www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277- 7695
ISSN (P): 2349-8242
NAAS Rating: 5.03
TPI 2019; 8(6): 627-632

www.thepharmajournal.com
Received: 22-04-2019
Accepted: 24-05-2019

Shaik Mahaboob Basha
Department of Chemistry, Thiruvalluvar University, Tamil Nadu, India

Paala Krishna
Department of chemistry, S.V. University, Tirupati, Andhra Pradesh, India

Shaik Thaslim Basha
Department of chemistry, S.V. University, Tirupati, Andhra Pradesh, India

Chintha Venkataramaiah
Department of Zoology, S. V. University-Tirupati, Andhra Pradesh, India

Suban Syed Shafi
Prof. Department of Chemistry, Thiruvalluvar University, Tamil Nadu, India

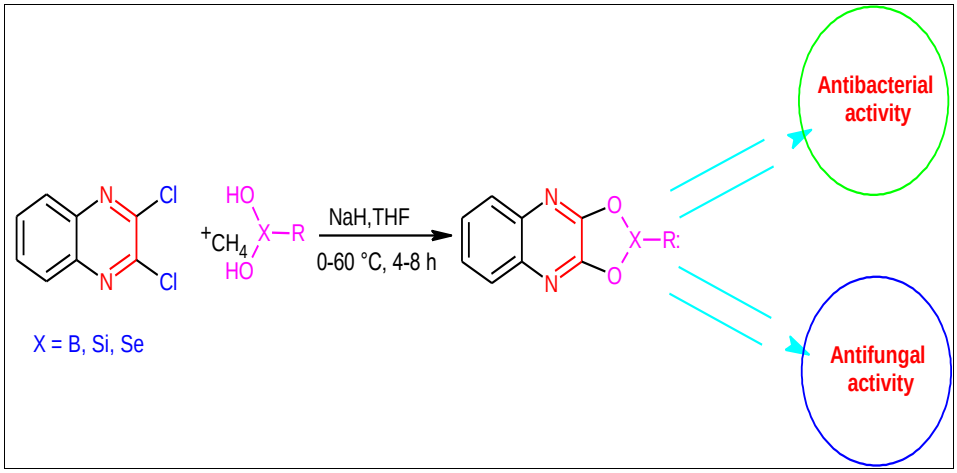
Chamarthi Naga Raju
Prof. Department of Chemistry, S.V. University, Tirupati, Andhra Pradesh, India

Correspondence
Suban Syed Shafi
Prof. Department of Chemistry, Thiruvalluvar University, Tamil Nadu, India

Synthesis, characterization and antimicrobial activity of boron, silicon and selenium substituted quinoxaline derivatives

Shaik Mahaboob Basha, Paala Krishna, Shaik Thaslim Basha, Chintha Venkataramaiah, Suban Syed Shafi and Chamarthi Naga Raju

Abstract
A series of new quinoxaline derivatives was synthesized by reacting 2, 3-dichloro quionoxaline with various boronic acids, silicic acid and selenous acid in mild, efficient and convenient method with good yields in less time. All the newly synthesized compounds were characterized by IR, NMR (^{1}H, ^{13}C & ^{11}B) and mass spectroscopy and also screened for their antimicrobial activity. Among the title compounds, 4-fluoro phenyl, 2,4-difluoro phenyl and 4-chloro phenyl groups substituted compounds at boron have showed potent antimicrobial activity when compared to the standard drugs.



Graphical Abstract

Keywords: Antimicrobial activity, 2, 3-dichloro quinoxaline, Quinoxaline derivatives, Boronic acid, silicic acid, Selenous acid

1. Introduction
Quinoxalines are the important class of *N*-containing heterocyclic compounds found in natural products and also as core moiety in several drugs currently on the market [1]. In addition several antibiotics such as Echinomycin, Levomycin and Actinoleutin which are known to inhibit growth of Gram-positive bacteria [2]. Quinacillin (1) is a quinoxaline containing moiety has a broad spectrum of antibacterial activity which is active against *Staphylococci* [3]. Furthermore, many quinoxaline derivatives have been reported to possess anticancer [4], beneficial effects for sleep disorders [5], antimycobacterial [6], antifungal [7], antiviral [8], anti-inflammatory [9] and antioxidant activities [10]. Among the quinoxalines derivatives, 2-substituted and 2,3-disubstituted aryl or heteroaryl quinoxaline derivatives have shown remarkable pharmacological activities. The antiprotozoal and antitrypanosomial activity has been reported for quinoxaline 1,4-di-N-oxide (2, 3) [11], 3-trifluoromethylquinoxaline N,N^{1}-dioxide (4) [12] and palladium and copper complexes of 3-aminoquinoxaline-2-carbonitrile 1,4-dioxide derivatives (5,6) [13]. In addition, anti-leishmanial activity has been reported for 4-substituted pyrrolo[1,2-a]quinoxalines (7) [14] and 3-phenyl-1-(1,4-di-N-oxide quinoxalin-2-.
-yl)-2-propen-1-one derivatives (8) [15] shown in Fig. I.

