An efficient and clean synthesis of thiophenyl thiazole depended novel triazolo[4,3-*a*]quinoxaline derivatives

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Keywords: Thiophenyl; Thiazole; [1,2,4]triazolo[4,3-*a*]quinoxaline; Iodobenzene diacetate

ABSTRACT. A simple and efficient approach for the synthesis of thiophenyl thiazole based triazolo[4,3-*a*]quinoxaline derivatives is described. In this methodology, 3-hydrazinyl-*N*-(4-(thiophen-2-yl)thiazol-2-yl)quinoxalin-2-amine derivatives treated with various aromatic aldehyde to form Schiff base which on treatment with iodobenzene diacetate in dichloromethane at room temperature to furnish title compounds. The synthesized compounds were characterized by ¹H NMR, ¹³C NMR, FT-IR, elemental analysis, and mass spectral data.

1 INTRODUCTION

1,2,4-triazoles are very interesting targets for medicinal and pharmaceutical applications. The recent literatures are enriched with progressive findings about the synthesis and pharmacological action of fused heterocyclic systems. The structural diversity and biological importance of nitrogen containing heterocyclic systems have made them attractive synthetic targets over many years and they are found in various natural products [1]. Quinoxalines are an important class of nitrogen containing heterocycles with a variety of biological activities. In particular quinoxaline scaffolds were found as a core unit in a number of biologically active compounds. These include anticancer [2, 3], antibacterial [4], antiviral [5], anti-inflammatory [6], anti HIV [7, 8] and antihelmintic activities [9]. Quinoxaline derivatives are also used in the development of novel organic dyes and organic semiconductors. Triazolo [4,3-*a*]quinoxaline [10] have been reported to possess antiviral, and antimicrobial activities. Many other triazolo quinoxaline derivatives have been reported [11-13] to possess other types of biological properties. Thus, triazolo quinoxaline derivatives continue to attract much attention as these molecules are of potential biological interest.

For synthesis purpose, triazolo quinoxalines can be achieved in several ways. Reaction of 1-(2-chloroquinoxalin-3-yl)hydrazine and triethyl orthoformate gave triazolo quinoxaline [14]. Reactions of benzyl bromide or benzyl cinnamate with *N*-(benzotriazol-1-ylmethyl)arylimidoyl chlorides in the presence of *t*-BuOK occur with opening of the benzotriazole ring affording 1,2,4-triazolo[1,5-*a*]quinoxalines [15]. Reaction of *N'*-(1,2-dihydro-2-oxoquinoxalin-3-yl)benzohydrazide and HMPA formed triazolo quinoxaline [16]. By heating 2-hydrazino 3-phenylquinoxaline with phenyl-1,3-butanedione produced triazolo quinoxaline [17]. *N*-(2-chloro-4*a*,8*a*-dihydroquinoline-3-yl-methyl)-*N*-3-chloro-quinoxalin-2-yl) hydrazones cyclised by iodobenzene diacetate under microwave irradiation technique to furnish the respective quinoliny-1, 2, 4-*s*-triazolo [4,3-*a*]quinoxalines [18]. Here we report an efficient and clean synthesis of thiophene thiazole depended novel triazolo quinoxaline derivatives by cyclisation 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 being used. 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 $\pm 0.4\%$ 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 ^{13}C NMR spectra were recorded in $\text{DMSO}-d_6$ 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 route for the synthesis of compound (1a)

Dry ethanol (10 ml), piperidine (1 ml), Substituted benzene-1,2-diamine (5 mmol), diethyl oxalate (5 mmol) were charged in a 100-ml round bottom flask with mechanical stirrer and condenser. The reaction mixture refluxed for 4 h. After the completion of reaction (checked by TLC), the separated substituted quinoxaline-2,3(1*H*,4*H*)-dione was filtered and washed with ethanol and dried. Now thionyl chloride (25 mmol) was added to a solution of substituted quinoxaline-2,3(1*H*,4*H*)-dione (10gm) in dry DCM (50 mL). Upon the addition of 1-2 drop of DMF a mixture was heated at reflux for 1 h. After the completion of reaction a mixture was washed with water followed by saturated NaHCO_3 solution. The organic phase was dried over anhydrous Na_2SO_4 and solvent was removed under reduced pressure to afford pure substituted 2,3-dichloroquinoxaline.

