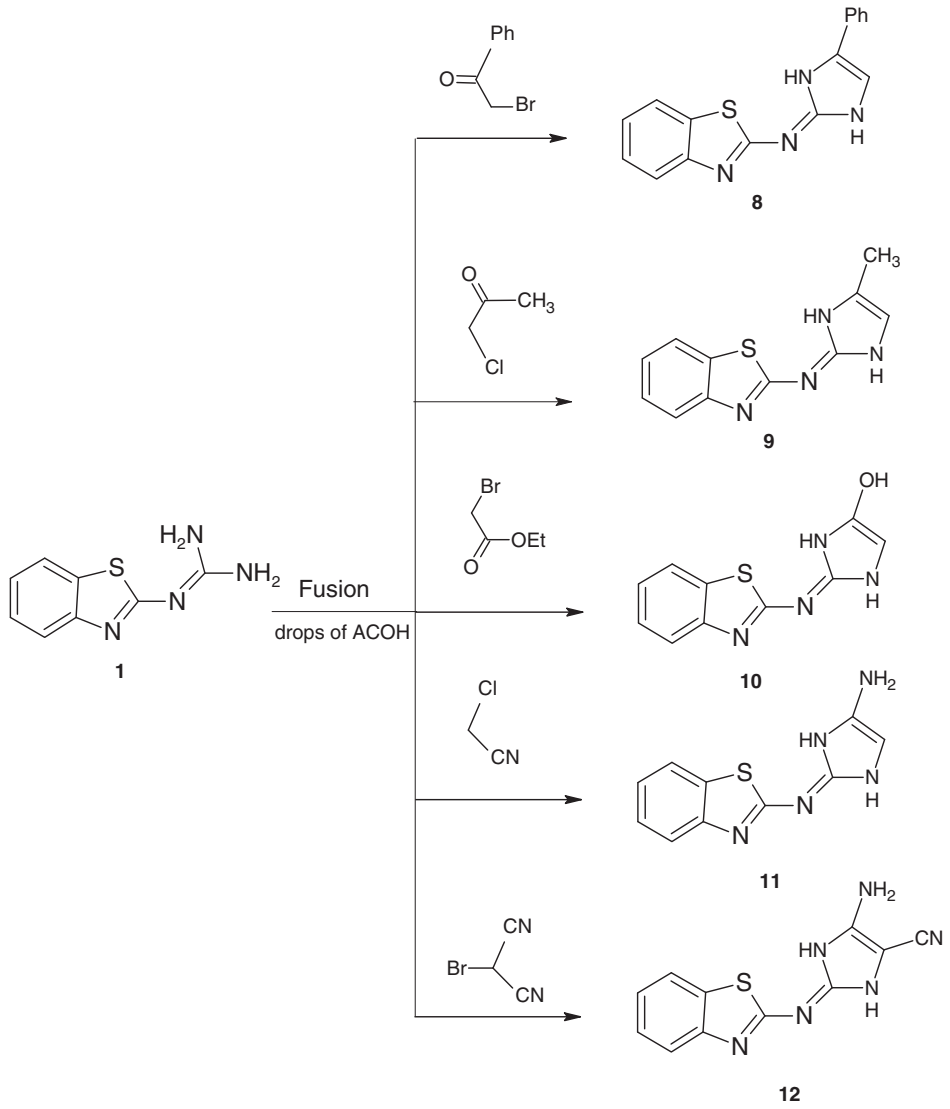


Table 1

Antibacterial evaluation of dipyrimidine and dihydropyrimidinone compounds **2–7**.

