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Synthesis and antimicrobial activity of some novel chalcones and their related compounds

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ABSTRACT

A number of chalcones have been prepared by Claisen-Schmidt condensation reaction between selected aldehyde and selected ketones. The synthesised chalcones are thiophen-2-aldehydeacetophenone (TAAP), furan-2-aldehydeacetophenone (FAAP), 2-hydroxynapthaldehyde acetophenone (HNAP), cinnamaldehydeacetophenone (CAAP), thiophen-2-aldehyde-2' hydroxy-4'methoxyacetophenone (TAHMAP), furan-2-aldehyde-2' hydroxy-4'methoxyacetophenone (FAHMAP), 2-hydroxynapth-aldehyde-2'-hydroxy-4'-methoxyacetophenone (HNHMAP), cinnam-aldehyde-2'-hydroxy-4'-methoxyacetophenone (CAHMAP), thiophen-2-aldehyde-3'-chloroacetophenone (TACAP), furan-2-aldehyde-3'-chloroacetophenone (FACAP),2-hydroxynapthaldehyde-3'-chloro-acetophenone (HNCAP), cinnamaldehyde-3'-chloroacetophenone (CACAP), The chalcones were converted into respective quinoxalines by treating them with bromine water and acetic acid and finally methanolic solution of tetramethylenediamine. All chalcones and quinoxalines have been characterised by melting point, elemental analyses and spectral studies. The antimicrobial activities of these compounds have also been studied.

Key words: Chalcones, Quinoxalines, antimicrobial activity.

INTRODUCTION

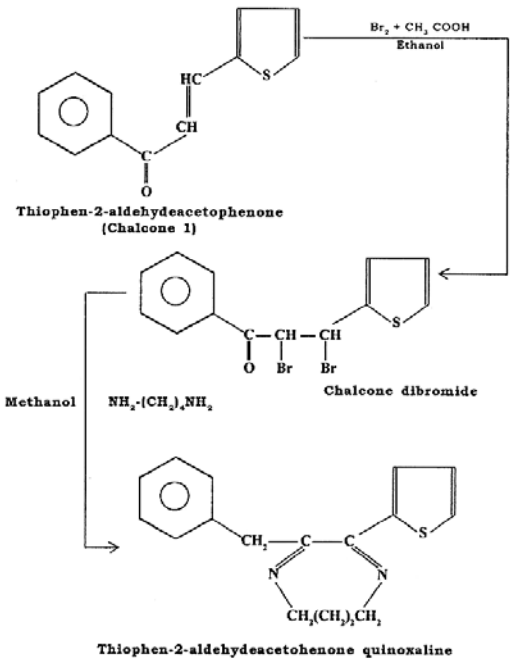
The chemistry of chalcones has been recognized as a significant field of study. Chalcons[1, 2] are useful intermediates in the synthesis of various heterocyclic compounds such as pyrzolines, isoxazolines pyrimidines, flavones, flavonols and quinoxalines. Chalcones have been associated with diverse biological activities, e.g. cardiovascular[3], antiviral[4], anticancer[5], etc. The literature survey reveals that are found to possess many biological activities and have variety of industrial applications[6].

In the present paper we report herein the synthesis of few chalcones by Claisen-Schmidt condensation by treating thiophen-2-aldehyde, furan--aldehyde and cinnamaldehyde with acetophenones like 2'-hydroxy-4'-methoxyacetophenone, 3'-chloroacetophenone and acetophenone.

Preparation of chalcones

Equimolar quantities of respective aldehydes and ketones were taken and dissolved in ethanol (20-30 ml) under stirring to which aqueous sodium hydroxide (50%, 5ml) was added dropwise. After stirring the reaction mixture was kept overnight at room temperature. It was diluted with ice cold water and then acidified with 10% hydrochloric acid. The precipitate was filtered off and recrystallized from ethanol and dried in vacuum. The purity of the sample was tested by TLC.

