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Synthesis, assessment of substituent effects from UV, IR, NMR spectra and antimicrobial activities of 2,4-dichloro-5-fluorophenyl chalcones

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ABSTRACT

A series of 2,4-dichloro-5-fluorophenyl chalcones were synthesized from 2,4-dichloro-5-fluoroacetophenone with various substituted benzaldehydes by crossed aldol condensation. The synthesized chalcones were characterized by their physical constants and spectral data. The UV absorption (λ max, nm), infrared spectral frequencies (v, cm⁻¹), and NMR chemical shifts (δ , ppm) of these chalcones were correlated with Hammett substituent constants, F and R parameter using single and multi-liner regression analysis. From the results of statistical analysis, the effects of substituent on the spectral group have been discussed. The antibacterial and antifungal activities of synthesized chalcones have been measured by Kirby-Bauerdisc-diffusion method.

Keywords: Crossed-Aldol condensation; Styryl 2,4-dichloro-5-fluorophenyl ketones;IR and NMR spectra; Substituent effects; Antimicrobial activities

INTRODUCTION

Science and technology plays an important role in the medical field especially the synthesis of new drugs and extraction core drugs ingredients from the medicinal plant which curing of particular disease. Latest research directed towards to synthesis [1] that type of core drug ingredients and evaluated biological activities [2]. This type research solving the medicinal need of mankind according to population growth which difficult met by cultivation. In this series researchers found out that flavonoids family plants contains 1, 3-diaryl propane skeleton is the reason for curing of diseases. Solvent-free methods [3-5] were useful for synthesis of 1, 3-diaryl propenone compounds. Chalcones are 1, 3 diaryl-2-propenones which available in the flavonoids family contains medicinal activities such as anti-microbial [7], anti-inflammatory [8], analgesic [9], anti-ulcerative [10], immune-modulatory [11], antimalarial [12], anti-cancer [13], anti-viral [14], anti-leishmanial [15], anti-oxidant [16], anti-tubercular[17], antihyperglycemic [18]etc. A compound having anti-oxidant activity prevents and counter acts the damage of the human tissue by the normal effects of physiological oxidation [19]. Spectral data were useful for prediction of ground state molecular equilibration such as *E s-cis*, *s-trans* and *Z s-cis* and *s-trans* conformers [20]. This correlation analysis were applied for studying the transition states of reaction mechanism[21], qualitative and quantitative analysis [22], assessment of substituent effects in oligo-peptides [23], enol-enone tautomerism [24]. Recently Subramanianet.al.[20] and Sathiyamoorthy et al.,[25]has studied the synthesis and spectral correlations of some heterocyclic chalcones and they observed satisfactory correlations. Sathiya moorthy et al., [25-27] also studied the same with some iodo- and hydroxy- substituted phenyl chalcones. With a view to above, there is no report available for UV, IR and NMR spectral correlation analysis with Hammett substituent constants, F and R parameters and antimicrobial activities in 2, 4-dichloro-5-fluorophenyl chalcones. Therefore the authors have taken efforts to study the spectral correlation and antimicrobial activities of the 2, 4-dichloro-5-fluorophenyl chalcones by synthesis of the chalcones and record their UV-Visible, IR and NMR spectra.

MATERIALS AND METHODS

General

All chemicals used were purchased from Sigma-Aldrich and E-Merck chemical company. Melting points of all chalcones were determined in open glass capillaries on V-SCIENTIFIC MP-DS melting point apparatus and are uncorrected. The Ultra-violet spectra of all chalcones were recorded using ELICO-double beam BL222 Bio-Spectrophotometer. Infrared spectra (KBr, 4000-400cm⁻¹) were recorded AVATAR-300 Fourier transform spectrophotometer. The NMR spectra of all chalcones were recorded fromINSTRUM AV300 operating at 500MHz for ¹H spectra and 125.46 MHz for ¹³C spectra in CDCl₃ solvent using TMS as internal standard.

Synthesisof2,4-dichloro-5-fluorophenylchalcones

An appropriate equi-molar quantities of 2,4-dichloro-5-fluoroacetophenone,substituted benzaldehydes(0.01 mol)and0.5g of sodium hydroxide in 15 mL of ethanol were shaken for 30 min(Scheme 1). The obtained crude yellow solid was filtered at the pump. Further this compound was purified by recrystallized with ethanol as pale yellow glittering solid. The analytical, physical constants and mass fragments data were presented in Table 1.



Scheme 1. Synthesis of 2,4-dichloro-5-fluorophenyl chalcones.

