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Synthesis and anticonvulsant activity of Schiff's bases of 3-{[2-({(*E*)-[(substituted) phenyl] methylidene} amino) ethyl] amino} quinoxalin-2(1H)-one

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Abstract

In an effort to develop potent anticonvulsant agents, we have synthesized some novel schiff's bases of 3-{[2-({(*E*)-[substituted) phenyl] methylidene} amino) ethyl] amino} quinoxalin-2(1H)-one and evaluated for *in vivo* anticonvulsant activity. All the compounds were characterized by IR, ^{1}H NMR data. This activity was carried out on pentylenetetrazole-induced seizure model. Compounds (IIIb) and (IIIc) showed maximum time for straub tail and clonic convulsions. That means, they possess good activity compared with the standard. Animals treated with compounds (IIIb) and (IIIe) were recovered from this activity.

Introduction

Quinoxaline (benzopyrazines), derivatives are an important class of nitrogen-containing heterocyclic compounds containing a ring complex made up of a benzene ring and a pyrazine ring; they are isomeric with the cinnolenes, phthalazines and quinazolines (Carta, 2002) They are part of various antibiotics such as echinomycin, levomycin, and actinoleutin which are known to inhibit the growth of Gram-positive bacteria and also active against various transplantable tumors. They have been reported for their applications in dyes and have also been used as building blocks for the synthesis of organic semiconductors. Quinoxalines are very important compounds due to their wide spectrum of biological activities behaving as anti-cancer (Moarbess and Masquefa, 2008) antibacterial (Refaat and Moneer, 2004) anti-inflammatory (Hashem and Gouda, 2010), anti-histaminic agent (Sridevi and Balaji, 2010) anti-trypanosomal activity (Urquiola, 2006) anti-herps (Harmenberg and Wahren, 1988) antiplasmodial activity (Zarranz et al., 2006) Ca uptake/release inhibitor (Xia et al., 2005) inhibit vascular smooth muscle cell proliferation (Chung, 2005), antimalarial (Vicente et al., 2008). These are useful as intermediates for many target molecules in organic synthesis and also as synthons.

Quinoxalines are in general, comparatively easy to prepare, and numerous derivatives have been designed and prepared for potential use as biologically active materials. The classical synthesis of quinoxalines involves the condensation of an aromatic 1,2-diamine with a 1,2-dicarbonyl in refluxing ethanol or acetic acid for 2–12 hours. The reaction is facile and is the most widely used synthetic method for both quinoxaline itself and its derivatives. A number of synthetic strategies have been developed for the preparation of substituted quinoxalines.

2, 3-Disubstituted quinoxalines have also been prepared by Suzuki–Miyaura coupling and also oxidative coupling of epoxides with ene-1,2-diamines (Antoniottia, 2002) Alkynes were oxidized efficiently using the

catalytic amount of $PdCl_2$ and by using gallium as catalyst (Cai et al., 2008) Quinoxaline derivatives also synthesized from amino acids (Faham et al., 2002). Solid -phase synthesis of quinoxaline derivatives using 6-amino-2,3-dichloroquinoxaline loaded on AMEBA (Jeon and Kim, 2005). Although great success has been obtained, many of these processes suffer from drawbacks such as drastic reaction conditions, low product yields, tedious work-up procedures, using toxic metal salts as catalysts, long reaction time and relatively expensive reagents they have limitations in some of the following areas: Low yield, long reaction time, difficult product isolation procedure and use of toxic metal catalysts as well as hazardous solvents. In this paper, we describe a conventional as well as microwave-assisted extremely rapid Schiff's bases synthesis of quinoxalines. The procedure is simple, convenient and does not require any aqueous work-up, thereby avoids the generation of waste and may contribute to the area of green chemistry.

