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Research Article

THE DESIGN AND SYNTHESIS OF NOVEL DERIVATIVES OF 3-HYDROXY-1, 2, 3, 4-TETRAHYDROQUINOXALINE-2-CARBOHYDRAZIDE DERIVATIVES

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ABSTRACT

O*-Phenylenediamine reacts with diethyl malonate to form ethyl 3-oxo-1,2,3,4- tetrahydroquinoxaline-2-carboxylate 2, which reacts with hydrazinehydrate to form ethyl 3-oxo-1,2,3,4- tetrahydroquinoxaline-2-carboxylate 3. Compound 3 on condensation with different aromatic aldehydes gives of 3-hydroxy-1, 2, 3, 4-tetrahydroquinoxaline-2-carbohydrazide. And The structures of these compounds are confirmed by* ^{1}*H NMR and LC-MS data.*

KEYWORDS: *Quinoxaline, Manolicacid, Hydrazinehydrate.*

INTRODUCTION

Heterocycles compounds are used in many various industries [1]. However most of hetero cycles compounds aren't extracted from nature source, but are synthesized. Almost all alkaloids that are used as drugs are formed from hetero aromatic molecules. Because these compounds cause to cancer, these chemicals must be removed from output materials of smokestack in factories [2, 3]. Quinoxaline derivatives are an important class of compounds that find use in medicinal chemistry [4, 5]. For example, quinoxaline is a part of various antibiotics such as echinomycin, levomycin, and actinoleutin that are known to inhibit growth of gram positive bacteria [6], and are active against various transplantable tumors [7].

Numerous methods are available for the synthesis of quinoxaline derivatives which involve condensation of 1,2-diamines with α-diketones [8], 1,4-addition of 1,2- diamines to diazenylbutenes, cyclization-oxidation of phenacyl bromides and oxidative coupling of epoxides with ene-1,2-diamines [11]. 2,3-Disubstituted quinoxalines have also been prepared via the Suzuki- Miyaura coupling reaction [12], condensation of *o*-phenylenediamines with 1,2-dicarbonyl compounds in MeOH/AcOH under microwave irradiation [9], and iodine catalyzed cyclocondensation of 1,2-dicarbonyl.

EXPERIMENTAL SECTION

Chemicals and solvents were reagent grade and used without further purification. Melting points were determined on a capillary melting point (Buchi B-540) apparatus and are uncorrected. The ^{1}H NMR spectra were recorded in the indicated solvent on a Varian 400 MHz spectrometer with TMS as internal standard. All chemical shifts (δ) were reported in ppm with TMS as internal standard. Mass spectra were measured on a Jeol JMS D-300 spectrometer. The homogeneity of the compounds was checked using precoated TLC plates (E. Merck Kieselgel 60 F_{254}).

Method 1 for Preparation of Synthesis of ethyl 3-oxo-1,2,3,4-tetrahydroquinoxaline-2-carboxylate,2:

A mixture of *o*-Phenalenediamine (5.12 gm, 0.05 mol) dissolved in 20 ml hot distilled water in 250 ml beaker stirred for 2 hours with drop wise addition of diethyl malonate (4.07 ml, 0.05 mol), after completion of the reaction (checked by TLC using Cyclohexane and Ethylacetate in ratio of 1:3 . Rf value 0.33). The solid mass was collected at the bottom of the beaker, filtered and recrystallized from aqueous ethanol.

Method 2 for Preparation of Synthesis of ethyl 3-oxo-1,2,3,4-tetrahydroquinoxaline-2-carboxylate,2:

A mixture of *o*-Phenalenediamine (5.12 gm, 0.05 mol) dissolved in 20 ml ethanol in 250 ml round bottom flask and filtered off then diethyl malonate (4.07 ml, 0.05 mol) was added with drop wise stirring, after completion of the reaction (checked by TLC Cyclohexane and Ethylacetate in the ratio 1:3. Rf value 0.42.). Then excess of alcohol is distilled off the solid mass was collected at the bottom of the beaker.

Based on the above two methods we have selected method 2 as it yields more outcome with high purity

3-hydroxy-1,2,3,4-tetrahydroquinoxaline-2-carbohydrazide, 3:

To a solution of ethyl 3-oxo-1,2,3,4-tetrahydroquin oxaline-2-carboxylate (SSP1-3) (3gm, 0.015 mol) in ethanol (10 ml), (0.935ml,0.015 mol) hydrazine hydrate 99% was added at