Table-1.Physical constants and mass spectral data of substituted styryl 2,4-dichloro-5-fluorophenyl ketenes

Entry	Х	M.F.	M.W.	Yield (%)	m.p.°C
1	Н	C15H9OFCl2	295	80	106
2	4-Br	C15H8OFCl2Br	374	78	148 (98)[28],95[39],105[30]
3	4-C1	C15H8OFCl3	329	78	124(102)[29], 102[30]
4	4-F	$C_{15}H_8OF_2Cl_2$	313	76	119(102)[28],102[39],102[30]
5	2-OH	$C_{15}H_8O_2FCl_2$	311	76	109
6	2-OCH ₃	$C_{16}H_{11}O_2FCl_2$	325	83	113(84)[28], 83[29]
7	4-OCH ₃	$C_{16}H_{11}O_2FCl_2$	325	83	116(80)[28], 64[29]
8	4-CH ₃	C ₁₆ H ₁₁ OFCl ₂	309	81	107
9	3-NO ₂	C15H8O3NFCl2	294	79	156(141)[28], 141[29], 144[30]
10	$4-NO_2$	C15H8O3NFCl2	340	79	163

RESULTS AND DISCUSSION

Spectral linearity

In the present investigation the Hammett spectral linearity of the synthesized chalcones has been studied by evaluating the substituent effects on the group frequencies. The assigned spectroscopic data of all chalcones such as absorption maxima $\lambda max(nm)$, infrared carbonyl stretches of vCOs-cis and s-trans, the deformation modes of vinyl part CH out of plane, in-plane, CH=CH and >C=C< out of planes(cm-1), NMR chemical shifts δ (ppm) of H α , H β , C α , C β , CO are assigned and these data are correlated with various substituent constants.

UVspectral study

The absorption maxima (λ maxnm) of synthesized 2,4-dichloro-5-fluorophenyl chalcones were assigned and resented in Table 2. These absorption maxima (λ maxnm) of these chalcones were correlated with Hammett substituent constants and F and R parameters using single and multi-linear regression analysis [1, 4, 22-27,31-36]. Hammett correlation involving the group frequencies and absorption maxima, the form of the Hammett equation employed is

 $\lambda = \rho \sigma + \lambda_o$

...(1)

Where λ_0 is the frequency for the parent member of these ries.

The results of statistical analyses [1, 4, 20, 25-27, 31-36] were presented in Table 3. The Hammett constants σ , σ + and σ I constants produced satisfactory correlations for all the substituents. The Hammett σ R constant, F and R parameters have shown poor correlation. The failure in correlation was due to the incapable of inductive and resonance effects of substituents on the absorption and is associated with the resonance-conjugative structure shown in Figure-1.



Fig. 1.The resonance-conjugative structure.

The multi-regression analysis of these frequencies of all ketones with inductive, resonance and Swain–Lupton's [37] constants produce satisfactory correlations as evident in equations (2 and 3).

UV(λ max, nm) = 311.99 (±4.365) + 15.988(±8.843) σ_{I} - 21.516(±7.514) σ_{R}	(2)
(R = 0.974, n = 10, P > 95%)	
UV(λ max, nm) = 312.20 (±4.295) + 13.734(±8.334)F - 18.298(±6.809)R	(3)
(R = 0.948, n = 10, P > 95%)	

IR spectral study

The measured carbonyl stretching frequencies (cm-1) of s-cis and s-trans isomers of present study are presented in Table-2 and the corresponding conformers were shown in Fig. 2. The stretching frequencies for carbonyl absorption are assigned based on the assignments made by Hays and Timmons [38] for *s*-*cis* and *s*-*trans* conformers at1690 and 1670 cm-1, respectively. These data have been correlated with Hammett substituent constants and Swain-Lupton's constants [37] and are presented in Table 3. In this correlation the structure parameter Hammett equation employed is as shown in the following equation:

$$v = \rho \sigma + v_o$$

...(4)

where v is the carbonyl frequencies of substituted system and vo is the corresponding quantity of unsubstitued system, σ is a Hammett substituent constant, which in principle is characteristics of the substituent and ρ is a reaction constant which is depend upon the nature of the reaction.

