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Synthesis of some new quinoxalines bearing pyridinyl thiazole moiety

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ABSTRACT. Keeping the objective to build up a new structural class of quinoxaline, a new series of quinoxaline derivatives bearing the pyridinyl thiazole nucleus have been synthesized by base-catalyzed chloro-amine condensation reaction approach. The protocol offers expeditious and easy synthesis with excellent yield. The chemical structures of the synthesized compounds were elucidated by ^{1}H NMR, ^{13}C NMR, FT-IR, elemental analysis, and mass spectral data.

1. INTRODUCTION

Quinoxaline and its derivatives are an important class of benzoheterocycles1 displaying a broad spectrum of biological activities which have made them privileged structures in combinatorial drug discovery libraries. Quinoxalines play an important role as a basic skeleton for the design of a number of antibiotics such as echinomycin, actinomycin, and leromycin. It has been reported that these compounds inhibit the growth of gram-positive bacteria, and are active against various transplantable tumors [1, 2] The quinoxaline ring is also a constituent of many pharmacologically and biologically active compounds such as insecticides, fungicides, herbicides, and anthelminitics [3, 4]. Quinoxaline derivatives have found application in dyes [5], electron luminescent materials [6], organic semiconductors [7], chemically controllable switches [8], as building blocks for the synthesis of anion receptors [9], cavitands [10], dehydroannulenes [11], DNA cleaving agents [12] and also serve as useful rigid subunits in macrocyclic receptors or in molecular recognition [13].

In recent years, the synthesis of quinoxalines has attracted considerable attention [14] and a wide range of synthetic methods has been developed for the synthesis of quinoxaline derivatives [15-17]. The conventional synthetic methods of quinoxaline derivatives were carried out in organic solvent via the condensation of arene-1,2-diamines with 1,2-dicarbonyl compounds for 2-12 hours under refluxing conditions with the yields of 34-85% [18] or in high boiling point solvent such as dimethylsulfoxide (DMSO) using the molecular iodine as the catalyst [19].

Now a days research effort has been focused on finding new catalysts to improve the yield of this condensation reaction. In addition to common Lewis acids, many other catalysts including I_2 [20, 21], SA [22], Montmorillonite K-10 [23], SSA [24], $H_6P_2W_{18}O_{62}$. $24H_2O$ [25], $InCl_3$ [26], $MnCl_2$ [27], $CuSO_4$. $5H_20$ [28], Zn/L-Proline [29] and CAN [30] have been explored. Oxidative couplings of epoxides and ene-1,2-diamines [31] catalyzed by Bi(0), $Pd(OAc)_2$, $RuCl_2$-$(PPh_3)_3$-TEMPO, and MnO_2 have been reported [32-34]. The condensation has also been accomplished under catalyst-free conditions, but needs microwave heating [35]. Here we report the synthesis of some new quinoxalines bearing pyridine thiazole moiety by condensation reaction. The constitutions of all the products were confirmed using ^{1}H NMR, ^{13}C NMR, FTIR, and elemental analysis.

2. EXPERIMENTAL

Required all reagents were obtained commercially. Solvents were purified and dried before being used. All melting points were taken in open capillaries and are uncorrected. Thin-layer chromatography (TLC, on aluminium plates precoated with silica gel, $60F_{254}$, 0.25 mm thickness) (Merck, Darmstadt, Germany) was used for monitoring the progress of all reactions, purity and homogeneity of the synthesized compounds; eluent-hexane:ethyl acetate: (3:7). UV radiation and/or

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iodine were used as the visualizing agents. Elemental analysis (% C, H, N) was carried out by Perkin-Elmer 2400 series-II elemental analyzer (Perkin-Elmer, USA) and all compounds are within ±0.4% of theory specified. The IR spectra were recorded in KBr on a Perkin-Elmer Spectrum GX FT-IR Spectrophotometer (Perkin-Elmer, USA) and only the characteristic peaks are reported in cm^{-1}. ^{1}H NMR and ^{13}C NMR spectra were recorded in DMSO-d_6 on a Bruker Avance 400F (MHz) spectrometer (Bruker Scientific Corporation Ltd., Switzerland) using solvent peak as internal standard at 400 MHz and 100 MHz respectively. Chemical shifts are reported in parts per million (ppm). Mass spectra were scanned on a Shimadzu LCMS 2010 spectrometer (Shimadzu, Tokyo, Japan).