	Compound **2**			Compound **3**			Compound **4**		
	Concentrations			Concentrations			Concentrations		
Types of bacteria	10,000 ppm	30,000 ppm	50,000 ppm	10,000 ppm	30,000 ppm	50,000 ppm	10,000 ppm	30,000 ppm	50,000 ppm
Bacillus cereus	0.7 cm	0.8 cm	0.9 cm	0.6 cm	0.8 cm	1.3 cm	0.5 cm	0.8 cm	1.1 cm
Bacillus subtilis	1 cm	1.5 cm	1.8 cm	0.9 cm	1.2 cm	1.5 cm	1.1 cm	1.5 cm	1.8 cm
Escherichia coli	0.5 cm	0.7 cm	1.0 cm	0.7 cm	0.9 cm	1.1 cm	0.7 cm	1.1 cm	1.5 cm
Micrococcus luteus	0.4 cm	0.6 cm	0.9 cm	0.4 cm	0.6 cm	0.8 cm	0.6 cm	0.8 cm	1.2 cm
Staphylococcus aureus	0.6 cm	0.7 cm	0.8 cm	0.6 cm	0.7 cm	0.8 cm	0.6 cm	0.7 cm	0.8 cm
Pseudomonas aeruginosa	0.4 cm	0.7 cm	0.9 cm	0.3 cm	0.7 cm	0.9 cm	1.1 cm	1.5 cm	1.8 cm
Micrococcus roseus	0.3 cm	0.7 cm	0.9 cm	0.9 cm	1.3 cm	1.9 cm	0.5 cm	0.7 cm	0.9 cm

(*Continued*)

ion peaks at *m/z* 258 and 320 respectively. ^{1}H NMR spectra illustrated sharp peaks in all compounds **2–7** ranging from 11.45 to 12.34 ppm for the NH group in addition to a singlet peak ranging between 5.05 to 6.27 ppm for CH proton of hydropyrimidine and hydropyrimidinone ring, respectively.

Aiming to compare the antibacterial potency between dihydropyrimidimes and dihydropyrimidinones, with dihydroimidazoles, we have synthesized a series of C2-amino benzothiazole substituted imidazoles **8–12**. Reaction of compound **1** with halogenated active methylenes such as phenacyl bromide, chloroacetone, ethyl bromoacetate, chloroacetonitrile, and bromo malononitril, in the presence of a few drops of glacial acetic acid as a benign catalyst afforded the formation of dihydroimidazole derivatives **8–12**, respectively (Scheme 3).

The reaction mechanism was proceeding via elimination of the corresponding hydrogen halide and elimination of either water molecules as in **8** and **9** or molecule of ethanol as in **10**, whereas an addition on the cyano group ultimately resulted in the amino dihydroimidazoles **11** and **12**.

IR spectra of compounds **8–12** illustrated absorption peaks at range between 3237 and 3175 cm^{-1} corresponding to the NH groups in dihydroimidazole ring and confirmed in ^{1}H NMR spectra appearing as singlet peaks between 9.86 and 10.19 ppm, whereas the CH group of dihydroimidazole ring was observed between 5.64 and 6.85 ppm as a singlet peak for compounds **8–11**. Mass spectra showed sharp molecular ion peaks at *m/z* 292, 239, 232, 231, and 256 of compounds **8–12**, respectively.

Evaluation of bacterial inhibiting effects of hydropyrimidine, dihydropyrimidinone, and dihydroimidazole compounds 2–12. The inhibitory effect of compounds **2–12** on the *in vitro* growth of broad spectrum of bacteria representing different types of Gram-positive and Gram-negative bacteria, namely, *Bacillus cereus*, *Bacillus subtilis*, *Escherichia coli*, *Micrococcus luteus*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Micrococcus roseus*, was evaluated using agar diffusion method (cup and plate method) [28–30]. DMSO was used as solvent control. All plates were incubated at 37 ± 0.5°C for 24 h. The zone of inhibition of compounds was measured using a centimeter scale. The results are summarized in Tables 1 and 2.

All of the tested compounds were able to inhibit the growth of the tested bacteria. The results indicated in Table 1 revealed that compound **4** showed the highest inhibitory effect against all types of bacteria. In addition, compounds **3** and **5** showed the best inhibitory effect against the Gram-positive bacteria *M. roseus* and *B. subtilis*, respectively, whereas compounds **4** and **10** showed high inhibitory effects against the Gram-negative bacterium *P. aeruginosa*. Compounds **2**, **7**, **8**, and **11** showed the lowest inhibitory effects against *M. luteus*, *S. aureus*, *P. aeruginosa*, and *M. roseus*, respectively. The rest of the compounds showed a moderate growth inhibitory effect. The results in Table 1 illustrated that the inhibiting effect of dihydropyrimidine **4** is higher against most of the applied bacteria than the corresponding dihydropyrimidine **2**; this can be attributed to the two amino groups in the former compound compared with the two methyl groups in the latter. By comparing the inhibitory effect of compound **2** with **5** against the Gram-negative *E. coli*, it is obvious that the presence of dihydropyrimidinone moiety in **5** resulted in higher potency than the dihydropyrimidine nucleus in **2**, whereas a direct comparison between results of **7** and **10** showed that the dihydroimidazole **10** was higher and broader in potency than the dihydropyrimidinone **7** at low concentration doses. Comparing the dihydropyrimidinones **3** (with the amino group) and **6** (with the phenyl group), the first has a greater inhibitory effect than the second towards the Gram-negative bacterium *P. aeruginosa*. We noticed from the results in Table 2 that the more diluted the doses of dihydroimidazoles were, the higher the inhibitory effect was over all types of bacteria;

