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Synthesis, spectral correlation and antimicrobial activities of some 3',4'-dimethyl phenyl chalcones

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ABSTRACT

About eleven substituted styryl3, 4-dimethyl phenyl ketones[1-(3, 5-dimethyl)-3-phenylprop-2-en-1-one] were synthesized using Crossed-aldol reaction. They are characterized by their analytical, ultraviolet, infrared and nmr spectral data. The spectroscopic data such as UV absorption λmax (nm), infrared νCOs-cis and s-trans stretches, the deformation modes of νCHin-plane, out of plane, CH=CH out of plane and C=C out of planes(cm^{-1}), NMR chemical shifts (ppm) of δHα, β and δCα, β and CO carbons were assigned their respective spectra. These data were correlated with Hammett substituent constants, F and R parameters using single and multi-linear regression analysis. From the results of statistical analysis, the effect of substituents on the above spectral frequencies were investigated. The antibacterial and fungal activities of these chalcones have been evaluated using Bauer-Kirby disc diffusion method with respective antibacterial and antifungal strains.

Keywords: Substituted styryl 3,5-dimethyl phenyl ketones; UV, IR and NMR spectra; Substituent effects; Hammett equation; Antibacterial and fungal activities

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INTRODUCTION

Chalcones are biosynthetic precursors of flavonoids found to possess cytotoxic and chemo preventive activities. Chalcones with 3, 4-dimethyl groups on ring were found to increase the biological activities. Chalcone compounds are natural compounds isolated from edible plants and are structurally chalcones having two phenyl rings separated by three carbon atom bridges with inhibitory property against bacterial and fungal strains[1-3]. Chalcone is an intermediate in the biosynthesis of flavonoid which substance is widespread in plants with an array of biological activities. Chalcones and their derivatives are also medicinally important as they were reported to display various biological activities such as antioxidant[4], antibacterial[5], antifungal[6], antitumor[7] and anti-inflammatory[8] activities. The presence of a reactive α, β-unsaturated keto function in chalcones was found to be responsible for their antimicrobial activity. A novel efficient synthesis chalcones by using $SOCl_2$-Ethanol as catalyst was used[9]. Various methods available for synthesizing chalcones such as Aldol, Crossed-Aldol, Claisen-Schmidt, Knovenagal, Greener methods Grinding of reactants, solvent free and oxides of nanoparticles with microwave heating. Also microwave assisted solvent free Aldol and Crossed-Aldol condensation[10-12] were useful synthesis of carbonyl compounds. Due to C-C single bond rotation[13] of carbonyl and alkene carbons, they exist as *Es-cis*and *s-trans* and *Zs-cis*and *Zs-trans* conformers. These structural conformers of chalcones have been confirmed by NMR and IR spectroscopy.

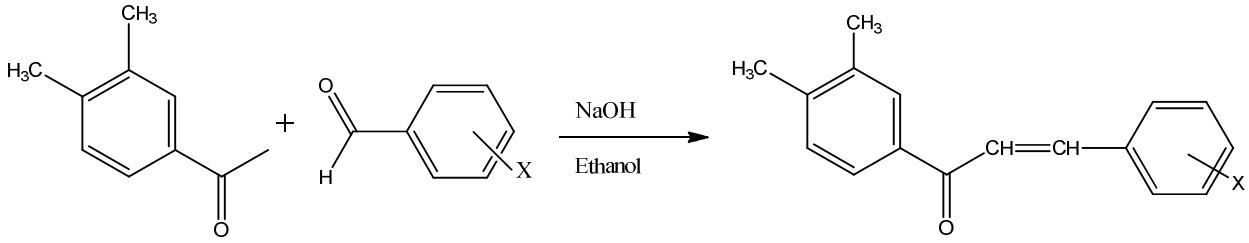
MATERIALS AND METHODS

General

All chemicals used were purchased from Sigma-Aldrich chemical company Bangalore. Melting points of all chalcones have been determined in open glass capillaries on Suntex melting point apparatus and are uncorrected. The Ultra violet spectra of the chalcones synthesized have been recorded using ELICO-double beam BL222 Bio-Spectrophotometer. Infrared spectra (KBr, 4000-400cm-1) have been recorded on AVATAR-300 Fourier transform spectrophotometer. BRUKER-500MHz NMR spectrometers have been utilized for recording ^{1}H and ^{13}C spectra in $CDCl_3$ solvent using TMS as internal standard.

