Synthesis of some new quinoxalines bearing pyridinyl thiazole moiety
Haresh G. Kathrotiya, Yogesh T. Naliapara*

Department of Chemistry, Saurashtra University, Rajkot-360005, Gujarat, India
*E-mail address: naliaparachem@yahoo.co.in

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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 1H NMR, 13C NMR, FT-IR, elemental analysis, and mass spectral data.

1. INTRODUCTION

Quinoxaline and its derivatives are an important class of benzenoheterocycles 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 anthelmintics [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], cavans [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-dicarboxyl 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 I2 [20, 21], SA [22], Montmorillonite K-10 [23], SSA [24], H2P2W18O62 . 24H2O [25], InCl3 [26], MnCl2 [27], CuSO4 . 5H2O [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), RuCl2(PPh₃)₃-TEMPO, and MnO₂ 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 1H NMR, 13C NMR, FTIR, and elemental analysis.

2. EXPERIMENTAL

Required all reagents were obtained commercially. Solvents were purified and dried before use. All melting points were taken in open capillaries and are uncorrected. Thin-layer chromatography (TLC, on aluminium plates precoated with silica gel, 60F₂₅₄, 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
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. ¹H NMR and ¹³C NMR spectra were recorded in DMSO-d₆ on a Bruker Avance 400F (MHz) spectrometer (Bruker Scientific Corporation Ltd., Switzerland) using 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(1H,4H)-dione was filtered and washed with ethanol and dried. Again a mixture of appropriate substituted quinoxaline-2,3(1H,4H)-dione (5gm) and 3 ml of DMF in POCl₃ (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 K₂CO₃ (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 K₂CO₃ (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](image-url)
Scheme 2 Synthetic pathway for the synthesis of intermediate 3c

\[
\text{1a} + \text{2b} \xrightarrow{\text{IPA / K}_2\text{CO}_3 / \text{Reflux}} \text{3c}
\]

Where \( R = \text{H, NO}_2 \)

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

\[
\text{3c} + \text{H}_2\text{N-}R_1 \xrightarrow{\text{IPA / K}_2\text{CO}_3 / \text{Reflux}} \text{4a-4t}
\]

Where \( R = \text{H, NO}_2 \), \( R_1 = \text{Aryl, Alkyl} \)

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

Where \( R = \text{H, NO}_2 \), \( R_1 = \text{Heterocycles} \), \( R_2 = \text{Aryl, Alkyl} \)
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

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

light yellow solid, yield 75%, m.p. 90-92°C, IR (KBr, v, cm\(^{-1}\)) : 3239 (N-H Str.), 3250 (N-H Str.), 3038 (Ar C-H Str.), \(^1\)H NMR (400 MHz, DMSO-d\(_6\)) \(\delta\) (ppm): \(\delta\) 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\(_6\)) \(\delta\) (ppm): 29.30 (NH-CH\(_3\)), 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-C). MS(M\(^+\)): 334.10, Anal. Calcd. for C\(_{11}\)H\(_{16}\)N\(_6\)S (334.4): C 61.06, H 4.22, N 25.13 Found: C 61.20, H 4.11, N 24.90%.

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

light yellow solid, yield 78%, m.p. 93-95°C, IR (KBr, v, cm\(^{-1}\)) : 3343 (N-H Str.), 3270 (N-H Str.), 3035 (Ar C-H Str.), \(^1\)H NMR (400 MHz, DMSO-d\(_6\)) \(\delta\) (ppm): \(\delta\) 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\(_6\)) \(\delta\) (ppm): 20.12 (CH\(_3\)), 34.68 (NH-CH\(_2\)), 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-C). MS(M\(^+\)): 348.12, Anal. Calcd. for C\(_{18}\)H\(_{16}\)N\(_6\)S (348.42): C 62.05, H 4.63, N 24.12 Found: C 62.20, H 4.50, N 24.25%.