Materials and Methods

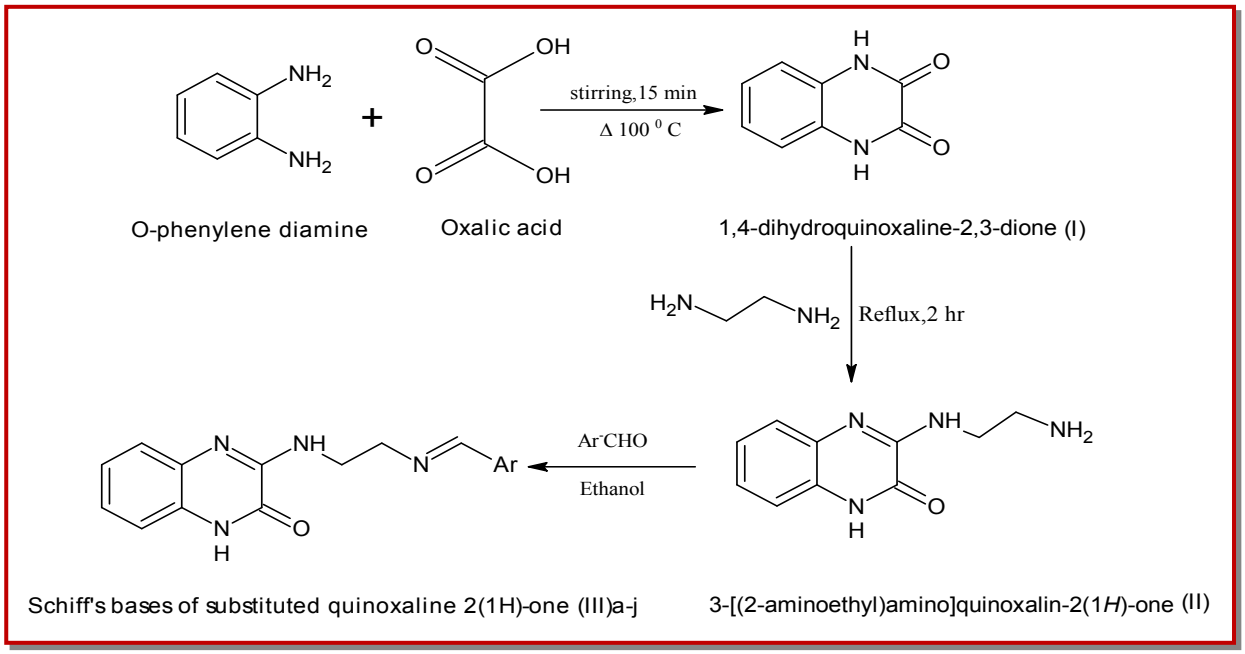
All chemicals and solvents were procured from the commercial sources, and were used without any additional purification. The chemicals were purchased from Sigma-Aldrich, Fine Chemicals and Merck Pvt. Ltd. (India), Laboratory (Pune), Research Lab (Poona), Loba chemicals Pvt. Ltd. (Mumbai) etc. The melting points of the compounds were determined on a VMP-I electric melting point apparatus and the values were uncorrected. Thin layer chromatography was used to assess the course of reactions and the purity of the intermediates and final compounds, giving a single spot on TLC plate (silica gel G), using various solvent systems. Visualization of the compounds on chromatographic plates was done by exposure to iodine vapors. The ^1H NMR spectra were recorded using TMS as the internal standard and with $CDCl_3$ as the solvents; the chemical shifts are reported in ppm. Signal multiplicities are represented by: s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet). Infrared (IR) spectra of the intermediates and final compounds were recorded on Jasco FTIR-410 spectrophotometer using KBr pellet method. The frequencies are expressed in cm^{-1}.

Synthesis of 1,4-dihydroquinoxaline-2,3-dione (I): A solution of oxalic acid dihydrate (0.238 mole, 30 g) in H_2O (100 mL) was heated to 100°C and concentrated HCl 4.5 mL was added, followed by O-phenylendiamine (0.204 mole, 22 g) with stirring, temperature was maintained at 100°C for 20 min. the mixture cooled by addition of ice. The precipitate was formed and washed with water. The product was recrystallized from ethanol.

Synthesis of 3-[(2-aminoethyl) amino] quinoxalin-2(1H)-one (II): A mixture of the quinoxalindione (I) (0.062 mole, 10.04 g), ethylene diamine (1 mole, 50 mL), and water (50 mL) was heated under reflux for 2 hours, then cooled to room temperature, the precipitate was filtered, washed with water and crystallized from 2-butanol.

Synthesis of 3-[(2-{[(E)-(substituted phenyl) methyl-idene] amino} ethyl) amino] quinoxalin-2(1H)-one (Schiff's bases) (III a-j)

Conventional synthesis: In this method, compound 3-[(2 aminoethyl) amino] quinoxalin-2(1*H*)-one (II) and the



Scheme 1

Table I

List of aromatic aldehyde used

Compound No.	Aromatic aldehyde
IIIa	$C_6H_5.CHO$
IIIb	3 NO_2-C_6H_4.CHO
IIIc	2 NO_2-C_6H_4.CHO
IIId	2 OH-C_6H_4 CHO
IIIe	CH_3O-C_6H_4 CHO
IIIf	$C_6H_5.CH_2CH$=CH CHO
IIIg	3 Cl - C_6H_4CHO
IIIh	$(CH_3)_2N$-C_6H_4CHO
IIIi	3, 4 Cl- C_6H_3 CHO
IIIj	1 OH $C_{12}H_8$CHO

corresponding aromatic aldehyde (0.01 mole of each) in ethanol as solvent (20 mL) was refluxed for 5 hours. Upon cooling the precipitate was obtained, filtered, dried and crystallized from ethanol.

