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Synthesis of New 2,3-Disubstituted Quinoxalines from 4,4′-Substituted Chalcones

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4′-Chlorochalcone **(Ia)**, 4′-chloro-4-methoxychalcone **(Ib)**, 4′-nitrochalcone **(Ic)** and 4′-nitro-4-methoxychalcone **(Id)** react with bromine in acetic acid to give chalcone dibromides **(IIa–d)**. The chalcone dibromides **(IIa–d)** condense with benzene 1,2-diamine (BDA) in presence of few drops of concentrated H_2SO_4 in methanol medium to affords 2,3-disubstituted quinoxalines **(IIIa–d)**. The structures of these compounds were confirmed by analytical and spectral data.

Key Words: Synthesis, 2,3-Disubstituted quinoxalines, 4,4′-Substituted chalcones.

INTRODUCTION

Quinoxalines are well known for their antibacterial[1], antitumour and antiviral[2] properties. Earlier workers reported various aziridinyl ketones and their cyclic anils by the reaction of chalcone dibromide with benzene-1,2-diamine (BDA) in presence of triethylamine and their subsequent acid catalyst isomerization to quinoxaline[3]. Similarly 2-monoalkylamino and 2-dialkylamino-4-phenylbenzo-diazepines are also reported[4]. Formation of novel Schiff bases containing tricyclic (7 + 12 + 7) inner ring system have also been suggested[5] in this reaction. Flavones are also condensed with BDA to give quinoxaline. The reaction of chalcone dibromide with BDA takes place *via* intermediates[5]. Cyclic anil which is isolable of triethylamine is used as a condensing agent which undergoes acid catalyzed isomerization of quinoxaline.

Aurone with hydrogen peroxide in alkaline methanol or dioxane gives aurone epoxide which on ring opening gives intermediate 2,3-dihydroxyl aurone isomers with 1,2-diketone structure[6], which subsequently condenses with BDA to give 2,3-disubstituted quinoxaline[7].

Chalcone dibromide or flavone condenses with BDA in presence of sulphuric acid in methanol to give 2,3-disubstituted quinoxaline[8, 9].

In the present work quinoxaline is synthesized from 4,4′-substituted chalcone dibromide condensed with BDA in presence of few drops of concentrated H_2SO_4 in methanol medium. Chalcones **(Ia–d)** were synthesized by reported methods[10]

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EXPERIMENTAL

Synthesis of 4″-chloro α,β-chalcone dibromide

4′-Chlorochalcone **(Ia)** (0.01 mole) was dissolved in glacial acetic acid by warming and the solution was cooled. A solution of bromine in acetic acid (6.4 mL, 25% w/v) was added to this solution with constant stirring. After 15 min the dibromide separated. It was filtered, washed with alcohol followed by petroleum ether to get the compound **(IIa)**, m.p. 193°C, yield 90%.

Properties and constitution of compound (IIa)

1. It is a white crystalline solid, m.p. 193°C.
2. Elemental analysis shows the presence of bromine in the molecule.
3. From the analytical data m.f. was found to be $C_{15}H_{11}Br_2ClO$ and the m.w. 402.3.
4. The R_f value in benzene was found to be 0.76 on silica gel-G plate with layer thickness of 0.3 mm.
5. IR spectrum of compound **(IIa)** was recorded in Nujol: 2485 ν(—CH), 1686 ν(—C=O), 785 ν(C—C1) 670 and 644 cm^{-1} ν(C—Br).
6. PMR ($CDCl_3$):

5–6 (d, 1H, —CH(Br)), 6. I (d, 1H, —CH(Br))

7.35 to 8.2 δ (m, 9H, Ar—H)