Entry	Х	UV	$\operatorname{IR} v(\operatorname{cm}^{-1})$						NMR δ(ppm)				
-		λmax	CO _(s-cis)	CO _(s-trans)	CH _{ip}	CH _{op}	CH=CH _{op}	C=C _{op}	H_{α}	H_{β}	CO	Cα	C _β
		(nm)											
1	Н	305	1632.88	1597.98	1259.34	886.00	1096.68	616.20	7.141	7.269	118.15	139.90	197.37
2	4-Br	325	1667.35	1595.03	1160.74	881.99	1019.11	540.02	7.058	7.495	117.41	138.74	190.82
3	4-C1	330	1666.73	1601.77	1172.95	879.28	1070.93	537.27	7.104	7.485	125.61	145.29	190.72
4	4-F	330	1660.27	1605.38	1156.16	821.34	1106.32	536.99	7.058	7.499	117.42	138.74	190.82
5	2-OH	330	1628.42	1604.87	1218.32	871.08	1091.74	621.40	7.308	7.807	121.48	143.41	192.47
6	2-OCH ₃	325	1654.07	1594.86	1170.65	882.29	1027.14	520.35	6.991	7.464	123.11	147.15	191.14
7	4-OCH ₃	325	1656.40	1593.94	1170.58	883.33	1075.87	599.52	6.988	7.462	117.30	139.14	191.14
8	4-CH ₃	320	1657.06	1589.02	1167.96	815.92	1073.71	575.34	7.076	7.486	117.35	142.04	191.22
9	3-NO ₂	310	1670.34	1608.55	1175.60	807.59	1074.95	532.81	7.271	7.652	122.94	143.19	190.18
10	4-NO ₂	325	1669.54	1600.08	1182.36	846.02	1121.26	541.62	7.336	7.604	117.69	140.20	190.07

Table 3. Results of statistical analysis of IR, ¹H-NMR, ¹³C-NMR and UV spectral values of substituted styryl-2,4-dichloro-5-fluorophenylketones with Hammett σ , σ^+ , σ_I , σ_R constants, F and Rparameters.

