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SYNTHESIS AND CHARACTERIZATION OF NOVEL QUINOXALINE DERIVATIVES

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ABSTRACT

Quinoxaline is the subject of considerable interest from both academic and industrial perceptive. Among the various classes of the nitrogen containing heterocyclic compounds quinoxaline are the important component of several pharmacologically active compounds. The starting compound quinoxaline,2,3-diol was prepared from o-phenylenediamine and diethyl oxalate. The quinoxaline 2,3-diol upon refluxing with POCl3 gives 2,3-dichloroquinoxaline, 2-chloro-3-hydrazinoquinoxaline was synthesized by reaction of 2,3-dichloroquinoxaline and hydrazine hydrate in methanolic medium. The Schiff's bases of 2-chloro-3-hydrazino quinoxaline were obtained by refluxing the furfuraldehyde and Thiophene-2-carbaldehyde with 2-chloro-3-hydrazinoquinoxaline in acetic acid medium. The progress of reaction was monitored by TLC. The synthesized compounds were characterized by their physical and IR and NMR spectral data.

***Keyword**: Quinoxaline, TLC, 2,3-dichloroquinoxaline, IR and NMR spectra, Pharmacologically Active Compounds, Schiff's bases.*

1. INTRODUCTION

Quinoxaline is the subject of considerable interest from both academic and industrial perceptive. Among the various classes of the nitrogen containing heterocyclic compounds quinoxaline are the important component of several pharmacologically active compounds. Although rarely described in nature synthetic quinoxaline ring is a part of number of antibiotics which are known to inhibit the growth of gram positive bacteria and are also active against various transplantable tumours. Studies on the synthesis of new quinoxalines derivatives have been of considerable importance because of their interesting chemical as well as biological properties. Quinoxaline derivatives are widely distributed in nature and many of them, such as the antibiotics, levomycin and actinomycin possess very useful biological activity. In addition, a large number of synthetic quinoxalines have also shown anti-bacterial, fungicidal, insecticidal, antiinflammory, tranquilizing and antidepressant properties. Quinoxaline is commonly called as 1,4diazonaphthalene or benzopyrine. Quinoxaline and its derivatives mostly are synthetic origin. Some quinoxaline derivatives are known to possess anti-bacterial activities. Piperazines is an organic compound that consists of six membered ring containing two opposing nitrogen's atoms. Piperazines exists as small alkaline deliquescent crystals with a saline taste. The Piperazines are broad class of chemical compounds, many with important pharmacological properties, which contain a core Piperazines functional group[1-15].

2. MATERIALS AND METHODS

Melting points were recorded with Thomas Hoover melting point apparatus and are uncorrected. ^{1}H-NMR (300 MHz) and ^{13}C NMR (75 MHz) NMR spectra were recorded in $CDCl_3$ as a solvent. Chemical shifts were reported in delta (ppm) units with reference to (tetra methyl silane) TMS as an internal standard. Column chromatography was carried out using silica gel (100-200 Mesh). Dimethyl formamide, Ethanol, Methanol, Triethyl amine and Pyridine were purified and dried before use.

2.1 Procedure for Preparation of 2,3-dihydroxy quinoxaline [a]

In to a clean dry round bottom flask introduced o-phenylenediamine (0.1mol) and diethyl oxalate (0.1mol) and contents were refluxed for 2h. Then cooled the reaction mixture and separated solid was collected by filtration, washed with 25ml ether and dried. The obtained 2,3-dihydroxyquinoxaline [a] was re-crystallized from DMF, the yield was 90% and the melting point was 360ºC.

Spectral Analysis

IR, (KBr disc):1620-1680 (C=C) cm^{-1}, 3450 (O-H)cm^{-1}

^{1}H NMR, (300 MHz, $CDCl_3$):11.8-12.09(s,2H of NH),7.0-7.2(m,4H of Ar-H).

