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Utilization of 2,3-hydrazinylquinoxalin-2-ol in the synthesis of fused quinoxaline ring systems

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ABSTRACT

The 3-hydrazinylquinoxalin-2-ol **(2)** and 2,3-dichloroquinoxaline **(3)** were prepared from 2,3-dihydroxyquinoxaline **(4)** and used as an intermediates in the syntheses of triazoloquinoxaline, imidazoquinoxaline, tetrazoloquinoxaline and piperazinoquinoxalines ring systems.
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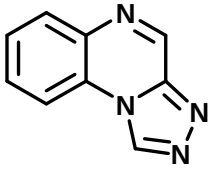
KEYWORDS

Organic Syntheses;
Tricyclic quinoxaline ring systems;
Triazoloquinoxaline;
Imidazoquinoxaline;
Tetrazoloquinoxaline;
Triazinoquionoxaline and piperazinoquinoxalines.

INTRODUCTION

In spite of the presence of several fused tricyclic quinoxaline ring systems have a great attention for their medical usefulness, specially the triazoloquinoxaline[1,2] ring system **(1)**, which works as adenosine receptor antagonists. Other ring systems; imidazoquinoxaline,[3] tetrazoloquinoxaline,[4] triazinoquinoxalie[5] and piperazinoquinoxalines[6] are rare in their presence and biological studies. This rarity helps us to study short procedure for their preparation and for evaluation of their biological properties. The readily prepared 3-hydrazinylquinoxalin-2-ol **(2)**[7] and 2,3-dichloroquinoxaline **(3)**[8,9] starting from 2,3-dihydroxyquinoxaline **(4)**[10] were suggested for the syntheses of these ring systems.



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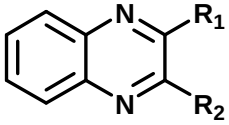


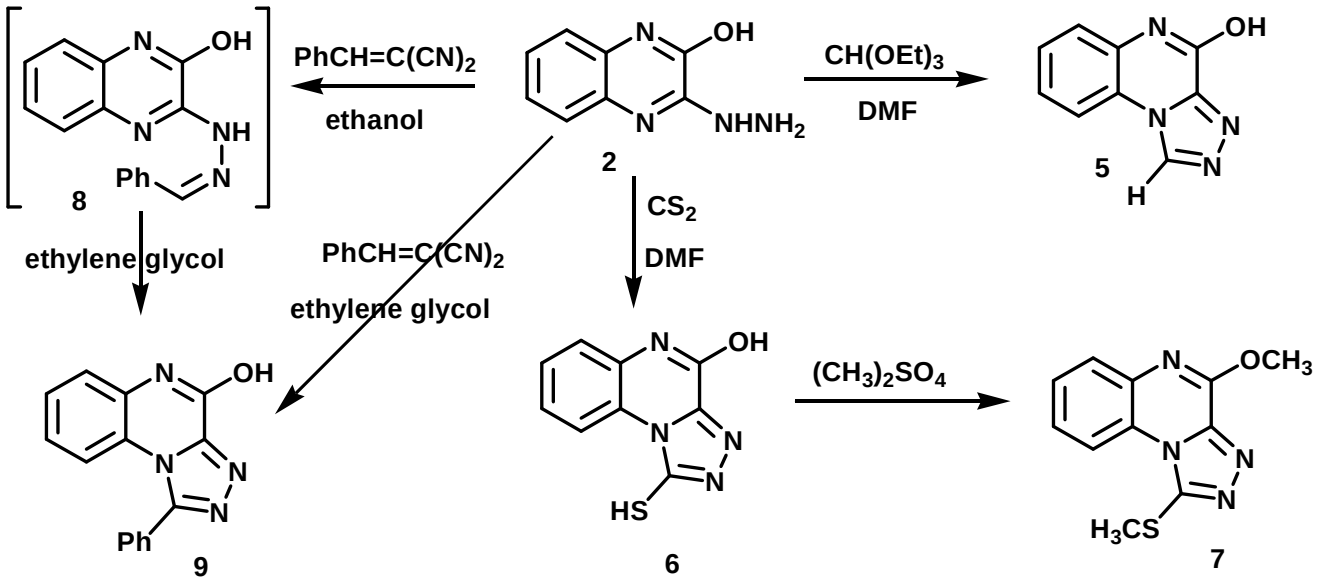
2; R_1 = $NHNH_2$, R_2 = OH
3; R_1 = R_2 = Cl
4; R_1 = R_2 = OH

RESULTS AND DISCUSSIONS

Our application for the reported solid synthetic method for 2,3-dihydroxyquinoxaline **(4)** (condensation of diethyl oxalate and *o*-phenylenediamine),[10] the reaction was not complete. When this procedure was repeated in tetrahydrofuran,[11] another problem appeared as a result of the reaction time (three days) and low yield. Our improved synthesis of compound **(4)**, involving condensation of *o*-phenylenediamine with diethyl oxalate in the presence of absolute ethanol and acetic acid, reduced the reaction time (two hours) and increased the reaction yield (92.5%). The hydrazide derivative **(2)** was prepared by refluxing of dihydroxy derivative **(4)** with hydrazine hydrate 50%.[7]