2.1 Synthetic way for substituted 2,3-dichloroquinoxaline (1a)

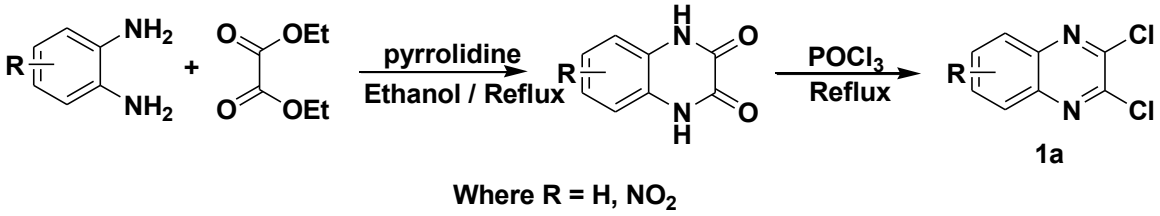
A mixture of appropriate substituted benzene-1,2-diamine (5 mmol), diethyl oxalate (5 mmol) and 1 ml of pyrrolidine in ethanol (10 ml) were charged in 100 ml round bottom flask equipped with condenser. The reaction mixture was stirred at reflux for 4 h. On completion of reaction, monitored by TLC, the the separated substituted quinoxaline-2,3(1*H*,4*H*)-dione was filtered and washed with ethanol and dried. Again a mixture of appropriate substituted quinoxaline-2,3(1*H*,4*H*)-dione (5gm) and 3 ml of DMF in $POCl_3$ (25 ml) were charged in 100 ml round bottom flask equipped with condenser. The reaction mixture was stirred at reflux for 4 h. On completion of reaction, monitored by TLC, The reaction mixture was poured in to chilled water. The separated solid was filtered, washed well with water and dried to get pure substituted 2,3-dichloroquinoxaline.

2.2 Synthetic way for substituted 3-chloro-*N*-(4-(pyridin-4-yl)thiazol-2-yl)quinoxalin-2-amine (3c)

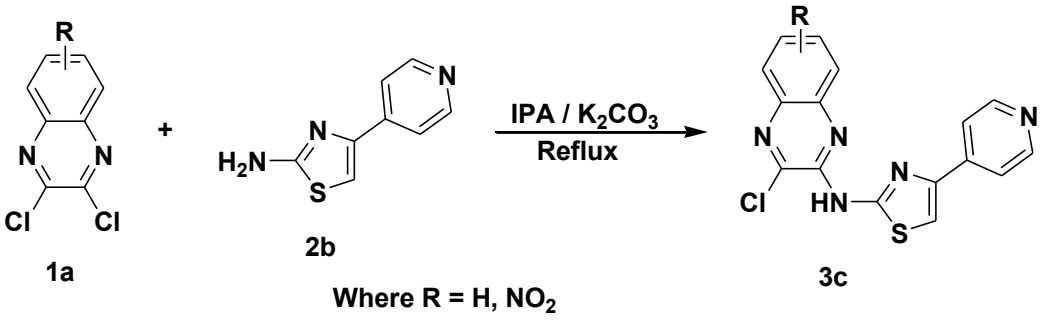
A mixture of substituted 2,3-dichloroquinoxaline **1a** (5 mmol), 4-(pyridin-4-yl)thiazol-2-amine **2b** (5 mmol) and K_2CO_3 (5 mmol) in 10 ml IPA was refluxed for 3 h. After completion of the reaction, monitored by TLC, reaction mixture was cooled. The separated solid was filtered, washed well with water and dried, and recrystallized from ethanol to afford analytically pure substituted 3-chloro-*N*-(4-(pyridin-4-yl)thiazol-2-yl)quinoxalin-2-amine.