2.2 Synthetic route for the synthesis of compound (3c)

Dry potassium carbonate (5 mmol) and dry DMF (10 ml) were taken in 100 ml RBF. Substituted 2,3-dichloroquinoxaline **1a** (5 mmol), 4-(thiophen-2-yl)thiazol-2-amine **2b** (5 mmol), were added to this solution. The suspension then was heated at 100°C 4 h. The reaction was monitored by TLC using Ethyl acetate: Hexane as a mobile phase. After completion of the reaction, 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-(thiophen-2-yl)thiazol-2-yl)quinoxalin-2-amine.

2.3 General synthetic route for the synthesis of compounds 4(a-t)

The mixture of substituted 3-chloro-*N*-(4-(thiophen-2-yl)thiazol-2-yl)quinoxalin-2-amine **3c** (5 mmol) and hydrazine hydrate (5 mmol) in ethanol was refluxed for 2 h. on water bath. After completion of the reaction, solid product was appeared in the reaction. Cool the reaction mixture up to rt and filter the separated product washed with ethanol and dried at rt to furnished analytically pure substituted 3-hydrazinyl-*N*-(4-(thiophen-2-yl)thiazol-2-yl)quinoxalin-2-amine. Now substituted 3-hydrazinyl-*N*-(4-(thiophen-2-yl)thiazol-2-yl)quinoxalin-2-amine (5 mmol) and various aromatic aldehydes (5 mmol) in ethanol was refluxed for 2 h. on water bath. After completion of the reaction, solid product was appeared in the reaction. Cool the reaction mixture up to rt and filter the separated product washed with ethanol and dried at rt to furnished analytically pure 3-((*E*)-2-benzylidenehydrazinyl)-*N*-(4-(thiophen-2-yl)thiazol-2-yl)quinoxalin-2-amine derivatives. Then to a solution of 3-((*E*)-2-benzylidenehydrazinyl)-*N*-(4-(thiophen-2-yl)thiazol-2-yl)quinoxalin-2-amine derivatives (5 mmol) in MDC (10 ml) was added Iodobenzene diacetate (15 mmol) while stirring at rt. This solution was stirred for 45-55 minutes at rt. After the completion of reaction, monitored by the TLC, the mixture was washed with water followed by saturated NaHCO_3 solution. The organic phase was dried over anhydrous Na_2SO_4 and solvent was removed under reduced pressure to afford solid product which recrystallized from chloroform to obtain pure compounds **4a-4t**. The physicochemical and spectral properties of all the newly synthesized compounds **4a-4t**. are presented 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 thiophenyl thiazole depended triazolo quinoxaline derivatives 4a-4t

Table 1 Synthesis of triazolo quinoxaline derivatives 4a-4t

Entry	R	R ₁	RT(min.)	Yield %	mp °C
4a	H	H	46	89	130-132
4b	H	4-CH ₃	45	90	142-144
4c	H	4-OCH ₃	47	88	124-126
4d	H	4-F	49	82	125-127
4e	H	4-Cl	49	80	133-135
4f	H	4-Br	48	81	138-142
4g	H	4-NO ₂	47	84	133-135
4h	H	4-OH	48	82	150-152
4i	H	3-NO ₂	51	73	161-163
4j	H	3-OH	51	71	157-159
4k	CH ₃	H	46	87	141-143
4l	CH ₃	4-CH ₃	47	86	147-149
4m	CH ₃	4-OCH ₃	46	88	161-163
4n	CH ₃	4-F	50	82	135-137
4o	CH ₃	4-Cl	48	83	115-117
4p	CH ₃	4-Br	47	80	149-151
4q	CH ₃	4-NO ₂	48	86	128-130
4r	CH ₃	4-OH	49	81	119-121
4s	CH ₃	3-NO ₂	52	74	167-169
4t	CH ₃	3-OH	54	70	143-145

Scheme 4 Mechanism for the synthesis of thiophene thiazole depended triazolo quinoxaline derivatives 4a-4t

The required 4-(thiophen-2-yl)thiazol-2-amine **2b** was prepared by solid phase reaction according to literature procedure [19].