Microwave synthesis: In this method, compound 3-[(2 amino ethyl)amino]quinoxalin-2(1*H*)-one (II) and the corresponding aromatic aldehyde (0.01 mole of each) in ethanol as solvent (20 mL) was added to it and irradiated with microwaves at 50%, 350 W. After specific time; depending on the derivative, the precipitate obtained was recrystallized using ethanol. List of aromatic aldehyde used (Table I) and data for microwave-assisted synthesis by Scheme reported in Table II.

1,4-dihydroquinoxaline-2, 3-dione (I): m.p. = 300°C, molecular formula ($C_8H_6N_2O_2$); IR: 3404, 3176, 3113, 1682, 1618, 1522, 1499, 1426, 1383, 755, 744; 1H-NMR ($CDCl_3$), δ ppm 8.003(s, 2H, NH), 6.978(t, 2H, CH), 6.715 (d.2H, CH).

3-[(2-aminoethyl) amino] quinoxalin-2(1H)-one (II): m.p. = 262°C, molecular formula ($C_{10}H_{12}N_4O$). IR: 3484, 3374, 3098, 2968, 2928, 1608, 1513, 1494, 1435, 820, 746; ^{1}HNMR($CDCl_3$):,δppm7.711(d,2H,CH),7.590 (t,2H,ArH),2.268(q,2H,CH_2),2.747(t,2H,CH_2),8.131 (s,2H,NHCO),3.631(s,1H,NH),5.929(s,2H,NH_2).

(3-[(2-{[(E)-phenylmethylidene] amino} ethyl) amino] quinoxalin-2(1H)-one (IIIa): m.p = 222°C, molecular formula ($C_{17}H_{16}$ N_4O). IR: 3429, 3037, 2924, 1655, 1617, 1570, 1458, 1418, 1384, 1346, 839, 751; ^{1}H-NMR ($CDCl_3$):, δ ppm: 7.962 (t, 2H, Ar-H), 7.737 (d, 2H, Ar-H), δ 9.953 (s, 1H, CH=N), δ 3.759 (s, 1H, NH), 8.622(s,1H,NHCO), 2.282 (q, 2H, CH_2), 2.523 (t, 2H, CH_2), 6.155-7.179 (m, 5H, Ar-H).

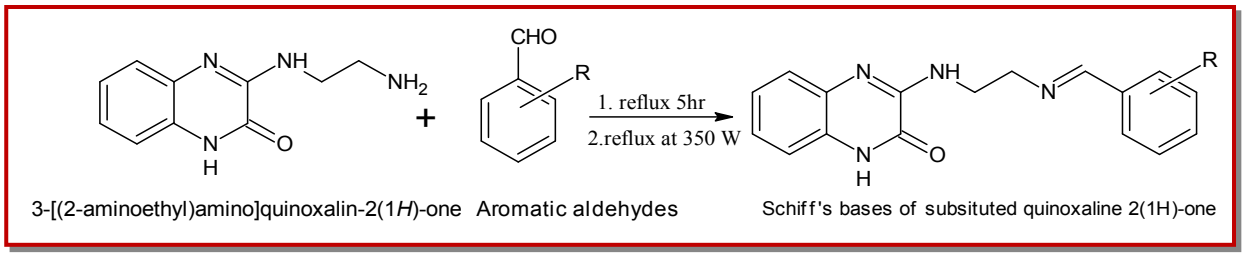
3-[(2-{[(E)-(3-nitrophenyl) methylidene] amino} ethyl) amino] quinoxalin-2(1H)-one (IIIb): m.p. = 247°C, molecular formula ($C_{17}H_{15}$ N_5O_3); IR: 3403, 3048, 3083, 2984, 1679, 1615, 1563, 1312, 1471, 1426, 1384, 807, 752; ^{1}H-NMR ($CDCl_3$):, δ ppm 7.764 (t, 2H, Ar-H), 6.690(d, 2H, Ar-H), δ 9.977 (s, 1H, CH=N), δ 3.890 (s, 1H, NH), 8.564(s,1H,NHCO),2.548 (q, 2H, CH_2), 3.036 (t, 2H, CH_2), 8.397 (S,1H,Ar-H), 7.89-8.101 (d,2H,Ar-H).7.892 (t,1H, Ar-H).

3-[(2-{[(E)-(2-nitrophenyl) methylidene] amino} ethyl) amino] quinoxalin-2(1H)-one (IIIc): m.p. = 232°C C, molecular formula ($C_{17}H_{15}$ N_5O_3); IR: 3434, 3011, 2899, 1675, 1567, 1506, 1384, 1430, 1470, 1356, 1301, 756, 742; ^{1}H-NMR ($CDCl_3$):, δ ppm; 7.361 (t, 2H, Ar-H), 7.290(d, 2H, Ar-H), δ 9.922 (s, 1H, CH=N), δ 3.774 (s, 1H, NH), 8.426(s,1H,NHCO), 2.348 (q, 2H, CH_2), 2.136 (t, 2H, CH_2), 7.654-8.197 (d, 5H, Ar-H).