2.3 General Synthetic way for the synthesis of compounds 4a-4t

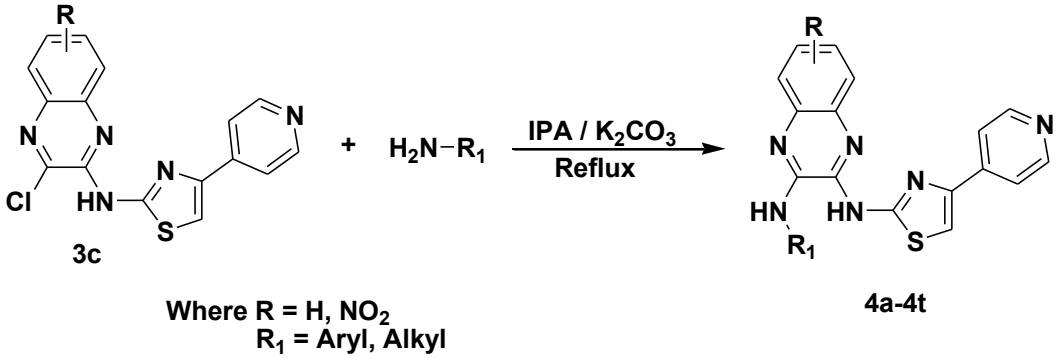
A mixture of substituted 3-chloro-*N*-(4-(pyridin-4-yl)thiazol-2-yl)quinoxalin-2-amine **3c** (5 mmol), various aliphatic/aromatic amines (5 mmol) and K_2CO_3 (5 mmol) in 10 ml IPA was refluxed for 4-5 h. After completion of the reaction, monitored by TLC, reaction mixture was cooled. The separated solid was filtered, washed well with water and dried, and recrystallized from chloroform to afford analytically pure compounds **4a-4t**. Analytical, physical, and spectroscopic characterization data of synthesized compounds **4a-4t** are mentioned below



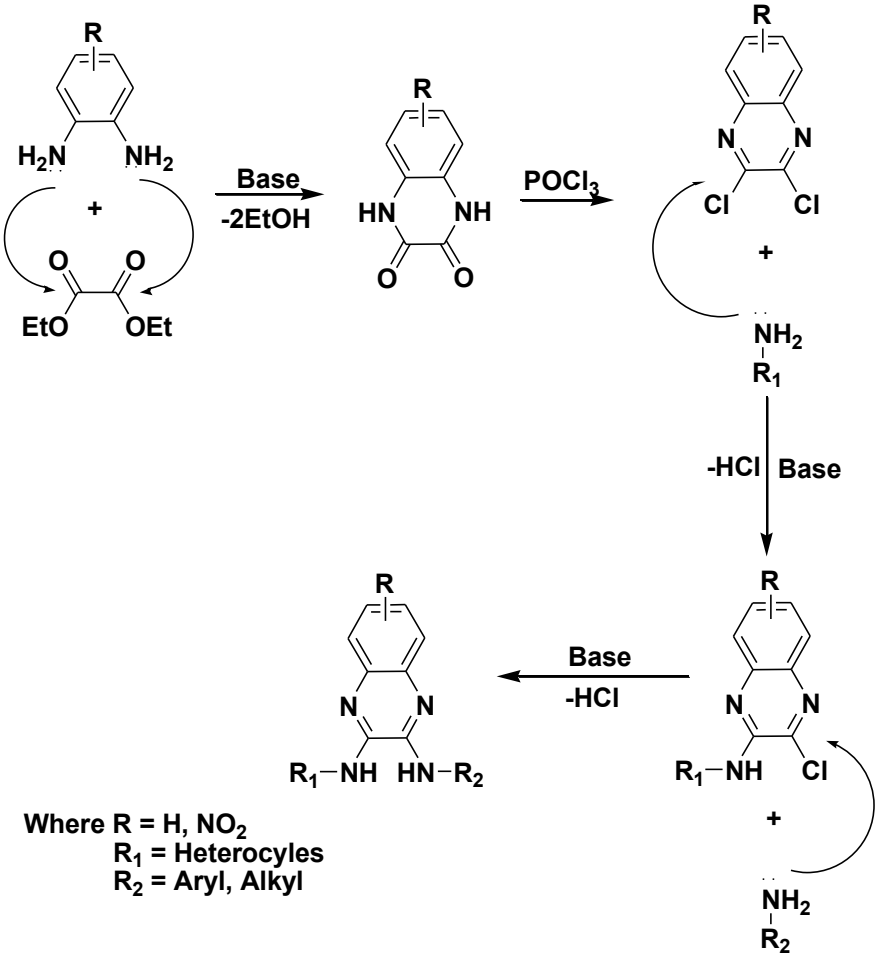
Scheme 1 Synthetic pathway for the synthesis of intermediate 1a