In this study, a series of triazolo quinoxaline derivatives **4a–4t** has been synthesized by dehydrogenative cyclisation reaction of 3-((*E*)-2-benzylidenehydrazinyl)-*N*-(4-(thiophen-2-yl)thiazol-2-yl)quinoxalin-2-amine derivatives using iodobenzene diacetate as catalyst (Scheme 3). In accordance with the mechanism suggested in (scheme-4), the first step of this process may involve electrophilic attack of iodobenzene diacetate on 3-((*E*)-2-benzylidenehydrazinyl)-*N*-(4-(thiophen-2-yl)thiazol-2-yl)quinoxalin-2-amine derivatives to generates the nitrile imine. Then due to loss of iodobenzene and acetic acid, finally ring closure occurs through quinoxaline ring nitrogen and leads to the formation of product **4a–4t**.

The structures of all the new synthesized compounds were confirmed by ^1H NMR, ^{13}C NMR, FTIR, elemental analysis, and molecular weight of some selected compounds confirmed by mass spectrometry. In ^1H NMR (DMSO- d_6) spectrum of compound **4c** exhibited singlet peak at δ 10.30 ppm for $-\text{NH}-$ proton while multiplets around δ 6.92–7.84 ppm for aromatic protons. Also exhibited singlet peak at δ 3.70 ppm for methoxy protons. In the ^{13}C NMR spectrum of compound **4c** showed signals around δ 109.22–142.10 ppm for aromatic carbons and δ 57.94 for aromatic methoxy carbon. The IR spectrum of compound **4c** exhibited characteristic absorption band at 3265 cm^{-1} for cyclic $-\text{NH}-$ and 3038 cm^{-1} for aromatic C–H stretching vibration. The mass spectra detected the expected molecular ion signals corresponding to respective molecular formula of synthesized compounds. Mass spectra of compound **4c** gave molecular ion peak at 456.0 ($M + 1$) corresponding to molecular formula $\text{C}_{23}\text{H}_{16}\text{N}_6\text{OS}_2$. 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

1-phenyl-*N*-(4-(thiophen-2-yl)thiazol-2-yl)-[1,2,4]triazolo[4,3-*a*]quinoxalin-4-amine (4a)

yellow solid, yield 89%, m.p. $130\text{--}132^\circ\text{C}$, IR (KBr, ν , cm^{-1}): 3265 (N-H Str.), 3040 (Ar C-H Str.), ^1H NMR (400 MHz, DMSO- d_6) δ_{H} (ppm): δ 6.713–7.698 (m, 13H, Ar-H), 10.580 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO- d_6) δ_{C} (ppm): 110.23, 111.10, 112.03, 113.26, 115.20, 116.90, 118.30, 119.90, 122.00, 123.60, 125.66, 127.33, 128.69, 129.35, 132.01, 133.65, 134.88, 136.04, 137.28, 138.33, 140.42, 143.00(Ar-C). MS(M^+): 426.07, Anal. Calcd. for $\text{C}_{22}\text{H}_{14}\text{N}_6\text{S}_2$ (426.52): C 61.95, H 3.31, N 19.70 Found: C 61.70, H 3.46, N 19.50%.

N-(4-(thiophen-2-yl)thiazol-2-yl)-1-*p*-tolyl-[1,2,4]triazolo[4,3-*a*]quinoxalin-4-amine (4b)

yellow solid, yield 90%, m.p. $142\text{--}144^\circ\text{C}$, IR (KBr, ν , cm^{-1}): 3214 (N-H Str.), 3026 (Ar C-H Str.), ^1H NMR (400 MHz, DMSO- d_6) δ_{H} (ppm): δ 2.416 (s, 3H, CH_3), 6.800–7.945 (m, 12H, Ar-H), 10.600 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO- d_6) δ_{C} (ppm): 24.13 (Ar- CH_3), 110.03, 111.22, 112.16, 114.66, 115.88, 116.99, 117.40, 119.10, 122.64, 123.14, 125.32, 126.56, 128.19, 130.32, 131.05, 132.66, 133.80, 136.04, 137.05, 138.13, 139.41, 142.06(Ar-C). MS(M^+): 440.09, Anal. Calcd. for $\text{C}_{23}\text{H}_{16}\text{N}_6\text{S}_2$ (440.54): C 62.71, H 3.66, N 19.08 Found: C 62.60, H 3.78, N 19.28%.