a- Syntheses of [1.2.4]triazolo[4,3-a]quinoxaline ring system

The [1,2,4]triazolo[4,3-a]quinoxaline ring system **(1)** was synthesized by three different procedures starting from the hydrazide derivative **(2)**. *The first two of them* depends on the condensation of the hydrazide **(2)** either with triethyl orthoformate in N,N-dimethylformamide (DMF) or refluxing with carbon disulphide to give two new triazoloquinoxaline derivatives **(5)** and **(6)** respectively, (Scheme 1). The ^{1}H NMR spectrum for compound **(5)** (DMSO-d_6, T = 60°C) indicated the presence of an exchangeable proton at δ 12.06 ppm for OH proton and the triazolo carbon proton at δ 9.82 ppm. The mass spectrometer determined the structure of compound **(5)**; 186 (M^+, 100), 187 (M^++1, 17.1), 158 (78.7), 130 (9.5), which showed that the M^+ fragment is consistent with its calculated molecular mass (186.17). Also the decomposition in spectrometer finally gave two fragments with ionic mass 105 ($C_6H_5N_2$, 25.5%), 104 ($C_6H_4N_2$,75.7%), which are common in the decomposition of quinoxaline compounds in mass spectrometer.



Scheme 1

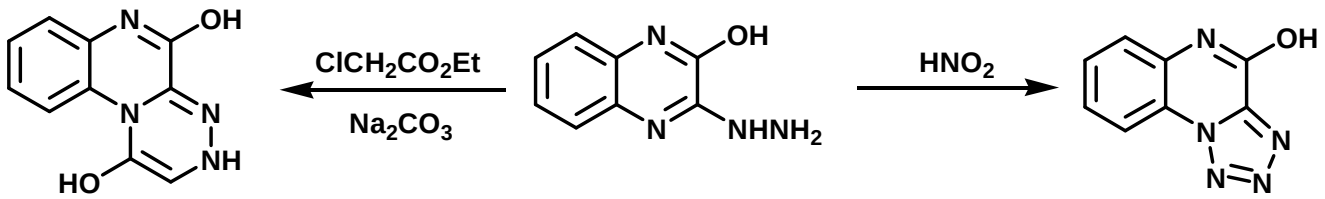
Compounds **(6)** was insoluble material and could not purify, so, it was methylated by treatment with dimethyl sulphate to give the dimethylated derivative **(7)** (Scheme 1). Compound **(7)** easily soluble in organic solvent and showed in ^{1}H NMR spectrum two different methyl protons at δ 2.98 and 4.49 ppm for SMe and OMe respectively.

The third methods including the reaction of compound **(2)** with arylidine derivative (PhCH=C(CN)$_2$) in ethanol and gave unexpected azomethine derivative **(8)**. Which was cyclized in boiling ethylene glycol to give the triazoloquinoxaline derivative **(9)**. Direct refluxing of the hydrazide **(2)** with the arylidine in ethylene glycol gave the triazoloquinoxaline derivative **(9)** (Scheme 1). The structure of the azomethine derivatives **(8)** was confirmed by independent chemical synthesis; condensation of the hydrazide derivative **(2)** with benaldehyde gave material consistent with corresponding azomethine **(8)** (TLC and melting point).

b- Synthesis of tetrazolo[1,5-a]quinoxaline ring system

The hydroxyl derivative of the tetrazolo[1,5-a]quinoxaline ring system was prepared from the hydrazide **(2)**; by diazotization with sodium nitrite in diluted hydrochloric acid and cyclization *in situ*, to give the tetrazolo[1,5-a]quinoxaline derivative **(10)** (Scheme 2). The IR spectrum of compound **(10)** has a sharp band of the stretching vibrations of a carbonyl group split into two $\nu_{C=O}$ bands at 1673.91and 1720.19 cm,$^{-1}$ this IR data are similar in its character

with those which published in literature.[3] The ^{1}H NMR spectrum of compound **(10)** shows the presence of four aromatic protons and exchangeable hydroxyl proton at δ 12.54 ppm.