The analytical data of chalcones suggested 1:1 molar ratio of respective aldehyde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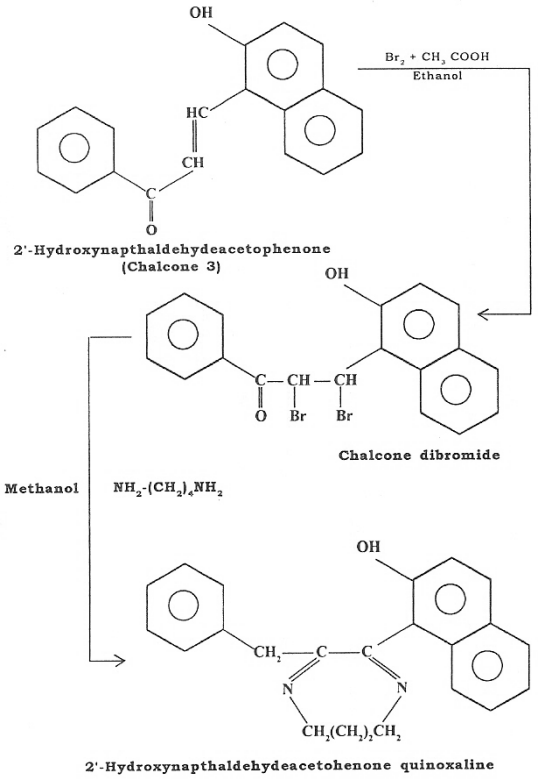
Ethanol
Thiophen-2-aldehydeacetophenone
(Chalcone 1)
Chalcone dibromide
Methanol
NH2-(CH2)4NH2
Thiophen-2-aldehydeacetohenone quinoxaline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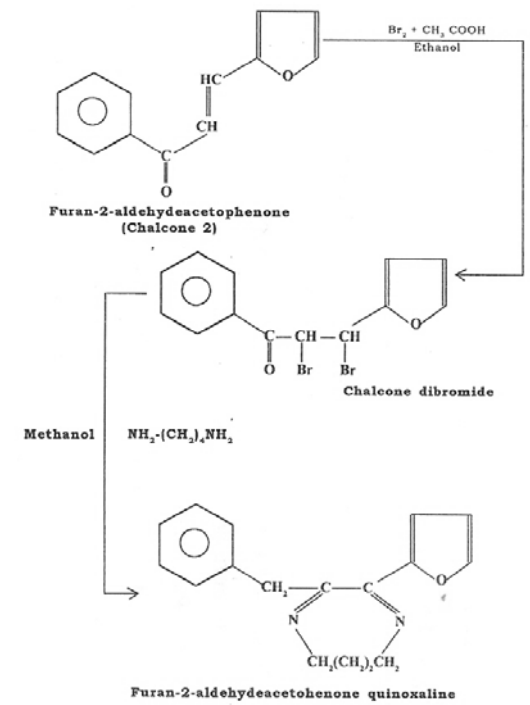