Frequency	Constant	r	T	0	c	n	Correlated derivatives
1 requeite y	Constant	0.041	322.08	P 1 007	8 8 1	10	H A Br A C A E 2 OH 2 OCH A OCH A CH 3 NO 4 NO
∧ _{max}	0 	0.941	222.90	-4.997	0.04	10	$H,4-B1,4-C1,4-F,2-OH,2-OCH_3,4-OCH_3,4-CH_3,3-NO_2,4-NO_2$
	0	0.931	210.00	-4.397	0.74	10	$H_4 - D_{1,4} - C_{1,4} - F_{1,2} - OH_{2,2} - OCH_{3,4} - OCH_{3,4} - CH_{3,5} - NO_{2,4} - NO_{2}$
	OI	0.947	210.00	10.222	0.70	10	$H,4-B1,4-C1,4-F,2-OH,2-OCH_3,4-OCH_3,4-CH_3,3-NO_2,4-NO_2$
	O _R	0.827	217.74	-10.421	7.13	10	$H,4-DI,4-CI,4-F,2-OH,2-OCH_3,4-OCH_3,4-CH_3,5-NO_2,4-NO_2$
	F	0.847	317.74	12.418	8.40	10	$H,4-Br,4-Cl,4-F,2-OH,2-OCH_3,4-OCH_3,4-CH_3,3-NO_2,4-NO_2$
70 ()	R	0.857	317.64	-17.639	6.99	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ ,4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
vCO _{s-cis} (cm ⁻)	σ +	0.906	1654.16	22.108	12.39	8	4-Br,4-Cl,4-F,2-OCH ₃ ,4-OCH ₃ , 4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ	0.905	1656.28	15.57	13.05	8	4-Br,4-Cl,4-F,2-OCH ₃ ,4-OCH ₃ , 4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σι	0.903	1641.51	41.785	11.24	8	H,4-Br,4-Cl,4-F,2-OCH ₃ , 4-OCH ₃ ,3-NO ₂ ,4-NO ₂
	σ_R	0.904	1661.48	23.006	13.94	8	4-Br,4-Cl,4-F,2-OCH ₃ ,4-OCH ₃ , 4-CH ₃ ,3-NO ₂ ,4-NO ₂
	F	0.906	1653.01	34.701	12.49	7	H,4-Br,4-Cl,4-OCH ₃ ,4-CH ₃ , 3-NO ₂ ,4-NO ₂
	R	0.905	1598.41	7.587	5.88	8	H,4-Br,4-Cl,2-OCH ₃ ,4-OCH ₃ , 4-CH ₃ ,3-NO ₂ ,4-NO ₂
$vCO_{s-trans}(cm^{-1})$	σ	0.844	1599.14	5.285	5.77	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ^+	0.906	1593.59	15.684	5.02	6	4-Br,4-Cl,4-F,4-OCH ₃ ,4-CH ₃ , 3-NO ₂
	σι	0.806	1599.44	1.326	6.44	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ_R	0.906	1592.82	16.517	4.68	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	F	0.806	1599.51	1.316	6.44	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	R	0.905	1598.41	7.587	5.88	8	H,4-Br,4-Cl,2-OCH ₃ ,4-OCH ₃ , 4-CH ₃ ,3-NO ₂ ,4-NO ₂
$vCH_{ip}(cm^{-1})$	σ	0.817	1183.67	-13.44	33.25	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
1. ,	σ^+	0.896	1182.37	-6.78	33.54	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σι	0.853	1207.16	-70.05	28.44	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ _R	0.8067	1184.18	8.06	33.65	10	H.4-Br.4-Cl.4-F.2-OH.2-OCH ₃ , 4-OCH ₃ , 4-OCH ₃ , 3-NO ₂ , 4-NO ₂
	F	0.854	1208.51	-68.27	28.28	10	H.4-Br.4-Cl.4-F.2-OH.2-OCH ₃ , 4-OCH ₃ , 4-OCH ₃ , 3-NO ₂ , 4-NO ₂
	R	0.811	1185.69	12.09	33.51	10	H 4-Br 4-Cl 4-F 2-OH 2-OCH ₂ 4-OCH ₂ 4-OCH ₂ 3-NO ₂ 4-NO ₂
$vCH_{r}(cm^{-1})$	σ	0.843	860.77	-33.92	30.23	10	H 4-Br 4-Cl 4-F 2-OH 2-OCH ₂ 4-OCH ₂ 4-CH ₂ 3-NO ₂ 4-NO ₂
ven _o p(em)	σ ⁺	0.837	857.50	-22 718	31.15	10	H 4-Br 4-Cl 4-F 2-OH 2-OCH2 4-OCH2 4-CH2 3-NO2 4-NO2
	o o	0.827	869.66	-34 403	32 35	10	H 4-Br 4-Cl 4-F 2-OH 2-OCH 2-O
	on on	0.835	8/8 78	-38 657	31.42	10	H A-Br A-C1 A-E 2-OH 2-OCH ₂ A-OCH ₂ A-OCH ₂ 3-NO ₂ A-NO ₂
	6 _R	0.835	875 71	-47 587	31.42	10	H 4-Br 4-C1 4-E 2-OH 2-OCH 4-OCH 4-CH 3-NO 4-NO
	P	0.820	8/0.21	30.084	32.06	10	H_{4} Br 4 Cl 4 F 2 OH 2 OCH 4 OCH 4 CH 3 NO 4 NO
VCH-CH (om ⁻¹)	κ σ	0.829	1070.64	-30.064	20.54	10	H_{4} $P_{r,4}$ $C_{1,4}$ $F_{2,2}$ $OH_{2,2}$ $OCH_{3,4}$ $+ OCH_{3,4}$ $+ CH_{3,5}$ $+ NO_{2,4}$ $+ NO_{2}$
vcn-cn _{op} (cm)	0 	0.800	1070.04	4.140	29.54	10	$H,4-B1,4-C1,4-F,2-OH,2-OCH_3,4-OCH_3,4-CH_3,3-NO_2,4-NO_2$
	0	0.807	1076.29	-4.200	29.5	10	$H_4 Pr_4 Cl_4 F_2 OH_2 OCH_4 OCH_4 CH_3 NO_4 NO_2$
	OI	0.812	1070.28	-14.70	29.55	10	$H,4-B1,4-C1,4-F,2-OH,2-OCH_3,4-OCH_3,4-CH_3,3-NO_2,4-NO_2$
	O _R	0.803	10/1.05	1.500	29.57	10	H_{4} = H_{2} = H_{2} = H_{2} = H_{2} = H_{2} = H_{3} = H_
	F	0.804	1009.28	4.590	29.57	10	$H,4-BF,4-CI,4-F,2-OH,2-OCH_3,4-OCH_3,4-CH_3,5-NO_2,4-NO_2$
wC C (and)	ĸ	0.802	10/0.44	-2.170	29.59	10	H,4-BF,4-CI,4-F,2-OH,2-OCH ₃ ,4-OCH ₃ ,4-OCH ₃ ,3-NO ₂ ,4-NO ₂
$vC = C_{op}(cm)$	σ +	0.742	505.48	-44.830	35.9	10	H,4-BF,4-CI,4-F,2-OH,2-OCH ₃ ,4-OCH ₃ ,4-OCH ₃ ,3-NO ₂ ,4-NO ₂
	0	0.732	501.18	-38.000	29.90	10	$H_4 - B_{1,4} - C_{1,4} - F_{1,2} - OH_{2,2} - OCH_{3,4} - OH_{3,4} - CH_{3,5} - NO_{2,4} - NO_{2}$
	OI	0.703	554.01	-110.76	20.09	10	$H_4 - B_{1,4} - C_{1,4} - F_{1,2} - OH_{2,2} - OCH_{3,4} - OCH_{3,4} - CH_{3,3} - NO_{2,4} - NO_{$
	σ _R	0.802	554.91	-27.00	39.80	10	$H,4-Br,4-Cl,4-F,2-OH,2-OCH_3,4-OCH_3,4-CH_3,5-NO_2,4-NO_2$
	F	0.806	597.84	-95.82	31.5	10	$H,4-Br,4-Cl,4-F,2-OH,2-OCH_3,4-OCH_3,4-CH_3,5-NO_2,4-NO_2$
SIL	ĸ	0.823	352.54	-31.20	39.41	10	$H,4-Br,4-Cl,4-F,2-OH,2-OCH_3,4-OCH_3,4-CH_3,3-NO_2,4-NO_2$
δHα(ppm)	σ	0.906	7.109	0.174	0.1	9	H,4-Br,4-Cl,4-F,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ	0.905	7.126	0.129	0.102	9	H,4-Br,4-Cl,4-F,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σι	0.828	7.076	0.142	0.119	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ _R	0.904	7.164	0.165	0.114	9	H,4-Br,4-Cl,4-F,2-OCH ₃ ,4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	F	0.828	7.059	0.132	0.12	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
ST10 (K	0.904	7.169	0.155	0.114	9	H,4-Br,4-Cl,4-F,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
ðHβ(ppm)	σ	0.902	7.513	0.085	0.145	8	4-Br,4-Cl,4-F,2-OCH ₃ ,4-OCH ₃ , 4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ^{-}	0.901	7.522	0.049	0.147	8	4-Br,4-Cl,4-F,2-OCH ₃ ,4-OCH ₃ , 4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σι	0.904	7.436	0.243	0.135	8	4-Br,4-Cl,4-F,2-OCH ₃ ,4-OCH ₃ , 4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ _R	0.901	7.504	-0.079	0.147	8	4-Br,4-Cl,4-F,2-OCH ₃ ,4-OCH ₃ , 4-CH ₃ ,3-NO ₂ ,4-NO ₂
	F	0.846	7.422	0.260	0.132	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	R	0.818	7.499	-0.082	0.147	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
δCO(ppm)	σ	0.805	191.75	-1.683	2.144	8	4-Br,4-Cl,4-F,2-OCH ₃ ,4-OCH ₃ , 4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ^+	0.806	191.59	-0.932	2.203	8	4-Br,4-Cl,4-F,2-OCH ₃ ,4-OCH ₃ , 4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ_{I}	0.792	193.65	-5.819	1.685	9	4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ_R	0.791	191.64	0.212	2.261	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	F	0.812	193.68	-5.465	1.716	8	4-Br,4-Cl,4-F,2-OCH ₃ ,4-OCH ₃ , 4-CH ₃ ,3-NO ₂ ,4-NO ₂
	R	0.790	191.71	0.435	2.581	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
δCa(ppm)	σ	0.801	119.8	0.422	3.314	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ^+	0.815	119.84	0.392	3.312	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ_{I}	0.804	118.79	2.953	3.229	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ_R	0.824	119.55	-1.288	3.295	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	F	0.813	119.27	1.478	3.295	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	R	0 791	119.82	-0.087	3 3 1 9	10	H 4-Br 4-Cl 4-F 2-OH 2-OCH, 4-OCH, 4-CH, 3-NO, 4-NO,