General procedure for synthesis of 3', 4'-dimethyl phenyl chalcones

Appropriate mixture of 3',4'-dimethyl acetophenone (100mmol) and substituted benzaledhydes (100mmol) and aqueous solution of sodium hydroxide (200 ml 0.5M) with absolute ethanol. The reaction mixture was vigorously stirred at room temperature for 30 minutes(Scheme 1). After complete conversion of the ketones as monitored by TLC, the mixture was allowed to stand 20 minutes. The reagents were removed by filtration. The filtrate was washed with distilled water and recrystallized from absolute ethanol, dried well and kept in a desiccator. The analytical, physical constants and mass fragments of these chalcones are presented in Table 1. The Ultraviolet, Infrared and NMR spectral data of these chalcones were presented in Table 2.



Where X = H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-CH_3, 4-OCH_3, 3-NO_2, 4-NO_2

Scheme 1.Synthesis of 3', 4'-dimethyl phenyl chalcones

Table-1: Physical constants and mass spectral data of substituted styryl 3, 4-dimethyl phenyl ketones

Entry	X	Molecular Formula	Mol. Weight	m.p.(°C)	Mass (m/z)
1	H	$C_{17}H_{16}O$	236	72	236[M^+], 221, 207, 133, 131, 103, 77 , 15
2	3-Br	$C_{17}H_{15}BrO$	314	76	314[M^+], 316[M^{2+}], 299, 284, 235, 208, 180, 133, 105, 78, 77, 15
3	4-Br	$C_{17}H_{15}BrO$	314	121	314[M^+], 316[M^{2+}], 299, 284, 235, 208, 180, 133, 105, 78, 77, 15
4	2-Cl	$C_{17}H_{15}ClO$	270	62	270[M^+], 272[M^{2+}], 255, 241, 235, 165, 137, 105, 77, 34, 15
5	3-Cl	$C_{17}H_{15}ClO$	270	79	270[M^+], 272[M^{2+}], 255, 241, 235, 165, 137, 105, 77, 34, 15
6	4-Cl	$C_{17}H_{15}ClO$	270	136	270[M^+], 272[M^{2+}], 255, 241, 235, 165, 137, 105, 77, 34, 15
7	4-F	$C_{17}H_{15}FO$	254	141	254[M^+], 256[M^{2+}], 239, 235, 225, 149, 133, 121, 105, 77, 18, 15
8	4-OCH_3	$C_{18}H_{18}O_2$	266	91	266[M^+], 251, 237, 235, 161, 133, 105, 77, 31, 15
9	4-CH_3	$C_{18}H_{18}O$	250	68	250[M^+], 235, 221, 145, 133, 117, 105, 77, 15
10	3-NO_2	$C_{17}H_{15}NO_3$	281	110	281[M^+], 235, 176, 148, 133, 105, 77, 45
11	4-NO_2	$C_{17}H_{15}NO_3$	281	124	281[M^+], 235, 176, 148, 133, 105, 77, 45

Table 2. UV, IR and NMR spectral data of substituted styryl 3, 4-dimethyl phenyl ketones

Entry	X	UVλmax (nm)	IR ν(cm^{-1})						NMR δ(ppm)				
			$CO_{(s\text{-}cis)}$	$CO_{(s\text{-}trans)}$	CH_{ip}	CH_{op}	$CH{=}CH_{op}$	$C{=}C_{op}$	H_α	H_β	CO	C_α	C_β
1	H	312.4	1654.92	1591.27	1192.01	752.24	1045.42	553.57	7.571	7.831	190.19	122.26	144.20
2	3-Br	306.0	1662.64	1598.99	1199.72	785.03	1049.28	569.00	7.304	7.723	189.66	123.06	142.70
3	4-Br	317.4	1658.78	1597.06	1130.29	785.03	1043.94	576.72	7.547	7.747	196.45	122.75	142.74
4	2-Cl	306.0	1660.71	1595.13	1130.29	752.24	1043.49	576.72	7.505	8.185	190.13	125.06	140.02
5	3-Cl	306.0	1670.35	1589.34	1138.00	763.81	1058.92	582.54	7.555	7.744	189.74	123.43	142.43
6	4-Cl	314.8	1658.78	1589.99	1132.21	771.53	1053.13	567.07	7.532	7.733	189.88	122.65	142.67
7	4-F	313.4	1662.64	1595.13	1147.65	734.88	1043.49	575.70	7.489	7.813	189.96	121.96	142.47
8	4-OCH_3	343.2	1654.92	1587.42	1151.50	732.95	1041.56	540.07	7.444	7.808	190.28	126.16	144.08
9	4-CH_3	325.8	1629.85	1585.49	1163.08	750.31	1058.92	547.78	7.524	7.817	190.33	121.28	144.31
10	3-NO_2	262.0	1670.35	1595.13	1139.93	746.45	1053.13	545.85	7.455	7.838	189.29	122.12	142.96
11	4-NO_2	318.8	1660.71	1598.99	1145.72	758.02	1022.27	532.35	7.67	7.827	189.27	125.93	140.92