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

light yellow solid, yield 89%, m.p. 110-112°C, IR (KBr, v, cm\(^{-1}\)) : 3356(N-H Str.), 3239 (N-H Str.), 3008 (Ar C-H Str.), \(^1\)H NMR (400 MHz, DMSO-d\(_6\)) \(\delta\) (ppm): \(\delta\) 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\(_6\)) \(\delta\) (ppm): 110.12, 110.03, 113.16, 115.32, 117.18, 118.98, 121.00, 122.36, 124.02, 125.66, 127.00, 128.18, 134.40, 131.45, 133.00, 135.24, 136.58, 137.85, 139.04, 141.22, 142.56, 143.12(Ar-C). MS(M\(^+\)): 396.12, Anal. Calcd. for C\(_{22}\)H\(_{16}\)N\(_6\)S (396.47): C 66.65, H 4.07, N 21.20 Found: C 66.50, H 4.02, N 21.30%.

\(\text{N}^2\text{-}(4\text{-methoxyphenyl)}\cdot\text{N}^3\text{-}(4\text{-pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4d)}\)

light yellow solid, yield 91%, m.p. 108-110°C, IR (KBr, v, cm\(^{-1}\)) : 3356 (N-H Str.), 3248 (N-H Str.), 3021 (Ar C-H Str.), \(^1\)H NMR (400 MHz, DMSO-d\(_6\)) \(\delta\) (ppm): \(\delta\) 3.920 (s, 3H, OCH\(_3\)), 6.882-7.914 (m, 13H, Ar-H), 10.712 (s, 1H, NH), 10.925 (s, 1H, NH). \(^13\)C NMR (100 MHz, DMSO-d\(_6\)) \(\delta\) (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-C). MS(M\(^+\)): 426.13, Anal. Calcd. for C\(_{23}\)H\(_{16}\)N\(_6\)OS (426.49): C 64.77, H 4.25, N 19.70 Found: C 64.85, H 4.20, N 19.80%.

\(\text{N}^2\text{-}(4\text{-pyridin-4-yl)thiazol-2-yl)}\cdot\text{N}^3\text{-p-tolylquinoxaline-2,3-diamine (4e)}\)

light yellow solid, yield 90%, m.p. 99-101°C, IR (KBr, v, cm\(^{-1}\)) : 3378(N-H Str.), 3242 (N-H Str.), 3021 (Ar C-H Str.), \(^1\)H NMR (400 MHz, DMSO-d\(_6\)) \(\delta\) (ppm): \(\delta\) 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\(_6\)) \(\delta\) (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-C). MS(M\(^+\)): 410.13, Anal. Calcd. for C\(_{23}\)H\(_{16}\)N\(_6\)S (410.49): C 67.30, H 4.42, N 20.47 Found: C 67.45, H 4.50, N 20.88%.
N²-(4-nitrophenyl)-N³-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4f)

light yellow solid, yield 88%, m.p. 129-131°C, IR (KBr, v, cm⁻¹): 3306 (N-H Str.), 3215(N-H Str.), 3020 (Ar C-H Str.), 1H NMR (400 MHz, DMSO-d₆) δH (ppm): δ 6.990-7.988 (m, 13H, Ar-H), 10.223 (s, 1H, NH), 10.425 (s, 1H, NH). 13C NMR (100 MHz, DMSO-d₆) δC (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 C₂₂H₁₃N₃O₂S (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, v, cm⁻¹): 3312 (N-H Str.), 3218 (N-H Str.), 3029 (Ar C-H Str.), 1H NMR (400 MHz, DMSO-d₆) δH (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). 13C NMR (100 MHz, DMSO-d₆) δC (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 C₂₂H₁₆N₆OS (417.51): C 64.06, H 3.91, N 20.38 Found: C 64.10, H 3.70, N 20.40%.

N²-(4-fluorophenyl)-N³-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4h)

light yellow solid, yield 83%, m.p. 113-115°C, IR (KBr, v, cm⁻¹): 3361 (N-H Str.), 3249 (N-H Str.), 3019 (Ar C-H Str.), 1H NMR (400 MHz, DMSO-d₆) δH (ppm): δ 6.856-7.842 (m, 13H, Ar-H), 10.658 (s, 1H, NH), 10.724 (s, 1H, NH). 13C NMR (100 MHz, DMSO-d₆) δC (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 C₂₂H₁₅FN₆S (414.46): C 63.75, H 3.65, N 20.28 Found: C 63.80, H 3.60, N 20.40%.