δCβ(ppm)	σ	0.903	141.91	-1.416	3.051	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ^+	0.902	141.77	-0.850	3.075	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ_{I}	0.906	141.96	-0.538	3.108	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	σ_R	0.802	141.22	-2.473	3.018	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	F	0.906	142.38	-1.588	3.081	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	R	0.806	141.48	-1.048	3.091	10	H,4-Br,4-Cl,4-F,2-OH,2-OCH ₃ , 4-OCH ₃ ,4-CH ₃ ,3-NO ₂ ,4-NO ₂
	r- apprelation	n acofficia		anti a-alan	as a at at	daud	deviation - n-number of completed devicesting

r=correlation coefficient; *I*=intercept; ρ =slope; *s*=standard deviation; *n*=number of correlated derivatives

The results of single parameter statistical analysis[1,4, 22-27,31-36]of carbonyl frequencies of *s*-*cis* and *s*-*trans*con formers with all Hammett substituent constants, F and R parameters were shown satisfactory correlation excluding H, 2-OH, 2-OCH₃and4-F_{substituents}. Hammett σ , σ _I constants and F parameters have shown satisfactory correlation for the carbonyl stretches of *s*-*trans*conformers excluding H, 2-OH, 2-OCH₃and4-F substituents. The remaining Hammett constants and R parameters were failed in correlation. The failure incorrelationisdue thereasons stated earlier and it is associated with the resonance-conjugative structure shown in Figure-1.All correlations gave positive ρ values. This may mean that the normal substituent effects operates in all system.



Fig. 2. The s-cis and s-trans conformers of 2,4-dichloro-5-fluorophenylchalcones

In view of the inability of some of the σ constants to produce individually satisfactory correlations, it was thought that worthwhile to seek multiple correlations involving either σ_I and σ_R constants or Swain-Lupton's [37] F and R parameters. The correlation equations for *s*-*cis*, *s*-*trans* and *deformation modes* are given in equations (5-16).