Scheme 2 Synthetic pathway for the synthesis of intermediate 3c



Scheme 3 Synthetic pathway for the synthesis of quinoxaline derivatives 4a-4t



Scheme 4 Mechanism for the synthesis of quinoxaline derivatives 4a-4t

Tabel-1 Synthesis of substituted quinoxalines

Entry	R	R_1	RT(h.)	Yield %	mp ^oC
4a	H	CH_3	5	75	90-92
4b	H	C_2H_5	4.5	78	93-95
4c	H	Ph	4.2	89	110-112
4d	H	(*p*-OCH_3)Ph	4	91	108-110
4e	H	(*p*-CH_3)Ph	4	90	99-101
4f	H	(*p*-NO_2)Ph	4.2	88	129-131
4g	H	(*p*-OH)Ph	4.5	85	121-123
4h	H	(*p*-F)Ph	4.6	83	113-115
4i	H	(*p*-Cl)Ph	4.6	79	119-121
4j	H	(*p*-Br)Ph	4.7	76	133-135
4k	NO_2	CH_3	4.8	72	140-142
4l	NO_2	C_2H_5	4.5	75	137-139
4m	NO_2	Ph	4.3	88	105-107
4n	NO_2	(*p*-OCH_3)Ph	4	90	117-119
4o	NO_2	(*p*-CH_3)Ph	4.2	85	123-125
4p	NO_2	(*p*-NO_2)Ph	4.3	80	143-145
4q	NO_2	(*p*-OH)Ph	4.4	79	139-141
4r	NO_2	(*p*-F)Ph	4.6	77	130-132
4s	NO_2	(*p*-Cl)Ph	4.8	75	114-116
4t	NO_2	(*p*-Br)Ph	4.9	73	138-140

The required 4-(pyridin-4-yl)thiazol-2-amine **2b** was prepared by solid phase reaction according to literature procedure [36].

In the present study, all the quinoxaline derivatives **4a-4t** were obtained in good yields by the potassium carbonate catalyzed chloro-amine condensation reaction of various aliphatic/aromatic amines with 3-chloro-*N*-(4-(pyridin-4-yl)thiazol-2-yl)quinoxalin-2-amine **3c** in IPA under reflux condition as depicted in (Scheme 3). The formation of compounds **4a-4t** may proceed via chloro-amine condensation in presence of potassium carbonate. Reaction of substituted benzene-1,2-diamine and diethyl oxalate gave substituted quinoxaline-2,3(1*H*,4*H*)-dione by removel of two ethanol molecule which treated by $POCl_3$ to achieve substituted 2,3-dichloroquinoxaline. In the end, nucleophilic attack of amine to the substituted 2,3-dichloroquinoxaline derivatives took place to result quinoxaline derivatives **4a–4t** (Scheme 4).

The identity of the product determined by ^1H NMR, ^{13}C NMR, FT-IR spectral data, and molecular weight of some selected compounds were confirmed by mass spectrometry. ^1H NMR (DMSO-d6) spectrum of **4d**, molecule of interest, exhibited singlet peak at d 3.92 ppm appeared for aromatic methoxy proton of phenyl ring. Aromatic protons as multiplets appeared at around d 6.88-7.91 ppm. Moreover, it exhibited two singlet peak at d 10.71 ppm and d 10.82 ppm appeared for two –NH– protons. The ^{13}CNMR spectrum is in consonance with the structure assigned. In the ^{13}C NMR spectra, signals around d 110.25–143.80 ppm are attributed to aromatic carbons of compound **4d**. Morver **4d** exhibited a distinctive signal at d 55.60 ppm for aromatic methoxy carben. The IR spectrum of compound **4d** exhibited characteristic absorption band at 3,356 and 3,248 cm^{-1} for cyclic –NH– group. And 3,021 cm^{-1} for aromatic C–H stretching. The mass spectra of compounds **4d** and **4f**, molecules of interest, detected the expected molecular ion signals corresponding to respective molecular formula, i.e., mass spectra of compounds **4d** and **4f** gave molecular ion peak at m/z 426.1 (M + 1) and m/z 441.1 (M + 1) corresponding to molecular formula $C_{23}H_{18}N_6OS$ and $C_{22}H_{15}N_7O_2S$. The obtained elemental analysis values are in good agreement with theoretical data. Similarly, all these compounds were characterized on the basis of spectral studies. All spectroscopic data have been given in spectral data.

3. SPECTRAL DATA

N^2-methyl-N^3-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4a)

light yellow solid, yield 75%, m.p. 90-92°C, IR (KBr, ν, cm^{-1}): 3329 (N-H Str.), 3250 (N-H Str.), 3038 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 3.800 (s, 3H, CH_3), 7.202-8.113 (m, 9H, Ar-H), 10.300 (s, 1H, NH), 10.413 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 29.30 (NH-<u>C</u>H_3), 110.12, 112.20, 114.30, 115.16, 116.80, 118.36, 122.40, 124.20, 126.12, 128.30, 129.03, 131.21, 133.12, 135.16, 136.00, 137.18 (Ar-<u>C</u>). MS(M^+): 334.10, Anal. Calcd. for $C_{17}H_{14}N_6S$ (334.4): C 61.06, H 4.22, N 25.13 Found: C 61.20, H 4.11, N 24.90%.