1-(4-methoxyphenyl)-*N*-(4-(thiophen-2-yl)thiazol-2-yl)-[1,2,4]triazolo[4,3-*a*]quinoxalin-4-amine (4c)

yellow solid, yield 88%, m.p. $124\text{--}126^\circ\text{C}$, IR (KBr, ν , cm^{-1}): 3265 (N-H Str.), 3038 (Ar C-H Str.), ^1H NMR (400 MHz, DMSO- d_6) δ_{H} (ppm): δ 3.700 (s, 3H, OCH_3), 6.920–7.845 (m, 12H, Ar-H), 10.300 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO- d_6) δ_{C} (ppm): 57.94 (OCH_3), 109.22, 110.16, 111.33, 112.16, 114.18, 115.91, 117.20, 119.82, 122.26, 123.33, 125.44, 127.17, 128.19, 129.45,

132.64, 133.36, 134.63, 136.27, 137.22, 138.31, 139.41, 142.10(Ar-C). MS(M⁺): 456.08, Anal. Calcd. for C₂₃H₁₆N₆OS₂ (456.54): C 60.51, H 3.53, N 18.41 Found: C 60.76, H 3.70, N 18.20%

1-(4-fluorophenyl)-N-(4-(thiophen-2-yl)thiazol-2-yl)-[1,2,4]triazolo[4,3-a]quinoxalin-4-amine (4d)

yellow solid, yield 82%, m.p. 125-127°C, IR (KBr, v, cm⁻¹): 3268 (N-H Str.), 3042 (Ar C-H Str.), ¹H NMR (400 MHz, DMSO-*d*₆) δ_H (ppm): δ 7.023-8.100 (m, 12H, Ar-H), 10.400 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-*d*₆) δ_C (ppm): 106.23, 107.40, 109.12, 110.24, 113.16, 114.98, 116.80, 118.00, 120.13, 121.16, 123.31, 124.80, 126.34, 128.18, 129.12, 131.18, 132.15, 133.00, 135.18, 137.01, 139.43, 141.12(Ar-C). MS(M⁺): 444.06, Anal. Calcd. for C₂₂H₁₃FN₆S₂ (444.51): C 59.44, H 2.95, N 18.91 Found: C 59.55, H 3.20, N 18.50%

1-(4-chlorophenyl)-N-(4-(thiophen-2-yl)thiazol-2-yl)-[1,2,4]triazolo[4,3-a]quinoxalin-4-amine (4e)

yellow solid, yield 80%, m.p. 133-135°C, IR (KBr, v, cm⁻¹): 3256 (N-H Str.), 3023 (Ar C-H Str.), ¹H NMR (400 MHz, DMSO-*d*₆) δ_H (ppm): δ 7.012-8.100 (m, 12H, Ar-H), 10.398 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-*d*₆) δ_C (ppm): 106.88, 107.65, 109.55, 110.21, 113.55, 115.90, 116.84, 118.26, 120.65, 121.33, 123.24, 124.55, 126.12, 128.13, 129.10, 130.10, 131.16, 133.12, 135.58, 137.11, 139.46, 141.88(Ar-C). MS(M⁺): 460.03, Anal. Calcd. for C₂₂H₁₃ClN₆S₂ (460.96): C 57.32, H 2.84, N 18.23 Found: C 57.20, H 3.02, N 18.35%

1-(4-bromophenyl)-N-(4-(thiophen-2-yl)thiazol-2-yl)-[1,2,4]triazolo[4,3-a]quinoxalin-4-amine (4f)

yellow solid, yield 81%, m.p. 138-142°C, IR (KBr, v, cm⁻¹): 3224 (N-H Str.), 3012 (Ar C-H Str.), ¹H NMR (400 MHz, DMSO-*d*₆) δ_H (ppm): δ 6.978-7.800 (m, 12H, Ar-H), 10.654 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-*d*₆) δ_C (ppm): 109.34, 111.02, 113.24, 114.12, 115.36, 116.24, 117.30, 118.54, 119.90, 121.20, 123.00, 124.56, 126.47, 128.03, 130.13, 132.45, 133.85, 136.30, 138.18, 140.16, 141.18, 142.89(Ar-C). MS(M⁺): 503.98, Anal. Calcd. for C₂₂H₁₃BrN₆S₂ (505.41): C 52.28, H 2.59, N 16.63 Found: C 52.36, H 2.72, N 16.80%