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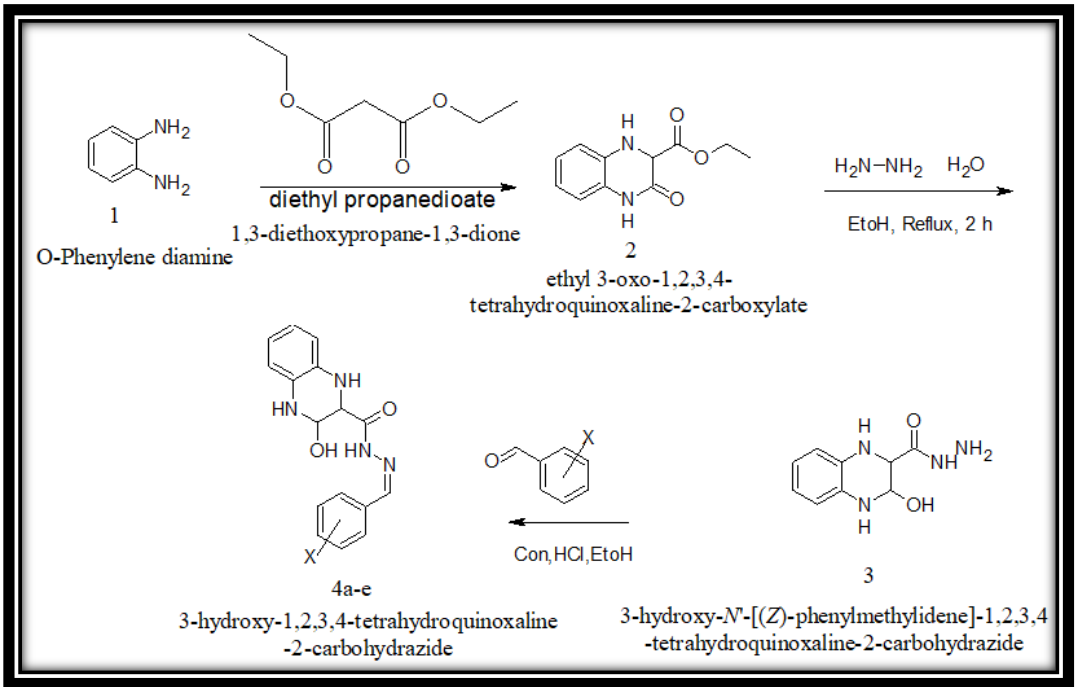
room temperature and the reaction mixture was refluxed for 8h. Then reaction was monitored by TLC using Cyclohexane and Ethylacetate in the ratio 1:3. Rf value 0.42. Reaction mixture was allowed to cool at bellow 10°C temperature resultant solid was filtered, dried and recrystallized from ethanol.



Compound	X	Compound	X
4a	2-CH_3	4d	2-NO_2
4b	2-Cl	4e	3-NO_2
4c	3-OCH_3		

Scheme I

Derivatives of 3-hydroxy-1,2,3,4-tetrahydroquinoxaline-2-carbohydrazide,4:

(500 mg, 2.45 mmol, 1 eq) in EtOH (10 mL) 2-methylbenzaldehyde (309 mg, 2.57 mmol, 1.05 eq.) and catalytic amount of conc. HCl were added at RT and the reaction mixture was stirred at RT for 1 hr. After completion of the reaction (checked by TLC). The mixture was diluted with water, basified with sat. aq. $NaHCO_3$ and resultant solid was filtered, washed with water and dried. The structure of the compound was confirmed by ^{1}H NMR and LC-MS data. Other members of this series were also prepared using this procedure.Yield: 600 mg (80%); Yellow solid.

3-hydroxy-1,2,3,4-tetrahydroquinoxaline-2-carbohydrazide, 4a:

^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.15 (s, 3H), 7.18-7.79 (m, 8H), 8.05 (s, 1H), 8.51 (brs, 1H), 12.01 (brs, 1H); LC-MS: *m/z* 306 (M^+), m.p. 228°C

3-hydroxy-1,2,3,4-tetrahydroquinoxaline-2-carbohydrazide, 4b:

^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.20-7.80 (m, 8H), 8.02 (s, 1H), 8.42 (brs, 1H), 12.03 (brs, 1H); MS: *m/z* 326 (M^+), m.p. 230°C

3-hydroxy-1,2,3,4-tetrahydroquinoxaline-2-carbohydrazide, 4c:

^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.86 (s, 3H), 7.15 (s, 1H), 7.19-7.89 (m, 8H), 7.99 (s, 1H), 8.48 (brs, 1H), 11.90 (brs, 1H); MS: *m/z* 322 (M^+), m.p. 232°C

3-hydroxy-1,2,3,4-tetrahydroquinoxaline-2-carbohydrazide, 4d:

^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.40-7.79 (m, 8H), 8.04 (s, 1H), 8.50 (brs, 1H), 12.56 (brs, 1H); MS: *m/z* 337 (M^+), m.p. 238°C

3-hydroxy-1,2,3,4-tetrahydroquinoxaline-2-carbohydrazide, 4e:

^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.38-7.80 (m, 8H), 8.05 (s, 1H), 8.48 (brs, 1H), 12.01 (brs, 1H); MS: m/z337 (M+), m.p.240°C

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