3-[(2-{[(E)-(2-hydroxyphenyl) methylidene] amino} ethyl) amino] quinoxalin-2(1H)-one (IIId): m.p. = 138°C, molecular formula ($C_{17}H_{16}N_4O_2$); IR: 3469, 3414, 3057, 2924, 2853, 1686, 1617, 1575, 1461, 1413, 1384, 1343, 815, 745; ^{1}H-NMR ($CDCl_3$):, δ ppm; 7.380 (t, 2H, Ar-H), 7.095 (d, 2H, Ar-H), δ 10.722 (s, 1H, CH=N), δ 3.741 (s, 1H, NH), 8.185 (s,1H,NHCO),2.369 (q, 2H, CH_2), 2.570 (t, 2H, CH_2),11.562(s,2H,OH), 6.668-6.843(d,5H, Ar-H.

3-[(2-{[(E)-(4-methoxyphenyl)methylidene] amino} ethyl) amino] quinoxaline-2(1H)-one (IIIe): m.p. = 273°C C, molecular formula ($C_{18}H_8N_4O_2$); IR: 3484, 3417, 3066, 2981, 2924, 1512, 1495, 1420, 1384, 1342, 1246, 1162, 820, 746; H-NMR($CDCl_3$) δ ppm; 7.982 (t, 2H, Ar-H), 7.645 (d, 2H, Ar-H), δ 10.474 (s, 1H, CH=N), δ 3.832 (s, 1H, NH), 8.943 (s,1H,NHCO),2.378 (q, 2H, CH_2), 2.870 (t, 2H, CH_2),3.616(s,3H,CH_3O), 6.798-6.864(d,4H, Ar-H).

3-[(2-{[(1E, 2E)-3-phenylprop-2-en-1-ylidene] amino} ethyl) amino]quinoxalin-2(1H)-one (IIIf): m.p. = 258°C, molecular formula ($C_{19}H_{18}N_4O$); IR: 3448, 3417, 3067,



Synthesis of 3-[(2-{[(E)-(substituted phenyl) methylidene] amino} ethyl) amino] quinoxalin-2(1H)-one (Schiff's bases) (III a-j), Where, 1: For conventional synthesis, reflux for 5 hours; and 2: For microwave synthesis, reflux at 350 W, 50% watt power

Table II

Data for microwave assisted synthesis by scheme

Compound No.	Power level	Output in watts	MW % Power	Time (min)
IIIa	5	350	50	7
IIIb	5	350	50	8
IIIc	5	350	50	9
IIId	5	350	50	8
IIIe	5	350	50	8
IIIf	5	350	50	9
IIIg	5	350	50	8
IIIh	5	350	50	7
IIIi	5	350	50	9
IIIj	5	350	50	7

),7.867(s,1H,Ar-H), 7.609(t,1H, Ar-H), 6.96-7.647(d,2H, Ar-H).

3-{[2-({(E)-[3, 4-(dimethylamino) phenyl] methylidene} amino)ethyl]amino}quinoxalin-2(1H)-one (IIIh): m.p. = 177° C, molecular formula ($C_{19}H_{21}N_5O$); IR: 3417, 3060, 2951, 1694, 1638, 1617, 1511, 1384, 1494, 1373, 858, 806; ^{1}H-NMR ($CDCl_3$):, δ ppm; 8.602(s,1H,NH), 7.608(d,2H,Ar-H),7.087(t,2H,Ar-H),3.832(s,1H,NH), 2.511 (m,2H,CH_2),2.832(t,2H,CH_2),9.672(s,1H,-CH=N-),6.702 (d,2H,Ar-H), 6.583(d,2H,Ar-H), 3.095(s,3H,CH_3).

3-[(2-{[(E)-(3, 4-dichlorophenyl) methylidene]amino}ethyl) amino]quinoxalin-2(1H)-one (IIIi): m.p. = 280°C, molecular formula ($C_{17}H_{14}N_4OCl_2$); IR: 3416, 3060, 2951, 2840, 1694, 1617, 1551, 1494, 1385, 1373, 806, 831791,765; ^{1}H-NMR ($CDCl_3$):, δ ppm; 8.943(s,1H,NH), 7.778 (d,2H,Ar-H), 7.532(t,2H,Ar-H), 3.870(s,1H,NH), 2.386 (m,2H,CH_2), 2.591(t,2H,CH_2), 9.763(s,1H,-CH=N-),7.448 (s,1H,Ar-H), 6.860(d,2H,Ar-H).