N^2-ethyl-N^3-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4b)

light yellow solid, yield 78%, m.p. 93-95°C, IR (KBr, ν, cm^{-1}): 3343 (N-H Str.), 3270 (N-H Str.), 3035 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 1.001 (t, 3H, CH_3), 2.980 (q, 2H, CH_2), 6.812-7.918 (m, 9H, Ar-H), 10.326 (s, 1H, NH), 10.563 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 20.12 (<u>C</u>H_3), 34.68 (NH-<u>C</u>H_2), 110.46, 112.80, 113.60, 114.17, 116.90, 118.56, 122.50, 124.60, 125.16, 128.40, 129.50, 131.80, 133.63, 135.18, 136.00, 137.88 (Ar-<u>C</u>). MS(M^+): 348.12, Anal. Calcd. for $C_{18}H_{16}N_6S$ (348.42): C 62.05, H 4.63, N 24.12 Found: C 62.20, H 4.50, N 24.25%.

N^2-phenyl-N^3-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4c)

light yellow solid, yield 89%, m.p. 110-112°C, IR (KBr, ν, cm^{-1}): 3356(N-H Str.), 3239 (N-H Str.), 3008 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 7.220-8.124 (m, 14H, Ar-H), 10.654 (s, 1H, NH), 10.735 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 110.12, 111.03, 113.16, 115.32, 117.18, 118.98, 121.00, 122.36, 124.02, 125.66, 127.00, 128.18, 130.44, 131.45, 133.00, 135.24, 136.58, 137.85, 139.04, 141.22, 142.56, 143.12(Ar-<u>C</u>). MS(M^+): 396.12, Anal. Calcd. for $C_{22}H_{16}N_6S$ (396.47): C 66.65, H 4.07, N 21.20 Found: C 66.50, H 4.02, N 21.30%.

N^2-(4-methoxyphenyl)-N^3-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4d)

light yellow solid, yield 91%, m.p. 108-110°C, IR (KBr, ν, cm^{-1}): 3356 (N-H Str.), 3248 (N-H Str.), 3021 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 3.920 (s, 3H, OCH_3), 6.882-7.914 (m, 13H, Ar-H), 10.712 (s, 1H, NH), 10.825 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 55.60 (OCH_3), 110.25, 112.06, 113.26, 115.45, 116.11, 118.88, 120.00, 122.26, 124.28, 125.88, 126.18, 128.23, 130.56, 131.90, 133.54, 134.24, 136.21, 137.12, 139.14, 141.25, 142.61, 143.80(Ar-<u>C</u>). MS(M^+): 426.13, Anal. Calcd. for $C_{23}H_{18}N_6OS$ (426.49): C 64.77, H 4.25, N 19.70 Found: C 64.85, H 4.20, N 19.80%.

N^2-(4-(pyridin-4-yl)thiazol-2-yl)-N^3-p-tolylquinoxaline-2,3-diamine (4e)

light yellow solid, yield 90%, m.p. 99-101°C, IR (KBr, ν, cm^{-1}): 3378(N-H Str.), 3242 (N-H Str.), 3021 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 2.325 (s, 3H, CH_3), 7.300-8.230 (m, 13H, Ar-H), 10.150 (s, 1H, NH), 10.260 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 26.30 (CH_3), 109.13, 110.06, 113.28, 115.64, 117.99, 120.11, 121.01, 122.44, 124.77, 125.16, 127.14, 128.18, 129.10, 131.2, 133.00, 134.26, 136.81, 137.56, 139.11, 141.38, 142.99, 144.00(Ar-<u>C</u>). MS(M^+): 410.13, Anal. Calcd. for $C_{23}H_{18}N_6S$ (410.49): C 67.30, H 4.42, N 20.47 Found: C 67.45, H 4.50, N 20.88%.

N^2-(4-nitrophenyl)-N^3-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4f)

light yellow solid, yield 88%, m.p. 129-131°C, IR (KBr, ν, cm^{-1}): 3306 (N-H Str.), 3215(N-H Str.), 3020 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 6.990-7.988 (m, 13H, Ar-H), 10.223 (s, 1H, NH), 10.425 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 110.23, 111.84, 112.36, 114.74, 115.80, 116.89, 118.00, 119.54, 121.47, 122.64, 124.01, 126.07, 127.24, 128.45, 130.33, 132.01, 133.45, 134.90, 136.00, 137.80, 139.12, 140.51(Ar-C). MS(M^+): 441.10, Anal. Calcd. for $C_{22}H_{15}N_7O_2S$ (441.47): C 59.85, H 3.42, N 22.21 Found: C 59.70, H 3.30, N 22.30%.