N²-(4-chlorophenyl)-N³-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4i)

light yellow solid, yield 79%, m.p. 119-121°C, IR (KBr, v, cm⁻¹): 3316 (N-H Str.), 3214 (N-H Str.), 3019 (Ar C-H Str.), 1H NMR (400 MHz, DMSO-d₆) δH (ppm): δ 7.125-8.213 (m, 13H, Ar-H), 10.523 (s, 1H, NH), 10.856 (s, 1H, NH). 13C NMR (100 MHz, DMSO-d₆) δC (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 C₂₂H₁₅ClN₆S (430.91): C 61.32, H 3.51, N 19.50 Found: C 61.28, H 3.40, N 19.55%.

N²-(4-bromophenyl)-N³-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4j)

light yellow solid, yield 76%, m.p. 133-135°C, IR (KBr, v, cm⁻¹): 3298 (N-H Str.), 3233 (N-H Str.), 3022 (Ar C-H Str.), 1H NMR (400 MHz, DMSO-d₆) δH (ppm): δ 6.798-7.623 (m, 13H, Ar-H), 10.118 (s, 1H, NH), 10.236 (s, 1H, NH). 13C NMR (100 MHz, DMSO-d₆) δC (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 C₂₂H₁₃BrN₆S (475.36): C 55.59, H 3.18, N 17.68 Found: C 59.50, H 3.30, N 17.72%. 
**N°-methyl-6-nitro-N°-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4k)**

Light yellow solid, yield 72%, m.p. 140-142°C, IR (KBr, v, cm⁻¹): 3326 (N-H Str.), 3223 (N-H Str.), 3042 (Ar C-H Str.). ¹H NMR (400 MHz, DMSO-d₆) δ_H (ppm): δ 3.200 (s, 3H, CH₃), 6.980-7.681 (m, 8H, Ar-H), 10.366 (s, 1H, NH), 10.513 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆) δ_C (ppm): 28.26 (NH-CH₂), 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-C). MS(M⁺): 379.09, Anal. Calcd. for C₁₁H₁₃N₅O₂S (379.40): C 53.82, H 3.45, N 25.84 Found: C 53.70, H 3.55, N 25.70%.

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

Light yellow solid, yield 75%, m.p. 137-139°C, IR (KBr, v, cm⁻¹): 3366 (N-H Str.), 3252 (N-H Str.), 3041 (Ar C-H Str.), ¹H NMR (400 MHz, DMSO-d₆) δ_H (ppm): δ 1.113 (t, 3H, CH₃), 2.756 (q, 2H, CH₂), 7.320-8.126 (m, 8H, Ar-H), 10.222 (s, 1H, NH), 10.306 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆) δ_C (ppm): 19.13 (CH₃), 35.14 (NH-CH₂), 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-C). MS(M⁺): 393.10, Anal. Calcd. for C₁₈H₁₅N₅O₂S (393.42): C 54.95, H 3.84, N 24.92 Found: C 54.80, H 3.90, N 24.80%.

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

Light yellow solid, yield 88%, m.p. 105-107°C, IR (KBr, v, cm⁻¹): 3376 (N-H Str.), 3280 (N-H Str.), 3022 (Ar C-H Str.), ¹H NMR (400 MHz, DMSO-d₆) δ_H (ppm): δ 7.120-8.156 (m, 13H, Ar-H), 10.118 (s, 1H, NH), 10.236 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆) 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-C). MS(M⁺): 441.10, Anal. Calcd. for C₂₂H₁₅N₅O₂S (441.47): C 59.85, H 3.42, N 22.21 Found: C 59.70, H 3.35, N 22.30%.

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

Light yellow solid, yield 90%, m.p. 117-119°C, IR (KBr, v, cm⁻¹): 3347 (N-H Str.), 3289 (N-H Str.), 3016 (Ar C-H Str.), ¹H NMR (400 MHz, DMSO-d₆) δ_H (ppm): δ 3.520 (s, 3H, OCH₃), 6.725-7.984 (m, 12H, Ar-H), 10.635 (s, 1H, NH), 10.758 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆) δ_C (ppm): 54.30 (OCH₃), 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-C). MS(M⁺): 471.11, Anal. Calcd. for C₂₃H₁₇N₅O₃S (471.49): C 58.59, H 3.63, N 20.80 Found: C 58.70, H 3.48, N 20.62%.

