Synthesis and Antibacterial Activity of Sulfur-linked Bis and Tris Heterocycles

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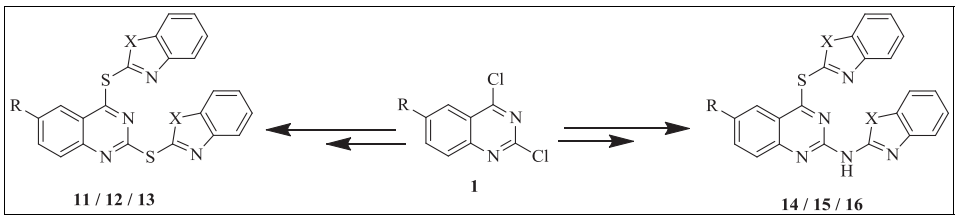

The bis and tris heterocycles-benzoxazolyl/benzothiazolyl/benzimidazolyl quinazolines linked by sulfur and/or nitrogen were prepared from 2,4-dichloroquinazoline and benzazolyl-2-thiol/benzazolyl-2-amine and studied their antibacterial activity. The nitro-substituted sulfur-linked bisbenzothiazolylquinazoline **(12f)**, bisbenzimidazolylquinazoline (**13f**), and nitro-substituted sulfur and nitrogen-linked bisbenzothiazolylquinazoline (**15f**) were found to be potential antibacterial agents against *Staphylococcus aureus*.

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INTRODUCTION

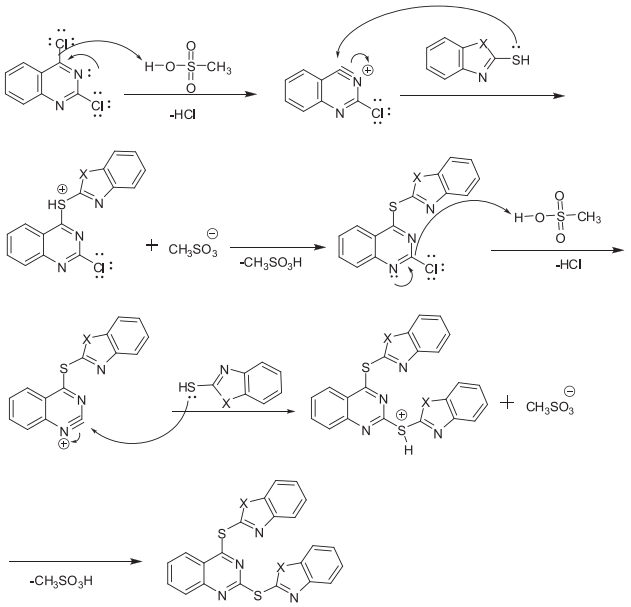
The heterocycles with two or more heteroatoms have intensively studied as they represent the most important structural units in a variety of bioactive molecules. Among these, benzimidazole, benzoxazole, and benzothiazole derivatives are frequently encountered in many therapeutic agents. Substituted benzoxazoles are associated with diverse pharmacological activities such as antibacterial, antifungal [1], analgesic [2], anti-inflammatory [3], and antioxidant [4]. Benzothiazoles have also been studied extensively for their antimicrobial [5], antitumor [6,7], and antiviral [8] activities. Benzimidazoles have been reported to possess potential antitumor and anticancer activities [9–11] along with antibacterial, antifungal [12], antiviral, and antioxidant [13]. In addition, as an important pharmacophore, quinazoline has a variety of biological activities such as anticancer [14,15], antibacterial [16], and anti-inflammatory [13,17], Although the medicinal chemistry fraternity has put up a brave front to cover a wide range of structurally and functionally derivatized heterocyclic compounds, the libraries of bis and tris heterocycles have not been extensively studied. Fascinated by multifarious bioactivity of these heterocycles and our continued efforts in this direction [18–20], we planned to synthesize compact molecules encompassing benzazole and quinazoline entities conjugated by a heteroatom with a scope to develop compounds possessing noteworthy pharmacological properties.

RESULTS AND DISCUSSION

The synthetic scheme involves the synthesis and antibacterial activity of multifaceted heterocycles linked by heteroatoms. The reactive intermediate 2,4-dichloroquinazoline (**1**) was obtained by the reaction of substituted anthranilic acid with urea followed by chlorination with $POCl_3$ in the presence of a base [21]. The compounds benzo[*d*]oxazole-2-thiol (**2**), benzo[*d*]thiazole-2-thiol (**3**), and 1*H*-benzo[*d*]imidazole-2-thiol (**4**) were prepared by the reaction of 2-aminophenol/2-aminothiophenol/*o*-phenylenediamine with CS_2 in the presence of KOH in ethanol [22]. The compounds benzo[*d*]oxazol-2-amine (**5**), benzo[*d*]thiazol-2-amine (**6**), and 1*H*-benzo[*d*]imidazol-2-amine (**7**) were obtained by the reaction of respective *o*-disubstituted benzenes with cyanogen bromide in ethanol [23–25]. The reaction of one equivalent of **1** with two equivalents of **2** in the presence of methanesulfonic acid gave 4-(benzo[*d*]oxazol-2-ylthio)-2-chloroquinazoline (**8**) instead of the expected 2,4-bis(benzo[*d*]oxazol-2-ylthio)quinazoline (**11**). Similarly, 4-(benzo[*d*]thiazol-2-ylthio)-2-chloroquinazoline (**9**) and 4-(1*H*-benzo[*d*]imidazol-2-ylthio)-2-chloroquinazoline (**10**) were obtained by treating one equivalent of **1** with two equivalents of **3** and **4**, respectively. The reaction was found to be regiospecific. In the presence of two equivalents of benzazole-2-thiol, only mono thioheteroarylation takes place leading to **8–10** along with unreacted benzazole-2-thiol, which was removed

by column chromatography. The ^{1}H NMR spectra of **8a**, **9a**, and **10a** displayed multiplets in the regions δ 6.95–8.25, 6.97–8.28, and 6.70–8.23 for aromatic protons. The compound **10a** showed a broad singlet at 12.07 ppm because of NH, which disappeared on deutiration. The ^{13}C NMR spectra of **8a**, **9a**, and **10a** exhibited signals at δ 167.3, 168.3, 165.4 (C-4), 155.6, 157.6, 154.2 (C-2), 156.2, 171.7, 150.4 ppm (C-2′) in addition to the signals of aromatic carbons. However, bisthioheteroarylation takes place when the reaction was performed with one equivalent of **1** and twofold excess of **2** in the presence of methanesulfonic acid in ethanol, which resulted in 2,4-bis(benzo[*d*]oxazol-2-ylthio) quinazoline (**11**). Adopting similar methodology, 2,4-bis(benzo[*d*]thiazol-2-ylthio)quinazoline (**12**) and 2,4-bis(1*H*-benzo[*d*]imidazol-2-ylthio)quinazoline (**13**) were prepared by the reaction of **1** with **3** and **4**, respectively. Under the aforementioned conditions, thioheteroarylation takes place at positions 2 and 4 of quinazoline. The 'N' of quinazoline activates the cites via quarternization as shown in the mechanism. The^{1}H NMR spectra of **11a**, **12a**, and **13a** exhibited multiplets in the regions δ 7.04–8.27, 6.88–8.29, and 6.72–8.24 because of aromatic protons. Moreover, **13a** showed a broad singlet at 11.90 ppm because of NH, which disappeared on deutiration. The ^{13}C NMR spectra of **11a**, **12a**, and **13a** exhibited signals at δ 156.6, 157.3, 154.2 (C-4), 162.1, 164.3, 160.1 (C-2) and 155.2, 160.7, 150.2 ppm (C-2′) besides the signals of aromatic carbons. The compounds **8**, **9**, and **10** were also utilized to prepare tris heterocycles linked by two different heteroatoms by nucleophilic displacement of chlorine at position 2 with appropriate heteroaryl amines. The compound **8** was treated with **5** in the presence of concentrated HCl in dry ethanol to obtain sulfanyl and amino-linked tris heterocycles-*N*-(benzo[*d*]oxazol-2-yl)-4-(benzo[*d*]oxazol-2-ylthio)quinazolin-2-amine (**14**). Likewise, *N*-(benzo[*d*] thiazol-2-yl)-4-(benzo[*d*]thiazol-2-ylthio)quinazolin-2-amine (**15**) and *N*-(1*H*-benzo[*d*]imidazol-2-yl)-4-(1*H*-benzo[*d*] imidazol-2-ylthio)quinazolin-2-amine (**16**) were prepared by the reaction of **9** with **6** and **10** with **7** (Scheme 1). The ^{1}H NMR spectra of **14a**, **15a**, and **16a** displayed a broad singlet at δ 9.05, 9.02, 8.95 ppm because of NH in addition to the signals of aromatic protons. The compound **16a** showed another broad singlet at 12.08 because of NH of benzimidazole. The signals of highly acidic protons disappeared on deutiration. The ^{13}C NMR spectra of **14a**, **15a**, and **16a** exhibited signals at δ 158.6, 159.3, 156.4 (C-4), 174.2, 175.4, 173.2 (C-2), 160.2, 167.7, 155.3 ppm (C-2′) apart from the signals of aromatic carbons. All the new compounds were further characterized by IR, mass, and elemental analysis.

Mechanism.