Table 1
(*Continued*)

Compound **5**			Compound **6**			Compound **7**		
Concentrations			Concentrations			Concentrations		
10,000 ppm	30,000 ppm	50,000 ppm	10,000 ppm	30,000 ppm	50,000 ppm	10,000 ppm	30,000 ppm	50,000 ppm
0.7 cm	0.8 cm	1.1 cm	0.6 cm	0.8 cm	0.9 cm	0.8 cm	0.9 cm	1.2 cm
1 cm	1.5 cm	1.9 cm	1 cm	1.5 cm	1.8 cm	1 cm	1.3 cm	1.7 cm
1.1 cm	1.5 cm	1.7 cm	0.7 cm	1 cm	1.3 cm	0.7 cm	0.9 cm	1.2 cm
0.4 cm	0.6 cm	0.7 cm	0.5 cm	0.7 cm	0.9 cm	0.6 cm	0.7 cm	0.8 cm
0.6 cm	0.7 cm	0.8 cm	0.6 cm	0.7 cm	0.8 cm	0.5 cm	0.7 cm	0.9 cm
0.7 cm	1 cm	1.3 cm	0.5 cm	0.7 cm	0.9 cm	0.6 cm	0.7 cm	0.8 cm
0.3 cm	0.7 cm	1.0 cm	0.7 cm	0.8 cm	1.1 cm	0.4 cm	0.7 cm	0.9 cm

Table 2
Antibacterial evaluation of dihydroimidazole compounds **8–12**.

Types of bacteria	Compound **8**			Compound **10**			Compound **11**			Compound **12**		
	Concentrations			Concentrations			Concentrations			Concentrations		
	10,000 ppm	30,000 ppm	50,000 ppm	10,000 ppm	30,000 ppm	50,000 ppm	10,000 ppm	30,000 ppm	50,000 ppm	10,000 ppm	30,000 ppm	50,000 ppm
Bacillus cereus	0.9 cm	0.8 cm	0.6 cm	1.0 cm	0.9 cm	0.4 cm	0.8 cm	0.7 cm	0.5 cm	1.2 cm	0.9 cm	0.8 cm
Bacillus subtilis	1.1 cm	0.7 cm	0.5 cm	1.1 cm	0.8 cm	0.3 cm	1.1 cm	0.8 cm	0.5 cm	1.4 cm	1.1 cm	0.8 cm
Escherichia coli	1.2 cm	0.7 cm	0.6 cm	1.3 cm	0.9 cm	0.4 cm	1.2 cm	0.7 cm	0.6 cm	1.1 cm	0.9 cm	0.4 cm
Micrococcus luteus	0.7 cm	0.6 cm	0.2 cm	1.0 cm	0.6 cm	0.2 cm	0.8 cm	0.5 cm	—	0.9 cm	0.8 cm	0.5 cm
Staphylococcus aureus	0.8 cm	0.6 cm	0.3 cm	0.9 cm	0.7 cm	0.2 cm	0.8 cm	0.6 cm	—	0.8 cm	0.6 cm	0.3 cm
Pseudomonas aeruginosa	0.8 cm	0.6 cm	0.4 cm	1.6 cm	1.0 cm	0.6 cm	0.7 cm	0.6 cm	0.4 cm	1.0 cm	0.8 cm	0.3 cm
Micrococcus roseus	0.9 cm	0.7 cm	0.3 cm	0.9 cm	0.5 cm	0.1 cm	0.9 cm	0.7 cm	0.2 cm	0.8 cm	0.7 cm	0.2 cm

whereas the more concentrated the doses of dihydropyrimidines and dihydropyrimidinones were, the more effective the inhibiting effect was (Table 1). The effect of substituents in compound **12** was recognized where its inhibitory effect against *B. subtilis* was higher compared with those of the corresponding dihydroimidazoles **8**, **10**, and **11**.