$vCO_{s-cis}(cm^{-1}) = 1646.54(\pm 7.554) + 37.568(\pm 15.301)\sigma_{I} + 15.734(\pm 3.003)\sigma_{R}$	(5)
(r = 0.975, n = 10, P > 95%)	
$vCO_{s-cis}(cm^{-1}) = 1648.54(\pm 7.917) + 33.385(\pm 15.373)F + 18.290(\pm 12.560)R$	(6)
(r = 0.971, n = 10, P > 95%)	
$vCO_{s-trans}(cm^{-1}) = 1593.01(\pm 3.689) + 16.167(\pm 7.473)\sigma_{I} - 1.802(\pm 0.351)\sigma_{R}$	(7)
(r = 0.963, n = 10 P > 95%)	
$vCO_{s-trans}(cm^{-1}) = 1592.98(\pm 3.383) + 16.479(\pm 6.569)F + 0.525(\pm 0.367) R$	(8)
(r = 0.968, n = 10, P > 95%)	
$vCH_{ip}(cm^{-1}) = 1214.45(\pm 20.410) - 76.163(\pm 41.343)\sigma_{I} + 22.804(\pm 5.133)\sigma_{R}$	(9)
(r = 0.956, n = 10, P > 95%)	
$vCH_{ip}(cm^{-1}) = 1213.186(\pm 20.117) - 69.389(\pm 39.06)F + 15.430(\pm 3.911) R$	(10)
(r = 0.956, n = 10, P > 95%)	
$vCH_{op}(cm^{-1}) = 858.867(\pm 22.730) - 25.358(\pm 6.043)\sigma_{I} - 33.749(\pm 9.127)\sigma_{R}$	(11)
(r = 0.939, n = 10, P > 95%)	
$vCH_{op}(cm^{-1}) = 867.270(\pm 21.417) - 45.581(\pm 4.583)F - 27.896(\pm 3.973) R$	(12)
(r = 0.947, n = 10, P > 95%)	
$vCH=CH_{op}(cm^{-1}) = 1078.457(\pm 21.636) - 16.611(\pm 4.826)\sigma_{I} + 6.797(\pm 3.243)\sigma_{R}$	(13)
(r = 0.914, n = 10, P > 95%)	
$vCH=CH_{op}(cm^{-1}) = 1068.56(\pm 21.376) + 4.765(\pm 1.505)F - 2.407(\pm 1.909) R$	(14)
(r = 0.904, n = 10, P > 95%)	
$vC = C_{op}(cm^{-1}) = 598.258(\pm 21.299) - 109.023(\pm 43.145)\sigma_{\Gamma} - 6.564(\pm 3.664)\sigma_{R}$	(15)
(r = 0.970, n = 10, P > 95%)	
$vC=Cop(cm^{-1}) = 589.74(\pm 21.868) - 93.896(\pm 42.460)F-26.752(\pm 4.690) R$	(16)
(r = 0.967, n = 10, P > 95%)	

NMR Spectral study ¹H NMR spectral study

The 1H NMR spectra of synthesized chalcones have been recorded using deuteriochloroform (CDCl₃) as solvent and employing tetramethylsilane (TMS) as internal standard. The ethylenic protons signals of the chalcones were assigned from their spectra. They were calculated as AB or AA' or BB' systems respectively. The lower chemical shifts (δ , ppm) obtained for H α and higher chemical shifts (δ , ppm) obtained for H β in this series of ketones. The vinyl protons give an AB pattern and the β -proton doublets were well separated from the signals of the aromatic protons. The assigned vinyl proton chemical shifts (δ , ppm) of all ketones were presented in Table 2. In nuclear magnetic resonance spectra, the proton or the 13Cchemical shifts (δ , ppm) depends on the electronic environment of the nuclei concerned. The assigned vinyl proton chemical shifts (δ , ppm) have been correlated with reactivity parameters using Hammett equation in the form of

$$Log\delta = Log\delta_{o} + \rho\sigma$$
 ... (17)

Where δo is the chemical shift (δ , ppm) of unsubstitued ketones.

The assigned H α and H β proton chemical shifts ((δ , ppm) ppm) are correlated with various Hammett sigma constants. The results of statistical analysis [1, 4, 22-27, 31-36] are presented in Table 3. The obtained correlation is satisfactory for both H α and H β with Hammett σ , σ +, σ I and σ R constants also with F and R parameters excluding H and 2-OH substituents.

While seeking the multi-correlation by the application of Swain-Lupton's [37] treatment to the relative chemical shifts (δ , ppm) of H α and H β with F and R values is successful with resonance, inductive effect generates the multi-regression equations (18-21).