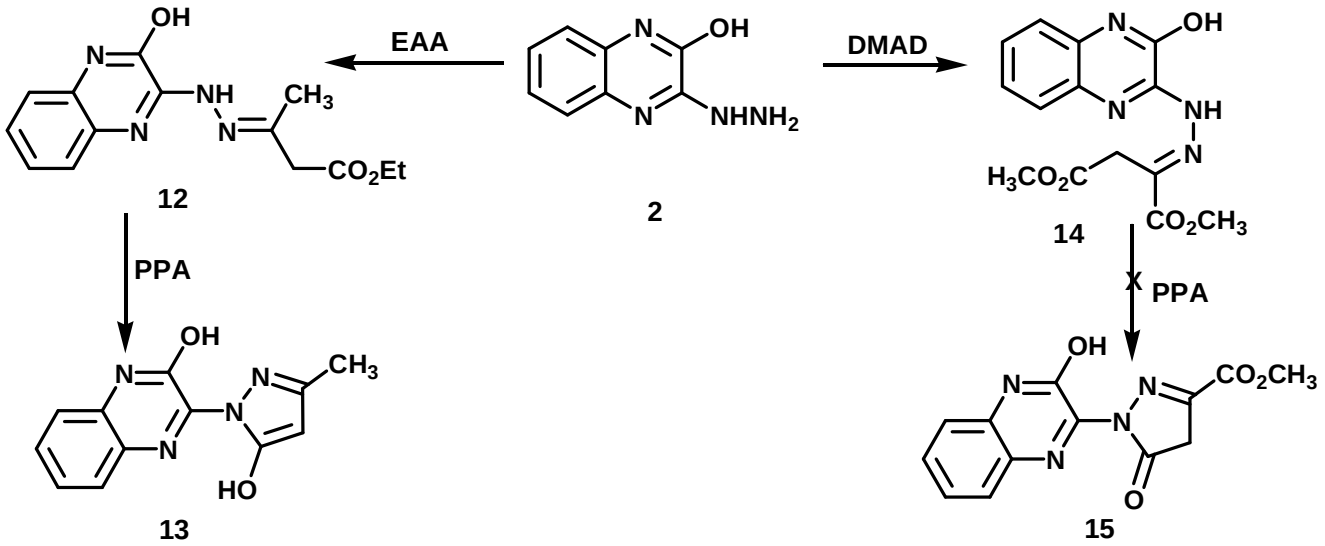
Scheme 2

c- Synthesis of the [1,2,4]triazino[4,3-a]quinoxaline ring system

For the synthesizing of the [1,2,4]triazino[4,3-a]quinoxaline ring system, by refluxing of the hydrazide derivative **(2)** with ethyl chloroacetate in the presence of sodium carbonate, gave the cyclized product **(11)** (Scheme 2). Compound **(11)** insoluble in organic solvents and was difficult to get on its ^{1}H NMR spectrum in normal temperature. While its ^{1}H NMR spectrum in DMSO-d_6 at 60°C showed the presence of three exchangeable protons at δ 11.75 ppm for two OH protons and at δ 10.55 ppm for NH proton. ^{13}C NMR spectrum (DEPT135, at T = 60°C in DMSO-d_6) and correlation diagram between proton and carbon (HMBC NMR) showed the presence of carbon signal characterized the CH of the triazine ring at δ 115.31 ppm and CH hydrogen at δ 8.03 ppm.

d- Synthesis of the new pyrazolyl-quinoxaline derivative

Attempting condensation of the hydrazide derivative **(2)** with ethyl acetoacetate (EAA) to give the pyrazolyl-quinoxaline derivative **(13)** failed, and gave the open structure **(12)** (Scheme 3). The ^{1}H NMR data for compound **(12)** showed the presence of ethyl ester group in addition to, two exchangeable protons for NH and OH protons at δ 9.17 and 11.32 ppm respectively, which ascertain the condensation reaction between NH2 and ketonic carbonyl group of ethyl acetoacetate, gave the open compound **(12)**. Further heating of the product **(12)** in PPA gave the cyclized material **(13)**. Compound **(13)** showed the disappearance of ester and NH protons in its NMR data.



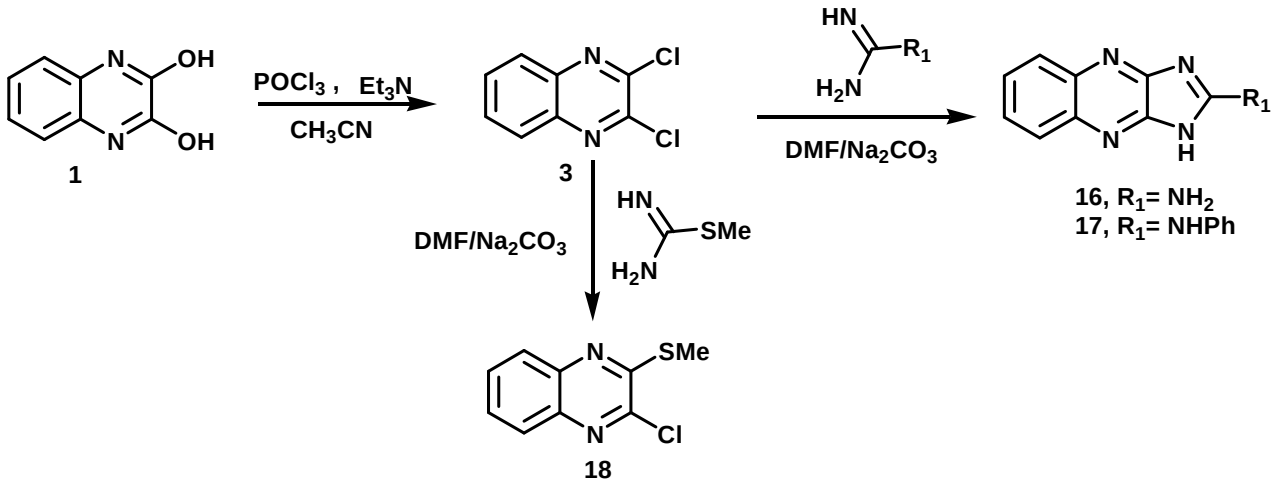
Scheme 3

In a similar procedure, the attempting further synthesis of the pyrazolyl-quinoxaline derivative by condensation of the hydrazide derivative **(2)** with dimethyl acetylene dicarboxylate (DMAD), the opened structure **(14)** was obtained (Scheme 3). The ^{1}H NMR spectrum for compound **(14)** shows two different methyl esters protons at δ 3.72 and 3.92 ppm, in addition to exchangeable NH and OH protons at δ 11.6 and 13.30 ppm respectively. Whatever cyclization of **(14)** with PPA failed to give the pyrazolyl-quinoxaline derivative **(15)** (Scheme 3).