3-[(2-{[(E)-(1-hydroxynaphthalen-2-yl) methylidene] amino} ethyl) amino] quinoxalin-2(1H)-one (IIIj): m.p. = 272°C,

Table III

Physicochemical data for the compound III (a-j)

Compound No.	Molecular Formula	M.P (°C)	% Yield		*R_f value
			Conventional	Microwave	
IIIa	$C_{17}H_{16}N_4O$	222	64	77	0.77
IIIb	$C_{17}H_{15}N_5O_3$	247	59	71	0.83
IIIc	$C_{17}H_{15}N_5O_3$	232	62	73	0.89
IIId	$C_{17}H_{16}N_4O_2$	138	67	75	0.87
IIIe	$C_{18}H_8N_4O_2$	273	54	70	0.64
IIIf	$C_{19}H_{18}N_4O$	258	71	88	0.51
IIIg	$C_{17}H_{15}N_4OCl$	282	60	69	0.81
IIIh	$C_{19}H_{21}N_5O$	177	57	65	0.86
IIIi	$C_{17}H_{14}N_4OCl_2$	280	55	67	0.84
IIIj	$C_{21}H_{18}N_4O_2$	272	62	69	0.90

[a](Mobile phase, Toluene: Acetone, 4:5)

2923, 1699, 1610, 1586, 1456, 1586, 1456, 1427, 1383, 1315, 739, 780; H-NMR($CDCl_3$) δ ppm ; 7778 (t, 2H, Ar-H), 7.678(d, 2H, Ar-H), δ 10.694 (s, 1H, CH=N), δ 3.446 (s, 1H, NH), 9.065 (s,1H,NHCO),2.291 (q, 2H, CH_2), 2.509 (t, 2H, CH_2),6.845(d,1H,Ar-H),7.074(t,1H,Ar-H),7.310-7.549(m,2H, Ar-H),7.742-7.254(d,2H, Ar-H).

3-[(2-{[(E)-(3-chlorophenyl) methylidene] amino} ethyl) amino] quinoxalin -2(1H)-one (IIIg): m.p. = 282°C, molecular formula ($C_{17}H_{15}N_4OCl$); IR : 3444, 3404, 3178, 3022, 2898, 1615, 1682, 1578, 1499, 1473, 1413, 1384, 754, 744, 721;^{1}H-NMR ($CDCl_3$):,δ ppm 8.095(s,1H,NH), 8.014(d,2H,CH), 7.431(t,2H,Ar-H), 3.832(s,1H,NH), 2.857(m,2H,CH_2), 2.267(t,2H,CH_2), 9.953(s,1H,-CH=N-

molecular formula ($C_{21}H_{18}N_4O_2$); IR: 3340, 3442, 3041, 2923, 2979, 1684, 1631, 1550, 1497, 1466, 1384, 1331, 827,802^{1}H-NMR($CDCl_3$)ppm;8.564(s,1H,NH),7.534 (d,2H,Ar-H),7.711(t,2H,Ar-H); 4.062(s,1H,NH),3.484 (m,2H,CH_2),2.147(t,2H,CH_2),10.739(s,1H,-CH=N-),11.566(S,1H,OH), 7.067-7.128(d,4H Ar-H), 7.908 (t,2H,Ar-H).

Proposed mechanism of the scheme:

Step I: Synthesis of 1, 4-dihydroquinoxaline-2, 3-dione (I): OPD (i.e. O-phenylenediame) condense with oxalic acid to form the heterocyclic compound 1, 4-dihydro-quinoxaline-2,3-dione via *Phillip's Condensation reaction.*

Condensation reaction: A chemical reaction in which two

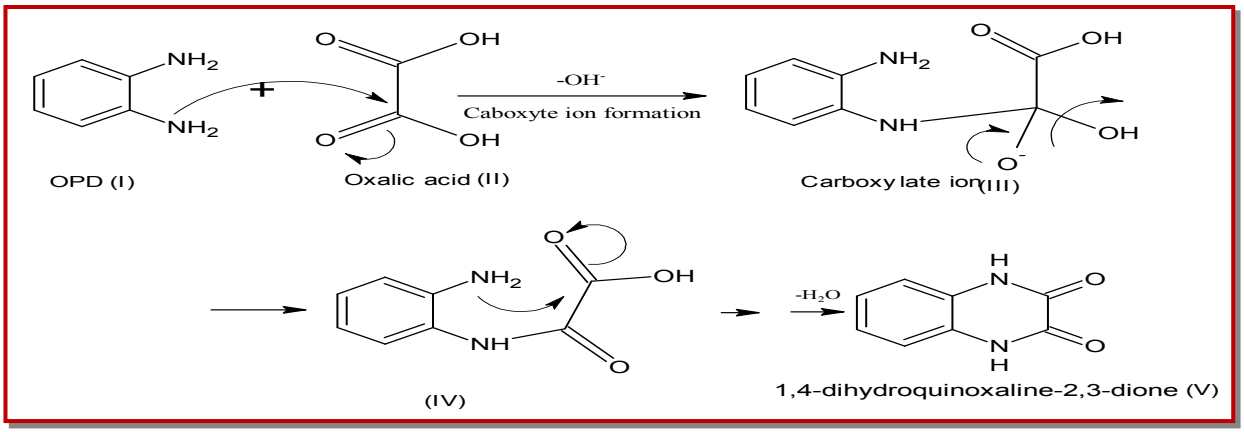
molecules or moieties combine to form a single molecule with loss of a small molecule, usually water.