4-(2-(4-(pyridin-4-yl)thiazol-2-ylamino)quinoxalin-3-ylamino)phenol (4g)

light yellow solid, yield 85%, m.p. 121-123°C, IR (KBr, ν, cm^{-1}): 3312 (N-H Str.), 3218 (N-H Str.), 3029 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 5.125 (s, 1H, OH), 7.223-8.324 (m, 13H, Ar-H), 10.108 (s, 1H, NH), 10.223 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 110.66, 111.70, 113.00, 114.25, 115.25, 116.44, 117.00, 120.22, 121.33, 122.36, 124.08, 126.44, 127.34, 128.13, 129.33, 132.51, 133.12, 134.18, 136.00, 137.61, 139.77, 140.19(Ar-C). MS(M^+): 412.11, Anal. Calcd. for $C_{22}H_{16}N_6OS$ (417.51): C 64.06, H 3.91, N 20.38 Found: C 64.10, H 3.70, N 20.40%.

N^2-(4-fluorophenyl)-N^3-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4h)

light yellow solid, yield 83%, m.p. 113-115°C, IR (KBr, ν, cm^{-1}): 3361 (N-H Str.), 3249 (N-H Str.), 3019 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 6.856-7.842 (m, 13H, Ar-H), 10.658 (s, 1H, NH), 10.724 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 109.36, 110.25, 112.77, 114.96, 115.35, 116.41, 117.05, 119.34, 121.87, 122.12, 123.01, 125.07, 126.28, 128.17, 130.51, 132.24, 133.14, 134.74, 136.02, 137.10, 140.00, 141.77(Ar-C). MS(M^+): 414.11, Anal. Calcd. for $C_{22}H_{15}FN_6S$ (414.46): C 63.75, H 3.65, N 20.28 Found: C 63.80, H 3.60, N 20.40%.

N^2-(4-chlorophenyl)-N^3-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4i)

light yellow solid, yield 79%, m.p. 119-121°C, IR (KBr, ν, cm^{-1}): 3316 (N-H Str.), 3214 (N-H Str.), 3019 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 7.125-8.213 (m, 13H, Ar-H), 10.523 (s, 1H, NH), 10.856 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 106.38, 107.85, 109.18, 110.33, 112.45, 114.51, 115.02, 116.33, 117.89, 118.20, 119.26, 121.00, 123.14, 125.14, 126.78, 127.88, 129.14, 130.01, 132.11, 133.17, 134.51, 136.00(Ar-C). MS(M^+): 430.08, Anal. Calcd. for $C_{22}H_{15}ClN_6S$ (430.91): C 61.32, H 3.51, N 19.50 Found: C 61.28, H 3.40, N 19.55%

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N^2-(4-bromophenyl)-N^3-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4j)

light yellow solid, yield 76%, m.p. 133-135°C, IR (KBr, ν, cm^{-1}): 3298 (N-H Str.), 3233 (N-H Str.), 3022 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 6.798-7.623 (m, 13H, Ar-H), 10.118 (s, 1H, NH), 10.236 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 106.88, 108.86, 109.36, 110.22, 111.26, 113.11, 114.06, 116.77, 117.99, 118.18, 119.98, 121.10, 123.44, 124.33, 126.20, 127.16, 128.16, 130.01, 132.6, 133.27, 134.37, 135.01(Ar-C). MS(M^+): 474.03, Anal. Calcd. for $C_{22}H_{15}BrN_6S$ (475.36): C 55.59, H 3.18, N 17.68 Found: C 59.50, H 3.30, N 17.72%.

N^3-methyl-6-nitro-N^2-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4k)

light yellow solid, yield 72%, m.p. 140-142°C, IR (KBr, ν, cm^{-1}): 3326 (N-H Str.), 3223 (N-H Str.), 3042 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 3.200 (s, 3H, CH_3), 6.980-7.681 (m, 8H, Ar-H), 10.366 (s, 1H, NH), 10.513 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 28.26 (NH-$\underline{C}H_3$), 112.42, 113.68, 114.00, 115.68, 116.78, 117.18, 119.54, 121.74, 122.64, 123.08, 125.00, 127.13, 129.44, 130.51, 132.44, 134.36 (Ar-$\underline{C}$). MS(M^+): 379.09, Anal. Calcd. for $C_{17}H_{13}N_7O_2S$ (379.40): C 53.82, H 3.45, N 25.84 Found: C 53.70, H 3.55, N 25.70%.