2.2 Procedure for preparation of 2,3-dichloro quinoxaline [b]

In the clean dry round bottom flask introduced 2,3-dihydroxy quinoxaline(0.01mol), $POCl_3$ (0.04mol) and DMF (1ml). The content was refluxed for 90 min and resulting solution was cooled at room temperature and then the solution was poured into crushed ice with constant stirring with glass rod. The solid thus separated was collected by filtration, washed with 25 ml of water and dried.The obtained 2,3-dichloroquinoxaline was re-crystallized from solution of chloroform and n-hexane,the yield was 85% and melting point was 150ºC.

Spectral Analysis

IR, (KBr disc):3042,3000 (Ar-H Stretching) cm^{-1}, 850(=C-Cl)cm^{-1}

^{1}H NMR, (300 MHz, $CDCl_3$):7.07-8.1(m,4H of Ar-H).

2.3 Procedure for Preparation of 3-chloro-2-hydrazino quinoxaline [c]

In a clean dry round bottom flask introduced 2,3-dichloro quinoxaline (0.01mol), hydrazine hydrate (0.01mol) and methanol (25ml).The contents in the flasks were refluxed for 30 min and then cooled. The separated solid was collected by filtration, washed with 25ml water and dried. The obtained 3-chloro-2-hydrazino quinoxaline was re-crystallized from methanol, the yield was 75% and melting point was 180ºC.

Spectral Analysis

IR, (KBr disc):3385(NH_2 stretching)cm^{-1},3266-3236(NH stretching) cm^{-1},

3051(Ar-H stretching)cm^{-1}.

^{1}H NMR, (300 MHz, $CDCl_3$):7.2-7.8(m,4H of Ar-H),6.7-6.8(s,1H of N-H),

4.1-4.2(s,2H of NH_2).

2.4 Procedure of Preparation of Quinoxaline Schiff's bases [d]

In to a clean dry round bottom flasks introduced the 3-chloro-2-hydrazino quinoxaline (0.01mol), furfuraldehyde (0.01mol) and ethanol (25ml) and glacial acetic acid (1ml) and reaction mixture was refluxed for 3h. After refluxing cool the reaction mixture at room temperature,the separated solid was collected by filtration and washed with water and dried.The obtained quinoxaline Schiff's bases of [d] was re-crystallized by using ethanol (90%) and the yield was 55% and melting point was 270ºC.

Spectral Analysis

IR, (KBr disc):3068(NH stretching)cm^{-1},2931-2837(Ar-H stretching)cm^{-1},

1620(CH=N,stretching) cm^{-1}

^{1}H NMR, (300 MHz, $CDCl_3$): 6.3-7.8 (m,7H of Ar-H), 12.20(s,1H of NH-N=C),

8.70-8.8(s,1H of CH=N-).

2.5 Procedure of Preparation of Quinoxaline Schiff's bases [e]

In to a clean dry round bottom flasks introduced the 3-chloro-2-hydrazino quinoxaline (0.01mol), thiophene-2-carbaldehyde (0.1mol), ethanol (25ml) and glacial acetic acid (1ml) and reaction mixture was refluxed for 3h. After refluxing cool the reaction mixture at room temperature, the separated solid was collected by filtration and washed with water and dried.The obtained quinoxaline Schiff's bases of [e] was re-crystallized by using ethanol (90%) and the yield was 78% and melting point was 138ºC.

Spectral Analysis

IR, (KBr disc):3068(NH stretching) cm^{-1},2931-2837(Ar-H stretching) cm^{-1},

1610(CH=N,stretching) cm^{-1}

^{1}H NMR, (300 MHz, $CDCl_3$): 6.3-7.3 (m,7H of Ar-H), 12.20(s,1H of NH-N=C),

8.65-8.8(s,1H of CH=N-).

2.6 Procedure for Preparation of Piperazinoquinoxaline [f]

In a clean dry round bottom flasks introduced the quinoxaline Schiff's bases [d] (0.01mol), Piperazine (0.01mol) in 25ml ethanol and 5 ml TEA. The reaction mixture was refluxed for 6h, cooled and separated solid was collected by filtration and dried. The obtained product was re-crystallized by using methanol, the yield was 55% and melting point was 243ºC.