$\delta H\alpha (ppm) = 7.123(\pm 10.082) + 0.1030(\pm 0.1671)\sigma_I + 0.145 (\pm 0.142) \sigma_R$	(18)
(r = 0.945, n = 10, P > 95%)	
$\delta H\alpha (ppm) = 7.1211(\pm 0.0792) + 0.122(\pm 0.153)F + 0.149(\pm 0.125)R$	(19)
(r = 0.948, n = 10, P > 95%)	
$\delta H\beta (ppm) = 7.493(\pm 0.0640) + 0.301(\pm 0.439)\sigma_{I} - 0.175(\pm 0.343)\sigma_{R}$	(20)
(r = 0.930, n = 10, P > 95%)	
$\delta H\beta (ppm) = 7.393(\pm 0.092) + 0.267(\pm 0.180)F - 0.094(\pm 0.147)R$	(21)
(r = 0.951, n = 10, P > 95%)	

¹³C NMR spectral study

Scientists and physical organic chemists [1, 4, 22-27, 31-36] have made extensive study of 13C NMR spectra for a large number of different ketones and styrenes. The assigned vinyl C α , C β and carbonyl carbon chemical shifts (δ , ppm) are presented in Table 2. The results of statistical analysis are given in Table 3. Both C α and C β chemical shifts (δ , ppm) gave satisfactory correlation with Hammett σ , σ +, σ I, σ R constants, F and R parameters.

The chemical shifts (δ , ppm) of CO carbons with Hammett substituent constants, F and R parameters gave poor correlation. The obtained correlation is satisfactory with Hammett σ , σ +, σ I and σ R constants also with F and R parameters excluding H and 2-OH substituents. This is due to the reason stated earlier and associated with resonance-conjugative structure shown in Figure. 1.

While seeking the multi-regression analysis through Swain-Lupton's [36] parameter correlations were satisfactorily obtained with in these carbon chemical shifts (δ , ppm) and the regression equations are given in (22-27).

$\delta CO(ppm) = 194.106(\pm 1.206) - 6.198(\pm 2.443)\sigma_{I} + 1.412(\pm 2.076)\sigma_{R}$	(22)
(r = 0.928, n = 10, P > 95%)	
δ CO (ppm) = 193.9(±1.230) - 5.515(±2.388)F+ 0.700(±1.951)R	(23)
(r = 0.912, n = 10, P > 95%)	
$\delta C\alpha (ppm) = 118.171 (\pm 2.347) + 3.479 (\pm 4.754) \sigma_{I} - 1.961 (\pm 4.040) \sigma_{R}$	(24)
(r = 0.934, n = 10, P > 95%)	
$\delta C\alpha (ppm) = 119.229 (\pm 2.382) + 1.489 (\pm 4.625) F - 0.159 (\pm 3.779) R$	(25)
(r = 0.917, n = 10, P > 95%)	
$\delta C\beta(ppm) = 141.169 (\pm 2.230) + 0.130(\pm 4.517)\sigma_{I} - 2.498(\pm 3.838) \sigma_{R}$	(26)
(r = 0.969, n = 10, P > 95%)	
$\delta C\beta$ (ppm) = 142.091 (±2.216) - 1.518(±4.302)F - 0.975(±3.515) R	(27)
(r = 0.965, n = 10, P > 95%)	

Antimicrobial Activity Antibacterial activity:

The newly synthesized chalcones were subjected to antimicrobial activity against gram positive bacteria *Bacillus subtilis,M.luteus* and *S.aureus* gram negative bacteria *Escherichia coli,P.aeruginosa* and *k.pneumonias* by using cup and plate method. The agar medium was purchased from *HI MEDIA* Laboratories Ltd, Mumbai,India. The agar medium prepared by dissolving 2.5 g of agar in 100 mL water at boiled condition as per standard procedure. The bubble free medium poured in to Petri dishes and allowed to cool under closed condition for gel formation.After streaking microorganism Whatman no-40 discs of 6.0 mm in diameter laid on the gel to identify the inhibition zones. The test compounds prepared by dissolving 5 mg each compound in 5 mL of dimethyl sulphoxide. The solution of each compound 0.1 mL were added on what man disc and incubated at 37 deg. C for 24 Hour. A reference standard drug of gram positive and gram negative bacteria was made by dissolving 5.0 mg of ampicillin in 5.0 mL of distilled water separately. All the experiments were carried out duplicate to avoid error.Simultaneously reference was tested with 0.1 mL of dimethyl sulphoxide which not reveal any zone of inhibition.Diameter of inhibition zone produced by each compound was measured in mm. The measurement of antibacterial activities[39] mm of zone of inhibition of all chalcones were shown in Fig. 3.(plates 1-12) and the clustered column chart is shown in Fig.5.