RESULTS AND DISCUSSION

Ultra violet spectral study

The UV spectra of all synthesized chalcones were recorded in SHIMADZU-1650 SPECTROMETER (λ_{max} nm) in spectral grade methanol. The measured absorption maxima (λ_{max} nm) of these chalcones are presented in **Table 2**. These values are correlated with Hammett substituent constants and F and R parameters using single and multi-linear regression analysis. Hammett correlation involving the group frequencies and absorption maxima, the form of the Hammett equation employed is

$$\lambda = \rho\sigma + \lambda_o \quad (1)$$

where$\lambda_o$is the frequency for the parent member of the series.

The results of statistical analysis of these values with Hammett substituent constants are presented in **Table 3**. From **Table 3,** Hammett substituent constants σ and σ^+ gave satisfactory correlations. From Table, Hammett substituent constants σ_I, σ_R and F and R values gave poor correlations with λmax. All constants gave negative ρ values. The poor correlation is due to the inability of predicting the substituent effects on the absorption maxima λmax and associated with the resonance-conjugative structure as shown in Fig. 1. The multi regression analysis of these

Fig. 1. The resonance conjugative-structure of ketones with inductive, resonance and Swain – Lupton's[14] constants produce satisfactory correlations as evident in equations 2 and 3.

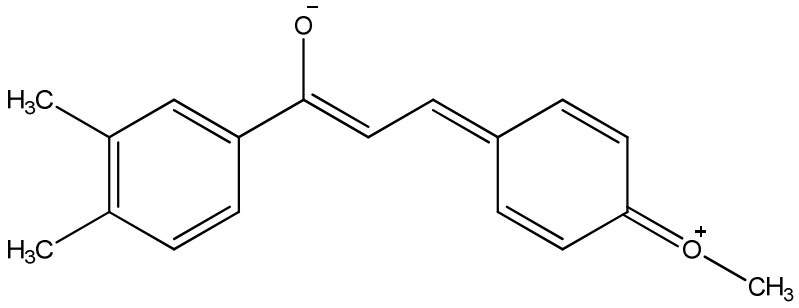


Table 3 Results of statistical analysis of substitutedstyryl 3, 4-dimethyl phenyl ketones

Frequency	Constants	r	I	ρ	s	n	Correlated derivatives
λ_{max}	σ	0.906	320.70	-40.109	15.14	9	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-CH_3, 3-NO_2
	σ^+	0.906	317.15	-29.525	14.80	9	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-CH_3, 3-NO_2
	σ_I	0.847	327.48	-40.122	18.22	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.852	303.83	-51.610	17.62	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.794	325.39	-34.127	18.82	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.795	302.44	-46.413	17.22	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
$\nu CO_{s\text{-}cis}$	σ	0.906	1653.86	20.524	8.83	10	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 3-NO_2, 4-NO_2
	σ+	0.905	1655.99	13.499	9.29	10	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 3-NO_2, 4-NO_2
	σ_I	0.907	1643.86	36.852	7.00	10	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 3-NO_2, 4-NO_2
	σ_R	0.876	1659.17	3.891	0.71	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.907	1645.38	32.301	8.00	10	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 3-NO_2, 4-NO_2
	R	0.865	1659.64	5.357	11.33	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
$\nu CO_{s\text{-}trans}$	σ	0.693	1590.85	9.642	3.51	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ+	0.907	1591.66	7.358	3.29	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.907	1587.49	13.970	3.49	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.827	1594.07	6.700	4.67	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.906	1587.78	12.966	3.64	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.827	1594.14	5.466	4.69	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
νCH_{ip}	σ	0.819	1161.30	-14.044	24.75	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.859	1162.43	-51.652	21.86	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.904	1159.09	-51.652	21.86	10	H, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.811	1170.51	14.335	25.06	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.854	1163.90	-45.837	22.45	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.806	1173.52	7.085	25.18	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
νCH_{op}	σ	0.833	753.23	18.418	17.37	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.841	753.96	18.226	16.26	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.818	752.01	13.717	18.24	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.823	761.11	24.579	17.81	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.818	757.25	0.596	18.54	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.798	761.89	22.713	17.67	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2