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

Light yellow solid, yield 85%, m.p. 123-125°C, IR (KBr, v, cm⁻¹): 3291 (N-H Str.), 3218 (N-H Str.), 3046 (Ar C-H Str.), ¹H NMR (400 MHz, DMSO-d₆) δ_H (ppm): δ 2.488 (s, 3H, CH₃), 6.925-7.846 (m, 12H, Ar-H), 10.236 (s, 1H, NH), 10.500 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆) δ_C (ppm): 27.20 (CH₃), 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-C). MS(M⁺): 455.12, Anal. Calcd. for C₂₃H₁₇N₅O₃S (455.49): C 60.65, H 3.76, N 21.53 Found: C 60.40, H 3.58, N 21.78%.
6-nitro-N³-(4-nitrophenyl)-N²-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4q)

light yellow solid, yield 80%, m.p. 143-145 °C, IR (KBr, v, cm⁻¹): 3364 (N-H Str.), 3274 (N-H Str.), 3021 (Ar C-H Str.), ¹H NMR (400 MHz, DMSO-d₆) δ_H (ppm): δ 7.236-8.200 (m, 12H, Ar-H), 10.820 (s, 1H, NH), 10.954 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆) 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 C₂₂H₁₄BrN₇OsS (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-nitroquinazolin-3-ylamino)phenol (4r)

light yellow solid, yield 79%, m.p. 139-141 °C, Anal. IR (KBr, v, cm⁻¹): 3388 (N-H Str.), 3263 (N-H Str.), 3018 (Ar C-H Str.), ¹H NMR (400 MHz, DMSO-d₆) 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). ¹³C NMR (100 MHz, DMSO-d₆) δ_C (ppm): 111.13, 114.62, 115.40, 116.42, 117.02, 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. Anal. Calcd. for C₂₂H₁₅N₅O₃S (457.46): C 57.76, H 3.30, N 21.43 Found: C 57.50, H 3.24, N 21.20%.

N³-(4-fluorophenyl)-6-nitro-N²-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4r)

light yellow solid, yield 77%, m.p. 130-132 °C, IR (KBr, v, cm⁻¹): 3328 (N-H Str.), 3260 (N-H Str.), 3006 (Ar C-H Str.), ¹H NMR (400 MHz, DMSO-d₆) δ_H (ppm): δ 7.210-8.126 (m, 12H, Ar-H), 10.366 (s, 1H, NH), 10.513 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆) 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 C₂₂H₁₄F₅N₅O₂S (459.46): C 57.51, H 3.07, N 21.34 Found: C 57.46, H 3.62, N 21.38%.

N³-(4-chlorophenyl)-6-nitro-N²-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4s)

light yellow solid, yield 75%, m.p. 114-116 °C, IR (KBr, v, cm⁻¹): 3358 (N-H Str.), 3290 (N-H Str.), 3042 (Ar C-H Str.), ¹H NMR (400 MHz, DMSO-d₆) δ_H (ppm): δ 7.100-8.123 (m, 12H, Ar-H), 10.636 (s, 1H, NH), 10.813 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆) 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, 141.21, 144.00 (Ar-C). MS(M⁺): 475.06. Anal. Calcd. for C₂₂H₁₄ClN₇O₂S (475.91): C 55.52, H 2.97, N 20.60 Found: C 55.30, H 3.08, N 20.80%.

N³-(4-bromophenyl)-6-nitro-N²-(4-(pyridin-4-yl)thiazol-2-yl)quinoxaline-2,3-diamine (4t)

light yellow solid, yield 73%, m.p. 138-140 °C, IR (KBr, v, cm⁻¹): 3295 (N-H Str.), 3219 (N-H Str.), 3056 (Ar C-H Str.), ¹H NMR (400 MHz, DMSO-d₆) δ_H (ppm): δ 6.963-7.890 (m, 12H, Ar-H), 10.654 (s, 1H, NH), 10.700 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆) 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 C₂₂H₁₄BrN₇O₂S (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 reaction. This synthetic strategy allows the assimilation of three promising heterocycles through an easy way.

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