CONCLUSIONS

In this study, we managed to synthesize newly C2-amino benzothiazole substituted dihydropyrimidines, dihydropyrimidinones, and dihydroimidazoles in an excellent yield under no solvent conditions. We carried out an antibacterial evaluation of the new products against several types of bacteria, namely, *B. cereus*, *B. subtilis*, *E. coli*, *M. luteus*, *S. aureus*, *P. aeruginosa*, and *M. roseus*. This showed that dihydropyrimidine **4** possessed an inhibitory effect against all types of bacteria. Compounds **3** and **5** showed the best inhibitory effect against the Gram-positive bacteria *M. roseus* and *B. subtilis*, respectively; whereas compounds **4** and **10** showed a high inhibitory effect against the Gram-negative bacterium *P. aeruginosa*.

EXPERIMENTAL

All melting points are uncorrected and were recorded on Melt-Temp II melting point apparatus. IR spectra were measured as KBr pellets on a Shimadzu DR-8001 spectrometer. ^{1}H NMR spectra were recorded on a Varian Gemini at 400 MHz using TMS as an internal reference and DMSO-d_6 as a solvent. Mass spectra were performed on a Shimadzu GCMS-QP 1000 mass spectrometer at 70 eV. The elemental analyses were carried out on a Perkin-Elmer 240C Microanalyzer. All compounds were checked for their purity on TLC plates. X-ray was measured on Bruker APEX2; cell refinement: Bruker SAINT; program(s) used to solve structure: SHELXS97; program(s) used to refine structure: SHELXL97; molecular graphics: XSEED.

Modified procedure for preparation of 2-benzothiazolylguanidine (1)

Method A. A mixture of *o*-aminothiophenol (1 mol), dicyandiamide (1 mol), concentrated hydrochloric acid (2 mol), and water (15 cm^3) was heated under reflux for 3 h. The reaction mixture allowed to cool down and treated with 10% NaOH to afford the product **1**, recrystallized from $CHCl_3$, with 95% yield.

Method B. *o*-Aminothiophenol (50 mmol) was dissolved upon heating in 50 mL of 10% sulfuric acid, and dicyandiamide (75 mmol) was added. The reaction mixture was heated for 20 min, and then 10 mL of 50% sodium hydroxide solution was added. After heating for additional 15 min, the reaction mixture was cooled. The solid was collected by filtration and washed with water. The prepared compound was sufficiently pure and used without further purification with 97% yield. Recrystallized samples have been prepared for analyses.

Method C. A mixture of *o*-aminothiophenol (1 mol), dicyandiamide (1 mol), eight drops of concentrated hydrochloric acid, and ethanol (15 mL) was heated under reflux for 3 h. The reaction mixture was allowed to cool down and treated with 10% NaOH to afford the product **1** with 98% yield.

General procedure for the synthesis of compounds (2–12): Synthesis of compound (2) as a typical example. A mixture of compound **1** (50 mmol) and 10 mL of acetylacetone in addition to few drops of catalytic glacial acetic acid was refluxed at 200°C. The solid product was observed after 15–20 min. The reaction was allowed to proceed with reflux for further 1 h. After cooling down, the solid was collected by filtration, washed with cold ethanol, and recrystallized from ethanol to afford the bright crystals of **2** with 92% yield.

N-[(2E)-4,6-Dimethylpyrimidin-2(1H)-ylidene]-1,3-benzothiazol-2-amine (2). This compound was obtained as bright crystals (ethyl alcohol), white color, yield 92%, mp 240°C; IR: cm^{-1} 3200 (NH); ^1H NMR: δ 12.19 (s, 1H, NH), 7.32–6.91 (br, 5H, arom), 5.55 (s, 1H, CH), 2.49 (s, 6H, $2CH_3$); MS *m/z* (%): M^+ 256 (100), 215 (38.40), 175 (10.50), 67 (37.30). *Anal*. Calcd for $C_{13}H_{12}N_4S$ (256.33): C (60.91%), H (4.72%), N (21.86%), S (12.51%). Found: C (60.81%), H (4.28%), N (21.05%), S (12.01%).

