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SYNTHESIS OF 2–HYDROXY SUBSTITUTED QUINOXALINE

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ABSTRACT

Synthesis of 2-hydroxy substituted quinoxaline prepared by using 2-hydroxy substituted chalcone dibromide and chalcone dibromide condensed with BDA in methanol solvent. The constitution of the synthesized compounds is supported by IR, UV, PMR and elemental analysis.

Key words: 2-Hydroxy substituted quinoxaline, Characterization.

INTRODUCTION

Heterocylic compounds represent an important class of biologically active molecules. Specially those containing quinoxaline derivatives have evoked considerable attention in recent years as these are endowed. Quinoxalines are versatile class of nitrogen containing heterocyclic compounds and they constitute useful intermediate in organic synthesis. Quinoxaline, also called a benzopyrazine in organic chemistry, is a heterocyclic compound contraining a ring complex made up of benzene ring and a pyrizine ring and they are isomeric with cinnoleness, pthalalazines and quinazolines.

Quinoxaline and substituted quinoxaline compound have their own identity in heterocyclic compound due to its various applications in each field. Various quinoxalines are found to be of wide clinical importance. A good amount of work has been done in studying various biological activities of different quinoxaline derivatives. Recently, coordination chemistry opens new path in medicinal, pharmaceutical and biochemical field. So, much more attention of chemists developed in physical and inorganic chemistry, which explore a new path in drug chemistry specially related to the drug activity and drug effect.

A simple highly efficient and green procedure for the condensation of aryl and alkyl

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1,2-diamines with α-diketones in the presence of catalytic amount of oxalic acid at room temperature is described. Using this method, quinoxaline derivatives as biologically interesting compounds are produced in high to excellent yields and short reaction times[1].

An efficient environmentally benign tandem synthetic route to prepare quinoxalines leading to reusable manganese oxide octahedral molecular sieves (OMS-2) is described[2].

Synthesis of new series of quinoxaline based MAO-inhibitors and docring were studied by Khattab et al.[3] Synthesis and antimicrobial activity of novel quinoxaline derivatives were studied by Badran et al[4]. Lead oxide (PbO) mediated synthesis quinoxaline were studied by Kotharkar & Shinde[5]. Anti-inflammatory activity of novel substituted quinoxaline heterocycles were studied by Noorulla and N. Sreenivasulu[6]. Anti-inflammatory activity of some new thio-ether derivatives of quinoxaline were studied by Singh et al[7]. Antibacterial activity of novel substituted quinoxaline were studied by Noorulla and Sreenivasulu[8]. Antimicrobial activities of some substituted quinoxaline-2(1H)-one derivatives were studied by Ghadge and Shriote[9]. The novel quinoxaline derivatives were studied by More et al[10].

EXPERIMENTAL

Preparation of 2-hydroxy substituted quinoxaline

Chalcone dibromide and BDA were condensed in methanol. A few drop of concentrated H_2SO_4 was added and the reaction mixture heated on water bath for 30 minutes. It was diluted with water and crude mass was extracted with solvent ether to remove insoluble BDA, the yellow product was obtained.

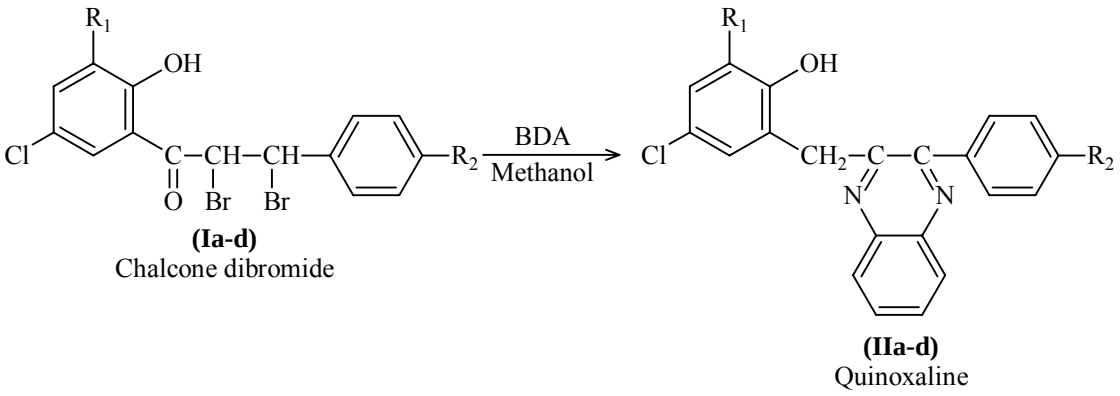
The following 2-hydroxy substituted quinoxalines were prepared.

(i) 2-(2-hydroxy-5-chloro) benzyl-3-(4-methoxyphenyl) quinoxaline **(IIa)**. m.p. 141°C, yield 80%.

(ii) 2-(2-hydroxy-5-chloro) benzyl-3-phenyl quinoxaline **(IIb)**. m.p. 174°C, yield 82%.

(iii) 2-(2-hydroxy-3-bromo-5-chloro) benzyl-3-(4-methoxyphenyl) quinoxaline **(IIc)**. m.p. 156°C, yield 85%

(iv) 2-(2-hydroxy-3-bromo-5-chloro) benzyl-3-phenyl quinoxaline **(IId)**. m.p. 130°C, yield 80%.



Where, R_1 = –H, –Br; R_2 = –H, –OCH_3

The structures of the compounds **(IIa-d)** were confirmed on the basis of chemical properties, analytical results and spectral data.