		Zone of Inhibition (mm)									
Entry	Х	Gram posit	tive bacteria		Gram negative bacteria						
		B.subtilis	M.luteus	S.aureus	E.coli	P.aeruginosa	k.pneumonias				
1	Н	6	6		6						
2	4-Br	6	7	6	7		6				
3	4-Cl	7	9	6	8	6	6				
4	4-F	6	10	8	7	6	7				
5	2-OH	6			8	6	6				
6	2-OCH ₃	6	6	6		6					
7	4-OCH ₃			6	6	6	8				
8	4-CH ₃	6		6							
9	3-NO ₂	6	6	7		8	6				
10	4-NO ₂	6	6	7		6	6				
Standa	rd	9	8	8	10	8	8				
Ampicillin											
Control											
DMSO	DMSO										



Plate - 1



Plate - 3



Plate - 2





Fig. 3 The antibacterial activities of (mm of zone of inhibition) substituted styryl 2,4-dichloro-5-fluorophenyl ketones-Perti plates.



Fig. 4.The antibacterial activities of substituted styryl 2,4-dichloro-5-fluorophenyl ketones-clustered column chart.

The antibacterial activities of all chalcones were measured by the mm of zone of inhibition against their bacterial strains and are presented in Table 4. From Table 4, all synthesized chalcones except 4-methoxy substituted shows good zone of inhibition against *B.subtilis*strains. The 4-F substituted chalcones shows excellent antibacterial activities against *M.luteus* strains. The chalcones containing the substituents 2-hydroxy, 4-methoxy and 4-methyl substituted were inactive against *M.luteus* strains. All compounds shown good antibacterial activities against *S.aureus* strains except the chalcones containing the substituents 2 hydroxy, 4-methyl and nitro groups. Except the chalcones containing H, 4-Br and 4-CH₃ substituents have shown good antibacterial activity against *P.aeruginosas*train. The substituted styryl 2,4-dichloro-5-fluorophenyl ketones except the substituents H, 2-OCH₃ and 4-CH₃ have shown good antibacterial activity against *k.pneumonias* strain.



Enters	v	Mean zone of inhibition (mm)							
Entry	Λ	Aspergillusniger	Tricodermaviride	Mucor species					
1	Н	6	6	6					
2	4-Br	6	7	6					
3	4-C1	7	6	6					
4	4-F	7	6	6					
5	2-OH	11	10						
6	2-OMe	7	6	6					
7	4-OMe	7	10						
8	4-Me	7	6	6					
9	3-NO ₂	6	6	6					
10	4-NO ₂	7	10	6					
18	DMF								
19	Fluconazole	14	13	8					

Fig. 5.The anti-fungal activities of substituted styryl 2,4-dichloro-5-fluorophenyl ketone-Petri plates

Table 5.Anti-fungal activity of substituted styryl 2,4-dichloro-5-fluorophenyl ketones

Antifungal Activity

All the those compounds screened for antimicrobial activity[39] were also tested for antifungal activity using potato –dextrose-agar (PDA) medium same cup and plate method against *Aspergillusniger,Tricodermaviride* and *Mucor species*. Preparation of nutrient broths, subculture, base layer medium and PDA-medium was done as per the standard procedure. A reference standard drug fluconazole 5 mg dissolved in 5 mL of water 0.1 mL of solution used as a control which did not reveal any inhibition. The experiments were duplicated to minimize the error. Diameter of inhibition zone of produced by each compound was measured in mm and are shown in Fig. 5 (plates 1-6), compared values are tabulated in Table 5 and the clustered column chart is shown in Fig. 6.

All chalcones shown good and excellent anti-fungal activities against *Aspergillusniger* and *Tricodermaviride* fungal species. The compounds congaing substituents except 2-OH and 4-OMe were shown good antifungal activities against *Mucor species*.



Fig. 6. Anti-fungal activity of substituted styryl 2,4-dichloro-5-fluorophenyl ketone derivatives-clustered column chart.

CONCLUSION

Some of 2, 4-dichloro-5-fluorophenyl chalcones have been synthesized by condensation of 2, 4-dichloro-5-fluoroacetophenone and substituted benzaldehydes using aldol condensation. The chalcones have been characterized by their physical constants, spectral data. The UV, IR, NMR spectral data of these chalcones has been correlated with Hammett substituent constants, F and R parameters. From the results of statistical analyses the effects of substituent on the spectral data have been studied. The antimicrobial activities of all synthesized chalcone have been studied using Bauer-Kirby method. The antimicrobial screening results revealed that compounds containing electron releasing group as substituent showed better antibacterial activity than compound containing electron with drawing group. Compounds containing pharmacopores such as chloro, fluoro and nitro functional group shows more antifungal activity.

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