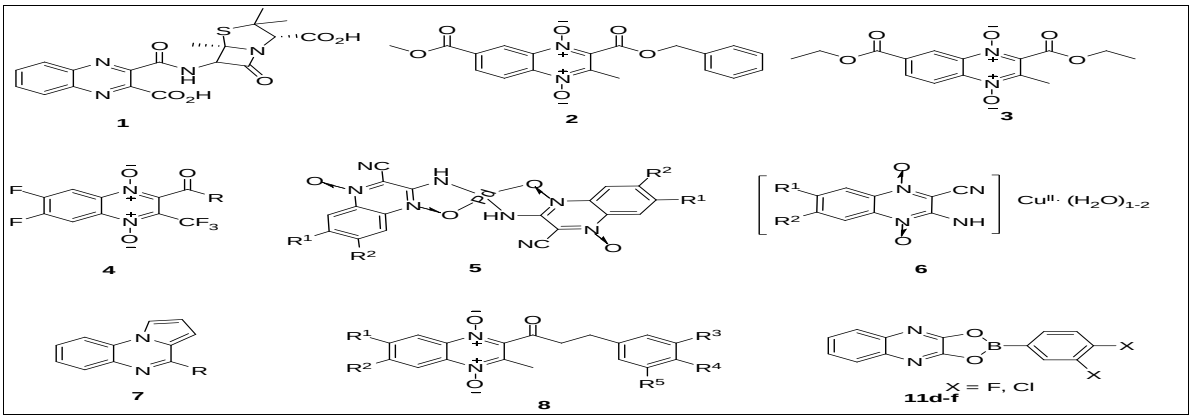


Fig 1: Biologically potent Quinoxaline derivatives.

In recent years, a number of research groups focused on the synthesis of organo functional compounds [16], biopolymers and drugs with ligands and evaluated their suitability for the bioengineering applications. Aromatic boronic acid and its functional derivatives has become a very important class of organic compounds, which are utilized in a variety of biological and medical applications, including carbohydrate recognition [17], neutron capture therapy for cancer treatment as effective tumour-targeting agents [18], especially for brain tumours [19] and protease enzyme inhibition [20]. A novel water-soluble polymer with lectin-like function by introducing phenylates, as sugar recognizing moieties, into the side chain of poly (*N*,*N*-dimethylacrylamide) was reported by Kataoka *et al.* [21] As per literature survey hetero-atom substituted quinoxaline derivatives were not obtained. By considering the importance of antimicrobial activity of quinoxaline and boron derivatives, we synthesized hetero-atom substituted quinoxaline derivatives and screened for their antimicrobial activity. To the best of literature knowledge, all the synthesized compounds are new molecules.

2. Experimental

2.1 Materials and Methods

All the reagents were commercially available and used as such without further purification. Solvents used for spectroscopic and other physical studies were reagent grade and were further purified by literature methods. Melting points were determined using a capillary thermometer by GUNA digital melting point apparatus and are uncorrected. Ethyl acetate and hexane used as solvents for the calculation of Rf values. IR spectra were recorded on BRUKER ALPHA Eco-ATR with ZnSe FT-IR spectrophotometer. Proton, carbon and boron NMR spectra were recorded in DMSO-d_6 on Bruker AVANCE-400 MHz spectrometer operating at 400 and 500 MHz for ^{1}H NMR, 100.64 and 125.77 MHz for ^{13}C NMR and 128.2 Hz for ^{11}B NMR. ^{1}H NMR and ^{13}C NMR spectra referenced to tetramethylsilane. ^{11}B NMR spectra referenced to $BF_3{\cdot}OEt_2$. Chemical shifts (δ) were expressed in ppm and J values in Hertz (Hz). Multiplicities are shown as the abbreviations: s (singlet), brs (broad singlet), d (doublet), t (triplet), m (multiplet).

2.2 General procedure for the synthesis of heterocyclic quinoxaline derivatives 11(a-j).

4-Fluoro phenyl boronic acid (10d) (1.0 mmol) was taken in a 50 mL round boom flask in 15 mL of tetrahydrofuron, cooled to 0 °C, to this hexane washed NaH (1.0 mmol) was added. The reaction was stirred at 0 °C for 30 mins and raised the temperature to 40 °C and stirred for 2 hrs. The progress of the reaction was monitored by thin layer chromatography (until disappearance of boronic acid). After completion, the reaction mixture was cooled to 20-30 °C, to this 2,3-dichloroquinoxaline (1.0 mmol) was added. The reaction temperature was raised to 50 °C and stirred for 3 hrs. The formation of compound 2-(4-fluorophenyl)-[1,3,2] dioxaborolo [4,5-*b*]quinoxaline (11d) ascertained by thin layer chromatography using hexane:ethylacetate (3:2). After completion, the reaction mixture was cooled to 20-30 °C, washed with 15 mL of water and extracted with ethyl acetate. The organic layer was separated and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to get crude compound. It was purified by column chromatography using hexane:ethyl acetate (7:3) to get pure compound 11d. The same method was adopted for the synthesis of remaining title compounds 11(a-j).