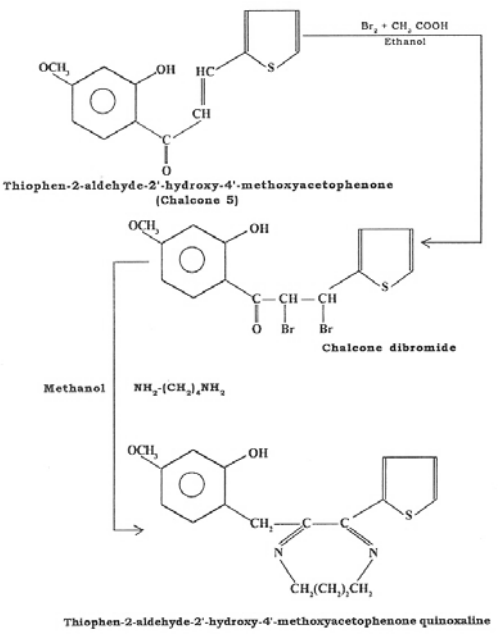
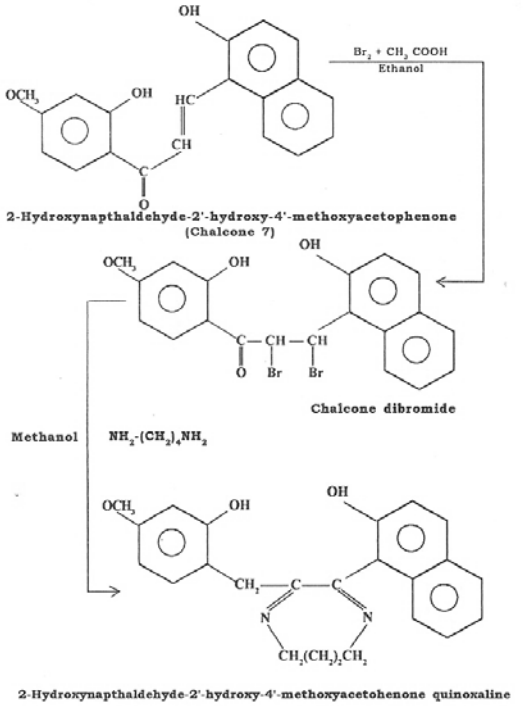
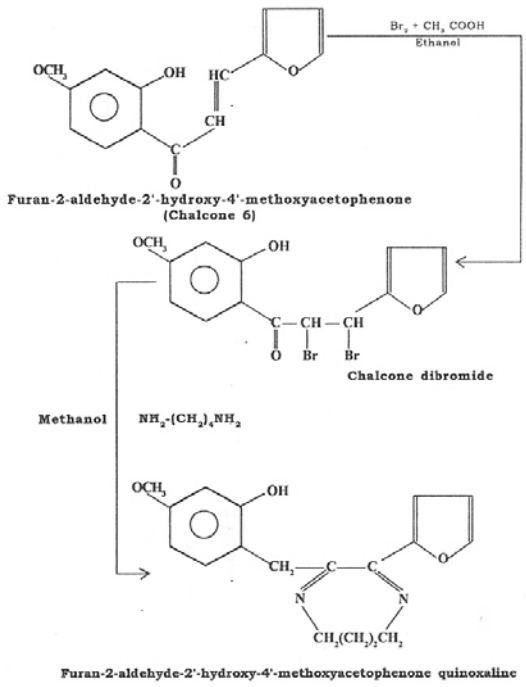
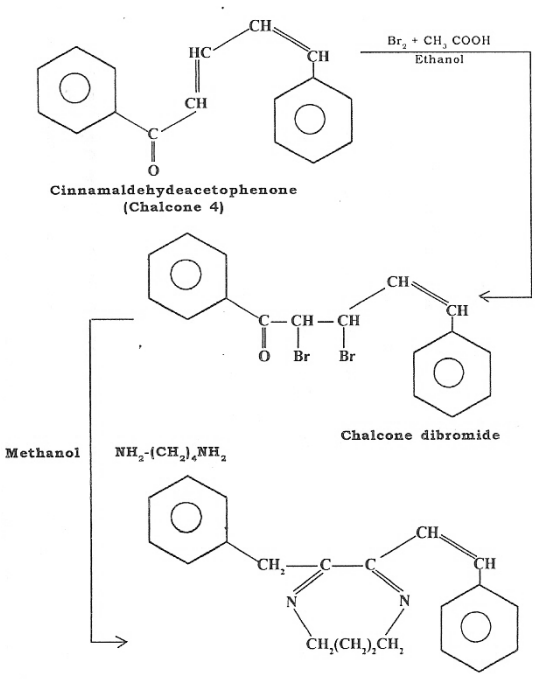
Ethanol
2'-Hydroxynapthaldehydeacetophenone
(Chalcone 3)
Chalcone dibromide
Methanol
NH2-(CH2)4NH2
2'-Hydroxynapthaldehydeacetohenone quinoxaline