Spectral Analysis

IR, (KBr disc):3273(N-H stretching)cm^{-1},2847(Ar-H stretching)cm^{-1},

1620(CH=N,stretching) cm^{-1},2723(CH_2 stretching) cm^{-1}

^{1}H NMR, (300 MHz, $CDCl_3$): 10.9 (s,1H of N-H), 8.5-8.7(s,1H of CH=N),

7.0-8.2(M,7H of Ar-H),4.3-4.4(s,1Hof NH),

3.8-4.0(s,4H of Piperazine), 3.1-3.2(s,1H of Piperazine).

2.7 Procedure for Preparation of Piperazinoquinoxaline [g]

In a clean dry round bottom flasks introduced the quinoxaline Schiff's bases [e] (0.01mol), Piperazine (0.01mol) in 25ml ethanol and 5 ml TEA. The reaction mixture was refluxed for 6h, cooled and separated solid was collected by filtration and dried. The obtained product was re-crystallized by using methanol, the yield was 63% and melting point was 203ºC.

Spectral Analysis

IR, (KBr disc):3280(N-H stretching) cm^{-1},2909(Ar-H stretching) cm^{-1},

1610(CH=N,stretching) cm^{-1},2723(CH_2 stretching) cm^{-1}

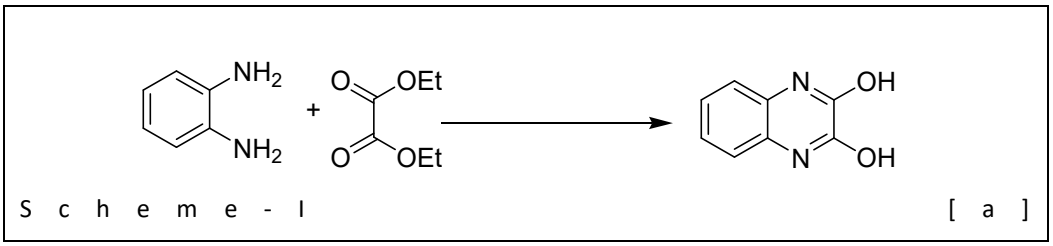
^{1}H NMR, (300 MHz, $CDCl_3$): 10.3 (s,1H of N-H), 8.3-8.5(s,1H of CH=N),

6.8-7.9(M,7H of Ar-H),4.2-4.3(s,1Hof NH),

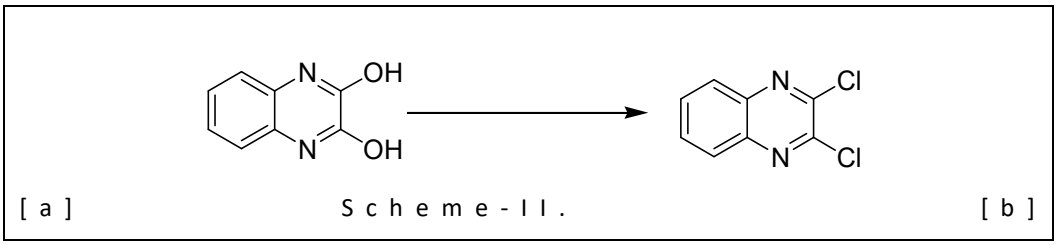
3.7-4.0(s,4H of Piperazine), 3.1-3.2(s,1H of Piperazine).