e- Synthesis of Imidazo[4,5-b]quinoxaline Ring System

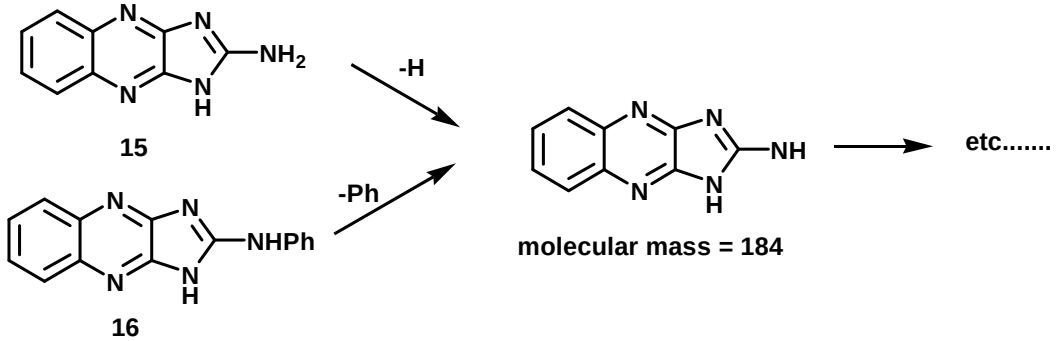
The published syntheses for this ring system involved building of the imidazole ring onto 2,3-quinoxalin-diamine.[4] In this work the imidazole ring was constructed by the condensation of 2,3-dichloroquinoxaline **(3)** with guanidine or phenylguanidine salts to give 1H-imidazo[4,5-b]quinoxalin-2-amine **(16)** or N-phenyl-1H-imidazo[4,5-b]quinoxalin-2-amine **(17)**, respectively, (Scheme 4). The ^{1}H NMR spectrum for the imidazoquinoxaline derivative **(16)**, reflect the presence of NH_2 protons at δ 3.77 ppm and the imidazole ring NH at δ 7.74 ppm. In addition, compound **(17)** showed the aromatic NH at δ 3.87 ppm and the imidazole ring NH at δ 7.91ppm.

The reported synthesis of 2,3-dichloroquinoxaline **(3)** from 2,3-dihydroxyquinoxaline **(1)**,[8,9] was developed to increase its yield and prevent the formation of monochloroquinoxaline derivative. Treatment of the dihydroxy derivative **(1)** with excess of phosphorus oxychloride (2 ml for each 1 g) in boiling acetonitrile using triethylamine as a catalyst, gave the dichloroquinoxaline derivative **(3)** in 87% yield.



Scheme 4

It was noted from the decomposition process of compounds **(16)** and **(17)** in mass spectrometer that, they gave the same ionic species as was pointed in Scheme 5.

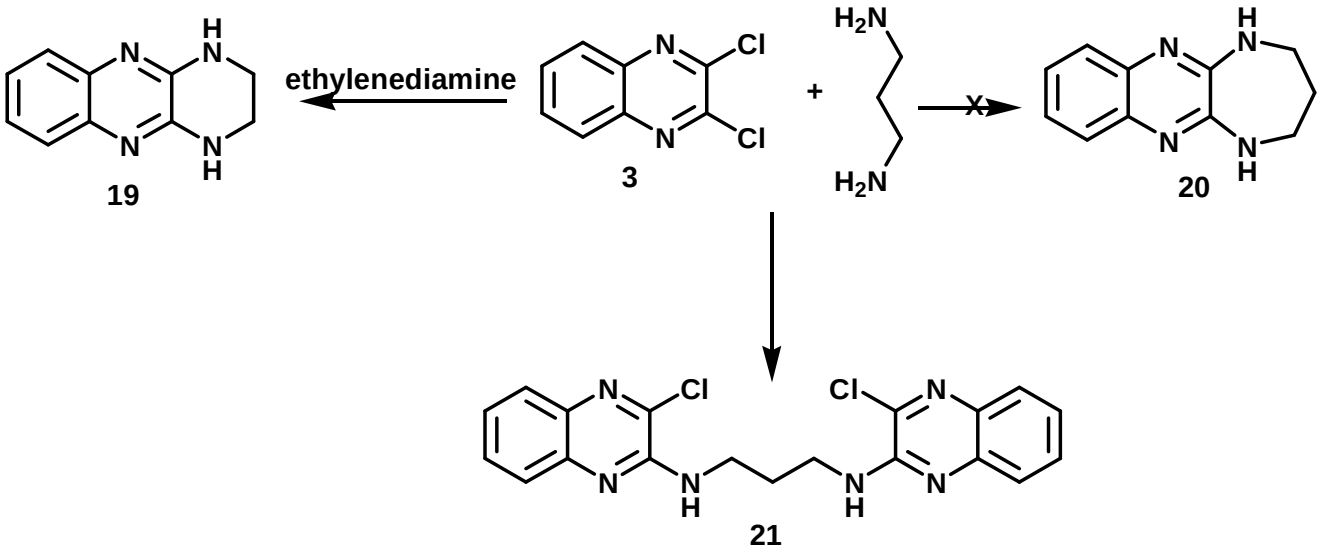


Scheme 5

The reaction product for the condensation of 2,3-dichloroquinoxaline **(3)** and S-methylisothiourea did not have signal related to NH protons in its ^{1}H NMR data, and showed new SCH_3 protons at δ 2.68 ppm. The elemental analyses and mass spectrum for this product are consistent with structure **(18)**, which showed that the imidazole ring did not formed during this condensation reaction. Instead of that, one of the two chloro atoms for compound **(3)** was substituted by SMe and the other chloro atom still present in the product (Scheme 4).

f- Synthesis of New Piperazinoquinoxaline Ring System

Reaction of the 2,3-dichloroquinoxaline **(3)** with excess of ethylenediamine gave 1,2,3,4-tetrahydropyrazino[2,3-b]quinoxaline (**(19)**, Scheme 6), as a new method of synthesis of this ring system. The ^{1}H NMR data of compound **(19)** showed two identical NH protons at δ 7.45 ppm and its IR data gave a broad NH band at 3232.11 cm^{-1}.