Br2 + CH3 COOH
Ethanol
Furan-2-aldehydeacetophenone
(Chalcone 2)
Chalcone dibromide
Methanol
NH2-(CH2)4NH2
Furan-2-aldehydeacetohenone quinoxaline


Br2 + CH3 COOH
Ethanol
Thiophen-2-aldehyde-2'-hydroxy-4'-methoxyacetophenone
(Chalcone 5)
Chalcone dibromide
Methanol
NH2-(CH2)4NH2
Thiophen-2-aldehyde-2'-hydroxy-4'-methoxyacetophenone quinoxaline


Br2 + CH3 COOH
Ethanol
2-Hydroxynapthaldehyde-2'-hydroxy-4'-methoxyacetophenone
(Chalcone 7)
Chalcone dibromide
Methanol
NH2-(CH2)4NH2
2-Hydroxynapthaldehyde-2'-hydroxy-4'-methoxyacetohenone quinoxaline


Br2 + CH3 COOH
Ethanol
Furan-2-aldehyde-2'-hydroxy-4'-methoxyacetophenone
(Chalcone 6)
Chalcone dibromide
Methanol
NH2-(CH2)4NH2
Furan-2-aldehyde-2'-hydroxy-4'-methoxyacetophenone quinoxaline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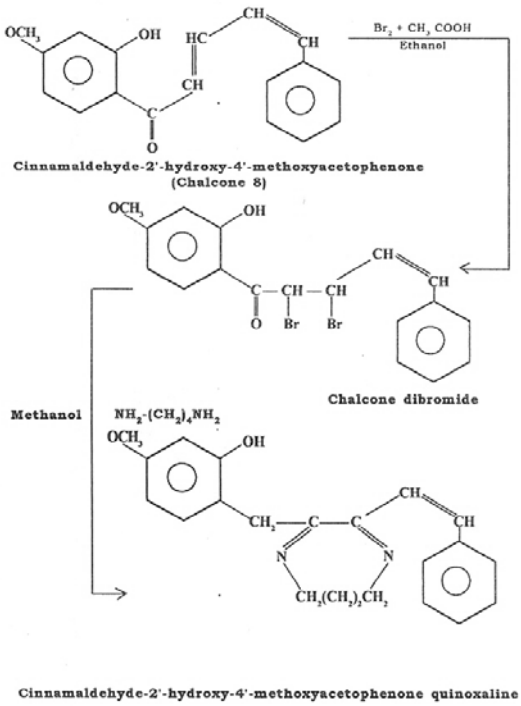
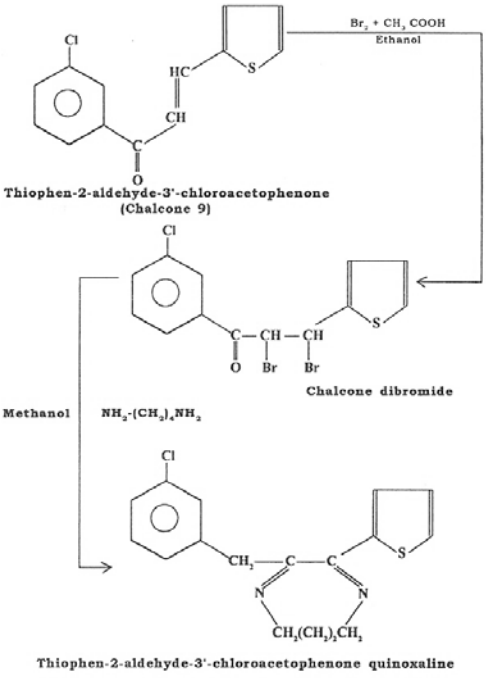
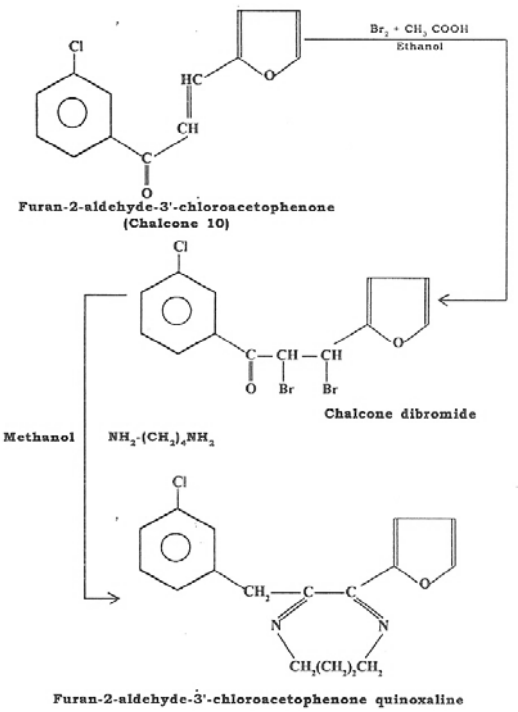
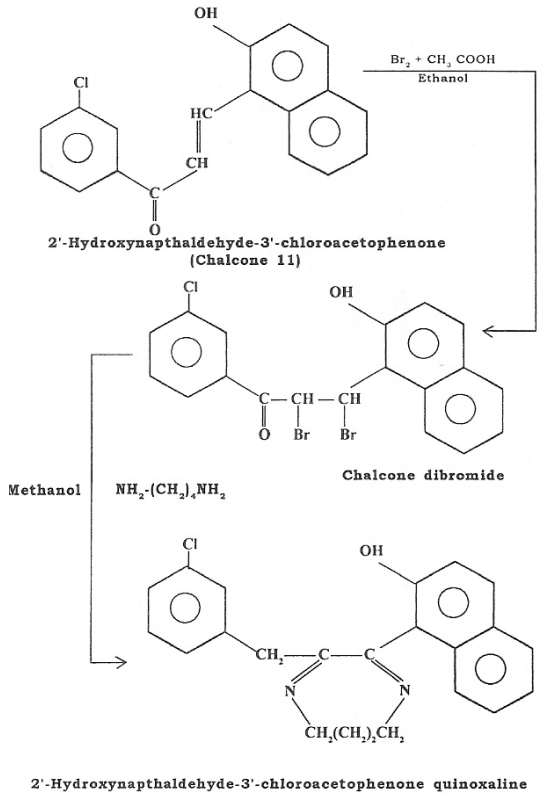
Ethanol
Cinnamaldehydeacetophenone
(Chalcone 4)
Chalcone dibromide
Methanol
NH2-(CH2)4NH2


Br2 + CH3 COOH
Ethanol
Cinnamaldehyde-2'-hydroxy-4'-methoxyacetophenone
(Chalcone 8)
Chalcone dibromide
Methanol
NH2-(CH2)4NH2
Cinnamaldehyde-2'-hydroxy-4'-methoxyacetophenone quinoxaline