3. RESULTS AND DISCUSSION

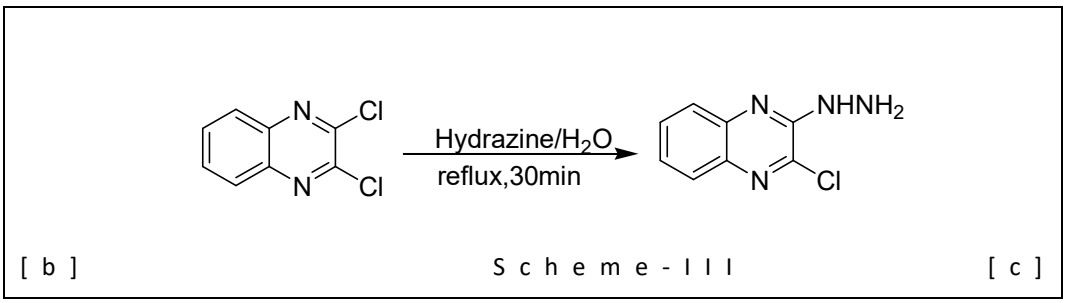
The starting compound quinoxaline,2,3-diol [a] was prepared from o-phenylenediaamine and diethyl oxalate upon refluxing for 1hours in single step. The quinoxaline, 2,3-diol [a] was refluxed for 90 min with POCl3, to furnish 2,3-dichloroquinoxaline[b], further the 2-chloro-3-hydrazinoquinoxaline[c] was synthesized by reaction of 2,3-dichloroquinoxaline[b] and hydrazine hydrate in methanolic medium upon refluxing for 60 min. The Schiff's bases [d] and [e] of 2-chloro-3-hydrazino quinoxaline[c] were obtained by refluxing the furfuraldehyde and Thiophene-2-carbaldehyde with 2-chloro-3-hydrazinoquinoxaline[c]in acetic acid medium for 3 hours respectively. The obtained quinoxalines Schiff's bases were further converted into the target compound [f] and [g] by reacting the Schiff' bases with Piperazine in presence of TEA in ethanolic medium. The progress of reaction was monitored by TLC. The synthesized compounds were characterized by their physical and spectral data.



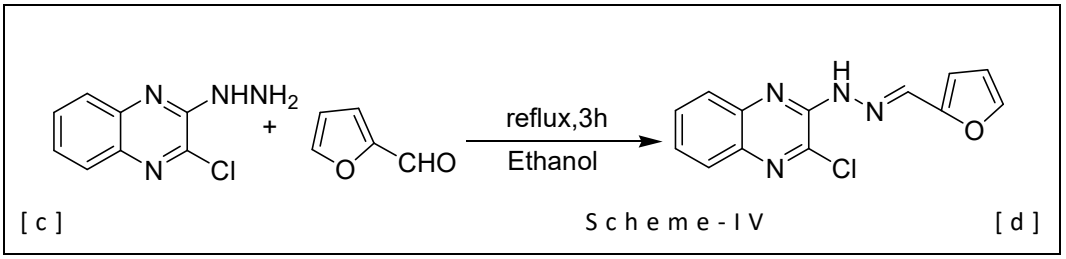
S c h e m e - I [a]



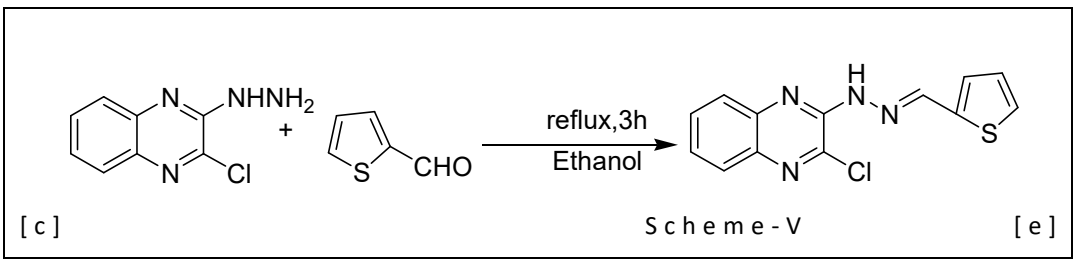
[a] S c h e m e - I I . [b]