Scheme 6

Whileas, the reaction of compound **(3)** with 1,3-diaminopropane, did not gave the 2,3,4,5-tetrahydro-1H-[1,4]diazepino[2,3-b]quinoxaline **(20)**, but the dimeric product **(21)** was produced (Scheme 6). The dimeric structure was deduced from the elemental analyses which indicated the presence of chlorine atom in its structure. The ^{1}H NMR data gave evidence on the increasing of the aromatic protons integration from 4H to 8H between δ 7.29, 7.70 ppm, which accertains that the product has two quinoxaline moieties.

CONCLUSION

A new pyrazino[2,3-b]quinoxaline ring system and new pyrazolyl-quinoxaline derivative were synthesized within two simple steps, starting from 2,3-dihydroxyquinoxaline. Further a new synthetic methods for imidazo[4,5-b]quinoxaline and [1,2,4]triazino[4,3-a]quinoxaline ring systems were established.

EXPERIMENTAL

Silica gel plates (Merck F, 254) and silica gel 60 (Merck, 70–230 mesh) were used for TLC and column chromatography, respectively. Melting points were determined on a Gallenkamp melting point apparatus. The IR spectra were recorded on a Jasco 4100 FTIR spectrophotometer in KBr discs (ν max in cm^{-1}). ^{1}H NMR spectra ($CDCl_3$) and (DMSO-d_6) on a Varian Mercury-VX-300 NMR spectrometer, chemical shifts are expressed in δ-scale downfield from TMS as an internal standard. The mass spectrum was recorded on a Shimadzu GCMS-QP 1000 EX mass spectrometer at 70 eV. Elemental analysis was recorded on Perkin-Elmer 2400 C,H,N Elemental analyzer.

2,3-Dihydroxyquinoxaline (4)

A mixture of *o*-phenylenediamine (10.8 g, 0.1mol), diethyl oxalate (14.7 g, 0.1mol) and glacial acetic acid

(1 ml) in absolute ethanol (30 ml) was refluxed for 2 hours. The precipitate was filtrated under suction to give the crude 2,3-dihydroxyquinoxaline (**(4)**, 10 g). The filtrate was concentrated *in vacue* and refluxed for another one hour. The precipitate was filtered off to give further the crude **(4)** (5.5 g). The crude substance was recrystallized from DMF to gave pure product **(4)** (15 g, 92.5 %yield), M.p.>300°C. (lit. >300 °C). ^{1}H NMR (DMSO): δ 7.07-7.14 {2H, m, H (6 and 7)}, 7.20-7.35, {2H, m, H (5 and 8)} and 12.18 (2H, br. exch., 2OH).

2,3-Dichloroquinoxaline (3)

Triethylamine (15 ml) was added gradually to a mixture of 2,3-dihydroxyquinoxaline (**(4)**, 16.2 g, 0.1 mol) and phosphorus oxychloride (32 ml) in acetonitrile (50 ml). the reaction mixture was vigorously refluxed in heating mantle for 14 hours. After cooling the reaction mixture to room temperature, the white crystals was filtered off to gave of 2,3-dichloroquinoxaline (**(3)**, 15 g). The filtrate was concentrated *in vacue* to the half and left to stand to give additional 3 g of compound **(3)**. Recystalization from methanol gave pure product **(3)** (17 g, 85.5% yield), m.p. 146-150°C. (Lit.145-152 °C). ^{1}H NMR (DMSO): δ 7.07-7.14 {2H, m, H (7 and 8)} and 7.20-7.35 {1H, m, H (9)}.

Syntheses of 3-(2-benzylidenehydrazinyl)-quinoxalin-2-ol (8)

Method a

A mixture of hydrazide **(2)** (1.76 g, 0.01mol) and 2-benzylidenemalononitrile (1.54 g, 0.01mol) in ethanol (20 ml) was refluxed for 12 hours and the solvent was evaporated *in vacue* to give crude product. It was transferred to column chromatography on silica gel for purification (methylene chloride) as eluent to give pure product **(8)** (1.6 g, 60% yield), m. p., 245-247 °C. IR (KBr cm^{-1}): 3336.25 (NH). ^{1}H NMR (CDCl3): δ 7.20-8.20 (9H, m, aromatic), 8.70 (1H, s, CH), 11.30 (H, s, exch., NH) and 12.5 (H, s, exch., NH). Anal. calcd. for $C_{15}H_{12}N_4O$ (264.28): C, 68.17; H, 4.58; N, 21.20 Found: C, 68.34; H, 4.19; N, 21.33

Method b

A solution of hydrazide **(2)** (1.76 g, 0.01mol) and benzaldehyde (1.06 g, 0.01mol) in ethanol (20 ml) was refluxed for 6 hours then was cooled and filtered off. Recystallization from ethanol gave pure product **(8)** (2.4 g, 91% yield), mp.245-247 °C.