(2E)-6-Amino-2-(1,3-benzothiazol-2-ylimino)-2,3-dihydropyrimidine-4(1H)-one (3). This compound was obtained as powder (ethyl alcohol), white color, yield 87%, mp 185°C; IR: cm^{-1} 3368, 3250, 3177 (2NH, NH_2), 1680 (CO); ^1H NMR: δ 11.67 (s, 1H, NH), 9.12 (s, 1H, NH), 7.76–7.04 (br, 4H, arom), 6.27 (s, 1H, CH), 4.11 (s, 2H, NH_2); MS *m/z* (%): M^+ 259 (38.40), 217 (58.24), 128 (13.52), 67 (38.40). *Anal*. Calcd for $C_{11}H_9N_5OS$ (259.29): C (50.95%), H (3.50%), N (27.01%), S (12.37%). Found: C (50.72%), H (3.11%), N (26.95%), S (12.03%).

(2E)-2-(1,3-Benzothiazol-2-ylimino)-1,2-dihydropyrimidine-4,6-diamine (4). This compound was obtained as light crystals (ethyl alcohol), white color, 95% yield, mp 198°C; IR: cm^{-1} 3391, 3277, 3182 (NH, $2NH_2$); ^1H NMR: δ 12.03 (s, 1H, NH), 7.90–7.04 (br, 5H, arom), 5.45 (s, 4H, $2NH_2$), 5.41 (s, 1H, CH); MS *m/z* (%): M^+ 258 (100), 216 (21.04), 177 (18.33), 67 (37.30). *Anal*. Calcd for $C_{11}H_{10}N_6S$ (258.30): C (51.15%), H (3.90%), N (32.54%), S (12.41%). Found: C (51.34%), H (3.26%), N (32.13%), S (12.10%).

(2E)-2-(1,3-Benzothiazol-2-ylimino)-6-methyl-2,3-dihydropyrimidine-4(1H)-one (5). This compound was obtained as powder (ethyl alcohol), buff color, 82% yield, mp 305°C; IR: cm^{-1} 3303, 3184 (2NH), 1691 (CO); ^1H NMR: δ 11.45 (s, 1H, NH), 7.67–7.05 (br, 5H, arom + NH), 5.18 (s, 1H, CH), 2.50 (s, 3H, CH_3); MS *m/z* (%): M^+ 258 (100), 210 (40.75), 128 (24.91), 76 (60.80). *Anal*. Calcd for $C_{12}H_{10}N_4OS$ (258.30): C (55.80%), H (3.90%), N (21.69%), S (12.41%). Found: C (55.61%), H (3.23%), N (21.01%), S (12.03%).

(2E)-2-(1,3-Benzothiazol-2-ylimino)-6-phenyl-2,3-dihydropyrimidine-4(1H)-one (6). This compound was obtained as light crystals (ethyl alcohol), creamy color, 88% yield, mp <360°C; IR: cm^{-1} 3393, 3177 (2NH), 1661 (CO); ^1H NMR: δ 12.34 (s, 1H, NH), 7.78–7.04 (br, 10H, 2arom + NH), 6.34 (s, 1H, CH); MS *m/z* (%): M^+ 320 (100), 292 (8.60), 251 (5.24), 176 (39.72), 69 (30.00). *Anal*. Calcd for $C_{17}H_{12}N_4OS$ (320.37): C (63.73%), H (3.78%), N (17.49%), S (10.01%). Found: C (63.46%), H (3.18%), N (17.01%), S (09.89%).

(2E)-2-(1,3-Benzothiazol-2-ylimino)-6-hydroxy-2,3-dihydropyrimidine-4(1H)-one (7). This compound was obtained as powder (ethyl alcohol), white color, 90% yield, mp 330°C; IR: cm^{-1} 3431 (OH), 3278, 3155 (2NH), 1666 (CO); ^1H NMR: δ 12.17 (s, 1H, NH), 10.58 (s, 1H, OH), 7.77–7.07 (br, 5H, arom + NH), 5.05 (s, 1H, CH); MS *m/z* (%): M^+ 260 (100), 215 (70.10), 177 (18.30), 134 (47.12), 69 (23.31). *Anal*. Calcd for $C_{17}H_{12}N_4OS$ (260.27): C (50.76%), H (3.10%), N (21.53%), S (12.32%). Found: C (50.44%), H (3.19%), N (21.11%), S (12.19%).