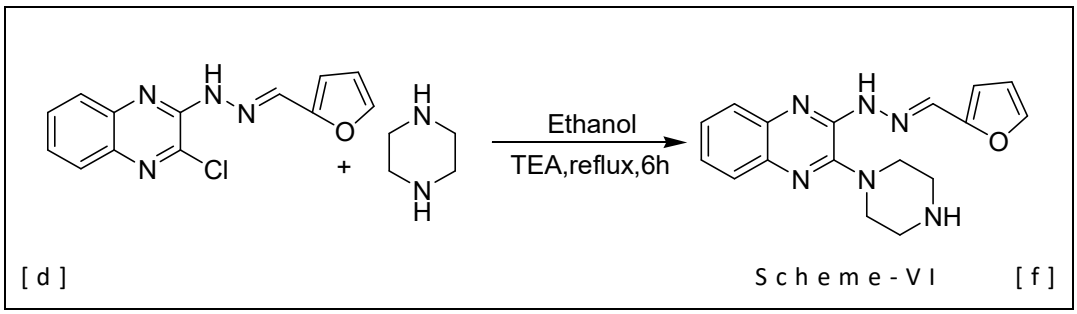
[b] S c h e m e - I I I [c]

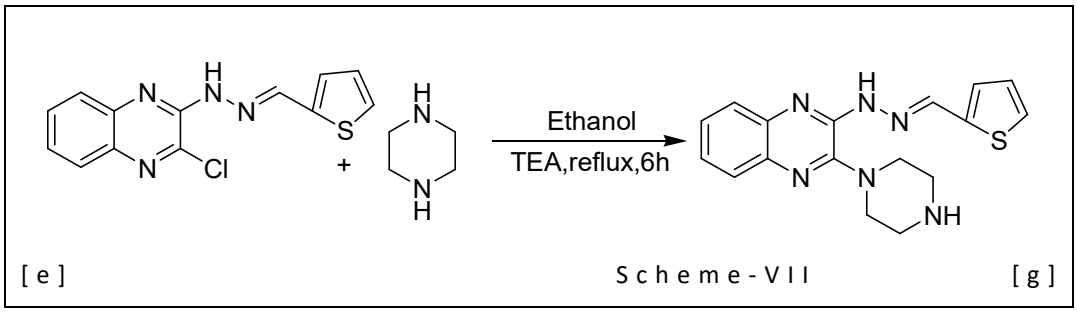


[c] S c h e m e - I V [d]



[c] S c h e m e - V [e]