1-(4-nitrophenyl)-N-(4-(thiophen-2-yl)thiazol-2-yl)-[1,2,4]triazolo[4,3-a]quinoxalin-4-amine (4g)

yellow solid, yield 84%, m.p. 133-135°C, IR (KBr, v, cm⁻¹): 3290 (N-H Str.), 3055 (Ar C-H Str.), ¹H NMR (400 MHz, DMSO-*d*₆) δ_H (ppm): δ 7.145-8.124 (m, 12H, Ar-H), 10.456 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-*d*₆) δ_C (ppm): 110.31, 111.25, 113.36, 115.02, 115.96, 116.33, 117.80, 118.94, 119.20, 122.10, 123.50, 124.46, 125.40, 127.06, 129.10, 131.15, 132.86, 134.40, 137.19, 141.16, 141.85, 141.80(Ar-C). MS(M⁺): 471.06, Anal. Calcd. for C₂₂H₁₃N₇O₂S₂ (471.51): C 56.04, H 2.78, N 20.79 Found: C 56.10, H 2.85, N 20.88%

4-(4-(4-(thiophen-2-yl)thiazol-2-ylamino)-[1,2,4]triazolo[4,3-a]quinoxalin-1-yl)phenol (4h)

yellow solid, yield 82%, m.p. 50-152°C, IR (KBr, v, cm⁻¹): 3265 (N-H Str.), 3021 (Ar C-H Str.), ¹H NMR (400 MHz, DMSO-*d*₆) δ_H (ppm): δ 4.800 (s, 1H, OH), 7.005-8.100 (m, 12H, Ar-H), 10.654 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-*d*₆) δ_C (ppm): 106.35, 108.36, 110.23, 112.10, 114.76, 116.34, 117.50, 118.61, 119.14, 121.23, 123.40, 124.50, 126.34, 128.01, 130.22, 132.41, 133.80, 134.20, 136.10, 138.19, 141.10, 141.98(Ar-C). MS(M⁺): 442.07, Anal. Calcd. for C₂₂H₁₄N₆OS₂ (442.52): C 59.71, H 3.19, N 18.99 Found: C 59.60, H 3.30, N 19.20%

1-(3-nitrophenyl)-N-(4-(thiophen-2-yl)thiazol-2-yl)-[1,2,4]triazolo[4,3-*a*]quinoxalin-4-amine (4i)

yellow solid, yield 73%, m.p. 161-163°C, IR (KBr, ν , cm^{-1}): 3233 (N-H Str.), 3016 (Ar C-H Str.), ^1H NMR (400 MHz, DMSO- d_6) δ_{H} (ppm): δ 7.140-8.042 (m, 12H, Ar-H), 10.400s (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO- d_6) δ_{C} (ppm): 113.18, 115.20, 116.25, 117.24, 119.80, 121.34, 122.00, 124.26, 125.67, 127.18, 129.14, 130.12, 132.63, 134.16, 135.78, 137.22, 139.14, 141.50, 143.27, 144.00, 145.03, 146.28(Ar-C). MS(M^+): 471.06, Anal. Calcd. for $\text{C}_{22}\text{H}_{13}\text{N}_7\text{O}_2\text{S}_2$ (471.51): C 56.04, H 2.78, N 20.79 Found: C 56.32, H 2.90, N 20.92%.

3-(4-(4-(thiophen-2-yl)thiazol-2-ylamino)-[1,2,4]triazolo[4,3-*a*]quinoxalin-1-yl)phenol (4j)

yellow solid, yield 71%, m.p. 157-159°C, IR (KBr, ν , cm^{-1}): 3280 (N-H Str.), 3050 (Ar C-H Str.), ^1H NMR (400 MHz, DMSO- d_6) δ_{H} (ppm): δ 4.980 (s, 1H, OH), 7.123-8.045 (m, 12H, Ar-H), 10.654 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO- d_6) δ_{C} (ppm): 112.31, 114.21, 116.20, 117.33, 119.81, 121.30, 122.22, 123.16, 125.65, 127.10, 129.11, 130.06, 132.55, 134.32, 135.18, 136.12, 138.24, 141.10, 142.22, 144.33, 145.58, 146.18(Ar-C). MS(M^+): 442.07, Anal. Calcd. for $\text{C}_{22}\text{H}_{14}\text{N}_6\text{O}_2\text{S}_2$ (442.52): C 59.71, H 3.19, N 18.99 Found: C 59.50, H 3.33, N 18.80%.