2.3. Spectral Data

2.3.1. [1,3,2]Dioxasilolo[4,5-b]quinoxalin-2-one (11a): Pale yellow color solid; Yield: 72%; m.p: 158-160 ˚C; R_f: 0.66; ^{1}H NMR (400 MHz, DMSO-d_6): δ= 7.50 (2H, d, J = 7.6 Hz, Ar-H), 7.78 (2H, d, J = 7.6 Hz, Ar-H); ^{13}C NMR (100.62 MHz, DMSO-d_6): 127.4, 129.3, 133.0, 157.0; IR (Cm^{-1}): 650, 1050, 1230, 1475, 1570; MS m/z: 205 (M+H); Anal. calcd. for $C_8H_4N_2O_3Si$: C, 47.05; H, 1.97; N, 13.72. Found: C, 47.12; H, 2.06; N, 13.66.

2.3.2. [1,3,2]dioxaselenolo[4,5-b]quinoxaline 2-oxide (11b): Pale yellow color solid; Yield: 74%; m.p: 183-185 ˚C; R_f: 0.40; ^{1}H NMR (400 MHz, DMSO-d_6): δ= 7.77 (2H, d, J = 8.0 Hz, Ar-H), 7.51 (2H, d, J = 8.0 Hz, Ar-H); ^{13}C NMR (100.62 MHz, DMSO-d_6): 127.1, 128.5, 133.7, 159.3; IR (Cm^{-1}): 1455, 1550; MS m/z: 256 (M+H); Anal. calcd. for $C_8H_4N_2O_3Se$: C, 37.67; H, 1.58; N, 10.98. Found: C, 37.75; H, 1.65; N, 10.88.

2.3.3. Pyrido[2',3':5,6][1,4]dioxino[2,3-b]quinoxaline (11c): Pale yellow color solid; Yield: 80%; m.p: 230-232 ˚C; R_f: 0.43; ^{1}H NMR (400 MHz, DMSO-d_6): δ= 6.42-6.45 (1H, m, Ar-H), 7.00-7.02 (1H, m, Ar-H), 7.24-7.26 (1H, m, Ar-H), 7.48 (2H, d, J = 8.0 Hz, Ar-H), 7.78 (2H, d, J = 7.6 Hz, Ar-H); ^{13}C NMR (100.62 MHz, DMSO-d_6): 124.3, 127.2, 127.3, 128.9, 129.4, 129.5, 134.1, 134.4, 137.2, 142.7, 150.2, 156.8, 157.1; IR (Cm^{-1}): 1020, 1150, 1440, 1515; MS m/z: 283 (M+H); Anal. calcd. for $C_{13}H_7N_3O_2$: C, 65.82; H, 2.97; N, 17.71. Found: C, 65.88; H, 2.90; N, 17.78.

2.3.4. 2-(4-Fluorophenyl)-[1,3,2]dioxaborolo[4,5-b]quinoxaline (11d): Yellow color solid; Yield: 82%; m.p: 200-202 ˚C; R_f: 0.56; ^{1}H NMR (500 MHz, DMSO-d_6): δ= 7.23 (2H, d, *J* = 8.0 Hz, Ar-H), 7.44-7.62 (4H, m, Ar-H), 7.77 (2H, d, *J* = 7.6 Hz, Ar-H); ^{13}C NMR (125.77 MHz, DMSO-d_6): 116.0, 126.5, 127.8, 129.4, 134.4, 135.5, 155.9, 163.5; IR (Cm^{-1}): 1050, 1170, 1410, 1500, 1680; ^{11}B NMR (128.2 Hz, DMSO-d_6): 38.40; MS m/z: 267 (M+H); Anal. calcd. for $C_{14}H_8BFN_2O_2$: C, 63.21; H, 3.03; N, 10.53. Found: C, 63.28; H, 3.10; N, 10.48.