Antibacterial Studies. The compounds **8–16** were tested for antibacterial activity at three different concentrations: 50, 75, and 100 μg/well**.** The results of antibacterial activity presented in Table 1 and Figure 1 indicated that Gram-positive bacteria were more susceptible toward the tested compounds than Gram-negative ones. Among bis and tris heterocycles, the latter compounds **11–16** displayed greater activity than **8–10**. Among tris heterocycles, those linked by two sulfur atoms (**11–13**) showed higher activity than the corresponding sulfur and amino-linked heterocycles (**14–16**). Further, it was observed that bisbenzothiazolylquinazolines (**12**, **15**) and bisbenzimidazolylquinazolines (**13**, **16**) exhibited greater activity than bisbenzoxazolylquinazolines (**11**, **14**). The presence of electron-withdrawing chloro, bromo, and nitro substituents on the aromatic ring increases the activity. It was noticed that with increasing electro negativity the activity also increased. In fact, the compounds having nitro substituent **12f**, **13f**, and **15f** exhibited excellent activity against *Staphylococcus aureus* greater than the standard drug, *Chloramphenicol* at all tested concentrations. However, the compounds **12c**, **13c**, **15c**, and **16f** showed good activity against *S. aureus.* On the other hand, the presence of electron-donating substituents decreases the activity. In fact the methyl and methoxy substituted compounds displayed less activity than unsubstituted compounds, which may be due to +I and +M effects. The structure-antibacterial activity of the tested compounds revealed that the presence of electronegative chloro, bromo, and nitro groups enhance the biological potency, bioavailability, metabolic stability, and lipophilicity. In fact, the increase in absorption and transportation of molecules within the biological system depends upon the lipophilicity.

Scheme 1. Synthesis of sulfur and/or nitrogen linked bis and tris heterocycles.

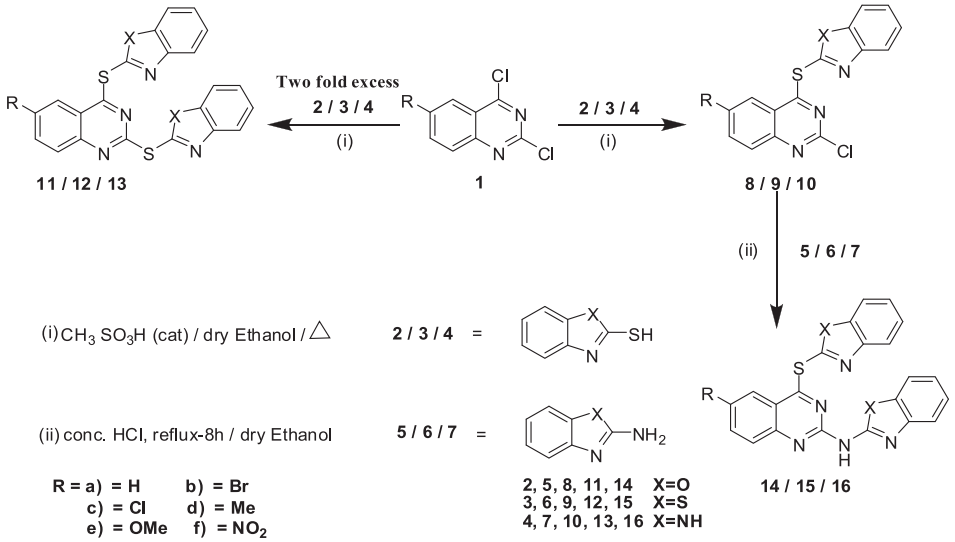


Table 1

The *in vitro* antibacterial activity of compounds **8**–**16**.

	Diameter of zone of inhibition (mm)											
	Gram-positive						Gram-negative					
	Staphylococcus aureus			*Bacillus substilis*			*Pseudomonas aeruginosa*			*Klebsiella pneumoniae*		
Compound	50 (μg/well)	75 (μg/well)	100 (μg/well)	50 (μg/well)	75 (μg/well)	100 (μg/well)	50 (μg/well)	75 (μg/well)	100 (μg/well)	50 (μg/well)	75 (μg/well)	100 (μg/well)
8a	—	—	—	—	—	—	—	—	—	—	—	—
8b	—	—	8 ± 2	—	—	—	—	—	—	—	—	—
8c	—	—	10 ± 2	—	—	9 ± 1	—	—	—	—	—	—
8d	—	—	—	—	—	—	—	—	—	—	—	—
8e	—	—	—	—	—	—	—	—	—	—	—	—
8f	—	9 ± 2	12 ± 1	—	—	—	—	—	—	—	—	8 ± 1
9a	—	—	—	—	—	—	—	—	—	—	—	—
9b	—	—	12 ± 2	—	—	9 ± 1	—	—	—	—	—	—
9c	8 ± 1	10 ± 2	13 ± 1	—	8 ± 2	10 ± 1		—	—	—	—	9 ± 1
9d	—	—	—	—	—	—	—	—	—	—	—	—
9e	—	—	—	—	—	—	—	—	—	—	—	—
9f	10 ± 2	12 ± 1	15 ± 2	9 ± 1	10 ± 2	12 ± 2	—	—	—	—	9 ± 2	11 ± 1
10a	—	—	—	—	—	—	—	—	—	—	—	—
10b	—	—	10 ± 1	—	—	—	—	—	—	—	—	—
10c	—	10 ± 1	11 ± 2	—	—	9 ± 2	—	—	—	—	—	8 ± 2
10d	—	—	—	—	—	—	—	—	—	—	—	—
10e	—	—	—	—	—	—	—	—	—	—	—	—
10f	9 ± 2	11 ± 2	13 ± 1	—	9 ± 2	11 ± 1	—	—	—	—	—	10 ± 1
11a	10 ± 2	12 ± 1	14 ± 2	9 ± 1	11 ± 1	13 ± 1	—	—	—	8 ± 2	10 ± 1	12 ± 2
11b	18 ± 1	20 ± 2	23 ± 1	10 ± 2	12 ± 1	14 ± 2	—	8 ± 2	11 ± 1	9 ± 1	11 ± 2	13 ± 2
11c	21 ± 2	22 ± 1	25 ± 2	12 ± 1	15 ± 1	17 ± 1	9 ± 1	10 ± 2	12 ± 1	11 ± 1	14 ± 1	16 ± 1
11d	—	—	—	—	—	—	—	—	—	—	—	
11e	—	10 ± 2	12 ± 1	—	—	12 ± 1	—	—	—	—	—	10 ± 1
11f	23 ± 1	25 ± 2	27 ± 2	17 ± 2	19 ± 2	21 ± 1	13 ± 1	15 ± 1	18 ± 1	14 ± 2	16 ± 1	19 ± 2
12a	18 ± 2	20 ± 1	23 ± 2	14 ± 1	15 ± 1	17 ± 2	—	—	10 ± 1	12 ± 2	14 ± 3	16 ± 2
12b	27 ± 1	30 ± 3	31 ± 2	21 ± 2	23 ± 2	25 ± 1	11 ± 2	12 ± 2	15 ± 2	18 ± 1	22 ± 1	24 ± 2
12c	29 ± 2	31 ± 2	33 ± 3	22 ± 2	24 ± 2	26 ± 2	14 ± 2	16 ± 2	19 ± 2	20 ± 2	23 ± 2	25 ± 1
12d	8 ± 1	11 ± 1	12 ± 2	—	—	—	—	—	—	—	8 ± 1	9 ± 1
12e	12 ± 2	14 ± 1	17 ± 1	10 ± 1	11 ± 1	14 ± 1	—	—	—	9 ± 2	10 ± 1	13 ± 2

(*Continued*)

Table 1

(*Continued*)

Compound	Diameter of zone of inhibition (mm)											
	Gram-positive						Gram-negative					
	Staphylococcus aureus			*Bacillus substilis*			*Pseudomonas aeruginosa*			*Klebsiella pneumoniae*		
	50 (μg/well)	75 (μg/well)	100 (μg/well)	50 (μg/well)	75 (μg/well)	100 (μg/well)	50 (μg/well)	75 (μg/well)	100 (μg/well)	50 (μg/well)	75 (μg/well)	100 (μg/well)
12f	35 ± 1	38 ± 2	41 ± 2	28 ± 1	31 ± 2	34 ± 2	18 ± 1	20 ± 1	23 ± 3	26 ± 2	27 ± 3	30 ± 2
13a	17 ± 1	18 ± 1	20 ± 2	12 ± 2	14 ± 2	15 ± 1	—	—	9 ± 1	10 ± 1	12 ± 2	14 ± 2
13b	26 ± 2	28 ± 1	30 ± 2	18 ± 1	21 ± 1	23 ± 3	—	10 ± 1	14 ± 1	15 ± 1	18 ± 1	20 ± 2
13c	28 ± 1	32 ± 2	34 ± 1	20 ± 1	22 ± 2	25 ± 1	13 ± 2	15 ± 1	18 ± 2	19 ± 1	21 ± 2	24 ± 2
13d	—	9 ± 2	11 ± 1	—	—	—	—	—	—	—	—	8 ± 2
13e	10 ± 2	11 ± 3	13 ± 2	—	9 ± 1	12 ± 1	—	—	—	—	8 ± 2	10 ± 2
13f	33 ± 2	36 ± 3	40 ± 2	27 ± 1	29 ± 2	32 ± 1	17 ± 1	19 ± 1	22 ± 2	24 ± 2	26 ± 1	29 ± 2
14a	9 ± 2	10 ± 1	12 ± 2	—	9 ± 2	11 ± 1	—	—	—	—	8 ± 2	10 ± 1
14b	13 ± 1	14 ± 1	17 ± 2	10 ± 1	11 ± 2	14 ± 2	—	—	—	9 ± 1	10 ± 2	12 ± 2
14c	15 ± 1	16 ± 2	18 ± 2	12 ± 1	13 ± 2	15 ± 2	—	—	—	10 ± 2	12 ± 1	14 ± 1
14d	—	—	—	—	—	—	—	—	—	—	—	—
14e	—	—	10 ± 2	—	—	—	—	—	—	—	—	9 ± 2
14f	17 ± 1	19 ± 2	20 ± 1	13 ± 2	16 ± 1	18 ± 1	—	8 ± 1	9 ± 1	11 ± 2	15 ± 1	17 ± 2
15a	14 ± 2	16 ± 2	17 ± 1	10 ± 2	12 ± 1	15 ± 2	—	—	10 ± 1	11 ± 2	12 ± 1	14 ± 2
15b	25 ± 1	26 ± 3	29 ± 3	16 ± 1	17 ± 1	19 ± 2	—	10 ± 1	13 ± 1	12 ± 2	14 ± 2	17 ± 1
15c	27 ± 2	30 ± 1	32 ± 1	18 ± 2	22 ± 1	24 ± 2	12 ± 1	14 ± 2	16 ± 2	15 ± 1	18 ± 2	21 ± 2
15d	—	9 ± 2	11 ± 2	—	—	—	—	—	—	—	—	—
15e	—	10 ± 3	11 ± 2	8 ± 2	10 ± 1	12 ± 2	—	—	—	8 ± 2	9 ± 1	11 ± 2
15f	32 ± 1	34 ± 2	37 ± 2	22 ± 2	24 ± 2	28 ± 1	16 ± 1	18 ± 1	20 ± 1	20 ± 2	22 ± 1	24 ± 2
16a	11 ± 2	13 ± 1	16 ± 2	8 ± 1	10 ± 2	12 ± 1	—	—	—	9 ± 2	12 ± 1	13 ± 2
16b	21 ± 1	24 ± 2	26 ± 1	12 ± 2	14 ± 1	15 ± 2	—	9 ± 2	12 ± 1	10 ± 1	12 ± 2	13 ± 2
16c	23 ± 2	25 ± 1	28 ± 2	15 ± 1	16 ± 1	18 ± 1	9 ± 1	11 ± 1	13 ± 1	12 ± 1	15 ± 1	14 ± 2
16d	—	—	9 ± 1	—	—	—	—	—	—	—	—	8 ± 2
16e	—	8 ± 1	10 ± 1	—	9 ± 1	11 ± 1	—	—	—	—	—	9 ± 2
16f	24 ± 1	27 ± 2	29 ± 2	17 ± 1	20 ± 3	23 ± 2	12 ± 1	14 ± 2	18 ± 1	17 ± 1	19 ± 2	21 ± 2
Chloramphenicol	30 ± 3	33 ± 1	35 ± 2	32 ± 3	34 ± 3	38 ± 1	25 ± 2	27 ± 3	30 ± 1	38 ± 1	40 ± 2	42 ± 3