N-[(2Z)-4-Phenyl-1,5-dihydro-2H-imidazol-2-ylidene]-1,3-benzothiazol-2-amine (8). This compound was obtained as powder (ethyl alcohol), white color, 88% yield, mp 188°C; IR: cm^{-1} 3237, 3175 (2NH); ^1H NMR: δ 09.66 (s, 1H, NH), 7.76–7.04 (br, 10H, 2arom + NH), 6.66 (s, 1H, CH); MS *m/z* (%): M^+ 292 (04.80), 192 (75.20), 175 (100), 150 (53.52), 123 (32.10), 96 (48.90). *Anal*. Calcd for $C_{16}H_{12}N_4S$ (292.36): C (65.73%), H (4.14%), N (19.16%), S (10.97%). Found: C (65.42%), H (3.98%), N (19.00%), S (10.27%).

N-[(2Z)-4-Methyl-1,5-dihydro-2H-imidazol-2-ylidene]-1,3-benzothiazol-2-amine (9). This compound was obtained as bright crystals (ethyl alcohol), white color, 83% yield, mp 350°C; IR: cm^{-1} 3257, 3187 (2NH); ^1H NMR: δ 11.74 (s, 1H, NH), 7.62–7.11 (br, 5H, arom + NH), 6.85 (s, 1H, CH), 2.5 (s, 3H, CH_3); MS *m/z* (%): M^+ 230 (28.40), 192 (26.90), 106 (80.60), 67 (100). *Anal*. Calcd for $C_{11}H_{10}N_4S$ (230.29): C (57.37%), H (4.38%), N (24.33%), S (13.92%). Found: C (57.59%), H (4.09%), N (24.01%), S (13.70%).

(2Z)-2-(1,3-Benzothiazol-2-ylimino)imidazolidin-4-ol (10). This compound was obtained as powder (ethyl alcohol), white color, 88% yield, mp 205°C; IR: cm^{-1} 3268, 3177 (2NH); ^1H NMR: δ 10.06 (s, 1H, NH), 7.87–7.03 (br, 5H, arom + NH), 6.60 (s, 1H, CH); MS *m/z* (%): M^+ 232 (53.10), 192 (40.60), 175 (50.00), 163 (65.60), 82 (100). *Anal*. Calcd for $C_{10}H_8N_4OS$ (232.26): C (51.71%), H (3.47%), N (24.12%), S (13.81%). Found: C (51.85%), H (3.08%), N (24.03%), S (13.77%).

N-[(2Z)-4-Amino-1,5-dihydro-2H-imidazol-2-ylidene]-1,3-benzothiazol-2-amine (11). This compound was obtained as powder (ethyl alcohol), white color, 82% yield, mp 265°C; IR: cm^{-1} 3371, 3236, 3177 (2NH, NH_2); ^1H NMR: δ 09.86 (s, 1H, NH), 7.67–7.04 (br, 5H, arom + NH), 5.64 (s, 1H, CH), 4.73 (s, 2H, NH_2); MS *m/z* (%): M^+ 231 (34.40), 192 (25.00), 163 (50.30), 139 (75.20), 82 (100). *Anal*. Calcd for $C_{10}H_9N_5S$ (231.28): C (51.93%), H (3.92%), N (30.26%), S (13.86%). Found: C (51.58%), H (3.77%), N (30.01%), S (13.53%).

(2Z)-4-Amino-2-(1,3-benzothiazol-2-ylimino)-2,5-dihydro-1H-imidazole-5-carbonitrile (12). This compound was obtained as light crystal (ethyl alcohol), brown color, 93% yield, mp 250°C; IR: cm^{-1} 3382, 3278, 3177 (2NH, NH_2), 2221 (CN); ^1H NMR: δ 10.19 (s, 1H, NH), 7.88–7.02 (br, 5H, arom + NH), 5.33 (s, 2H, NH_2); MS *m/z* (%): M^+ 256 (47.80), 192 (32.10), 170 (39.10), 148 (65.20), 107 (43.50), 60 (100). *Anal*. Calcd for $C_{11}H_8N_6S$ (256.27): C (51.55%), H (3.15%), N (32.79%), S (12.51%). Found: C (51.24%), H (2.99%), N (32.60%), S (12.29%).

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