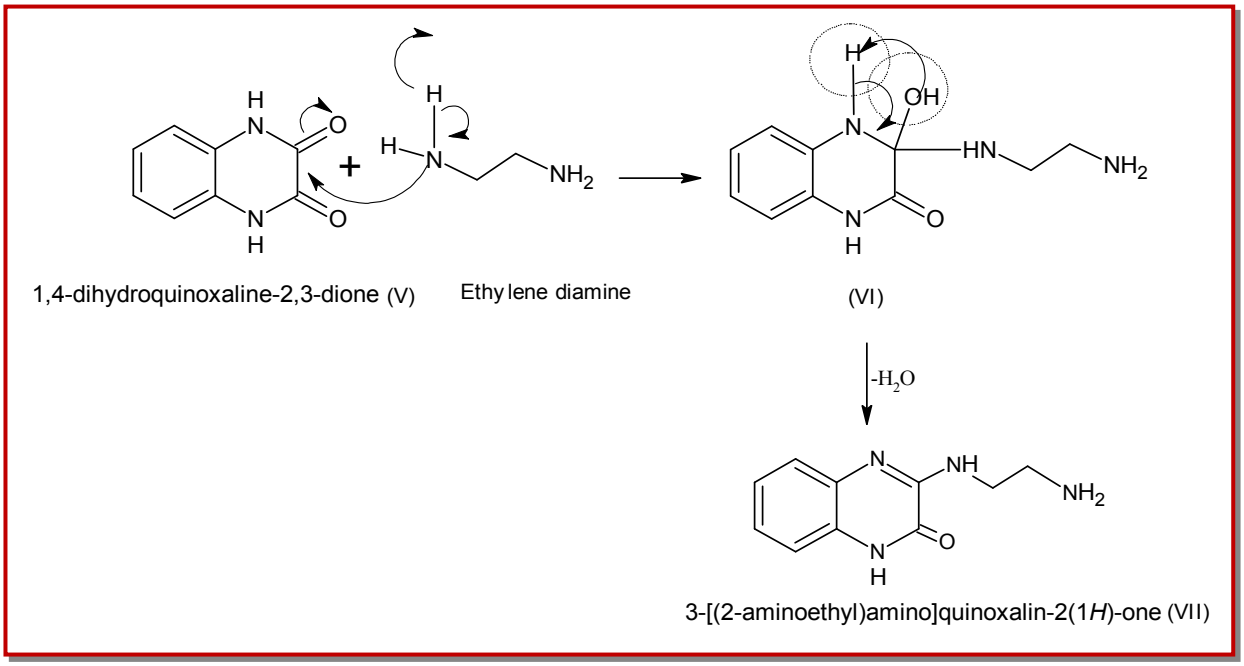
In this step, lone pair from the amine of OPD (I) attacks the partial positive carbon of carbonyl group from oxalic acid (II) leading to cleavage of C-O pi bond. This results in an intermediate containing caboxylate ion (III). The delocalized bond pair electron on oxygen reforms the C-O pi bond resulting in the loss of hydroxyl group which is an easy leaving group (IV). Subsequently, a similar reaction takes place between the remaining amino and carbonyl group which yields the cyclic condensed molecule with amide linkage quinoxaline ring by Phillips condensation mechanism. (V).