Em dash (—) means no activity; "±" indicates standard deviation.

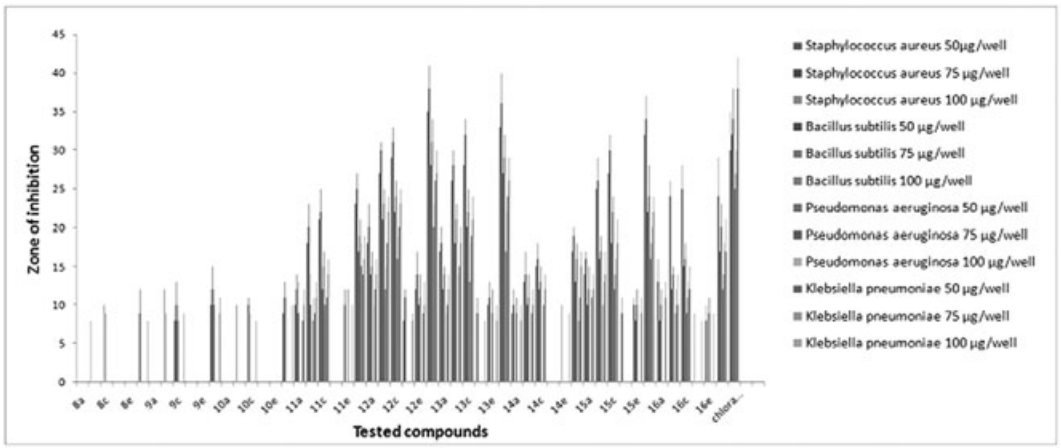


Figure 1. The *in vitro* antibacterial activity of compounds **8**–**16**.

The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values of the compounds tested are listed in Table 2. MIC is the lowest concentration of an antimicrobial that will inhibit the visible growth of a microorganism. (But it is not sure that the microorganisms are completely killed.) The MBC is the lowest concentration of antibiotic required to kill a particular bacterium. The MBC involves an additional set

Table 2

MIC and MBC of compounds **12c**, **12f**, **13c**, **13f**, **15c**, **15f**, and **16f**.

Compound	Minimum inhibitory concentration MIC (MBC) μg/well			
	Staphylococcus aureus	*Bacillus subtilis*	*Pseudomonas aeruginosa*	*Klebsiella pneumoniae*
12c	12.5 (50)	100 (>200)	—	—
12f	6.25 (12.5)	12.5 (50)	50 (200)	100 (>200)
13c	12.5 (50)	100 (>200)	—	—
13f	6.25 (12.5)	12.5 (50)	50 (200)	100 (>200)
15c	12.5 (50)	100 (>2000)	—	—
15f	6.25 (12.5)	50 (200)	100 (>200)	200 (>200)
16f	25 (100)	100 (>200)	—	—
Chloramphenicol	6.25	6.25	6.25	12.5
Ketoconazole	—	—	—	—

Em dash (—) means no activity.

of steps performed once the MIC is determined. The antimicrobials are usually regarded as bactericidal if the MBC is not greater than four times the MIC [26]. The compounds **12f**, **13f**, and **15f** exhibited low MIC values in case of *S. aureus*. In fact, in these compounds, the MBC value is 2xMIC against *S. aureus*.

CONCLUSIONS

The bis and tris heterocycles-benzoxazolyl/ benzothiazolyl/benzimidazolyl quinazolines linked by sulfur and/or nitrogen were prepared from 2,4-dichloroquinazoline and benzazolyl-2-thiol/ bezazolyl-2-amine adopting simple and versatile synthetic methodologies and tested for their antibacterial activity. The nitro-substituted sulfur linked bisbenzothiazolylquinazoline (**12f**), bisbenzimidazolylquinazoline (**13f**), and sulfur and nitrogen-linked bisbenzothiazolylquinazoline (**15f**) are the potential antibacterial agents against *S. aureus.*

EXPERIMENTAL

Melting points were determined in open capillaries on a Mel-Temp apparatus and are uncorrected. The purity of the compounds was checked by TLC (silica gel H, BDH, ethyl acetate/hexane, 1:3). The IR spectra were recorded on a Thermo Nicolet IR 200 FTIR spectrometer as KBr pellets, and the wave numbers were given in cm^{-1}. The ^1H and ^{13}C NMR spectra were recorded in DMSO-d_6 on a Bruker-400 spectrometer operating at 400 and 100 MHz, respectively. All chemical shifts are reported in δ (ppm) using TMS as an internal standard. The mass spectra were recorded on Jeol JMS-D 300 and Finnigan Mat 1201 B at 70 eV with an emission current of 100 μA. The microanalyses were performed on a Perkin-Elmer 240C elemental analyzer. The compounds 2,4-dichloroquinazoline(**1**) [20], benzo[*d*]oxazole-2-thiol (**2**) [25], benzo[*d*]thiazole-2-thiol (**3**) [25] and 1*H*-benzo[*d*]imidazole-2-thiol(**4**) [25], benzoxazol-2-amine (**5**) [26], benzothiazol-2-amine (**6**) [27], and 1*H*-benzimidazol-2-amine **(7)** [28] were prepared by adopting the literature precedents.

General procedure. ***4-(Benzo[d]oxazol-2-ylthio)-2-chloroquinazoline (8a–f)/4-(benzo[d]thiazol-2-ylthio)-2-chloroquinazoline (9a–f)/4-(1H-benzo[d]imidazol-2-ylthio) -2-chloroquinazoline (10a–f).*** A mixture of 2,4-dichloroquinazoline (**1**) (1 mmol), benzoxazole-2-thiol (**2**)/benzothiazole-2-thiol (**3**)/1*H*-benzimidazole-2-thiol (**4**) (2 mmol), dry ethanol (10 mL), and a catalytic amount of methanesulfonic acid (0.3 mL) was refluxed for 3–5 h. The contents of the flask were cooled and diluted with water (20 mL). The separated solid was filtered, washed with water, and dried. It was purified by column chromatography (silica gel, 60–120 mesh) using hexane-ethyl acetate (3:1) as eluent.

4-(Benzo[d]oxazol-2-ylthio)-2-chloroquinazoline (8a). Yield 68%; mp 146–148°C; IR (KBr): 1564 (C═N), 1598, 1487, 1466 (Ar, C═C) cm^{-1}; ^1H-NMR (400 MHz, DMSO-d_6): δ 6.95–8.25 (m, 8H, Ar—H) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 167.3 (C-4), 156.2 (C-2′), 155.6 (C-2), 153.4, 150.6, 138.7, 132.4, 131.2, 128.6, 127.1, 126.2, 125.6, 124.5, 111.3, 109.3 (aromatic carbons) ppm; MS: (*m/z*): 313.76 [M^+]. *Anal*. Calcd for $C_{15}H_8ClN_3OS$: C, 57.42; H, 2.57; N, 13.39; found: C, 57.49; H, 2.59; N, 13.54%.

4-(Benzo[d]oxazol-2-ylthio)-6-bromo-2-chloroquinazoline (8b). Yield 65%; mp 162–164°C; IR (KBr): 1568 (C═N) 1601, 1447, 1450 (Ar, C═C) cm^{-1}; ^1H-NMR (400 MHz, DMSO-d_6): δ 7.02–8.28 (m, 7H, Ar—H)ppm ; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 168.3 (C-4), 157.5 (C-2′), 156.2 (C-2), 150.2, 149.3, 136.5, 131.6, 128.4, 127.4, 124.3, 123.6, 122.6, 120.3, 110.4, 109.5 (aromatic carbons) ppm; MS: (*m/z*): 392.66 [M^+]. *Anal*. Calcd for $C_{15}H_7BrClN_3OS$: C, 45.88; H, 1.80; N, 10.70; found: C, 45.99; H, 1.83; N, 10.87%.