N^3-ethyl-6-nitro-N^2-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4l)

light yellow solid, yield 75%, m.p. 137-139°C, IR (KBr, ν, cm^{-1}): 3366 (N-H Str.), 3252 (N-H Str.), 3041 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 1.113 (t, 3H, CH_3), 2.756 (q, 2H, CH_2), 7.320-8.126 (m, 8H, Ar-H), 10.222 (s, 1H, NH), 10.306 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 19.13 ($\underline{C}H_3$), 35.14 (NH-$\underline{C}H_2$), 111.6, 112.70, 114.6, 115.4, 116.1, 117.7, 20.00, 121.65, 122.2, 123.16, 125.50, 127.7, 129.14, 131.51, 132.34, 135.30 (Ar-$\underline{C}$). MS(M^+): 393.10, Anal. Calcd. for $C_{18}H_{15}N_7O_2S$ (393.42): C 54.95, H 3.84, N 24.92 Found: C 54.80, H 3.90, N 24.80%.

6-nitro-N^3-phenyl-N^2-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4m)

light yellow solid, yield 88%, m.p. 105-107°C, IR (KBr, ν, cm^{-1}): 3376 (N-H Str.), 3280 (N-H Str.), 3022 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 7.120-8.156 (m, 13H, Ar-H), 10.118 (s, 1H, NH), 10.236 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 111.03, 112.36, 113.00, 114.56, 115.36, 117.00, 118.36, 119.68, 121.45, 122.36, 123.78, 125.01, 127.36, 129.33, 131.47, 133.26, 134.78, 136.08, 137.45, 138.39, 140.2, 142.30 (Ar-$\underline{C}$). MS(M^+): 441.10, Anal. Calcd. for $C_{22}H_{15}N_7O_2S$ (441.47): C 59.85, H 3.42, N 22.21 Found: C 59.70, H 3.35, N 22.30%.

N^3-(4-methoxyphenyl)-6-nitro-N^2-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4n)

light yellow solid, yield 90%, m.p. 117-119°C, IR (KBr, ν, cm^{-1}): 3347 (N-H Str.), 3289 (N-H Str.), 3016 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 3.520 (s, 3H, OCH_3), 6.725-7.984 (m, 12H, Ar-H), 10.635 (s, 1H, NH), 10.758 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 54.30 (OCH_3), 111.27, 112.33, 113.18, 114.90, 115.23, 116.00, 117.35, 120.68, 121.46, 122.27, 123.44, 125.36, 127.29, 130.30, 131.83, 133.11, 134.64, 136.26, 137.33, 138.21, 140.01, 140.90(Ar-$\underline{C}$). MS(M^+): 471.11, Anal. Calcd. for $C_{23}H_{17}N_7O_3S$ (471.49): C 58.59, H 3.63, N 20.80 Found: C 58.70, H 3.48, N 20.62%.

6-nitro-N^2-(4-(pyridin-4-yl)thiazol-2-yl)-N^3-p-tolylquinoxaline-2,3-diamine (4o)

light yellow solid, yield 85%, m.p. 123-125°C, IR (KBr, ν, cm^{-1}): 3291 (N-H Str.), 3218 (N-H Str.), 3046 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 2.488 (s, 3H, CH_3), 6.925-7.846 (m, 12H, Ar-H), 10.236 (s, 1H, NH), 10.500 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 27.20 (CH_3), 110.06, 111.26, 112.01, 113.46, 115.11, 117.8, 118.2, 119.70, 121.23, 122.27, 123.11, 125.19, 127.22, 128.12, 130.42, 132.16, 134.3, 136.17, 137.11, 138.20, 140.11, 141.30(Ar-$\underline{C}$). MS(M^+): 455.12, Anal. Calcd. for $C_{23}H_{17}N_7O_2S$ (455.49): C 60.65, H 3.76, N 21.53 Found: C 60.40, H 3.58, N 21.78%.