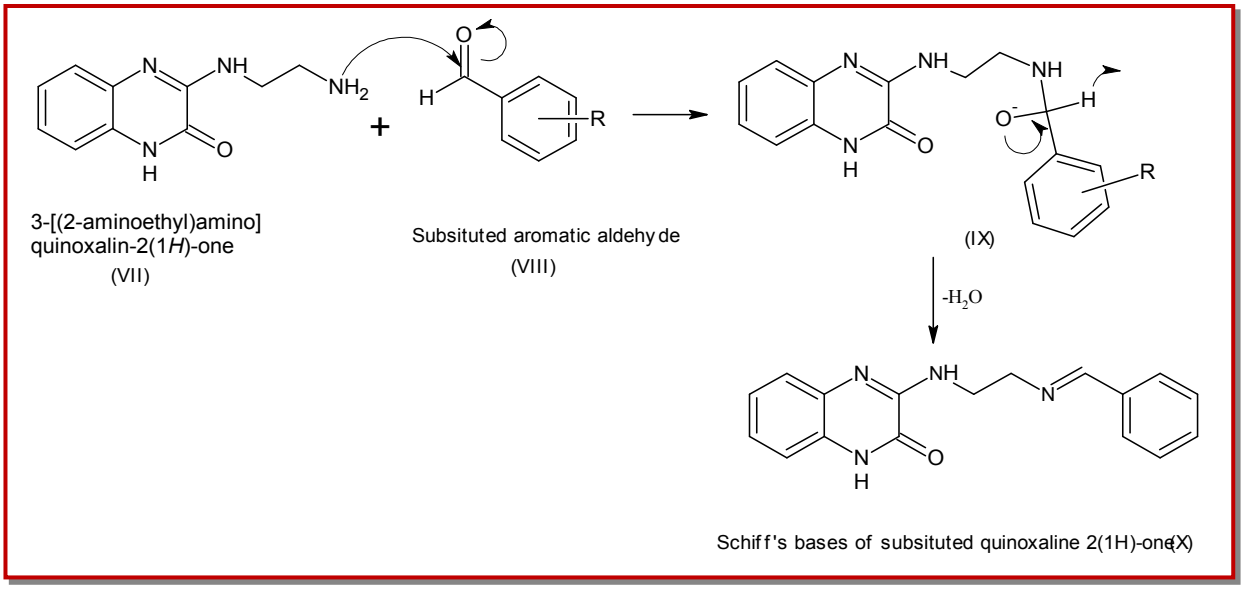
Step II: Synthesis of 3-[(2-aminoethyl) amino] quinoxalin-2 (1H)-one (II): In the next step, the quinoxaline-2, 3-dione (i.e. 1, 4-dihydroquinoxaline-2, 3-dione) in presence of ethylene diamine undergoes substitution reaction at position 3 and gives 3-[(2-aminoethyl) amino] quinoxalin-2(1H)-one with a loss of one water molecule. Here, the electron rich nitrogen center of ethylene diamine targets the electron deficient carbonyl carbon of quinoxaline ring which leads to the substitution of carbonyl oxygen by amine with a loss of one water molecule.

Step III: Synthesis of 3-[(2-{[(E)-(substituted Phenyl) methylidene]amino}ethyl)amino] quinoxalin-2(1H)-one: When 3-[(2-aminoethyl)amino]quinoxalin-2(1H)-one (VII) is made to react with aromatic aldehyde it results as follows; condensation of primary amine of ethylene diamine with carbonyl group of aromatic aldehydes take place by nucleophillic addition followed by dehydration which results in a formation of an imine (CH=N) functional moiety. i.e. formation of Schiff's base. Schiff's base [named after Hugo Schiff; (1834-1915, German chemist]. Which gives3-[(2-{[(*E*)-(substituted phenyl) methylidene] amino} ethyl)amino]quinoxalin-2(1*H*)-one.

Pharmacological evaluation: Pentylenetetrazole-induced







seizure model is utilized for this study. This is because MES induced model doesn't give any idea regarding the mechanism of action of the drug. Pentylenetetrazole is a central nervous system stimulant. It produces jerky clonic convulsions in rats/mice. The convulsive effect produced by this chemical is considered to be analogous to petit mal type of convulsions. Recently it has been found that pentylenetetrazole binds to an allosteric site on $GABA_A$ receptor and act as a negative modulator, thus interfering with chloride conductance.

All animals were screened using pentylenetetrazole-induced clonic seizures method. Pentylenetetrazole was used as convulsant and diazepam (Ranbaxy Laboratories, India) was used as standard drug. Pentylenetetrazole was dissolved in normal saline. Convulsion was induced 1 hour after the administration of the standard drug or the test compounds by i.p. injection of pentylenetetrazole (80 mg/kg), Swiss albino mice (20-25 g) of either sex were used for the study. Animals were divided into three groups control, standard and test each comprising of six mice. Test groups were treated with synthesized drugs (10, 20 mg/kg, oral) in distilled water. While standard and control groups were administered diazepam (4 mg/kg) and saline water (oral) respectively. After 30 min, pentylenetetrazole (80 mg/kg, i.p.) was administered to all the three groups. Each animal was placed in an individual plastic cage for observation. Convulsion appearance time and death or survival after 24 hours were recorded. Observations were taken in terms of Strobe's tail was observed as "S" shaped tail, clonic convulsions were observed as muscular jerks. Tonic convulsions were exhibited as the extension of the hind limb. Time for convulsions (min) for Straube's Tail and clonic convulsions recorded in (Table IV).