8-methyl-1-phenyl-N-(4-(thiophen-2-yl)thiazol-2-yl)-[1,2,4]triazolo[4,3-*a*]quinoxalin-4-amine (4k)

yellow solid, yield 87%, m.p. 141-143°C, IR (KBr, ν , cm^{-1}): 3266 (N-H Str.), 3014 (Ar C-H Str.), ^1H NMR (400 MHz, DMSO- d_6) δ_{H} (ppm): δ 2.486 (s, 3H, Ar-CH₃), 6.985-8.001 (m, 12H, Ar-H), 10.358 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO- d_6) δ_{C} (ppm): 26.10 (Ar-CH₃), 112.30, 114.32, 115.60, 116.36, 118.30, 119.00, 120.54, 121.00, 123.06, 125.66, 126.90, 127.88, 130.00, 131.65, 132.55, 134.03, 136.98, 138.00, 139.01, 142.30, 143.00, 145.01(Ar-C). MS(M^+): 440.09, Anal. Calcd. for $\text{C}_{23}\text{H}_{16}\text{N}_6\text{S}_2$ (440.54): C 62.71, H 3.66, N 19.08 Found: C 62.80, H 3.90, N 19.23%.

8-methyl-N-(4-(thiophen-2-yl)thiazol-2-yl)-1-p-tolyl-[1,2,4]triazolo[4,3-*a*]quinoxalin-4-amine (4l)

yellow solid, yield 86%, m.p. 147-149°C, IR (KBr, ν , cm^{-1}): 3288 (N-H Str.), 3023 (Ar C-H Str.), ^1H NMR (400 MHz, DMSO- d_6) δ_{H} (ppm): δ 2.420 (s, 3H, Ar-CH₃), 2.500 (s, 3H, Ar-CH₃), 6.900-7.845 (m, 11H, Ar-H), 10.336 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO- d_6) δ_{C} (ppm): 25.30 (Ar-CH₃), 27.14 (Ar-CH₃), 111.23, 112.55, 113.62, 115.30, 116.10, 118.12, 120.55, 121.22, 123.18, 125.54, 126.17, 127.32, 130.01, 131.33, 132.15, 134.18, 135.90, 138.10, 139.55, 142.20, 143.17, 145.21(Ar-C). MS(M^+): 454.10, Anal. Calcd. for $\text{C}_{24}\text{H}_{18}\text{N}_6\text{S}_2$ (522.39): C 63.41, H 3.99, N 18.49 Found: C 63.52, H 4.09, N 18.85%.

1-(4-methoxyphenyl)-8-methyl-N-(4-(thiophen-2-yl)thiazol-2-yl)-[1,2,4]triazolo[4,3-*a*]quinoxalin-4-amine (4m)

yellow solid, yield 88%, m.p. 161-163°C, IR (KBr, ν , cm^{-1}): 3298 (N-H Str.), 3025 (Ar C-H Str.), ^1H NMR (400 MHz, DMSO- d_6) δ_{H} (ppm): δ 2.451 (s, 3H, Ar-CH₃), 4.002 (s, 3H, OCH₃), 7.001-8.120 (m, 11H, Ar-H), 10.500 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO- d_6) δ_{C} (ppm): 23.16 (Ar-CH₃), 54.96 (OCH₃), 112.22, 114.55, 115.14, 116.66, 118.88, 119.70, 120.35, 121.12, 123.88, 125.66, 126.82, 127.44, 130.11, 131.60, 132.15, 133.13, 135.93, 137.01, 140.06, 142.33, 143.54, 145.08(Ar-C). MS(M^+): 470.10, Anal. Calcd. for $\text{C}_{24}\text{H}_{18}\text{N}_6\text{O}_2\text{S}_2$ (470.57): C 61.26, H 3.86, N 17.86 Found: C 61.82, H 4.10, N 17.80%.