4-(Benzo[d]oxazol-2-ylthio)-2,6-dichloroquinazoline (8c). Yield 68%; mp 153–155°C; IR (KBr): 1576 (C═N), 1610, 1470, 1441 (Ar, C═C) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.12–8.34 (m, 7H, Ar─H) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 169.3 (C-4), 158.7 (C-2′), 157.2 (C-2), 151.3, 150.5, 134.3, 132.4, 131.2, 130.6, 128.2, 127.4, 126.3, 124.2, 111.3, 110.9 (aromatic carbons) ppm; MS: (*m/z*): 348.21 [M^+]. *Anal*. Calcd for $C_{15}H_7Cl_2N_3OS$: C, 51.74; H, 2.03; N, 12.07; found: C, 51.83; H, 2.02; N, 12.19%.

4-(Benzo[d]oxazol-2-ylthio)-2-chloro-6-methylquinazoline (8d). Yield 63%; mp 134–136°C; IR (KBr): 1558 (C═N), 1610, 1467, 1438 (Ar, C═C) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.02–8.13 (m, 7H, Ar─H), 2.42 (s, 3H, Ar─CH_3) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 166.1 (C-4), 155.4 (C-2′), 154.3 (C-2), 25.1 (CH_3), 148.4, 147.3, 137.6, 132.4, 131.5, 130.1, 129.3, 127.2, 123.8, 123.2, 111.5, 108.4 (aromatic carbons) ppm; MS: (*m/z*): 327.79 [M^+]. *Anal*. Calcd for $C_{16}H_{10}ClN_3OS$: C, 58.63; H, 3.07; N, 12.82; found: C, 58.75; H, 3.11; N, 13.00%.

4-(Benzo[d]oxazol-2-ylthio)-2-chloro-6-methoxyquinazoline (8e). Yield 69%; mp 130–131°C; IR (KBr): 1554 (C═N), 1589, 1480, 1423 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.98–8.22 (m, 7H, Ar─H), 3.78 (s, 3H, Ar─OCH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 165.6 (C-4), 154.6 (C-2′), 153.2 (C-2), 54.6 (OCH_3), 158.6, 147.6, 144.7, 129.6, 127.2, 126.3, 125.2, 123.2, 121.4, 109.3, 108.3, 107.4 (aromatic carbons) ppm; MS: (*m/z*): 343.79 [M^+]. *Anal*. Calcd for $C_{16}H_{10}ClN_3O_2S$: C, 55.90; H, 2.93; N, 12.22; found: C, 56.00; H, 2.94; N, 12.15%.

4-(Benzo[d]oxazol-2-ylthio)-2-chloro-6-nitroquinazoline (8f). Yield 70%; mp 157–158°C; IR (KBr): 1582 (C═N), 1602, 1493,1445 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.16–8.42 (m, 7H, Ar─H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.3 (C-2), 167.4 (C-4), 158.6 (C-2′), 151.7, 150.3, 146.3, 133.4, 129.7, 128.1, 127.3, 124.1, 123.4, 121.2, 113.1, 112.1 (aromatic carbons) ppm; MS: (*m/z*): 358.76 [M^+]. *Anal*. Calcd for $C_{15}H_7ClN_4O_3S$: C, 50.22; H, 1.97; N, 15.62; found: C, 50.34; H, 1.96; N, 15.80%.

4-(Benzo[d]thiazol-2-ylthio)-2-chloroquinazoline (9a). Yield 72%; mp 160–162°C; IR (KBr): 1572 (C═N), 1603, 1499, 1466 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.97–8.28 (m, 8H, Ar─H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.7 (C-2′), 168.3 (C-4), 157.6 (C-2), 154.8, 153.4, 139.5, 137.3, 132.4, 128.7, 127.4, 126.6, 125.4, 124.2, 123.1, 122.6 (aromatic carbons) ppm; MS: (*m/z*): 329.83 [M^+]. *Anal*. Calcd for $C_{15}H_8ClN_3S_2$: C, 54.62; H, 2.44; N, 12.74; found: C, 54.70; H, 2.46; N, 12.58%.

4-(Benzo[d]thiazol-2-ylthio)-6-bromo-2-chloroquinazoline (9b). Yield 73%; mp 178–180°C; IR (KBr): 1578 (C═N), 1593, 1478, 1460 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.01–8.25 (m, 7H, Ar─H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.3 (C-2′),169.2 (C-4), 158.4 (C-2), 152.4, 150.3, 137.5, 132.5, 129.2, 128.4, 126.4, 123.3, 122.4, 121.4, 120.4, 118.4 (aromatic carbons) ppm; MS: (*m/z*): 408.72 [M^+]. *Anal*. Calcd for $C_{15}H_7BrClN_3S_2$: C, 44.08; H, 1.75; N, 10.28; found: C, 44.15; H, 1.74; N, 10.40%.

4-(Benzo[d]thiazol-2-ylthio)-2,6-dichloroquinazoline (9c). Yield 75%; mp 172–174°C; IR (KBr): 1584 (C═N), 1576, 1445, 1436 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.08–8.35 (m, 7H, Ar─H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.5(C-2′), 170.4(C-4), 159.5 (C-2), 154.3, 150.3, 137.2, 135.3, 132.2, 131.4, 130.2, 128.2, 126.1, 124.7, 123.4, 122.1 (aromatic carbons) ppm; MS: (*m/z*): 364.27 [M^+]. *Anal*. Calcd for $C_{15}H_7Cl_2N_3S_2$: C, 49.46; H, 1.94; N, 11.54; found: C, 49.38; H, 1.98; N, 11.45%.

4-(Benzo[d]thiazol-2-ylthio)-2-chloro-6-methylquinazoline (9d). Yield 71%; mp 156–158°C; IR (KBr): 1564 (C═N), 1602, 1490, 1466 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.88–8.20 (m, 7H, Ar─H), 2.36 (s, 3H, Ar─CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 170.4 (C-2′), 167.1 (C-4), 156.2 (C-2), 25.3 (CH_3), 152.4, 148.4, 138.3, 136.4, 131.1, 130.6, 130.3, 128.4, 124.5, 123.4,121.3, 120.1 (aromatic carbons) ppm; MS: (*m/z*): 343.85 [M^+]. *Anal*. Calcd for $C_{16}H_{10}ClN_3S_2$: C, 55.89; H, 2.93; N, 12.22; found: C, 56.00; H, 2.96; N, 12.38%.

4-(Benzo[d]thiazol-2-ylthio)-2-chloro-6-methoxyquinazoline (9e). Yield 76%; mp 165–166°C; IR (KBr): 1558 (C═N), 1604, 1467, 1456 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.85–8.22 (m, 7H, Ar─H), 3.82 (s, 3H, Ar─OCH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.1 (C-2′), 166.4 (C-4), 155.4 (C-2), 55.2 (OCH_3), 159.6, 150.1, 145.2, 130.4, 128.4, 127.3, 126.2, 124.6, 119.6, 118.4, 116.8, 108.3 (aromatic carbons) ppm; MS: (*m/z*): 359.85 [M^+]. *Anal*. Calcd for $C_{16}H_{10}ClN_3OS_2$: C, 53.40; H, 2.80; N, 11.68; found: C, 53.46; H, 2.79; N, 11.58%.

4-(Benzo[d]thiazol-2-ylthio)-2-chloro-6-nitroquinazoline (9f). Yield 78%; mp 169–171°C; IR (KBr): 1592 (C═N), 1578, 1498, 1471 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.12–8.31 (m, 7H, Ar─H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 174.0 (C-2′), 160.8 (C-2), 160.6 (C-4), 154.5, 152.5, 147.2, 133.6, 130.4, 129.5, 127.6, 124.3, 123.9, 122.8, 121.2, 119.5 (aromatic carbons) ppm; MS: (*m/z*): 374.82 [M^+]. *Anal*. Calcd for $C_{15}H_7ClN_4O_2S_2$: C, 48.07; H, 1.88; N, 14.95; found: C, 48.15; H, 1.90; N, 15.13%.

4-(1H-Benzo[d]imidazol-2-ylthio)-2-chloroquinazoline (10a). Yield 73%; mp 149–150°C; IR (KBr): 3273 (NH),1563 (C═N), 1607, 1493, 1466 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.07 (bs, 1H, Imidazole-NH), 6.70–8.23 (m, 8H, Ar-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 165.4 (C-4),154.2 (C-2), 150.4 (C-2′), 151.5, 137.2, 131.2, 130.7, 126.3, 125.6, 125.4, 121.6,

109.5 (aromatic carbons) ppm; MS: (*m/z*): 312.78 [M^+]. *Anal*. Calcd for $C_{15}H_9ClN_4S$: C, 57.60; H, 2.90; N, 17.91; found: C, 57.67; H, 2.89; N, 18.04%.

4-(1H-Benzo[d]imidazol-2-ylthio)-6-bromo-2-chloroquinazolin (10b). Yield 66%; mp 176–178°C; IR (KBr): 3279 (NH), 1569 (C═N), 1589, 1467, 1437 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 12.15 (bs, 1H, Imidazole-NH),6.75–8.29 (m, 7H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 166.2 (C-4), 155.7 (C-2), 152.7 (C-2′), 148.9, 135.4, 132.6, 127.6, 126.8, 122.4, 120.2, 119.3, 109.5 (aromatic carbons) ppm; MS: (*m/z*): 391.67 [M^+]. *Anal*. Calcd for $C_{15}H_8BrClN_4S$: C, 46.00; H, 2.06; N, 20.40; found: C, 46.09; H, 2.09; N, 20.28%.

4-(1H-Benzo[d]imidazol-2-ylthio)-2,6-dichloroquinazoline (10c). Yield 76%; mp 157–159°C; IR (KBr): 3286 (NH), 1576 (C═N), 1578, 1478, 1456 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 12.24 (bs, 1H, Imidazole-NH),6.79–8.32 (m, 7H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.4 (C-4), 156.6 (C-2), 154.3 (C-2′), 148.6, 132.6, 130.6, 129.7, 128.6, 127.6, 126.4, 122.8, 110.8 (aromatic carbons) ppm; MS: (*m/z*): 347.22 [M^+]. *Anal*. Calcd for $C_{15}H_8Cl_2N_4S$: C, 51.89; H, 2.32; N, 16.14; found: C, 52.00; H, 2.34; N, 16.29%.