Results and Discussion

In the current research work, we aimed to synthesize some novel Schiff's bases of quinoxalines. The aforementioned compounds were prepared according to the synthetic process illustrated in Scheme 1. The final step III derivatives yield 3-[(2-{[(E)-(substituted phenyl)methylidene]amino}ethyl) amino] quinoxalin-2 (1*H*)-one upon cooling, the precipitate was obtained, filtered, dried and crystallized from the ethanol. The structural elucidation of the synthesized compounds was carried out with the help of IR spectroscopy and ^1H NMR spectroscopy. Screening of the *in vivo* anti-convulsant activity of the novel Schiff's bases of 3-{[2-({(E)-[substituted) phenyl] methylidene} amino) ethyl] amino} quinoxalin-2(1H)-one allowed us to identify interesting anti-convulsant candidates based on their potency, making them valid new leads for synthesizing new compounds that might improve the previously methods of synthesis. This activity was carried out on pentylenetetrazole (PTZ)-induced seizure model. Time for convulsions (min) for Strobe's tail and clonic convulsions is given in (Table IV). Compound 3-[(2-{[(E)-(2 nitrophenyl)methylidene]amino}ethyl)amino] quinoxalin-2(1H)-one (IIIb) for Strobe's tail 7.1 ± 0.0 and 11.1 ± 0.0 for clonic convulsions and 3-[(2-{[(E)-(2-nitrophenyl)methylidene]amino}ethyl)amino]quinoxalin-2 (1H)-one (IIIc) for Strobe's tail 3.5 ± 0.0 and 0.0 ± 0.0 for clonic convulsions showed maximum time for Strobe's tail and clonic convusions. That means, they possess good activity compared with the standard. Only animals treated with compounds 3-[(2-{[(E)-(2 nitrophenyl)methylidene] amino}ethyl)amino]quinoxalin-2(1H) one (IIIb) and 3-{[2-({(E)-[4-(dimethylamino)phenyl]methylidene}amino)ethyl] amino}quinoxalin-2(1H)-one (IIIe) were recovered from this study. Compound 3-[(2-{[(E)-(2-hydroxyphenyl) methylidene]amino}ethy)amino] quinoxalin-2(1H)-one

Table IV

Time for convulsions (min) for Straube's tail and clonic convulsions

Treatment	Dose (mg/kg)	Time for convulsions (min)		Death/Recovery
		Straube's Tail[a]	Clonic convulsions[a]	
Saline + PTZ	10	1.0 ± 0.0	1.1 ± 0.0	Death
Diazepam + PTZ	4	--	--	Recovery
IIIa+ PTZ	10	1.0 ± 0.0	2.2 ± 0.0	Death
	20	2.2 ± 0.0	4.1 ± 0.0	
IIIb+ PTZ	10	2.2 ± 0.0	9.2 ± 0.0	Recovery
	20	7.1 ± 0.0	11.1 ± 0.0	
IIIc+ PTZ	10	3.5 ± 0.0	10.0 ± 0.0	Recovery
	20	3.6 ± 0.0	0.0 ± 0.0	
IIId+ PTZ	10	2.5 ± 0.0	3.4 ± 0.0	Death
	20	3.2 ± 0.0	6.1 ± 0.0	
IIIe+ PTZ	10	3.5 ± 0.0	6.1 ± 0.0	Recovery
	20	2.7 ± 0.0	10.0 ± 0.0	
IIIf+ PTZ	10	1.5 ± 0.0	1.6 ± 0.0	Death
	20	1.6 ± 0.0	2.1 ± 0.0	
IIIg+ PTZ	10	2.5 ± 0.0	5.1 ± 0.0	Death
	20	3.5 ± 0.0	5.3 ± 0.0	
IIIh+ PTZ	10	1.5 ± 0.0	2.3 ± 0.0	Death
	20	2.2 ± 0.0	2.6 ± 0.0	
IIIi+ PTZ	10	1.4 ±0.0	3.3 ± 0.0	Death
	20	1.6 ± 0.0	3.5 ± 0.2	
IIIj+ PTZ	10	2.3 ± 0.0	4.4 ± 0.1	Death
	20	4.2 ± 0.0	6.4 ± 0.0	

Values are mean ± SEM; n = 6 in each group; [a]p<0.01 considered as significant when compared with the control (One-way ANOVA followed by Dunnet's Test). All the compounds show significant "p" value

(IIId) showed moderate activity. And 3-[(2-{[(1E, 2E)-3-phenylprop-2-en-1-ylidene] amino} ethyl) amino] quinoxalin-2(1H)-one (IIIf) showed minimum anti-convulsant activity.

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