Br2 + CH3 COOH
Ethanol
Thiophen-2-aldehyde-3'-chloroacetophenone
(Chalcone 9)
Chalcone dibromide
Methanol
NH2-(CH2)4NH2
Thiophen-2-aldehyde-3'-chloroacetophenone quinoxaline


Br2 + CH3 COOH
Ethanol
Furan-2-aldehyde-3'-chloroacetophenone
(Chalcone 10)
Chalcone dibromide
Methanol
NH2-(CH2)4NH2
Furan-2-aldehyde-3'-chloroacetophenone quinoxaline


Br2 + CH3 COOH
Ethanol
2'-Hydroxynapthaldehyde-3'-chloroacetophenone
(Chalcone 11)
Chalcone dibromide
Methanol
NH2-(CH2)4NH2
2'-Hydroxynapthaldehyde-3'-chloroacetophenone quinoxaline

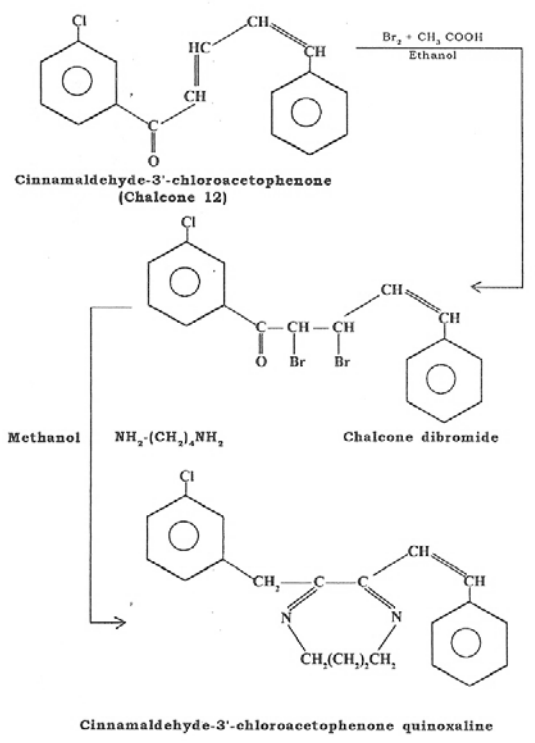

Br2 + CH3 COOH
Ethanol
Cinnamaldehyde-3'-chloroacetophenone
(Chalcone 12)
Chalcone dibromide
Methanol
NH2-(CH2)4NH2
Cinnamaldehyde-3'-chloroacetophenone quinoxaline

Table 1:

S. No.	Molecular formula of Chalcones	Colour	m.p. °C	Elemental Analysis % Calc (Found) C	H	S	Cl
1.	$C_{13}H_{10}OS$	Light Orange	142	72.98 (72.13)	4.67 (4.31)	14.95 (14.29)	
2.	$C_{19}H_{14}O_2$	Light Orange	156	78.78 (78.71)	5.05 (5.00)		
3.	$C_{17}H_{14}O_2$	Light Yellow	168	83.21 (82.18)	5.10 (5.00)		
4.	$C_{17}H_{14}O$	Light Yellow	140	87.17 (87.08)	5.98 (5.92)		
5.	$C_{14}H_{12}O_3S$	Light Yellow	192	64.61 (64.56)	4.61 (4.56)	12.30 (12.26)	
6.	$C_{14}H_{12}O_4$	Yellowish White	169	68.85 (68.72)	4.91 (4.82)		
7.	$C_{20}H_{16}O_3$	Light Yellow	168	78.94 (78.82)	5.26 (5.20)		
8.	$C_{18}H_{16}O_3$	Dark Cream	142	77.14 (77.10)	5.71 (5.55)		
9.	$C_{13}H_9OClS$	Light Yellow	197	62.77 (62.56)	3.62 (3.56)	12.87 (12.56)	14.28 (14.13)
10.	$C_{13}H_9O_2Cl$	Yellowish Orange	172	67.09 (67.00)	3.87 (3.79)		15.26 (15.13)
11.	$C_{19}H_{13}O_2Cl$	Light Orange	174	73.90 (73.89)	4.21 (4.18)		11.50 (11.34)
12.	$C_{17}H_{13}OCl$	Light Orange	178	75.97 (75.89)	4.84 (4.72)		13.22 (13.12)

Table 2:

S. No.	Molecular Formula	Characteristic peaks of in IR Spectra		Characteristics peak of chalcone in NMR Spectra
1.	$C_{13}H_{10}OS$	1735(-C = 0)	(1)	7.91 (1H, d, J = 16Hz, C-5-H,
		1640 (-CH = CH-)	(2)	7.80 (1H, d, J = 16Hz, C-6-H)
		730 (C-S-C)	(3)	7.04 (1H, dd, CH = CH), 6.75 (n, 70d)
		(C = C) 1590	(4)	(Ar -H)
2.	$C_{13}H_{10}O_2$	1740 (-C = O), 1645 (-CH = CH-)		7.89 (1H, d, J = 16Hz, C - 5-H)
		1595 (C = C), 1235 υ(-C-O-C) (5)		7.81 (1H, d, J = 16Hz, C - 4- H)
3.	$C_{19}H_{14}O_2$	3100(-OH), 1720 (-C = O)		7.88 (1H, d, J = 16Hz, C-5-H)
		1635 (-CH = CH-)		7.3 (m, 20H, Ar - H)

4.	$C_{17}H_{14}O$	1670 u(C = 0) (Chalcone moiety) 1580 u(-CH = CH -) (Chalcone moiety) 1590 u(-C = C)	8.1 (d, 1H, Ar - CH =) (6) 7.0 (m, 18H, Ar - H)
5.	$C_{13}H_{10}O_3$	3106 u(-OH) 1725 u(-C = O) 1642 u(-CH = CH-) 1192 (-O-CH_3) 1580 υ(- C = C-)	7.98 (1H, d, J = 16 Hz, C - 5 - H) 7.77 (1H, d, J = 16 Hz, C - 4 - H)
6.	$C_{14}H_{12}O_4$	3100 υ(-OH) 1721 υ(-C = O) 1640 (-CH = CH-) 1180 υ(-O - CH_3) 1590 υ(-C = C-)	7.85 (1H, d, J = 16 Hz, C - 5 - H) 7.78 (1H, d, J = 16 Hz, C- 4- H)
7.	$C_{20}H_{16}O_3$	3110 υ(-OH) 1720 υ(-C = O) 1645 υ(-CH = CH-) 1195 υ(-O - CH_3)	7.96 (1H, d, J = 16 Hz, C - 5 - H) 7.77 (1H, d, J = 16 Hz, C - 4 - H)
8.	$C_{18}H_{16}O_3$	3090 υ(-OH) 1715 υ(-C = O) 1640 υ(-CH = CH-) 1190 (-O-CH_3)	7.98 (1H, d, J = 16 Hz, C - 5 - H) 7.77 (1H, d, J = 16 Hz, C - 4 - H)
9.	$C_{13}H_9OClS$	3075 υ(-OH) 1720 υ(-C = O) 1639 υ(-CH = CH-) 845 υ(-C - Cl)	7.96 (1H, d, J = 16 Hz, C - 5 - H) 7.77 (1H, d, J = 16 Hz, C- 6- H)
10.	$C_{13}H_9O_2Cl$	3110 υ(-OH) 1725 υ(-C = O) 1645 υ(-CH = CH-) 848 υ(-C - Cl)	7.96 (1H, d, J = 16 Hz, C - 5 - H) 7.77 (1H, d, J = 16 Hz, C - 6 - H)
11.	$C_{13}H_9O_2Cl$	3090 υ(-OH) 1720 υ(-C = O) 1640 υ(-CH = CH-) 840 (-C-Cl)	7.99 (1H, d, J = 16 Hz, C - 7 - H) 7.77 (1H, d, J = 16 Hz, C - 8 - H)
12.	$C_{17}H_{13}OCl$	3100 υ(-OH) 1725 υ(-C = O) 1645 υ(-CH = CH-) 838 υ(-C - Cl)	7.62(2H, m, C - 4 and 5H) 7.71 (2H, bs, C - 2 and 4-H)

The characteristics peaks given in the above table indicate the formation of the chalcone

Table 3:

S. No.	Molecular formula of quinoxalines	Colour	m.p. °C	Elemental Analysis % Calc (Found) C	H	N	S	Cl
1.	$C_{17}H_{18}N_2S$	Light Yellow	189	72.34 (72.12)	6.38 (6.21)	9.92 (9.89)	11.34 (11.28)	
2.	$C_{17}H_{18}N_2O$	Yellowish white	210	79.69 (76.65)	6.76 (6.71)	10.52 (10.48)		
3.	$C_{23}H_2N_2O$	White	212	80.70 (80.67)	6.43 (6.41)	8.18 (8.16)		
4.	$C_{21}H_{23}N_2$	White	192	83.16 (83.12)	7.59 (7.51)	9.24 (9.20)		
5.	$C_{17}H_{20}N_2O_2S$	Light Cream	211	65.55 (64.51)	6.32 (6.29)	8.86 (8.82)	10.12 (10.10)	
6.	$C_{17}H_{20}N_2O_3$	Yellowish white	208	68.00 (67.5)	6.66 (6.61)	9.33 (9.29)		
7.	$C_{23}H_{24}N_2O_3$	Yellow	192	73.40 (73.36)	6.39 (6.32)	7.44 (7.39)		
8.	$C_{21}H_{25}N_2O_2$	Dark cream	195	74.77 (74.72)	7.41 (7.40)	8.30 (8.27)		
9.	$C_{17}H_{17}M_2OCl$	Light cream	250	64.45 (64.43)	5.37 (5.32)	8.84 (8.80)	10.11 (10.08)	11.21 (11.18)
10.	$C_{17}H_{17}N_2OCl$	Light cream	255	67.88 (67.79)	5.65 (5.61)	9.31 (9.28)		11.81 (11.78)
11.	$C_{23}H_{21}N_2OCl$	Yellowish white	262	73.30 (73.27)	5.57 (5.52)	7.43 (7.39)		
12.	$C_{21}H_{22}N_2Cl$	Dark green	279	74.66 (74.64)	6.51 (6.49)	8.30 (8.28)		10.51 (10.48)

The quinoxalines were characterised by a I.R. and N.M.R. spectra. The important peaks are given in the table 4.

Table 4:

S. No.	Molecular Formula of quinoxalines	Characteristic peaks of in IR Spectra		Characteristics peak of chalcone in NMR Spectra
1.	$C_{17}H_{18}N_2S$	υ(-CH) - 2986 cm^{-1} υ(-C = N) -1589 cm^{-1} υ(-CN) -1220 cm^{-1} υ(-CH_2) - 785 cm^{-1} υ(-C-S-C) -730 cm^{-1}	(7)	5.2 to 5.4 (dd, 2H - CH_2) (7) 7.2 to 8.1 d(m, 13H (Ar -H)
2.	$C_{17}H_{18}N_2O$	υ(-CH) - 3000 cm^{-1} υ(-C = N) -1595 cm^{-1} υ(-CN) -1230 cm^{-1} υ(-CH_2) - 1380 cm^{-1}	(7)	5.1 to 5.3 (dd, 2H - CH_2) 7.1 to 8.0 d(m, 13H (Ar -H)
3.	$C_{23}H_{22}N_2O$	υ(-OH) - 3100 cm^{-1} υ(-CH) -3000 cm^{-1} υ(-C=N) -1590 cm^{-1} υ(-C≡N) - 1225 cm^{-1} υ(-CH_2) -1375 cm^{-1}		5.2 to 5.4 (dd, 2H - CH_2) 5.7 to 8.1 d(m, 13H (Ar -H)
4.	$C_{21}H_{23}N_2$	υ(-C-H) - 2980 cm^{-1}		5.1 to 5.3 (dd, 2H - CH_2)