Syntheses of [1,2,4]triazolo[4,3-a]quinoxaline Ring System

Method a: [1,2,4]triazolo[4,3-a]quinoxalin-4-ol (5)

Triethyl orthoformate (6 ml) was added to a solution of hydrazide (1.76 g, 0.01 mol) in DMF (20 ml) and the reaction mixture was refluxed for 12 hours then poured onto ice water mixture (40 ml). The precipitate was filtered off, recrystallized from aqueous DMF to give pure product **(5)** (1.4 g, 75% yield), m. p.>300°C. IR (KBr cm^{-1}): 1693.19 (C=N). ^{1}H NMR (400 MHz, DMSO-d_6, T = 60°C); δ 7.24-7.29 {1H, m, H (6)}, 7.39-7.40 {2H, m, H (7 and 8)}, 8.10-8.14 {1H, m, H (9)}, 9.82 (1H, s, C-1) and 12.06 (1H, br., exch., OH). MS (*m/z*, %): 186 (M^+, 100), 187 (M^++1, 17.1), 158 (M^+-28, CO, 78.7), 158 (M^+-28, N_2, 78.7), 130 ($C_8H_6N_2$, 9.5), 105 ($C_6H_5N_2$, 25.5), 104 ($C_6H_4N_2$, 75.7). Anal. calcd for $C_9H_6N_4O$ (186.17): C, 58.06; H, 3.25; N, 30.09. Found: C, 58.32; H, 3.43; N, 30.18.

Method b : 1-phenyl-[1,2,4]triazolo[4,3-a]quinoxalin-4-ol (9)

A mixture of hydrazide **(2)** (1.76 g, 0.01mol) and 2-benzylidenemalononitrile (1.54 g, 0.01mol) in of ethylene glycol (5 ml) was refluxed for 24 hours. The reaction mixture was poured onto ice-water (30 ml) and filtered off to give the triazoloquinoxaline derivative **(9)**. Which was purified by column chromatography using methylene chloride as eluent to give pure product **(9)** (1.3 g, 49 % yield), m.p.>300 °C. IR: 1685.00 (CO, amide). ^{1}H NMR ($CDCl_3$): δ 7.21-7.7 (9H, m, aromatic), 12.60 (1H, s, OH). Anal. calcd. for $C_{15}H_{10}N_4O$ (262.27): C, 68.69; H, 3.84; N, 21.36. Found: C, 68.44; H, 3.99; N, 21.29.

4-Methoxy-1-(methylthio)-[1,2,4]triazolo[4,3-a]quinoxaline (7)

A mixture of hydrazide **(2)** (1.94 g, 0.01 mol) and carbon disulphide (4 ml) in DMF (15 ml) was refluxed over night. The reaction mixture was poured onto ice (30 g), and flittered off to give crude product **(6)** (2.3 g). The latter product **(6)**, was heated with dimethyl sulphate (10 ml) at 120 °C in oil bath for 2 hours. Decant the excess of dimethyl sulphate and the oil was triturated with triethylamine (5 ml) and poured onto

cooled water. The yellow precipitate was collected by filtration and transferred to column chromatography for purification (ethyl alcohol: methylene chloride 10%) to give pure product **(7)** (0.74 g, 60% yield), m.p.170-172 °C. IR: 1708.62 (C=N). ^{1}H NMR (DMSO): δ 2.98 (3H, S, S*CH*$_3$), 4.49 (3H, S, O*CH*$_3$), 7.55-7.60 {2H, m, H(7 and 8)}, 7.60-7.76 {1H, m, H (9)}, 8.34-8.37 {1H, m, H (6)}. MS (*m/z*, %): 247 (M^++1, 0.9), 218 (M^+-28, N_2 7.1), 203 ($C_{10}H_7N_2OS$, 4.5), 187 ($C_{10}H_7N_2S$, 8.9), 168 ($C_9H_4N_4$, 3.6) and 104 ($C_6H_4N_2$, 11.6). Anal. Calcd. for $C_{11}H_{10}N_4OS$ (246.29): C, 53.64; H, 4.09; N, 22.75; S, 13.02. Found: C, 53.54; H, 4.09; N, 22.98; S, 13.39.

Tetrazolo[1,5-a]quinoxalin-4(5H)-one (10)

To a solution of hydrazide **(2)** (1.94 g, 0.01mol) in dilute hydrochloric acid at 0 °C, a solution of sodium nitrite (0.5 g, in 5ml) of water was added with stirring during 10 min and left the temperature raised to room temperature gradually. The precipitate was filtered off to give the crude product. The product was Recrystallized from aqueous DMF to give pure product **(10)** (1.63 g, 87% yield), mp.272-274 °C. IR (KBr cm^{-1}): 1673.91, 1720.19. ^{1}H NMR (DMSO): δ 7.42-7.52 {2H, m, H(7 and 8)}, 7.60-7.65 {1H, m, H (9)}, 8.25-8.28 {1H, m, H (6)}. MS (*m/z*, %): 187 (M^+, 1.6), 170 (M^+-17, OH, 14.3), 142 ($C_8H_4N_3$, 10.2), 129 ($C_8H_5N_2$, 100), 128 ($C_8H_4N_2$, 42.0) Anal. calcd. for $C_8H_5N_5O$ (187.16): C, 51.34; H, 2.69; N, 37.42. Found: C, 51.22; H, 2.35; N, 37.52.

3H-[1,2,4]triazino[4,3-a]quinoxaline-1,5-diol (11)

A mixture of hydrazide **(2)** (1.94 g, 0.01mol), ethyl chloroacetate (1.22 g, 0.01mol) and sodium carbonate (1g, 0.01mol) in DMF (20 ml) was refluxed for 6 hours. The reaction mixture was poured onto ice (50 g) and the precipitate was filtered off to give the crude product. Recystalization from aqueous DMF gave pure product **(11)** (1.6 g, 74 %), m. p.>300°C. IR (KBr cm^{-1}): 3350.00, 3400.00 (NH), 1718.00 and 1689.34 (CO). ^{1}H NMR (400 MHz, DMSO-d_6, T = 60°C); δ 7.13 – 7.17 {1H, m, H (6)}, 7.20-7.24 {2H, m, H(7 and 8)}, 8.03 (1H, s, C-2), 8.96-8.98 {1H, m, H (9)}, 10.55 (1H, br., exch., NH) and 11.75 (2H, br., exch., OH). ^{13}C NMR (DEPT135, T = 60°C): 115.31, 116.48, 123.24 and 126.24. Anal. calcd. for $C_{10}H_8N_4O_2$ (216.2): C, 55.55; H, 3.73; N, 25.91. Found: C, 55.11; H, 3.39; N, 25.72.