2.3.5. 2-(2,4-Difluorophenyl)-[1,3,2]dioxaborolo[4,5-b]quinoxaline (11e): Yellow color solid; Yield: 85%; m.p: 220-222 ˚C; R_f: 0.43; ^{1}H NMR (500 MHz, DMSO-d_6): δ= 7.06 (1H, d, *J* = 7.2 Hz, Ar-H), 7.21 (1H, s, Ar-H), 7.46 (2H, d, *J* = 7.6 Hz, Ar-H), 7.59 (1H, d, *J* = 7.2 Hz, Ar-H), 7.76 (2H, d, *J* = 7.6 Hz, Ar-H); ^{13}C NMR (125.77 MHz, DMSO-d_6): 103.9, 115.7, 116.2, 127.8, 129.3, 134.2, 135.8,155.9, 159.6, 164.3; IR (Cm^{-1}): 1075, 1150, 1390, 1520; ^{11}B NMR (128.2 Hz, DMSO-d_6): 35.67; MS m/z: 285 (M+H); Anal. calcd. for $C_{14}H_7BF_2N_2O_2$: C, 59.20; H, 2.48; N, 9.86. Found: C, 59.29; H, 2.54; N, 9.81.

2.3.6. 2-(4-Chlorophenyl)-[1,3,2]dioxaborolo[4,5-b]quinoxaline (11f): Brown color solid; Yield: 80%; m.p: 170-172 ˚C; R_f: 0.56; ^{1}H NMR (500 MHz, DMSO-d_6): δ= 7.21-7.40 (4H, m, Ar-H), 7.61 (2H, d, *J* = 6.4 Hz, Ar-H), 7.77 (2H, d, *J* = 7.6 Hz, Ar-H); ^{13}C NMR (125.77 MHz, DMSO-d_6): 127.8, 128.7, 129.4, 130.2, 133.2, 135.3, 136.4, 155.7; IR (Cm^{-1}): 600, 1220, 1380, 1520, 1620; ^{11}B NMR (128.2 Hz, DMSO-d_6): -39.5; MS m/z: 284 (M+H), Anal. calcd. for $C_{14}H_8BClN_2O_2$: C, 59.52; H, 2.85; N, 9.92. Found: C, 59.61; H, 2.82; N, 9.85.

2.3.7. 2-(3,4-Dichlorophenyl)-[1,3,2]dioxaborolo[4,5-b]quinoxaline (11g): Pale yellow color solid; Yield: 85%; m.p: 157-159 ˚C; R_f: 0.47; ^{1}H NMR (500 MHz, DMSO-d_6): δ= 7.36 (1H, s, Ar-H), 7.45-7.64 (4H, m, Ar-H), 7.78 (2H, d, *J* = 6.4 Hz, Ar-H); ^{13}C NMR (125.77 MHz, DMSO-d_6): 127.6, 129.5, 129.9, 130.2, 131.1, 133.3, 134.2, 134.6, 135.6, 155.6; IR (Cm^{-1}): 665, 1000, 1380, 1515, 1650; ^{11}B NMR (128.2 Hz, DMSO-d_6): 37.23; MS m/z: 317 (M+H); Anal. calcd. for $C_{14}H_7BCl_2N_2O_2$: C, 53.06; H, 2.23; N, 8.84. Found: C, 53.11; H, 2.31; N, 8.75.

2.3.8. 2-(Thiophen-2-yl)-[1,3,2]dioxaborolo[4,5-b]quinoxaline (11h): Grey color solid; Yield: 87%; m.p: 248-250 ˚C; R_f: 0.40; ^{1}H NMR (500 MHz, DMSO-d_6): δ= 7.14 (1H, d, *J* = 4.8 Hz, Ar-H), 7.20-7.22 (1H, m, Ar-H), 7.47 (2H, d, *J* = 7.6 Hz, Ar-H), 7.63 (1H, d, *J* = 4.4 Hz, Ar-H) 7.76 (2H, d, *J* = 7.6 Hz, Ar-H); ^{13}C NMR (125.77 MHz, DMSO-d_6): 124.2, 125.9, 127.1, 127.5, 128.4, 129.3, 134.3, 156.2; IR (Cm^{-1}): 1275, 1380, 1525, 1670; ^{11}B NMR (128.2 Hz, DMSO-d_6): 40.2; MS m/z: 255 (M+H); Anal. calcd. for $C_{12}H_7BN_2O_2S$: C, 56.73; H, 2.78; N, 11.03. Found: C, 56.78; H, 2.84; N, 11.05.

2.3.9. 2-Phenyl-[1,3,2]dioxaborolo[4,5-b]quinoxaline (11i): Grey color solid; Yield: 82%; m.p: 131-133 ˚C; R_f: 0.53; ^{1}H NMR (500 MHz, DMSO-d_6): δ= 7.06-7.26 (5H, m, Ar-H), 7.45-7.48 (2H, m, Ar-H), 7.76 (2H, d, *J* = 8.0 Hz, Ar-H); ^{13}C NMR (125.77 MHz, DMSO-d_6): 123.5, 126.0, 127.8, 129.4, 130.4, 133.2, 134.5, 155.6; IR (Cm^{-1}): 1250, 1370, 1525, 1710; ^{11}B NMR (128.2 Hz, DMSO-d_6): 43.62; MS m/z: 249 (M+H); Anal. calcd. for $C_{14}H_9BN_2O_2$: C, 67.79; H, 3.66; N, 11.29. Found: C, 67.84; H, 3.72; N, 11.26.