4-(1H-Benzo[d]imidazol-2-ylthio)-2-chloro-6-methylquinazoline (10d). Yield 74%; mp 136–138°C; IR (KBr): 3270 (NH), 1558 (C═N), 1589, 1497, 1460 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 12.02 (bs, 1H, Imidazole-NH), 6.74–8.13 (m, 7H, Ar—H), 2.44 (s, 3H, Ar—CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 23.6 (CH_3), 149.2 (C-2′), 153.4 (C-2), 164.5 (C-4), 147.6, 134.2, 131.5, 130.4, 129.5, 128.4, 126.3, 119.8, 109.4 (aromatic carbons) ppm; MS: (*m/z*): 326.80 [M^+]. *Anal*. Calcd for $C_{16}H_{11}ClN_4S$: C, 58.80; H, 3.39; N, 17.14; found: C, 58.72; H, 3.42; N, 17.26%.

4-(1H-Benzo[d]imidazol-2-ylthio)-2-chloro-6-methoxyquinazoline (10e). Yield 71%; mp 141–143°C; IR (KBr): 3264 (NH), 1552 (C═N), 1587, 1489, 1470 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 11.97 (bs, 1H, Imidazole-NH), 6.67–8.18 (m, 7H, Ar—H), 3.73 (s, 3H, Ar—OCH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.1 (C-4), 152.5 (C-2), 147.1 (C-2′), 52.4 (OCH_3), 157.5, 143.4, 130.1, 126.7, 125.4, 124.5, 120.1, 108.1, 106.2 (aromatic carbons) ppm; MS: (*m/z*): 342.80 [M^+]. *Anal*. Calcd for $C_{16}H_{11}ClN_4OS$: C, 56.06; H, 3.23; N, 16.34; found: C, 56.12; H, 3.20; N, 16.22%.

4-(1H-Benzo[d]imidazol-2-ylthio)-2-chloro-6-nitroquinazoline (10f). Yield 77%; mp 163–165°C; IR (KBr): 3292 (NH), 1583 (C═N), 1607, 1493, 1466 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 12.28 (bs, 1H, Imidazole-NH), 6.85–8.36 (m, 7H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.4 (C-4), 158.5 (C-2), 155.6 (C-2′), 150.2, 145.6, 133.4, 128.6, 127.2, 123.2, 122.6, 120.2, 110.3 (aromatic carbons) ppm; MS: (*m/z*): 357.77 [M^+]. *Anal*. Calcd for $C_{15}H_8ClN_5O_2S$: C, 50.36; H, 2.25; N, 19.57; found: C, 50.43; H, 2.27; N, 19.70%.

General procedure. ***2,4-Bis(benzo[d]oxazol-2-ylthio) quinazoline (11a–f)/2,4-bis(benzo[d]thiazol-2-ylthio)quinazoline (12a–f)/2,4-bis(1H-benzo[d]imidazol-2-ylthio)quinazoline (13a–f).*** To a solution of 2,4-dichloroquinazoline (**1**) (1.0 mmol), benzoxazole-2-thiol (**2**)/benzothiazole-2-thiol (**3**)/1*H*-benzimidazole-2-thiol (**4**) (4 mmol) in dry ethanol (15 mL), a catalytic amount of methanesulfonic acid (0.6 mL) was added and refluxed for 3–5 h. The contents of the flask were cooled and diluted with water (25 mL). The separated solid was filtered, washed with water, dried, and recrystallized from 2-propanol.

2,4-Bis(benzo[d]oxazol-2-ylthio)quinazoline (11a). Yield 64%; mp 156–158°C; IR (KBr): 1567 (C═N), 1567, 1474, 1456 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 7.04–8.27 (m, 12H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.1 (C-2), 156.6 (C-4), 155.2 (C-2′), 152.6, 148.4, 137.3, 131.1, 130.2, 127.6, 126.1, 125.6, 124.5, 123.2, 110.1, 108.4 (aromatic carbons) ppm; MS: (*m/z*): 428.49 [M^+]. *Anal*. Calcd for $C_{22}H_{12}N_4O_2S_2$: C, 61.67; H, 2.82; N, 13.08; found: C, 61.78; H, 2.84; N, 13.21%.

2,4-Bis(benzo[d]oxazol-2-ylthio)-6-bromoquinazoline (11b). Yield 65%; mp 185–187°C; IR (KBr): 1572 (C═N), 1565, 1467, 1451 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 7.06–8.31 (m, 11H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.8 (C-2), 157.2 (C-4), 156.4 (C-2′), 151.2, 150.1, 136.3, 132.4, 131.3, 127.4, 125.2, 124.3, 122.5, 121.2, 111.2, 110.9 (aromatic carbons) ppm; MS: (*m/z*): 507.38 [M^+]. *Anal*. Calcd for $C_{22}H_{11}BrN_4O_2S_2$: C, 52.08; H, 2.19; N, 11.04; found: C, 52.19; H, 2.22; N, 10.93%.

2,4-Bis(benzo[d]oxazol-2-ylthio)-6-chloroquinazoline (11c). Yield 66%; mp 168–170°C; IR (KBr): 1580 (C═N), 1571, 1472, 1443 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 7.08–8.36 (m, 11H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.4 (C-2), 158.4 (C-4), 157.7 (C-2′), 149.1, 148.2, 133.2, 132.1, 130.6, 129.5, 128.6, 126.4, 125.1, 123.8, 110.9, 109.1 (aromatic carbons) ppm; MS: (*m/z*): 462.93 [M^+]. *Anal*. Calcd for $C_{22}H_{11}ClN_4O_2S_2$: C, 57.08; H, 2.40; N, 12.10; found: C, 57.16; H, 2.38; N, 12.23%.

2,4-Bis(benzo[d]oxazol-2-ylthio)-6-methylquinazoline (11d). Yield 63%; mp 140–142°C; IR (KBr): 1562 (C═N), 1579, 1480, 1445 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 7.02–8.23 (m, 11H, Ar—H),2.63 (s, 3H, Ar—CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.6 (C-2), 155.3 (C-4), 154.2 (C-2′), 24.5 (CH_3), 147.8, 146.4, 136.7, 132.3, 130.6, 129.3, 128.1, 126.7, 124.1, 122.8, 110.9, 107.8 (aromatic carbons) ppm; MS: (*m/z*): 442.51 [M^+]. *Anal*. Calcd for $C_{23}H_{14}N_4O_2S_2$: C, 62.43; H, 3.19; N, 12.66; found: C, 62.50; H, 3.21; N, 12.80%.

4-(1H-Benzo[d]imidazol-2-ylthio)-2-chloro-6-methoxyquinazoline (11e). Yield 62%; mp 162–164°C; IR (KBr): 1558 (C═N), 1553, 1445, 1430 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz,

DMSO-d_6): δ 6.97–8.18 (m, 11H, Ar—H), 3.81 (s, 3H, Ar—OCH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.2 (C-2), 153.3 (C-4), 152.6 (C-2′), 55.3 (OCH_3), 158.2, 148.6, 146.2, 132.1, 130.3, 127.4, 126.1, 124.1, 122.3, 109.3, 108.7, 106.3 (aromatic carbons) ppm; MS:(*m/z*): 458.51[M^+]. *Anal*. Calcd for $C_{23}H_{14}N_4O_3S_2$: C, 60.25; H, 3.08; N, 12.22; found: C, 60.33; H, 3.10; N, 12.36%.

2,4-Bis(benzo[d]oxazol-2-ylthio)-6-nitroquinazoline (11f). Yield 69%; mp 178–180°C; IR (KBr): 1586 (C═N), 1562, 1456, 1434 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.13–8.41 (m, 11H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.3 (C-2), 160.2 (C-4), 158.5 (C-2′), 153.2 152.1, 146.7, 134.2, 131.2, 128.2, 126.2, 125.4, 124.8, 123.2, 113.2, 112.3 (aromatic carbons) ppm; MS: (*m/z*): 473.48 [M^+]. *Anal*. Calcd for $C_{22}H_{11}N_5O_4S_2$: C, 55.81; H, 2.34; N, 14.79; found: C, 55.91; H, 2.43; N, 14.65%.

2,4-Bis(benzo[d]thiazol-2-ylthio)quinazoline (12a). Yield 65%; mp 174–176°C; IR (KBr): 1576 (C═N) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.88–8.29 (m, 12H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.3 (C-2), 160.7 (C-2′), 157.3 (C-4), 153.4, 152.3, 138.6, 136.2, 131.5, 127.6, 126.5, 125.3, 124.5, 123.4, 122.1, 121.3 (aromatic carbons) ppm; MS: (*m/z*): 460.62 [M^+]. *Anal*. Calcd for $C_{22}H_{12}N_4S_4$: C, 57.37; H, 2.63; N, 12.16; found: C, 57.30; H, 2.64; N, 12.28%.

2,4-Bis(benzo[d]thiazol-2-ylthio)-6-bromoquinazoline (12b). Yield 61%; mp 192–194°C; IR (KBr): 1582 (C═N), 1574, 1464, 1446 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.91–8.34 (m, 11H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 165.9 (C-2), 161.1 (C-2′), 158.5 (C-4), 152.4, 152.1 137.6, 133.6, 132.7, 128.7, 127.21, 123.1, 122.3, 121.6, 120.8, 119.2 (aromatic carbons) ppm; MS: (*m/z*): 539.51 [M^+]. *Anal*. Calcd for $C_{22}H_{11}BrN_4S_4$: C, 48.98; H, 2.06; N, 10.38; found: C, 49.07; H, 2.09; N, 10.55%.