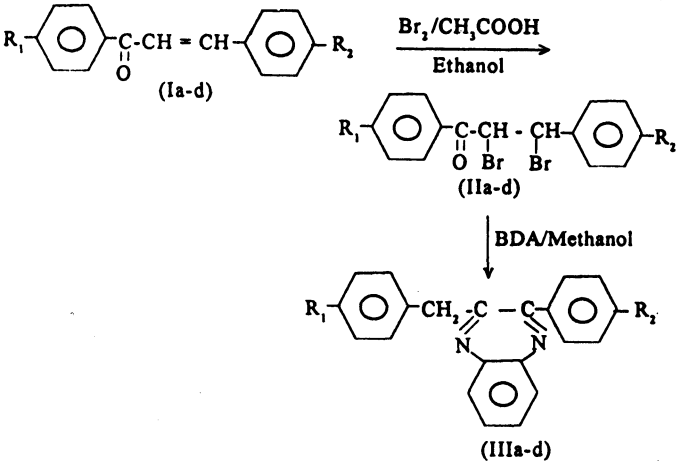
Synthesis of 2-(4″-chlorophenyl)-3-phenyl quinoxaline

4″-Chloro, α,β-chalcone dibromide **(IIa–j)** (0.01 mole) and benzene 1,2-diamine (BDA) (0.01 mole) was taken in 25 mL methanol, and 2–3 drops of concentrated H_2SO_4 were added. The reaction mixture was heated on a water bath for about 30 min. It was then diluted with water, the crude mass extracted with solvent petroleum ether (to remove the insoluble BDA). Ether was evaporated and the solid was crystallized from ethanol to get **(IIIa)**, m.p. 179°C, yield 90%.

Properties and constitution of compound (IIIa)

1. It is white crystalline solid, m.p. 1790C.
2. From the analytical data the m.f. was found to be $C_{21}H_{15}N_2CI$ and m.w. 330.5.
3. The R_f values in benzene were found to be 0.82 on silica gel-G plate with a layer thickness of 0.3 mm.
4. IR spectrum of compound **(IIIa)** was recorded in Nujol: 2986 ν(—CH), 1589 ν(—C=N), 1220 ν(—C—N), 1375 ν(—CH_2), 785 cm^{-1} ν(C—C1).
5. PMR ($CDCl_3$):
   5.2 to 5.4 (dd, 2H, —CH_2), 7.2 to 8.1 δ (m, 13H, Ar—H).

The other chalcone dibromides and quinoxalines were prepared by the same method.



(Ia-d)

(IIa-d)

(IIIa-d)

The chalcones, chalcone dibromides and corresponding quinoxalines prepared are listed in Table-1.

TABLE-1
CHALCONES, CHALCONE DIBROMIDES AND CORRESPONDING QUINOXALINES

Compd. No.	R_1	R_2	m.f.	m.w.	m.p. (°C)	Yield (%)	R_f values (benzene)
Ia	—Cl	—H	$C_{15}H_{11}ClO$	242.5	95	76	0.76
Ib	—Cl	—OCH_3	$C_{16}H_{13}ClO_2$	272.5	113	80	0.74
Ic	—NO_2	—H	$C_{15}H_{11}NO_3$	253.0	117	72	0.92
Id	—NO_2	—OCH_3	$C_{16}H_{13}NO_4$	283.0	175	78	0.87
IIa	—Cl	—H	$C_{15}H_{11}Br_2ClO$	402.3	193	74	0.76
IIb	—Cl	—OCH_3	$C_{16}H_{13}Br_2ClO_2$	432.3	159	80	0.80
IIc	—NO_2	—H	$C_{15}H_{11}Br_2NO_3$	412.8	198	76	0.80
IId	—NO_2	—OCH_3	$C_{16}H_{13}Br_2NO_4$	442.8	170	82	0.86
IIIa	—Cl	—H	$C_{21}H_{15}N_2Cl$	330.5	179	90	0.82
IIIb	—Cl	—OCH_3	$C_{22}H_{17}N_2ClO$	360.5	153	92	0.84
IIIc	—NO_2	—H	$C_{21}H_{15}N_3O_2$	341.0	173	90	0.90
IIId	—NO_2	—OCH_3	$C_{22}H_{17}N_3O_3$	371.0	161	90	0.92

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