2.3.10. 2-(5-Chlorothiophen-2-yl)-[1,3,2]dioxaborolo[4,5-b]quinoxaline (11j): Grey color solid; Yield: 88%; m.p: 257-259 ˚C; R_f: 0.60; ^{1}H NMR (500 MHz, DMSO-d_6): δ= 6.77 (1H, d, *J* = 4.0 Hz, Ar-H), 6.81 (1H, d, *J* = 4.0 Hz, Ar-H), 7.49 (2H, d, *J* = 7.6 Hz, Ar-H), 7.78 (2H, d, *J* = 6.4 Hz, Ar-H); ^{13}C NMR (125.77 MHz, DMSO-d_6): 125.4, 126.5, 127.5, 127.7, 128.0, 129.3, 134.2, 156.0; IR (Cm^{-1}): 1375, 1540, 1680; ^{11}B NMR (128.2 Hz, DMSO-d_6): 38.9; MS m/z: 290 (M+H), Anal. calcd. for $C_{12}H_6BClN_2O_2S$: C, 49.95; H, 2.10; N, 9.71. Found: C, 50.02; H, 2.15; N, 9.75.

2.4. Antibacterial activity

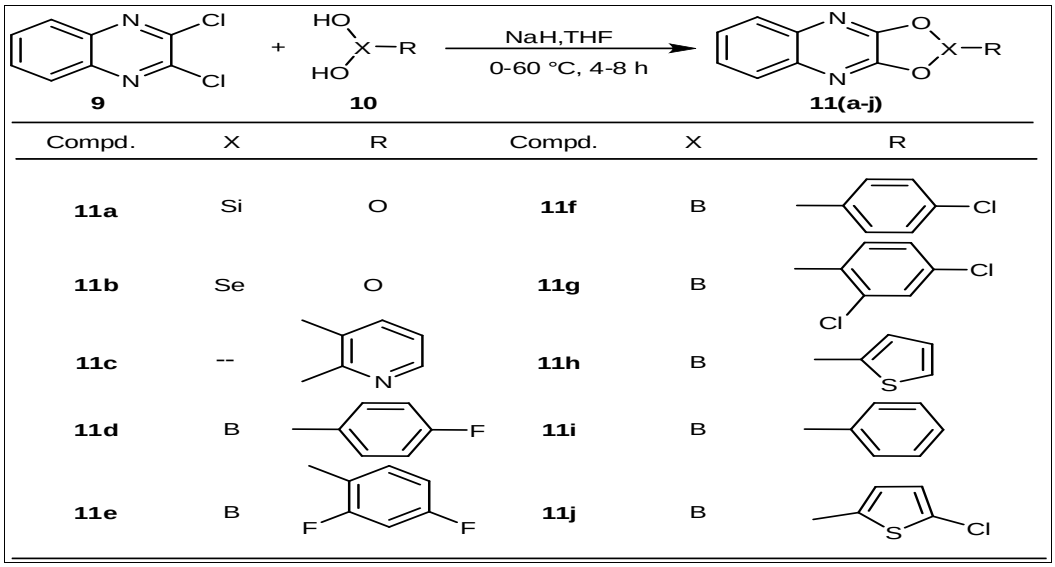
Antibacterial activity was assayed for the title compounds against *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis and Klebsiella pneumoniae* by agar well diffusion method [22]. 5 µg/mL of the test compounds were dissolved in 1 mL of DMSO solvent. Centrifuged pellets of bacteria from 24 h old culture containing approximately 10^4-10^6 colony forming unit (CFU) per mL was spread on the surface of Muller Hinton Agar (MHA) plates. Nutrient agar medium was prepared by suspended nutrient agar 28 g in 1 liter of distilled water, autoclaved and cooled to 45 °C, and then it was seeded with 15 mL of prepared inocula to have 10^6 CFU/mL. Petri dishes were prepared by pouring 10 mL of seeded nutrient agar. Wells were created in medium with the help of a sterile metallic borer and test solution was added. Experimental plates were incubated for 24 h at 37 °C and antibacterial activity was defined as the diameter (mm) of the clear inhibition zone formed around the well. Ciprofloxacin was used as standard drug for antibacterial activity. For each treatment, three replicates were carried out and the mean of the diameter of the inhibition zone values were calculated and presented in Table 2.