1-(4-fluorophenyl)-8-methyl-N-(4-(thiophen-2-yl)thiazol-2-yl)-[1,2,4]triazolo[4,3-*a*]quinoxalin-4-amine (4n)

yellow solid, yield 82%, m.p. 135-137°C, IR (KBr, ν , cm^{-1}): 3214 (N-H Str.), 3038 (Ar C-H Str.), ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ_{H} (ppm): δ 2.612 (s, 3H, Ar-CH₃), 6.987-7.856 (m, 11H, Ar-H), 10.200 (s, 1H, NH). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ_{C} (ppm): 27.16 (Ar-CH₃), 111.00, 112.69, 114.03, 116.48, 117.80, 119.20, 121.37, 122.36, 124.30, 126.39, 127.89, 129.60, 131.33, 133.12, 135.14, 137.18, 139.15, 140.12, 141.20, 142.36, 144.08, 146.34(Ar-C). MS(M^+): 458.08, Anal. Calcd. for $\text{C}_{23}\text{H}_{15}\text{FN}_6\text{S}_2$ (458.53): C 60.25, H 3.30, N 18.33 Found: C 60.35, H 3.10, N 18.26%.

1-(4-chlorophenyl)-8-methyl-N-(4-(thiophen-2-yl)thiazol-2-yl)-[1,2,4]triazolo[4,3-*a*]quinoxalin-4-amine (4o)

yellow solid, yield 83%, m.p. 115-117°C, IR (KBr, ν , cm^{-1}): 3288 (N-H Str.), 3006 (Ar C-H Str.), ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ_{H} (ppm): δ 2.456 (s, 3H, Ar-CH₃), 6.900-7.890 (m, 11H, Ar-H), 10.356 (s, 1H, NH). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ_{C} (ppm): 25.31 (Ar-CH₃), 110.25, 111.79, 112.13, 114.44, 116.60, 118.22, 121.30, 122.26, 124.11, 126.35, 127.55, 129.96, 131.14, 132.10, 133.16, 136.20, 139.10, 140.22, 141.31, 142.30, 144.14, 146.20(Ar-C). MS(M^+): 474.05, Anal. Calcd. for $\text{C}_{23}\text{H}_{15}\text{ClN}_6\text{S}_2$ (474.99): C 58.16, H 3.18, N 17.69 Found: C 58.33, H 3.45, N 17.50%.

1-(4-bromophenyl)-8-methyl-N-(4-(thiophen-2-yl)thiazol-2-yl)-[1,2,4]triazolo[4,3-*a*]quinoxalin-4-amine (4p)

yellow solid, yield 80%, m.p. 149-151°C, IR (KBr, ν , cm^{-1}): 3241 (N-H Str.), 3033 (Ar C-H Str.), ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ_{H} (ppm): δ 2.200 (s, 3H, Ar-CH₃), 6.756-7.600 (m, 11H, Ar-H), 10.700 (s, 1H, NH). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ_{C} (ppm): 24.26 (Ar-CH₃), 107.64, 109.13, 111.02, 112.36, 114.15, 116.18, 117.20, 119.65, 121.30, 122.08, 124.15, 126.33, 127.69, 128.77, 130.14, 132.51, 133.87, 135.17, 136.45, 137.10, 139.40, 141.14(Ar-C). MS(M^+): 518.00, Anal. Calcd. for $\text{C}_{23}\text{H}_{15}\text{BrN}_6\text{S}_2$ (519.44): C 53.18, H 2.91, N 16.18 Found: C 53.23, H 3.00, N 16.03%.

8-methyl-1-(4-nitrophenyl)-N-(4-(thiophen-2-yl)thiazol-2-yl)-[1,2,4]triazolo[4,3-*a*]quinoxalin-4-amine (4q)

yellow solid, yield 86%, m.p. 128-130°C, IR (KBr, ν , cm^{-1}): 3276 (N-H Str.), 3046 (Ar C-H Str.), ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ_{H} (ppm): δ 2.600 (s, 3H, Ar-CH₃), 6.600-7.020 (m, 11H, Ar-H), 10.345 (s, 1H, NH). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ_{C} (ppm): 26.00 (Ar-CH₃), 108.14, 109.23, 110.22, 111.56, 113.10, 115.44, 116.29, 118.60, 121.25, 122.87, 124.35, 126.13, 127.28, 128.57, 130.34, 132.50, 133.80, 135.11, 136.15, 137.88, 138.42, 140.15(Ar-C). MS(M^+): 485.07, Anal. Calcd. for $\text{C}_{23}\text{H}_{15}\text{N}_7\text{O}_2\text{S}_2$ (485.54): C 56.89, H 3.11, N 20.19 Found: C 56.60, H 3.20, N 20.28%.