Ethyl 3-{2-(3-oxo-3,4-dihydroquinoxalin-2-yl)hydrazono}butanoate (12)

A mixture of hydrazide **(2)** (1.94 g, 0.01mol) and excess of ethyl acetoacetate (10 ml) was heated at 120 °C for two hours, cooled and the precipitate was filtered off to give the crude product. It was purified using column chromatography on silica gel and use the mixture (petroleum ether: ethyl acetate 50%) as an eluent to give pure product **(12)** (2.5 g, 71%yield), m.p.272-274 °C. IR (KBr cm^{-1}): 3440.39, 3316.96 (NH), 1735.62 (CO ester), 1681.62 (CO amide). ^{1}H NMR ($CDCl_3$): δ 1.28-1.35 (3H, t, *CH*$_3$CH$_2$, ester), 2.18 (3H, s, CH_3), 3.56 (2H, s, CH_2), 4.15-4.23 (2H, q, CH$_3$*CH*$_2$, ester), 7.26-7.28 {3H, m, H(5, 6 and 7)}, 7.75-7.78 {1H, m, H(8)}, 9.16 (1H, s, exch., NH), 11.32 (1H, s, exch., OH). MS (*m/z*, %): 289 (M^+, 18.5), 290 (M^++1, 3.5), 243 (M^+-43, OEt, 13.9), 215 (M^+-73, CO_2Et, 3.1), 201 (M^+-87, CH_2CO_2Et, 100), 117 ($C_7H_5N_2$, 8.8), 105 ($C_6H_5N_2$, 8.8). Anal. Calcd. for $C_{14}H_{16}N_4O_3$ (288.30): C, 58.32; H, 5.59; N, 19.43. Found: C, 58.52; H, 5.50; N, 19.22.

3-(5-Hydroxy-3-methyl-1H-pyrazol-1-yl)quinoxalin-2-ol (13)

Ethyl 3-{2-(3-oxo-3,4-dihydroquinoxalin-2-yl)hydrazono}butanoate **(12)** (1.44 g, 0.005 mol) was added to polyphosphuric acid, prepared from phosphorous pentaoxide (5 g) and phosphoric acid (3.3 g) at 80°C. The reaction mixture was heated for 1 hour then poured onto ice-water (100 ml). The precipitate was filtered off and recrystallized from methanol to give pure product **(13)** (0.74 g, 61%yield), m. p. > 300. IR: 3445.23 (OH) and 1682.22 (CO, amide). ^{1}H NMR (DMSO), 2.37 (3H, s, CH_3), 3.28 (2H, s, CH_2), 7.12 – 7.18 {2H, m, H(6 and 7)}, 7.61-7.65 {2H, m, H(5 and 8)} and 11.78 (1H, br., exch., OH). Anal. calcd for $C_{12}H_{10}N_4O_2$ (242.23): C, 59.50; H, 4.16; N, 23.13. Found: C, 59.33; H, 4.23; N, 23.50

Dimethyl 2-{2-(3-oxo-3,4-dihydroquinoxalin-2-yl)hydrazinyl}but-2-enedioate (14)

To a solution of hydrazide **(2)** (1.76 g, 0.01mol) in DMF (10 ml), dimethyl acetylenedicarboxylate (1.42 g, 0.01mol) was added dropwise, with stirring

at room temperature. The reaction mixture was kept at this temperature for 4 hours, the was poured onto cooled water (50 ml). The solid product was filtered off and purified by chromatography using mixture (ethyl alcohol: methylene chloride 1%) as eluent to give pure product **(14)** (3 g, 95% yield), m. p.210-212 °C. IR (KBr cm^{-1}): 3455.81, 3251.4 (NH), 1739.48 (CO ester), 1700.91 (CO ester), 1670.00 (CO amide). ^{1}H NMR ($CDCl_3$): δ 3.71 (3H, s, CH_3, ester), 3.77 (2H, s, CH_2) 3.93 (3H, s, CH_3, ester), 7.28-7.38 {3H, m, H(5, 6 and 7)}, 7.80-7.84 {1H, m, H(8)}, 11.60 (1H, s, exch., NH), 13.30 (1H, s, exch., OH). Anal. calcd for $C_{14}H_{14}N_4O_5$ (318.28): C, 52.83; H, 4.43; N, 17.60. Found: C, 52.65; H, 4.78; N, 17.23.