2,4-Bis(benzo[d]thiazol-2-ylthio)-6-chloroquinazoline (12c). Yield 68%; mp 183–185°C; IR (KBr): 1586 (C═N), 1561, 1472, 1430 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.96–8.36 (m, 11H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 166.2 (C-2), 163.2 (C-2′), 159.8 (C-4), 153.1, 149.6, 136.8, 134.2, 131.4, 130.6, 129.6, 127.4, 125.2, 124.1, 122.8, 120.1 (aromatic carbons) ppm; MS: (*m/z*): 495.06 [M^+]. *Anal*. Calcd for $C_{22}H_{11}ClN_4S_4$: C, 53.37; H, 2.24; N, 11.32; found: C, 53.45; H, 2.27; N, 11.4%.

2,4-Bis(benzo[d]thiazol-2-ylthio)-6-methylquinazoline (12d). Yield 62%; mp 165–167°C; IR (KBr): 1568 (C═N), 1567, 1474, 1456 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.90–8.21 (m, 11H, Ar—H),2.65 (s, 3H, Ar—CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.1 (C-2), 159.2 (C-2′), 156.3 (C-4), 26.5 (CH_3), 151.9, 147.6, 137.6, 135.8, 131.5, 130.4, 129.5, 127.5, 123.4, 122.3, 121.8, 120.6 (aromatic carbons) ppm; MS: (*m/z*): 474.64 [M^+]. *Anal*. Calcd for $C_{23}H_{14}N_4S_4$: C, 58.20; H, 2.97; N, 11.80; found: C, 58.31; H, 2.95; N, 11.92%.

2,4-Bis(benzo[d]thiazol-2-ylthio)-6-methoxyquinazoline (12e). Yield 64%; mp 176–178°C; IR (KBr): 1562 (C═N), 1570, 1471, 1452 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.86–8.16 (m, 11H, Ar—H),3.85 (s, 3H, Ar—OCH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.5 (C-2), 156.2 (C-2′), 154.6 (C-4), 56.3 (OCH_3), 159.8, 151.2, 147.3, 133.2, 131.2, 128.4, 127.6, 125.3, 120.3, 119.3, 118.1, 108.2 (aromatic carbons) ppm; MS: (*m/z*): 490.64 [M^+]. *Anal*. Calcd for $C_{23}H_{14}N_4OS_4$: C, 56.30; H, 2.88; N, 11.42; found: C, 56.40; H, 2.92; N, 11.53%.

2,4-Bis(benzo[d]thiazol-2-ylthio)-6-nitroquinazoline (12f). Yield 72%; mp 188–190°C; IR (KBr): 1596 (C═N), 1589, 1470, 1436 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.03–8.43 (m, 11H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 166.2 (C-2), 165.3 (C-2′), 160.3 (C-4), 155.2, 153.2, 148.3, 134.1, 132.4, 129.3, 128.1, 125.4, 124.6, 123.2, 122.8, 120.5 (aromatic carbons) ppm; MS: (*m/z*): 505.62 [M^+]. *Anal*. Calcd for $C_{22}H_{11}N_5O_2S_4$: C, 52.26; H, 2.19; N, 13.85; found: C, 52.33; H, 2.18; N, 14.00%.

2,4-Bis(1H-benzo[d] imidazol-2-ylthio)quinazoline (13a). Yield 70%; mp 162–164°C; IR (KBr): 3305 (NH), 1567 (C═N), 1598, 1469, 1443 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.90 (bs, 2H, Imidazole-NH), 6.72–8.24 (m, 12H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.1 (C-2), 154.2 (C-4), 150.2 (C-2′), 150.7 136.5, 132.6, 129.3, 125.3, 124.5, 123.4, 122.6, 110.3 (aromatic carbons) ppm; MS: (*m/z*): 426.52 [M^+]. *Anal*. Calcd for $C_{22}H_{14}N_6S_2$: C, 61.95; H, 3.31; N, 19.70; found: C, 62.04; H, 3.32; N, 19.82%.

2,4-Bis(1H-benzo[d]imidazol-2-ylthio)-6-bromoquinazoline (13b). Yield 67%; mp 181–183°C; IR (KBr): 3313(NH), 1573 (C═N), 1540, 1464, 1436 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): 11.96 (bs, 2H, Imidazole-NH), 6.78–8.29 (m, 11H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.6 (C-2), 155.7 (C-4), 151.6 (C-2′), 150.1, 135.6, 133.2, 131.2, 126.7, 123.4, 121.2, 120.3, 110.3 (aromatic carbons) ppm; MS: (*m/z*): 505.41 [M^+]. *Anal*. Calcd for $C_{22}H_{13}BrN_6S_2$: C, 52.28; H, 2.59; N, 16.63; found: C, 52.30; H, 2.63; N, 16.81%.

2,4-Bis(1H-benzo[d]imidazol-2-ylthio)-6-chloroquinazoline (13c). Yield 75%; mp 171–173°C; IR (KBr): 3321 (NH), 1578 (C═N), 1567, 1474, 1456 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.04 (bs, 2H, Imidazole-NH),6.81–8.34 (m, 11H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): 162.1 (C-2), 156.6 (C-4), 153.1 (C-2′), 147.5, 133.5, 132.1, 129.4, 128.3, 127.6, 125.3, 123.5, 111.6 (aromatic carbons) ppm; MS: (*m/z*): 460.96 [M^+]. *Anal*. Calcd for $C_{22}H_{13}ClN_6S_2$: C, 57.32, H, 2.84; N, 18.23; found: C, 57.39; H, 2.83; N, 18.34%.

2,4-Bis(1H-benzo[d]imidazol-2-ylthio)-6-methylquinazoline (13d). Yield 69%; mp 144–145°C; IR (KBr): 3302

(NH), 1562 (C═N), 1570, 1470, 1430 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 11.88 (bs, 2H, Imidazole-NH),6.76–8.15 (m, 11H, Ar—H), 2.42 (s, 3H, Ar—CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.5 (C-2), 153.5 (C-4), 149.2 (C-2′), 25.6 (CH_3), 145.6 135.4, 130.2, 129.3, 128.2, 127.3, 125.6, 120.3, 108.1 (aromatic carbons) ppm; MS: (*m/z*): 440.54 [M^+]. *Anal*. Calcd for $C_{23}H_{16}N_6S_2$: C, 62.71; H, 3.66; N, 19.08; found: C, 62.81; H, 3.70; N, 19.25%.

2,4-Bis(1H-benzo[d]imidazol-2-ylthio)-6-methoxyquinazoline (13e). Yield 74%; mp 150–152°C; IR (KBr): 3297 (NH), 1554 (C═N), 1580, 1470, 1456 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 11.82 (bs, 2H, Imidazole-NH), 6.71–8.09 (m, 11H, Ar—H), 3.75 (s, 3H, Ar—OCH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 157.2 (C-2), 151.2 (C-4), 147.2 (C-2′), 53.5 (OCH_3), 157.3, 145.4, 132.4, 131.3, 126.2, 125.2, 121.3, 109.3, 105.6 (aromatic carbons) ppm; MS: (*m/z*): 456.54 [M^+]. *Anal*. Calcd for $C_{23}H_{16}N_6OS_2$: C, 60.51; H, 3.53; N, 18.41; found: C, 60.58; H, 3.55; N, 18.54%.

2,4-Bis(1H-benzo[d]imidazol-2-ylthio)-6-nitroquinazoline (13f). Yield 77%; mp 166–168°C; IR (KBr): 3226 (NH), 1587 (C═N), 1560, 1457, 1446 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 12.12 (bs, 2H, Imidazole-NH), 6.81–8.34 (m, 11H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.4 (C-2), 156.2 (C-4), 153.3 (C-2′), 151.2 145.3, 134.2, 130.2, 127.3, 124.6, 123.4, 122.4, 111.5 (aromatic carbons) ppm; MS: (*m/z*): 471.51 [M^+]. *Anal*. Calcd for $C_{22}H_{13}N_7O_2S_2$: C, 56.04; H, 2.78; N, 20.79; found: C, 55.90; H, 2.79; N, 20.92%.

General procedure. *N-(benzo[d]oxazol-2-yl)-4-(benzo[d]oxazol-2-ylthio)quinazolin-2-amine (14a–f)*/*N-(benzo[d]thiazol-2-yl)-4-(benzo[d]thiazol-2-ylthio)quinazolin-2-amine (15a–f)*/*4-(1H-benzo[d]imidazol-2-ylthio)-N-(1H-benzo[d]imidazol-2-yl) quinazolin-2-amine (16a–f).* A solution of 2-(2-chloroquinazolin-4-ylthio)benzo[*d*]oxazole (**8**)/2-(2-chloroquinazolin-4-ylthio)benzo[*d*]thiazole (**9**)/4-(1*H*-benzo[*d*]imidazol-2-ylthio)-2-chloroquinazoline (**10**) (1 mmol) and benzo[*d*]oxazol-2-amine (**5**)/benzo[*d*]thiazol-2-amine (**6**)/1*H*-benzo[*d*]imidazol-2-amine (**7**) (2 mmol) in dry ethanol (10 mL) was taken and to this a drop of concentrated HCl was added and stirred at room temperature for 8–10 h. The solid separated was filtered, dried, and recrystallized from 2-propanol.

N-(benzo[d]oxazol-2-yl)-4-(benzo[d]oxazol-2-ylthio)quinazolin-2-amine (14a). Yield 66%; mp 160–162°C; IR (KBr): 3283 (NH), 1560 (C═N), 1556, 1474, 1456 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 9.05 (bs, 1H, NH),7.07–8.28 (m, 12H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 174.2 (C-2), 160.2 (C-2′), 158.6 (C-4), 155.5 (C-2″), 151.4, 149.5, 145.6, 143.3, 133.5, 131.2, 128.4, 126.3, 125.7, 124.8, 123.7, 123.6, 122.5, 121.2, 115.1, 111.4, 110.1, 109.6 (aromatic carbons) ppm; MS: (*m/z*): 411.44 [M^+]. *Anal*. Calcd for $C_{22}H_{13}N_5O_2S$: C, 64.22; H, 3.18; N, 17.02; found: C, 64.31; H, 3.21; N, 17.16%.