4-(4-(4-(thiophen-2-yl)thiazol-2-ylamino)-8-methyl-[1,2,4]triazolo[4,3-*a*]quinoxalin-1-yl)phenol (4r)

yellow solid, yield 81%, m.p. 119-121°C, IR (KBr, ν , cm^{-1}): 3268 (N-H Str.), 3046 (Ar C-H Str.), ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ_{H} (ppm): δ 2.563 (s, 3H, Ar-CH₃), 4.500 (s, 1H, OH), 6.980-7.800 (m, 11H, Ar-H), 10.212 (s, 1H, NH). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ_{C} (ppm): 25.30 (Ar-CH₃), 106.60, 108.10, 109.65, 111.36, 113.18, 115.20, 117.36, 119.66, 121.33, 122.51, 124.25, 126.40, 127.61, 128.19, 130.54, 131.50, 133.80, 134.10, 136.20, 137.88, 138.30, 140.19(Ar-C). MS(M^+): 456.08, Anal. Calcd. for $\text{C}_{23}\text{H}_{16}\text{N}_6\text{OS}_2$ (456.54): C 60.51, H 3.53, N 18.41 Found: C 60.72, H 3.74, N 18.20%.

8-methyl-1-(3-nitrophenyl)-N-(4-(thiophen-2-yl)thiazol-2-yl)-[1,2,4]triazolo[4,3-a]quinoxalin-4-amine (4s)

yellow solid, yield 74%, m.p. IR (KBr, ν , cm^{-1}): 3250 (N-H Str.), 3040 (Ar C-H Str.), ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ_{H} (ppm): δ 2.400 (s, 3H, Ar-CH₃), 7.002-8.100 (m, 11H, Ar-H), 10.220 (s, 1H, NH). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ_{C} (ppm): 26.00 (Ar-CH₃), 110.34, 112.26, 113.68, 115.02, 117.18, 119.30, 121.45, 123.36, 125.41, 126.37, 128.12, 129.40, 131.25, 132.16, 133.88, 135.40, 137.20, 138.16, 140.12, 141.33, 143.00, 145.11(Ar-C). MS(M^+): 485.07 Anal. Calcd. for $\text{C}_{23}\text{H}_{15}\text{N}_7\text{O}_2\text{S}_2$ (485.54): C 56.89, H 3.11, N 20.19 Found: C 56.70, H .20, N 20.30%.

3-(4-(4-(thiophen-2-yl)thiazol-2-ylamino)-8-methyl-[1,2,4]triazolo[4,3-a]quinoxalin-1-yl)phenol (4t)

yellow solid, yield 70%, m.p. 143-145°C, IR (KBr, ν , cm^{-1}): 3288 (N-H Str.), 3047 (Ar C-H Str.), ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ_{H} (ppm): δ 2.560 (s, 3H, Ar-CH₃), 4.400 (s, 1H, OH), 7.010-8.005 (m, 11H, Ar-H), 10.546 (s, 1H, NH). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ_{C} (ppm): 23.98 (Ar-CH₃), 110.55, 111.20, 112.24, 114.05, 116.10, 117.35, 119.40, 121.30, 123.51, 125.36, 127.15, 129.20, 131.00, 132.34, 133.85, 135.46, 137.21, 138.22, 139.03, 141.53, 144.00, 145.99(Ar-C). MS(M^+): 456.08, Anal. Calcd. for $\text{C}_{23}\text{H}_{16}\text{N}_6\text{O}_2\text{S}_2$ (456.54): C 60.51, H 3.53, N 18.41 Found: C 60.62, H 3.60, N 18.52%.

4 CONCLUSION

In summary, novel series of triazolo quinoxalines having thiophene and thiazole moiety synthesized by dehydrogenative cyclisation reaction through iodobenzene diacetate. The synthetic method produced a single scaffold with triazole, quinoxaline, thiophene and thiazole heterocyclic systems.

Acknowledgments

The authors are thankful to the Head, Department of Chemistry, Saurashtra University, Rajkot for providing ^1H NMR, ^{13}C NMR, mass and FT-IR spectroscopy and research facilities.

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