2.5. Antifungal activity

Antifungal activity of newly synthesized compounds were screened against the fungal strains like *Aspergillus flavus*, *Aspergillus niger*, *Aspergillus fumigatus* and *Candida albicans* by the poison plate technique [23]. All the tested compounds were dissolved in DMSO before mixing with potato dextrose agar (PDA). The final concentration of the compounds in the medium was fixed at 50 µg/mL. The fungi were incubated in PDA at 25±1 °C for 5 days to get new mycelium for antifungal activity, and then a mycelia disc of approximately 0.45 cm diameter cut from the culture medium was picked up with a sterilized inoculation needle and inoculated in the center of the PDA plate. The inoculated plates were incubated at 25±1 °C for 5 days. Amphotericin-B was used as a standard drug for antifungal activity. The radial growth of the fungal colonies was measured on the sixth day. For each treatment, three replicates were carried out and the mean of the diameter of the inhibition zones were calculated and presented in Table 3.

3. Results and Discussion

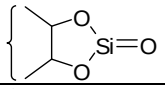
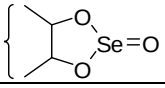
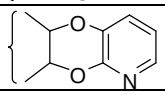
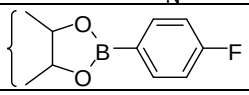
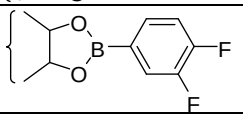
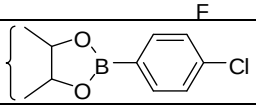
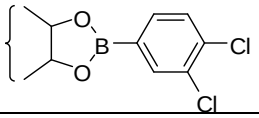
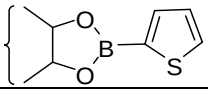
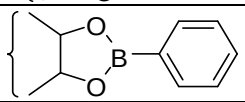
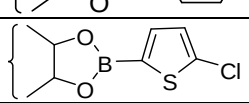
The synthetic route for the synthesis of title compound 11(a-j) is outlined in Scheme 1. A series of new quinoxaline derivatives were synthesized by the reaction of 2,3-dichloroquinoxaline (**9**) with silicic acid, selenous acid, pyridine-2,3-diol and various boronic acid derivatives using NaH as base and THF as solvent at 0-60°C to obtain corresponding quinoxaline derivatives.



Scheme 1: Synthesis of boron, silicon and selenium substituted quinoxaline derivatives 11(a-j).

The structures of the compound were depicted in table 1. In IR spectra, the absorption bands in the region 1500-1540 cm^{-1} corresponds to B-O stretching. The absorption bands for B-Ph, Si-O, C-Cl and C-F were obtained in the region of 1375-1410, 1050, 650-665 and 1150-1170 cm^{-1} respectively. In ^{1}H NMR spectra, doublets *at* δ 7.80-7.75 and δ 7.53-7.47 were corresponds to quinoxaline protons and remaining aromatic protons were resonated in the region of δ 6.44 -7.81 as singlet, doublet and multiplet based on the structures. In ^{13}C NMR spectra, chemical shift observed in the region of δ 103.9-164.3 were assigned to aromatic carbons. In ^{11}B NMR, the signal for boron resonated in the region of 35.67-43.62. Further the structures of the compounds were supported by mass and elemental analysis.

Table 1: Structures of the synthesized compounds 11(a-j).

Entry	Structure	R_f	Time (h)	Yield (%)[a]	Melting point (°C)
11a		0.66	4.00	72	158-160
11b		0.40	4.15	74	183-185
11c		0.43	5.30	80	230-232
11d		0.56	4.30	82	200-202
11e		0.43	5.30	85	220-222
11f		0.56	5.45	80	170-172
11g		0.47	8.00	85	157-159
11h		0.40	6.30	77	248-250
11i		0.53	7.15	82	131-133
11j		0.60	6.00	81	257-259

[a] Isolated yield

Antibacterial activity

All the newly synthesized heterocyclic quinoxaline derivatives were screened against Gram -ve bacteria such as *Escherichia coli* and *Staphylococcus aureus* and Gram +ve

bacteria such as *Bacillus subtilis* and *Klebsiella pneumoniae* by agar well diffusion method. Ciprofloxacin was used as a standard drug for antibacterial activity. The diameters of the inhibition zone (DIZ in mm) values are presented in Table 2. Among the synthesized compounds 11d, 11e and 11f showed potent activity against all bacterial strains than that of the remaining title compounds. Compound 11e exhibited excellent activity against *Escherichia coli*, *Staphylococcus aureus* and *Basillus subtilis*. Compounds 11d and 11f showed potent activity against *Klebsiella pneumoniae* than that of remaining compounds. The reason might be the presence of fluoro and chloro substituents in dioxaborolo [4,5-b]quinoxaline derivatives.

Table 2: Antibacterial activity of newly synthesized quinoxaline derivatives 11(a-j).