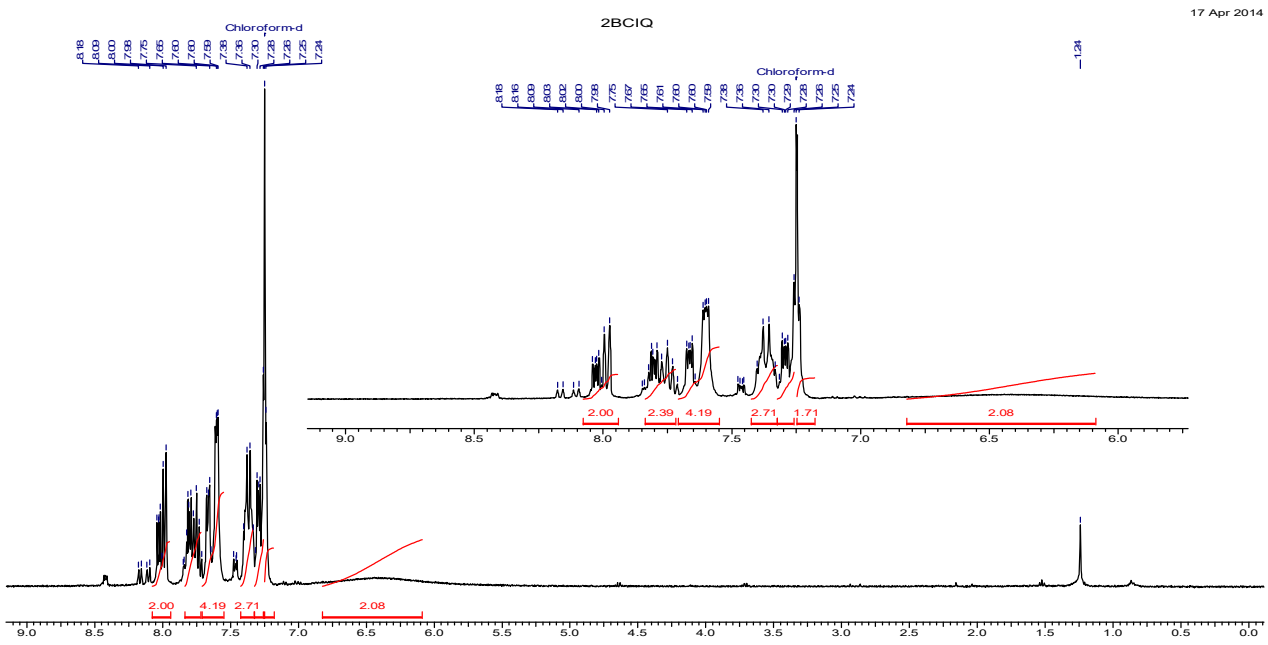


Fig. 1: Quinoxaline Schiff's bases [d]

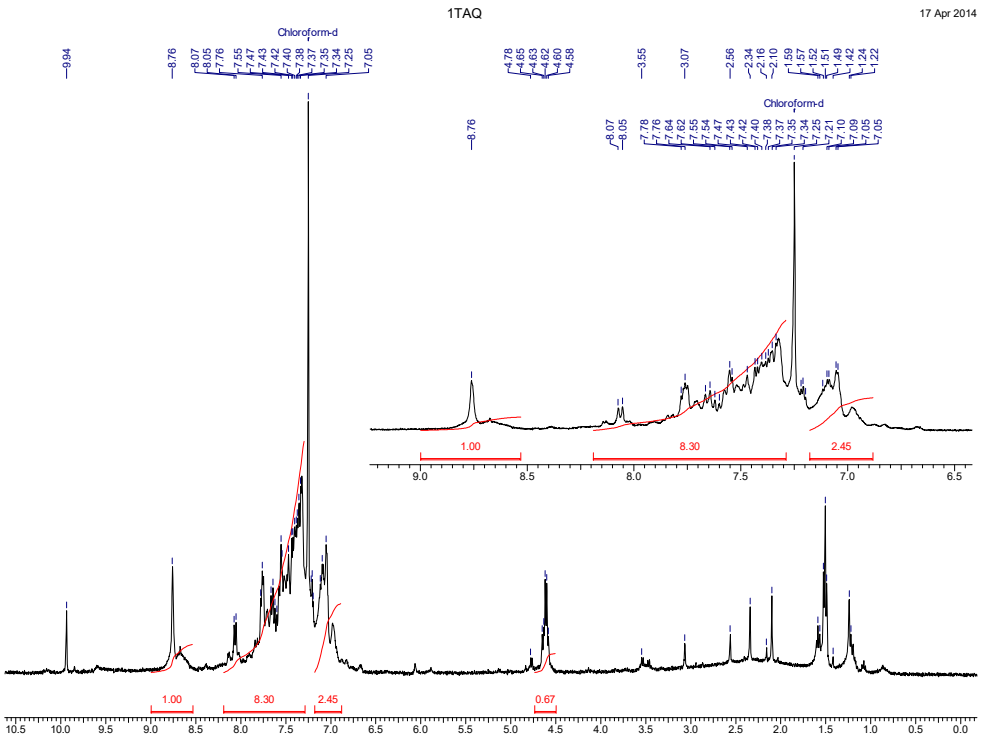


Fig.2: Quinoxaline Schiff's bases [e]

4. CONCLUSION

In conclusion, we have prepared some biologically and pharmacologically active quinoxaline derivatives like quinoxaline,2,3-diol, 2,3-dichloroquinoxaline, 2-chloro-3-hydrazinoquinoxaline, Schiff's bases of 2-chloro-3-hydrazino quinoxaline. The advantages of this method are extremely mild reaction conditions, short reaction times, high yields simple and time conserving techniques.

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