N-(benzo[d]oxazol-2-yl)-4-(benzo[d]oxazol-2-ylthio)-6-bromoquinazolin-2-amine (14b). Yield 64%; mp 174–176° C; IR (KBr): 3288 (NH), 1563(C═N), 1607, 1484, 1466 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 9.08 (bs, 1H, NH), 7.12–8.33 (m, 11H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.8 (C-2), 161.2 (C-2′), 159.7 (C-4), 156.2 (C-2″), 149.6, 147.6, 146.3, 144.6, 135.4, 129.5, 128.6, 127.2, 126.2, 123.6, 122.3, 121.1, 119.2, 118.3, 117.6, 111.3, 108.6, 107.6 (aromatic carbons) ppm; MS: (*m/z*): 490.33 [M^+]. *Anal*. Calcd for $C_{22}H_{12}BrN_5O_2S$: C, 53.89; H, 2.47; N, 14.28; found: C, 54.01; H, 2.49; N, 14.44%.

N-(benzo[d]oxazol-2-yl)-4-(benzo[d]oxazol-2-ylthio)-6-chloroquinazolin-2-amine (14c). Yield 69%; mp 166–168° C; IR (KBr): 3294 (NH), 1572 (C═N), 1601, 1484, 1476 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 9.12 (bs, 1H, NH),7.16–8.37 (m, 11H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.2 (C-2), 163.8 (C-2′), 160.2 (C-4), 157.5 (C-2″), 150.2, 148.5, 146.2, 144.3, 133.4, 132.4, 129.2, 128.4, 127.2, 126.4, 125.2, 124.2, 123.1, 121.3, 116.2, 112.6, 111.4, 110.5 (aromatic carbons) ppm; MS: (*m/z*): 445.88 [M^+]. *Anal*. Calcd for $C_{22}H_{12}ClN_5O_2S$: C, 59.26; H, 2.71; N, 15.71; found: C, 59.39; H, 2.76; N, 15.89%.

N-(benzo[d]oxazol-2-yl)-4-(benzo[d]oxazol-2-ylthio)-6-methylquinazolin-2-amine (14d). Yield 65%; mp 158–160°C; IR (KBr): 3278 (NH), 1554 (C═N), 1587, 1484, 1426 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 9.01 (bs, 1H, NH),7.07–8.22 (m, 11H, Ar—H), 2.38 (s, 3H, Ar—CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.2 (C-2), 159.4 (C-2′), 157.5 (C-4), 154.1 (C-2″), 23.5 (CH_3), 148.6, 146.1, 144.3, 142.1, 134.5, 131.6, 130.4, 129.5, 125.4, 124.5, 123.6, 122.3, 121.4, 117.2, 114.6, 110.6, 109.4, 108.9 (aromatic carbons) ppm; MS: (*m/z*): 425.46 [M^+]. *Anal*. Calcd for $C_{23}H_{15}N_5O_2S$: C, 64.93; H, 3.55; N, 16.46; found: C, 65.01; H, 3.58; N, 16.63%.

N-(benzo[d]oxazol-2-yl)-4-(benzo[d]oxazol-2-ylthio)-6-methoxyquinazolin-2-amine (14e). Yield 68%; mp 163–165°C; IR (KBr): 3272 (NH), 1550 (C═N), 1597, 1484, 1476 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 8.96 (bs, 1H, NH), 7.02–8.18 (m, 11H, Ar—H), 3.71 (s, 3H, Ar—OCH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.3 (C-2), 171.3 (C-2), 157.5 (C-2′), 156.3 (C-4), 55.4 (OCH_3), 152.3 (C-2″), 153.4, 147.2, 146.3, 145.7, 142.5, 128.6, 127.3, 125.2, 124.6, 122.3, 121.3, 120.6, 119.3, 115.3, 109.5, 106.5, 105.2, 102.3 (aromatic carbons) ppm; MS: (*m/z*): 441.46 [$M^{+\cdot}$]. *Anal*. Calcd for $C_{23}H_{15}N_5O_3S$: C, 62.58; H, 3.42; N, 15.86; found: C, 62.71; H, 3.47; N, 16.07%.

N-(benzo[d]oxazol-2-yl)-4-(benzo[d]oxazol-2-ylthio)-6-nitroquinazolin-2-amine (14f). Yield 71%; mp 170–172° C; IR (KBr): 3297 (NH), 1578 (C═N), 1604, 1467, 1445 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 9.17 (bs, 1H, NH), 7.20–8.43 (m, 11H, Ar—H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.3 (C-2), 163.9

(C-2′), 162.5 (C-4), 158.5 (C-2″), 152.3, 150.6, 148.3, 146.1, 145.6, 131.5, 129.3, 128.6, 127.6, 126.3, 125.3, 124.3, 123.6, 119.2, 118.4, 112.5, 110.5, 109.3 (aromatic carbons) ppm; MS: (*m/z*): 456.43 [M$^+$]. *Anal*. Calcd for $C_{22}H_{12}N_6O_4S$: C, 57.89; H, 2.65; N, 18.41; found: C, 58.00; H, 2.68; N, 18.59%.

N-*(benzo[d]thiazol-2-yl)-4-(benzo[d]thiazol-2-ylthio)quinazolin-2-amine (15a)*. Yield 77%; mp 171–173°C; IR (KBr): 3261 (NH), 1568 (C═N), 1596, 1484, 1443 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.02 (bs, 1H, NH),6.78–8.22 (m, 12H, Ar─H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): 175.4 (C-2), 167.7 (C-2′), 161.5 (C-2″), 159.3 (C-4), 153.4, 152.8, 151.3, 136.7, 134.6, 130.2, 129.2, 127.6, 126.4, 125.6, 124.9, 124.8, 123.4, 122.6, 121.3, 120.5, 119.3, 118.5 (aromatic carbons) ppm; MS: (*m/z*): 443.57 [M$^+$]. *Anal*. Calcd for $C_{22}H_{13}N_5S_3$: C, 59.57; H, 2.95; N, 15.79; found: C, 59.71; H, 2.91; N, 15.99%.

N-*(benzo[d]thiazol-2-yl)-4-(benzo[d]thiazol-2-ylthio)-6-bromoquinazolin-2-amine (15b)*. Yield 76%; mp 190–192°C; IR (KBr): 3268 (NH), 1575 (C═N), 1587, 1487, 1456 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.07 (bs, 1H, NH), 6.85–8.27 (m, 11H, Ar─H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 176.2 (C-2), 168.4 (C-2′), 162.4 (C-2″), 160.1 (C-4), 155.3, 151.5, 150.4, 137.2, 132.6, 130.2, 128.6, 127.3, 126.4, 125.4, 123.6, 122.4, 121.5, 120.1, 119.8, 119.3, 118.4, 116.8 (aromatic carbons) ppm; MS: (*m/z*): 522.46 [M$^+$]. *Anal*. Calcd for $C_{22}H_{12}BrN_5S_3$: C, 50.57; H, 2.32; N, 13.40; found: C, 50.66; H, 2.34; N, 13.57%.

N-*(benzo[d]thiazol-2-yl)-4-(benzo[d]thiazol-2-ylthio)-6-chloroquinazolin-2-amine (15c)*. Yield 79%; mp 184–186°C; IR (KBr): 3272 (NH), 1581 (C═N), 1587, 1484, 1435 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.13 (bs, 1H, NH), 6.89–8.35 (m, 11H, Ar─H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.2 (C-2), 169.2 (C-2′), 163.1 (C-2″), 161.3 (C-4), 154.5, 153.2, 149.5, 137.6, 134.2, 131.5, 130.2, 129.6, 127.4, 126.7, 125.3, 124.5, 123.8, 123.4, 122.4, 121.6, 120.4, 119.5 (aromatic carbons) ppm; MS: (*m/z*): 478.01 [M$^+$]. *Anal*. Calcd for $C_{22}H_{12}ClN_5S_3$: C, 55.28; H, 2.53; N, 14.65; found: C, 55.24; H, 2.54; N, 14.78%.

N-*(benzo[d]thiazol-2-yl)-4-(benzo[d]thiazol-2-ylthio)-6-methylquinazolin-2-amine (15d)*. Yield 72%; mp 175–177°C; IR (KBr): 3257 (NH), 1560 (C═N), 1594, 1467, 1456 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.06 (bs, 1H, NH),6.93–8.20 (m, 11H, Ar─H), 2.36 (s, 3H, Ar─CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 174.5 (C-2), 166.1 (C-2′), 160.6 (C-2″), 158.6 (C-4), 26.4 (CH_3), 151.4 150.6, 147.5, 136.5, 135.4, 132.4, 130.5, 129.3, 126.2, 125.4, 124.3, 123.2, 122.1, 121.5, 120.4, 119.3, 118.6, 117.2 (aromatic carbons) ppm; MS: (*m/z*): 457.59 [M$^+$]. *Anal*. Calcd for $C_{23}H_{15}N_5S_3$: C, 60.37; H, 3.30; N, 15.30; found: C, 60.49; H, 3.33; N, 15.49%.

N-*(benzo[d]thiazol-2-yl)-4-(benzo[d]thiazol-2-ylthio)-6-methoxyquinazolin-2-amine (15e)*. Yield 78%; mp 180–182°C; IR (KBr): 3252 (NH), 1555 (C═N), 1597, 1487, 1435 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.95 (bs, 1H, NH), 6.85–8.24 (m, 11H, Ar─H), 3.76 (s, 3H, Ar─OCH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.3 (C-2), 164.6 (C-2′), 158.6 (C-2″), 157.5 (C-4), 56.3 (OCH_3), 154.5, 153.1, 150.4, 148.6, 130.2, 129.6, 128.5, 126.3, 124.9, 123.5, 121.4, 120.6, 119.3, 118.3, 117.1, 116.5, 115.2, 103.5 (aromatic carbons) ppm; MS: (*m/z*): 473.59 [M$^+$]. *Anal*. Calcd for $C_{23}H_{15}N_5OS_3$: C, 58.33; H, 3.19; N, 14.79; found: C, 58.27; H, 3.21; N, 14.87%.