Compound	Diameter of inhibition zone (in mm)			
	Escherichia coli	***Staphylococcus aureus***	***Bacillus subtilis***	***Klebsiella pneumoniae***
11a	15	20	16	14
11b	15	21	18	6
11c	21	15	20	6
11d	28	35	33	16
11e	30	35	34	9
11f	21	28	25	18
11g	18	25	30	8
11h	15	20	10	9
11i	16	22	14	11
11j	19	19	13	14
Std	20	28	25	26

Std: Ciprofloxacin

Antifungal activity

Antifungal activity of newly synthesized heterocyclic quinoxaline compounds were screened against *Aspergillus flavus, Aspergillus niger, Aspergillus fumigatus* and *Candida albicans* by the poison plate technique. Amphotericin-B was used as a standard drug for antifungal activity. The diameters of the inhibition zone (DIZ in mm) values were presented in Table 3. 11a, 11c, 11d, 11e, 11f compounds exhibited potent activity against *Aspergillus niger.* 11a, 11b, 11d, 11e and 11f showed very good activity than that of the standard drug against *Aspergillus fumigatus*. 11b, 11c and 11d showed activity greater than that of the standard drug against *Candida albicans.* Among the newly synthesized compounds 11b and 11d exhibited good activity than that of the remaining title compounds and also standard drug, ciprofloxacin. Compound 11c exhibited high antifungal activity, but it did not show good activity against *Aspergillus fumigatus*. Compound 11j showed moderate activity against *Candida albicans* only.

Table 3: Antifungal activity of newly synthesized quinoxaline derivatives 11(a-j).

Compound	Diameter of the inhibition zone (in mm)			
	Aspergillus flavus	***Aspergillus niger***	***Aspergillus fumigatus***	***Candida albicans***
11a	20	23	22	10
11b	24	18	20	23
11c	18	28	9	21
11d	25	23	30	27
11e	25	24	25	10
11f	20	25	17	15
11g	16	22	18	12
11h	13	17	13	10
11i	15	15	12	13
11j	12	11	10	15
Std	20	22	21	22

Std: Amphotericin-B

From these results, the compounds 11d, 11e and 11f exhibited potent antibacterial and antifungal activity than that of the remaining title compounds and also when compared to the standard drugs due to the attachment of 4-fluorophenyl; 2,4-difluorophenyl and 4-chloro phenyl groups to boron.

4. Conclusion

In this study we synthesized a series of heteroatom substituted quinoxaline heterocyclic derivatives in single step with high yields in short time. Among the newly synthesized compounds 11d, 11e and 11f have showed potent antibacterial and antifungal activity than that of the remaining synthesized compounds compared to the standard drugs respectively. From these results, we conclude that these three compounds exhibited potent antimicrobial activity than that of standard drugs. So these compounds might be useful as antibiotic and antifungal agents without modification and also act as intermediates for the synthesis of new drugs.

5. Supporting information

IR, ^{1}H, ^{13}C, ^{31}P NMR and Mass spectra for the compounds (11a-j) were given in the supporting information.

6. Acknowledgment

The author, S. Mahaboob Basha would like to express his grateful thanks to Mrs. T. Gayathri and Dr. P. Sivamani, Director, Micro Labs Institute of Research and Technology, Arcot, Vellore, Tamil Nadu.