6-nitro-N^3-(4-nitrophenyl)-N^2-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4q)

light yellow solid, yield 80%, m.p. 143-145°C, IR (KBr, ν, cm^{-1}): 3364 (N-H Str.), 3274 (N-H Str.), 3021 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 7.236-8.200 (m, 12H, Ar-H), 10.820 (s, 1H, NH), 10.954 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 113.24, 114.21, 115.36, 116.47, 117.36, 118.30, 119.01, 122.36, 123.47, 125.19, 127.40, 129.30, 131.21, 133.00, 134.51, 136.12, 137.00, 138.36, 139.99, 141.20, 142.39, 144.00(Ar-C). MS(M^+): 486.09, Anal. Calcd. for $C_{22}H_{14}N_8O_4S$ (486.46): C 54.32, H 2.90, N 23.03 Found: C 54.15, H 2.77, N 23.09%.

4-(2-(4-(pyridin-4-yl)thiazol-2-ylamino)-6-nitroquinoxalin-3-ylamino)phenol (4r)

light yellow solid, yield 79%, m.p. 139-141°C, Anal. IR (KBr, ν, cm^{-1}): 3388 (N-H Str.), 3263 (N-H Str.), 3018 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 4.900 (s, 1H, OH), 6.714-7.864 (m, 12H, Ar-H), 10.364 (s, 1H, NH), 10.412 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 112.33, 113.01, 115.63, 116.11, 117.42, 118.10, 120.44, 122.31, 123.17, 124.11, 127.35, 129.42, 131.10, 133.03, 135.41, 136.77, 137.01, 138.63, 139.88, 141.10, 142.26,143.90(Ar-C). MS(M^+): 457.10, Calcd. for $C_{22}H_{15}N_7O_3S$ (457.46): C 57.76, H 3.30, N 21.43 Found: C 57.50, H 3.24, N 21.20%

.

N^3-(4-fluorophenyl)-6-nitro-N^2-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4r)

light yellow solid, yield 77%, m.p. 130-132°C, IR (KBr, ν, cm^{-1}): 3328 (N-H Str.), 3260 (N-H Str.), 3006 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 7.210-8.126 (m, 12H, Ar-H), 10.366 (s, 1H, NH), 10.513 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 112.26, 113.20, 114.30, 116.18, 117.20, 118.11, 119.34, 122.56, 123.64, 125.18, 128.41, 129.10, 131.11, 133.18, 134.41, 135.64, 136.01, 138.4, 139.64, 141.34, 142.30, 143.00 (Ar-C). MS(M^+): 459.09, Anal. Calcd. for $C_{22}H_{14}FN_7O_2S$ (459.46): C 57.51, H 3.07, N 21.34 Found: C 57.46, H 3.62, N 21.38%.

N^3-(4-chlorophenyl)-6-nitro-N^2-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4s)

light yellow solid, yield 75%, m.p. 114-116°C, IR (KBr, ν, cm^{-1}): 3358 (N-H Str.), 3290 (N-H Str.), 3042 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 7.100-8.123 (m, 12H, Ar-H), 10.636 (s, 1H, NH), 10.813 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 114.30, 115.34, 116.18, 117.01, 119.56, 120.45, 122.13, 124.36, 125.61, 126.87, 128.03, 129.54, 131.66, 133.00, 135.44, 136.88, 137.24, 139.64, 140.20, 141.22, 143.00, 144.29(Ar-C). MS(M^+): 475.06, Anal. Calcd. for $C_{22}H_{14}ClN_7O_2S$ (475.91): C 55.52, H 2.97, N 20.60 Found: C 55.30, H 3.08, N 20.80%.

N^3-(4-bromophenyl)-6-nitro-N^2-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4t)

light yellow solid, yield 73%, m.p. 138-140°C, IR (KBr, ν, cm^{-1}): 3295 (N-H Str.), 3219 (N-H Str.), 3056 (Ar C-H Str.), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H (ppm): δ 6.963-7.890 (m, 12H, Ar-H), 10.654 (s, 1H, NH), 10.700 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C (ppm): 114.26, 115.18, 116.29, 116.91, 117.56, 120.22, 121.14, 124.35, 125.36, 126.0, 127.9, 129.60, 131.62, 133.01, 135.22, 136.78, 137.64, 138.94, 140.30, 141.64, 143.18, 143.99 (Ar-C). MS(M^+): 519.01, Anal. Calcd. for $C_{22}H_{14}BrN_7O_sS$ (520.36): C 50.78, H 2.71, N 18.84 Found: C 50.60, H 2.82, N 18.86%.

4. CONCLUSION

New substituted quinoxaline derivatives bearing the thiazole and pyridine nucleus have been synthesized through chloro-amine condensation reacton. This synthetic strategy allows the assimilation of three promising heterocycles through an easy way.

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