RESULTS AND DISCUSSION

2-(2-hydroxy-5-chloro) benzyl-3,4-methoxyphenyl quinoxaline **(IIa)**, 2-(2-hydroxy-5-chloro) benzyl-3-phenyl quinoxaline **(IIb)**, 2-(2-hydroxy-3-bromo-5-chloro) benzyl-3-(4-methoxyphenyl) quinoxaline **(IIc)** and 2-(2-hydroxy-3-bromo-5-chloro) benzyl-3-phenyl quinoxaline **(IId)** were prepared and the UV, IR and PMR are discussed.

It is pale yellow crystalline compound, m.p. 141^{o}C.

It gives green colouration with neutral $FeCl_3$ solution indicating the presence of phenolic –OH group all compounds **(IIa –IId)** contain same properties.

IVa: 2-(2-hydroxy-5-chloro) benzyl-3-(4-methoxyphenyl) quinoxaline

IR (KBr) cm^{-1}: 3516 (Ar-OH), 3100 (Ar-C-H), 1600-1720 (Ar-C-C), 1583 (C=N), 1440 (--CH-C), 1260 and 1080 (Ar, -O-CH_3), 1220 and 1192 (Ar, C-Cl), 860 (p-substitution), 847 (m-substitution), 763 (o-substitution); ^{1}H NMR ($CDCl_3$ with TMS): δ 2.4 (q, 2H, -CH_2), 3.96 (s, 3H, -OCH_3), 6.76-8.34 (m, 7H, Ar-H), 13.3 (s, 1H, -OH); Mass (m/z): 376.5. Anal Calcd for $C_{22}H_{17}O_2N_2Cl$ % C, 72.73; H, 4.33; O, 4.62; N, 8.08; Cl, 10.23; Found: C, 73.31; H, 4.23; O, 4.71; N, 7.99; Cl, 10.12; UV (nm): 237 ($\pi \rightarrow \pi^*$) and 306 ($n \rightarrow \pi^*$).

IVb: 2-(2-hydroxy-5-chloro) benzyl-3-phenyl quinoxaline

IR (KBr) cm^{-1}: 3745 (Ar-OH), 3035 (Ar-C-H), 2874 (-CH_2), 1697 and 1602 (Ar-C-C), 1556 (C=N), 1236 and 1174 (Ar-C-Cl), 864 (m-substitution), 792 (o-substitution); ^{1}HNMR

($CDCl_3$ with TMS): δ 2.62 (q, 2H, -CH_2), 6.70-7.72 (m, 7H, Ar-H), 12.83 (s, 1H, -OH); Mass (m/z) : 346.5. Anal Calcd for $C_{21}H_{15}ON_2Cl$ % C, 72.73; H, 4.33; O, 4.62; N, 8.08; Cl, 10.23; Found: C, 73.31; H, 4.23; O, 4.71; N, 7.99; Cl, 10.12; UV (nm) : 238 ($\pi \rightarrow \pi^*$) and 345 ($n \rightarrow \pi^*$).

IVc: 2-(2-hydroxy-3-bromo-5-chloro) benzyl-3-(4-methoxyphenyl) quinoxaline

IR (KBr) cm^{-1}: 3540 (Ar-OH), 3080 (Ar-C-H), 1640-1600 (Ar-C-C), 1560 (C=N), 1433 (--CH-C), 1303 and 1100 (Ar-O-CH_3), 1236 and 1140 (Ar-C-Cl), 1170 and 1080 (Ar-Br), 875 (p-substitution), 810 and 790 (m-substitution), 750 (o-substitution); ^{1}H NMR ($CDCl_3$ with TMS): δ 2.64 (q, 2H, -CH_2), 3.96 (s, 3H, -OCH_3), 6.81-8.08 (m, 7H, Ar-H), 12.2 (s, 1H, -OH); Mass (m/z) : 455.4. Anal Calcd for $C_{22}H_{16}O_2N_2ClBr$ % C, 57.97; H, 3.51; O, 7.03; N, 6.15; Cl, 7.80; Br, 17.55; Found: C, 59.12; H, 3.44; O, 7.13; N, 6.06; Cl, 7.73; Br, 17.42; ; UV (nm) : 243 ($\pi \rightarrow \pi^*$) and 314 ($n \rightarrow \pi^*$).

IVd : 2-(2-hydroxy-3-bromo-5-chloro) benzyl-3-phenyl quinoxaline

IR (KBr)[11-13] cm^{-1}: 3570 (Ar-OH), 3091 (Ar-C-H), 1697-1651 (Ar-C-C), 1556 (C=N), 1435 (-CH-C), 1220 and 1055 (Ar-C-Cl), 1203 and 1022 (Ar-Br), 817 and 794 (m-substitution); ^{1}HNMR ($CDCl_3$ with TMS)[14-15]: δ 2.67 (q, 2H, -CH_2), 6.70-8.09 (m, 7H, Ar-H), 12.86 (s, 1H, -OH); Mass (m/z) : 425.4. Anal Calcd for $C_{21}H_{14}ON_2ClBr$ % C, 59.24; H, 3.29; O, 3.76; N, 6.58; Cl, 8.33; Br, 18.78; Found : C, 60.12; H, 3.14; O, 3.92; N, 6.48; Cl, 8.21; Br, 18.65; ; UV (nm) : 235 ($\pi \rightarrow \pi^*$) and 342 ($n \rightarrow \pi^*$).

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