7. Conflict of interest

None declared

8. References

1. Cheeseman GWH, Cookson RF. In the Chemistry of Heterocyclic Compounds A Weissberger and E C Taylor (Eds.) (Wiley; New York), 1979, 35, Chapter 10.
2. Islami MR, Hassani Z. One-pot and efficient protocol for synthesis of quinoxaline derivatives, ARKIVOC. 2008; 23:280-287.
3. Hugo WB, Stretton RG. Action of quinacillin on staphylococcus aureus, Nature. 1964; 202:1217-1217.
4. Chen Q, Bryant VC, Lopez H, Kelly DL, Luo X, Natarajan A. 2,3-Substituted quinoxalin-6-amine analogs as antiproliferatives: A structure-activity relationship study, Bioorg. Med. Chem. Lett. 2011; 21:1929-1932.
5. Ancizu S, Castrillo N, Perez-Silanes S, Aldana I, Monge A, Delagrange P *et al*. New quinoxaline derivatives as potential MT1 and MT2 receptor ligands, Molecules. 2012; 17:7737-7757.
6. Moreno E, Ancizu S, Perez-Silanes S, Torres E, Aldana I, Monge A. Synthesis and antimycobacterial activity of new quinoxaline-2-carboxamide 1,4-di-N-oxide derivatives, Eur. J Med. Chem. 2010; 45:4418-4426.
7. Ishikawa H, Sugiyama T, Yokoyama A. Synthesis of 2,3-bis (halomethyl) quinoxaline derivatives and evaluation of their antibacterial and antifungal activities. Chem. Pharm. Bull. 2013; 61:438-444.
8. You L, Cho EJ, Leavitt J, Ma LC, Montelione GT, Anslyn EV *et al*. Synthesis and evaluation of quinoxaline derivatives as potential influenza NS1A protein inhibitors. Bioorg. Med. Chem. Lett. 2011; 21:3007-3011.
9. Burguete A, Pontiki E, Hadjipavlou-Litina D, Villar R, Vicente E, Solano B *et al*. Synthesis and anti-inflammatory/antioxidant activities of some new ring substituted 3-phenyl-1-(1,4-di-N-oxide quinoxalin-2-yl)-2-propen-1-one derivatives and of their 4,5-dihydro-(1H)-pyrazole analogues. Bioorg. Med. Chem. Lett. 2007; 17:6439-6443.
10. Burguete A, Pontiki E, Hadjipavlou-Litina D, Ancizu S, Villar R, Solano B *et al*. Synthesis and biological evaluation of new quinoxaline qerivatives as antioxidant and anti-Inflammatory agents. Chem. Biol. Drug Des. 2011; 77:255-267.
11. Ancizu S, Moreno E, Torres E, Burguete A, Perez-Silanes S, Benitez D *et al*. Heterocyclic-2-carboxylic acid (3-cyano-1,4-di-Noxidequinoxalin-2-yl)amide derivatives as hits for the development of neglected diseases drugs. Molecules. 2009; 14:2256-2272.
12. Estevez Y, Quiliano M, Burguete A, Cabanillas B, Zimic M, Malaga E *et al*. Trypanocidal properties, structure-activity relationship and computational studies of quinoxaline 1,4-di-N-oxide derivatives. Exp. Parasitol. 2011; 127:745-751.
13. Benitez D, Cabrera M, Hernandez P, Boiani L, Lavaggi ML, Di Maio R *et al*. 3-Trifluoromethylquinoxaline N,N'-dioxides as anti-Trypanosomatid agents. Identification of optimal anti-*T. cruzi* Agents and mechanism of action studies. J Med. Chem. 2011; 54:3624-3636.
14. Varela J, Lessa JA, Lavaggi ML, Beraldo H, Cerecetto H, Gonzalez M. Coordination of 3-aminoquinoxaline-2-carbonitrile 1,4-dioxides to antimony(III) as a strategy for anti-*Trypanosoma cruzi* activity improvement. Med. Chem. Res. 2012; 21:4120-4128.
15. Guillon J, Forfar I, Mamani-Matsuda M, Desplat V, Saliege M, Thiolat D *et al*. Synthesis, analytical behaviour and biological evaluation of new 4-substituted pyrrolo[1,2-a]quinoxalines as antileishmanial agents. Bioorg. Med. Chem. 2007; 15:194-210.
16. Thaslim Basha SK, Rasheed S, Chandra Sekhar K, Naga Raju C, Subhan Ali Md, Appa Rao Ch. Ultrasonicated, nano-ZnO Catalyzed green synthesis of *α*-hydroxyphosphonates and their antioxidant activity. Phosphourus, Sulphur Silicon Relat. Elem. 2014; 189:1546-1556.
17. Meryem P, Hikmet A, Fatma B, Onur S. Synthesis, characterization, antimicrobial activity, and QSAR studies of some new 6-substituted phenyl 3-(4-chlorophenyl)-3a,4,8,8a-tetrahydro-[1,3,2]dioxaborepino[5,6-d]isoxazoles. Heteroat. Chem. 2017; 28:21363.
18. James TD, Sandanayake S, Shinkay S. Saccharide Sensing with Molecular Receptors Based on Boronic Acid. Angew Chem Inter Ed Eng. 1996; 35:1910-1922.
19. Mishima Y. Cancer Neutron Capture Therapy New York, Plenum Press, (Ed.), 1996.
20. Kettner CA, Shenvi AB. Inhibition of the serine proteases leukocyte elastase, pancreatic elastase, cathepsin G, and chymotrypsin by peptide boronic acids. J Biol Chem. 1984; 259:15106-15114.
21. Miyazaki H, Kikuchi A, Kitano S, Koyama Y, Okano T, Sakurai Y *et al*. Boronate-containing polymer as novel mitogen for lymphocytes. Biochem Biophys Res Commun. 1993; 195: 829-836.
22. Atta-ur-Rehman MI, Choudhary W, Thomson J. Bioassay techniques for drug development (Harwood Academic Publishers: Amsterdam). 2001.
23. Barry AL. The Antimicrobial Susceptibility Test: Principle and Practices Illus lea and Febiger (Ed.) (Philadelphia, PA USA), 1976, 180.