		υ(-C = N) -1590 cm^{-1}	7.1 to 8.0 d(m, 13H (Ar -H)
		υ(-C - N) - 1225 cm^{-1}	
		υ(-CH_2) -1380 cm^{-1}	
5.	$C_{17}H_{20}N_2O_2S$	υ(-OH) - 3100 cm^{-1}	5.2 to 5.4 (dd, 2H - CH_2)
		υ(-CH) -2985 cm^{-1}	7.1 to 8.1 d(m, 13H (Ar -H)
		υ(-C=N) -1588 cm^{-1}	
		υ(-C N) - 1222 cm^{-1}	
		υ(-CH_2) -1378 cm^{-1}	
		υ(-C-S-C) -732 cm^{-1}	
		υ(-O-CH_3) - 1190 cm^{-1}	
6.	$C_{17}H_{20}N_2O_3$	υ(-OH) - 3100 cm^{-1}	5.1 to 5.2 (dd, 2H - CH_2)
		υ(-CH) -2990 cm^{-1}	7.2 to 8.1 d(m, 13H (Ar -H)
		υ(-C=N) -1592 cm^{-1}	
		υ(-C N) - 1225 cm^{-1}	
		υ(-CH_2) -1375 cm^{-1}	
		υ(O-CH_3) - 1192 cm^{-1}	
7.	$C_{23}H_{24}N_2O_3$	υ(-OH) - 3100 cm^{-1}	5.1 to 5.3 (dd, 2H - CH_2)
		υ(-CH) -2988 cm^{-1}	7.2 to 8.0 d(m, 13H (Ar -H)
		υ(-C=N) -1590 cm^{-1}	
		υ(-C≡N) - 1220 cm^{-1}	
		υ(-CH_2) -1375 cm^{-1}	
		υ(-O-CH_3) - 1190 cm^{-1}	
8.	$C_{21}H_{25}N_2O_2$	υ(-OH) - 3115 cm^{-1}	5.2 to 5.4 (dd, 2H - CH_2)
		υ(-CH) -3000 cm^{-1}	7.1 to 8.1 d(m, 13H (Ar -H)
		υ(-C=N) -1605 cm^{-1}	
		υ(-CN) - 1230 cm^{-1}	
		υ(-CH_2) -1380 cm^{-1}	
		υ(-O-CH_3) - 1195 cm^{-1}	
9.	$C_{17}H_{17}N_2ClS$	υ(-CH) - 2990 cm^{-1}	5.1 to 5.3 (dd, 2H - CH_2)
		υ(-C=N) -1592 cm^{-1}	7.2 to 8.0 d(m, 13H (Ar -H)
		υ(-C≡N) - 1222 cm^{-1}	
		υ(-CH_2) -1377 cm^{-1}	
		υ(C-S-C) - 730 cm^{-1}	
		υ(C-Cl) - 785 cm^{-1}	
10.	$C_{17}H_{17}N_2ClO$	υ(-CH) - 2990 cm^{-1}	5.1 to 5.3 (dd, 2H - CH_2)
		υ(-C=N) -1595 cm^{-1}	7.2 to 8.0 d(m, 13H (Ar -H)
		υ(-C≡N) - 1225 cm^{-1}	
		υ(-CH_2) -1380 cm^{-1}	
		υ(C-Cl) - 788 cm^{-1}	
11.	$C_{23}H_{21}N_2OCl$	υ(-OH) - 3100 cm^{-1}	5.2 to 5.4 (dd, 2H - CH_2)
		υ(-CH) -2990 cm^{-1}	7.1 to 8.1 d(m, 13H (Ar -H)
		υ(-C=N) -1592 cm^{-1}	
		υ(-C N) - 1222 cm^{-1}	
		υ(-CH_2) -1375 cm^{-1}	
		υ(C-Cl) - 785 cm^{-1}	
12.	$C_{21}H_{22}N_2Cl$	υ(-CH) - 2985 cm^{-1}	5.1 to 5.3 (dd, 2H - CH_2)
		υ(-C=N) -1590 cm^{-1}	7.2 to 8.0 d(m, 13H (Ar -H)
		υ(-C≡N) - 1220 cm^{-1}	
		υ(-CH_2) -1375 cm^{-1}	
		υ(C-Cl) - 785 cm^{-1}	
		υ(-CH=CH) -1640 cm^{-1}	

Table 5: AntiMicrobial activity of quinoxalines

S. No.	Molecular Formula of quinoxalines	Antifungal activity % inhibition	Antibacterial activity Zone of Inhibition in m.m.			
			S. aureus	*E. Coli*	*S. Parafyphia*	*B. Subtilis*
1.	$C_{17}H_{18}N_2S$	23	-	-	18	18
2.	$C_{17}H_{18}N_2O$	42	15	25	12	-
3.	$C_{23}H_{22}N_2O$	33	9	-	-	-
4.	$C_{21}H_{23}N_2$	54	10	-	9	-
5.	$C_{17}H_{20}N_2O_2S$	25	12	-	11	9
6.	$C_{17}H_{20}N_2O_3$	26	14	-	-	12
7.	$C_{23}H_{24}N_2O_3$	42	10	-	10	-
8.	$C_{21}H_{25}N_2O_2$	54	21	-	16	10
9.	$C_{17}H_{17}N_2ClS$	50	13	-	-	-
10.	$C_{17}H_{17}N_2ClO$	52	8	11	-	-
11.	$C_{23}H_{21}N_2OCl$	42	9	-	-	-
12.	$C_{21}H_{22}N_2Cl$	61	12	8	8	-
	Ciprofloxacine	-	25	24	20	23
	Fusarium saloni	83	-	-	-	

and ketone. The difference in the melting points of the constituents and product indicated the formation of chalcones.

Spectral Studies

The IR and NMR spectra of synthesised chalcones were recorded. The important peaks are given in table 2.

Synthesis of Aminoderivatives (Quinoxalines)

The chalcones were treated with bromine water and acetic acid in ethanolic solution when chalcone dibromide were obtained. This on treatment with tetramethylinediamine in methanolic solution gave quioxaline.

Characterisation of quinoxalines

The quinoxalines were characterized by a determination of m.p. and elemental analysis. The results are tabulated in Table 3.

Characterisation of chalcones

These chalcones were characterised by determination of m.p. and elemental analysis. The results of these studies are tabulated in Table-1.

Antimicrobial Activity

The antifungal and antibacterial activities of quinoxalines were carried out. And results are given in table-5.

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