N-*(benzo[d]thiazol-2-yl)-4-(benzo[d]thiazol-2-ylthio)-6-nitroquinazolin-2-amine (15f)*. Yield 72%; mp 188–189°C; IR (KBr): 3279 (NH), 1589 (C═N), 1592, 1478, 1463 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.17 (bs, 1H, NH), 6.92–8.37 (m, 11H, Ar─H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 180.2 (C-2), 170.2 (C-2′), 165.3 (C-2″), 163.5 (C-4), 156.8, 154.2, 153.6, 147.1, 133.6, 132.5, 129.5, 128.2, 127.4, 126.3, 125.6, 124.6, 123.6, 122.3, 121.5, 120.5, 119.2, 118.9 (aromatic carbons) ppm; MS: (*m/z*): 488.56 [M$^+$]. *Anal*. Calcd for $C_{22}H_{12}N_6O_2S_3$: C, 54.08; H, 2.48; N, 17.20; found: C, 54.17; H, 2.46; N, 17.35%.

***4-(1*H*-benzo[d]imidazol-2-ylthio)-*N*-(1*H*-benzo[d]imidazol-2-yl)quinazolin-2-amine (16a)*.** Yield 67%; mp 152–154°C; IR (KBr): 3291 (NH), 1560 (C═N), 1605, 1484, 1472 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.08 (bs, 2H, Imidazole-NH), 8.95 (bs, 1H, NH), 6.75–8.29 (m, 12H, Ar─H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.2 (C-2), 156.4 (C-4), 155.3 (C-2′), 150.1 (C-2″), 150.5, 137.6, 133.4, 132.1, 127.5, 125.6, 122.3, 121.7, 120.3, 119.5, 111.2, 109.1 (aromatic carbons) ppm; MS: (*m/z*): 409.47 [M$^+$]. *Anal*. Calcd for $C_{22}H_{15}N_7S$: C, 64.53; H, 3.69; N, 23.95; found: C, 64.68; H, 3.74; N, 24.16%.

***4-(1*H*-benzo[d]imidazol-2-ylthio)-*N*-(1*H*-benzo[d]imidazol-2-yl)-6-bromoquinazolin-2-amine (16b)*.** Yield 72%; mp 185–187°C; IR (KBr): 3296 (NH), 1565 (C═N), 1607, 1574, 1566 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.12 (bs, 2H, Imidazole-NH), 9.00 (bs, 1H, NH), 6.78–8.32 (m, 11H, Ar─H)ppm ; ^{13}C NMR (100 MHz, DMSO-d_6): δ 174.3 (C-2), 157.5 (C-4), 156.3 (C-2′), 151.5 (C-2″), 147.2, 140.2, 133.6, 130.6, 128.4, 126.1, 122.4, 120.5, 118.3, 117.3, 115.3, 107.4 (aromatic carbons) ppm; MS: (*m/z*): 488.36 [M$^+$]. *Anal*. Calcd for $C_{22}H_{14}BrN_7S$: C, 54.11; H, 2.89; N, 20.08; found: C, 54.23; H, 2.93; N, 20.10%.

***4-(1*H*-benzo[d]imidazol-2-ylthio)-*N*-(1*H*-benzo[d]imidazol-2-yl)-6-methylquinazolin-2-amine (16c)*.** Yield 75%; mp 163–165°C; IR (KBr): 3305 (NH), 1571 (C═N), 1597, 1488, 1476 (Ar, C═C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.18 (bs, 2H, Imidazole-NH), 9.04 (bs, 1H, NH), 6.83–8.36 (m, 11H, Ar─H) ppm; ^{13}C NMR (100 MHz,

DMSO-d_6): δ 175.2 (C-2), 159.5 (C-4), 158.6 (C-2′), 153.3 (C-2″), 147.8, 138.6, 133.2, 132.4, 128.1, 127.5, 124.2, 123.4, 121.3, 120.6, 112.4, 110.2 (aromatic carbons) ppm; MS: (*m/z*): 443.91 [M^+]. *Anal*. Calcd for $C_{22}H_{14}ClN_7S$: C, 59.52; H, 3.18; N, 22.09; found: C, 59.62; H, 3.16; N, 22.27%.

4-(1H-benzo[d]imidazol-2-ylthio)-N-(1H-benzo[d]imidazol-2-yl)-6-chloroquinazolin-2-amine (16d). Yield 76%; mp 157–159°C; IR (KBr): 3288 (NH), 1553(C═N), 1600, 1474, 1448 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 11.92 (bs, 2H, Imidazole-NH), 8.98 (bs, 1H, NH), 6.78–8.17 (m, 11H, Ar─H), 2.43 (s, 3H, Ar─CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 170.1 (C-2), 155.4 (C-4), 154.8 (C-2′), 149.2 (C-2″), 24.6 (CH_3), 145.6, 136.5, 133.6, 131.2, 130.4, 128.9, 122.2, 121.6, 118.4, 116.1, 110.8, 108.6 (aromatic carbons) ppm; MS: (*m/z*): 423.49 [M^+]. *Anal*. Calcd for $C_{23}H_{17}N_7S$: C, 65.23; H, 4.05; N, 23.15; found: C, 65.36; H, 4.09; N, 23.35%.

4-(1H-benzo[d]imidazol-2-ylthio)-N-(1H-benzo[d]imidazol-2-yl)-6-methoxyquinazolin-2-amine (16e). Yield 77%; mp 168–170°C IR (KBr): 1548 (C═N), 3284 (NH), 1607, 1485, 1467 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 11.85 (bs, 2H, Imidazole-NH), 8.94 (bs, 1H, NH), 6.72–8.26 (m, 11H, Ar─H), 3.74 (s, 3H, Ar─OCH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.6 (C-2), 153.8 (C-4), 152.3 (C-2′), 147.1 (C-2″), 54.5 (OCH_3), 151.6, 146.5, 138.3,128.3, 126.5, 123.9, 120.4, 119.6, 118.6, 113.1, 107.2, 101.3 (aromatic carbons) ppm; MS: (*m/z*): 439.49 [M^+]. *Anal*. Calcd for $C_{23}H_{17}N_7OS$: C, 62.86; H, 3.90; N, 22.31; found: C, 62.94; H, 3.91; N, 22.47%.

4-(1H-benzo[d]imidazol-2-ylthio)-N-(1H-benzo[d]imidazol-2-yl)-6-nitroquinazolin-2-amine (16f). Yield 79%; mp 173–175°C; IR (KBr): 3312 (NH), 1578 (C═N), 1597, 1486, 1463 (Ar, C═C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 12.22 (bs, 2H, Imidazole-NH), 9.11 (bs, 1H, NH), 6.87–8.39 (m, 11H, Ar─H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.6 (C-2), 159.3 (C-4), 158.3 (C-2′), 154.3 (C-2″), 150.5, 143.6, 141.3, 132.1, 127.6, 126.2, 123.6, 122.4, 121.6, 117.3, 116.2, 108.6 (aromatic carbons) ppm; MS: (*m/z*): 454.46 [M^+]. *Anal*. Calcd for $C_{22}H_{14}N_8O_2S$: C, 58.14; H, 3.11; N, 24.66; found: C, 58.54; H, 3.14; N, 24.84%.

Antibacterial assays. The compounds **8**–**16** were evaluated for antibacterial activity at three different concentrations: 50, 75, and 100 μg/well. Bacterial strains *S. aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* were obtained from the Department of Microbiology, S.V. University, Tirupati.

The *in vitro* antibacterial studies were carried out by agar well diffusion method against test organisms [27,28]. Nutrient broth (NB) plates were swabbed with 24-h old broth culture (100 μl) of test bacteria. Using the sterile cork borer, wells (6 mm) were made into each petriplate. The compounds were dissolved in DMSO of 5 mg/mL, and from this, 10, 15, and 20 μL (50, 75, and 100 μg/well) were added into the wells by using sterile pipettes. The standard antibiotic, Chloramphenicol, for antibacterial activity (as positive control) was simultaneously tested against the pathogens. The samples were dissolved in DMSO, which showed no zone of inhibition acts as a negative control. The plates were incubated at 37°C for 24 h. After appropriate incubation, the diameter of zone of inhibition of each well was measured. Duplicates were maintained, and the average values were calculated for eventual antibacterial activity.

Minimum inhibitory concentration assay. Broth dilution test was used to determine MIC of the above-mentioned samples [29,30]. Freshly prepared nutrient broth was used as diluents. The 24-h old culture of the test bacteria *S. aureus*, *B. subtilis*, *P. aeruginosa*, and *K. pneumoniae* were diluted 100-fold in nutrient broth (100-μL bacterial cultures in 10-m**L** NB). The stock solution of the synthesized compounds was prepared in DMSO by dissolving 5 mg of the compound in 1 m**L** of DMSO. Increasing concentrations of the test samples (1.25, 2.5, 5, 10, 20, **and** 40 μL of stock solution contain 6.25, 12.5, 25, 50, 100, **and** 200 μg of the compounds) were added to the test tubes containing the bacterial cultures. All the tubes were incubated at 37°C for 24 h. The tubes were examined for visible turbidity and using NB as control. Control without test samples and with solvent was assayed simultaneously. The lowest concentration that inhibited visible growth of the tested organisms was recorded as MIC.

Minimum bactericidal concentration. For the determination of the MBC [31] for each set of test tubes in the MIC determination, a loopful of broth was collected from those tubes, which did not show any growth and inoculated on sterile nutrient broth (for bacteria) by streaking. Plates inoculated with bacteria were incubated at 37°C for 24 h. After incubation, the lowest concentration was noted as MBC at which no visible growth was observed.

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