1-H-Imidazo[4,5-b]quinoxalin-2-amine (16)

A mixture of 2,3-dichloroquinoxaline (4 g, 0.02 mol), guanidine nitrate (2.5 g, 0.02 mol), and of sodium carbonate (3 g) in DMF (30 ml) was refluxed for 12 hour then was poured onto ice-water mixture (50 ml). Extraction with chloroform, washing with water, drying over sodium sulphate anhydrous and evaporation *in vacue* to give product. The crude material was recrystallized from benzene and drops of methanol to give pure product **(16)** (4.6 g, 62% yield), m.p.207-208°C. IR: 3463.53, 3328.35 (NH_2) and 3151.11 (NH). ^{1}H NMR ($CDCl_3$): 3.42 (2H, s, exch., NH_2), 7.12 – 7.18 {2H, m, H(6 and 7)}, 7.31-735 {2H, m, H(5 and 8)} and 7.45 (1H, s, exch., NH). MS (*m/z*, %): 185 (M^+, 39.6), 186 (M^++1, 100), 184 (M^+-H, 3.6), 169 (M^+-16, NH_2, 32.9), 143 ($C_8H_5N_3$, 39.6), 116 ($C_7H_4N_2$, 28.1) and 104 ($C_6H_4N_2$, 2.5). Anal. calcd. for $C_9H_7N_5$ (185.19): C, 58.37; H, 3.81; N, 37.82. Found C, 58.11; H, 3.64; N, 37.59.

N-Phenyl-1H-imidazo[4,5-b]quinoxalin-2-amine (17)

2,3-Dichloroquinoxaline (4 g, 0.02 mol), phenyl guanidine sulphate (3.68 g, 0.01 mol), and sodium carbonate (3 g) in DMF (30 ml) were refluxed for 12 hour. After the reaction was completed, it was poured onto cooled water and crude product was filtered off. It was transferred to column chromatography for purification using (ethanol: methylene chloride 10%) to give pure product **(17)** (3 g, 57% yield), m. p. 275-276°C. IR: 3459.67 (NH, aromatic) and 3336.25 (NH, imidazole). ^{1}H NMR (DMSO): 3.87 (1H, br. exch., *NH*Ph) and 7.44–7.92 (10H, m, NH and aromatic protons). MS (*m/z*, %): 261 (M^+, 61.6), 262 (M^++1, 11.4), 184 (M^+-Ph, 5.2), 169 (M^+-92, NHPh, 2.3), 143 ($C_8H_5N_3$, 9), 116 ($C_7H_4N_2$, 8) and 104 ($C_6H_4N_2$, 8.2). Anal. calcd. for $C_{15}H_{11}N_5$ (261.28): C, 68.95; H, 4.24; N, 26.80. Found: C, 68.88; H, 4.34; N, 26.71.

2-Chloro-3-(Methylthio)quinoxaline (18)

The 2,3-dichloroquinoxaline (4 g, 0.02 mol), S-methyisolthiourea sulphate (2.78 g, 0.01 mol), and sodium carbonate (3 g) in DMF (30 ml) were refluxed for 6 hour and was poured onto ice (50 g). The precipitate was filtered off to obtain crude product, which was transferred to column chromatography for purification using (ethyl acetate: petroleum ether 8%). Recystallization from methanol to give pure imidazoquinoxaline **(18)** (2.46 g, 57 % yield), m.p.91-93 °C. IR: 2923.56 and 1523.49. ^{1}H NMR ($CDCl_3$): 3.68 (3H, s, SMe), 7.59-7.74 {2H, m, H(6 and 7)} and 7.90-7.98 {2H, m, H(5 and 8)}. MS (*m/z*, %): 212 (M^+ +2, 37.8), 174 ($C_9H_6N_2S$, 37.8), 160 ($C_8H_4N_2S$, 13.5) and 104 ($C_6H_4N_2$, 2.7). Anal. calcd. for $C_{10}H_8N_4S$ (216.26): C, 55.54; H, 3.73; N, 25.91; S, 14.83. Found: C, 55.66; H, 3.32; N, 25.78; S, 14.90.

1,2,3,4-Tetrahydropyrazino[2,3-b]quinoxaline (19)

Ethylenediamine (2 ml) was added to the solid 2,3-dichloroquinoxaline (2 g, 0.01 mol) at room temperature and left at this temperature for 15 min. The mixture was dissolved in methanol (10 ml), poured onto ice-water (30 ml) and the separated solid material was filtered off to obtain crude product. It was transferred to column chromatography on silica gel for purification (ethanol: dichloromethane 2%) and recrystallized from benzene-methanol mixture to give pure product **(19)** (1.45 g, 78 % yield), m.p. 287-289 °C. IR: 3131.83 (NH). ^{1}H NMR (DMSO): 3.42 (4H, s, CH_2CH_2), 7.11-7.18 {2H, m, H(6 and 7)} and 7.30-7.35 {2H, m, H(5 and 8)} and 7.45 (2H, br., exch., NH). MS (*m/z*, %): Anal. calcd. for $C_{10}H_{10}N_4$ (186.21): C, 64.50; H, 5.41; N, 30.09.Found: C, 64.23; H, 5.78; N, 30.44.

Full Paper

N_1,N_3-Bis(3-chloroquinoxalin-2-yl)propane-1,3-diamine.(21)

The same procedure as was described for compound **(19)**, with yield 90 %, m.p.160-161 °C. IR: 3397.96 (NH). ^{1}H NMR (DMSO): δ 2.00 (2H, s, $CH_2CH_2CH_2$), 7.59 (4H, s, $CH_2CH_2CH_2$), 7.29-7.70 (10H, m, aromatic and *2*NH). MS (*m/z*, %): 228 (M^+-71, 2Cl, 7.8), 227 ($C_{19}H_{16}N_6$, 7.8), 157 ($C_9H_7N_3$, 28.6), 104 ($C_6H_4N_2$, 11.7). Anal. calcd. for $C_{19}H_{16}C_{l2}N_6$ (399.28): C, 57.15; H, 4.04; Cl, 17.76; N, 21.05. Found: C, 57.43; H, 4.23; Cl, 17.87; N, 21.11.

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