νCH=CH$_{op}$	σ	0.833	1048.70	-8.753	10.30	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.832	1047.58	-4.661	10.51	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.793	1052.84	-15.389	10.07	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.795	1045.61	-7.278	10.64	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.796	1053.12	-15.749	9.98	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.874	1045.79	-4.605	10.69	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
νC=C$_{op}$	σ	0.908	561.64	-4.212	18.17	9	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3
	σ^+	0.915	559.55	-5.735	18.01	9	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3
	σ_I	0.879	555.42	13.100	17.95	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.877	554.60	-41.179	16.04	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.815	555.96	11.513	18.00	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.835	555.31	-27.667	16.90	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
$\delta_{H\alpha}$	σ	0.823	7.502	-0.054	0.07	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.809	7.493	-0.015	0.07	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.833	7.533	-0.107	0.07	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.902	7.491	-0.010	0.07	9	H, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 4-NO_2
	F	0.833	7.532	-0.104	0.07	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.901	7.496	0.032	0.07	9	H, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 4-NO_2
$\delta_{H\beta}$	σ	0.871	7.827	-0.006	0.13	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.814	0.818	0.147	0.13	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.801	7.816	0.023	0.13	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.795	7.821	-0.028	0.13	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.864	7.824	0.002	0.13	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.804	7.830	0.025	0.13	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
δCO	σ	0.919	190.72	-1.201	2.10	10	H, 3-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.918	190.46	-0.080	2.14	10	H, 3-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.905	190.65	-0.524	2.14	10	H, 3-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.673	190.23	-1.394	2.12	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.671	190.74	0.776	2.13	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.599	190.17	-1.405	2.11	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
δCα	σ	0.903	123.30	-1.477	1.44	8	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 4-F, 4-CH_3, 3-NO_2
	σ^+	0.903	123.17	-1.084	1.44	9	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-CH_3, 3-NO_2
	σ_I	0.803	122.86	0.236	1.53	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.800	122.40	-3.780	1.31	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.805	123.10	-0.354	1.53	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.845	122.38	-2.958	1.35	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
δCβ(ppm)	σ	0.903	143.15	-1.423	1.14	9	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2
	σ^+	0.905	143.30	-1.422	1.03	9	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2
	σ_I	0.906	144.09	-3.161	0.97	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.791	142.93	0.743	1.23	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.908	143.90	-2.637	1.05	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.709	142.83	0.050	1.24	11	H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2

$\lambda_{(nm)}$ = 318.77 (±11.229)-35.679(±22.345)σ_I - 47.060(±25.968) σ_R (2)
(R = 0.967, n = 11, *P > 95%)*

$\lambda_{(nm)}$= 316.88 (±10.337) -35.977(±20.607)F -47.856(±20.994) R (3)
(R = 0.970, n = 11, *P > 95%*)

IR spectral study

The synthesized chalcones in the present study are shown in **Scheme 1**. The carbonyl stretching frequencies (cm^{-1}) of *s-cis* and *s-trans* isomers of present study are presentedin **Table 2**.The stretching frequencies for carbonyl absorption are assigned based on the assignments made by Hays and Timmons[15]for *s-cis* and *s-trans* conformers at 1690 and 1670 cm^{-1}, respectively. As anticipated the lowest carbonyl frequency is observed in both the conformers when strongest electron withdrawing group is present in phenyl ring while highest frequency is noted when strongest electro attracting group present in phenyl ring. A similarly trend in absorption was earlier noted by Perjessy and Hrnciar[16] too whose investigated on chalcones demonsrates that *s-trans* conformers transmit more effectively than *s-cis* conformers due to reason stated earlier. The difference in carbonyl frequencies between the *s-cis* and *s-trans* conformers is higher in this study than the difference observed by Silver and Boykin[17] between similar conformers in phenyl styryl ketones. These data have been correlated with Hammett substituent constants and Swain-Lupton constants[14]. The same trend was followed in the present study. The *s-cis* and *s-trans* conformers of the carbonyl stretches are presented in Table 2 and the correspondingconformers are shown in Fig. 2.

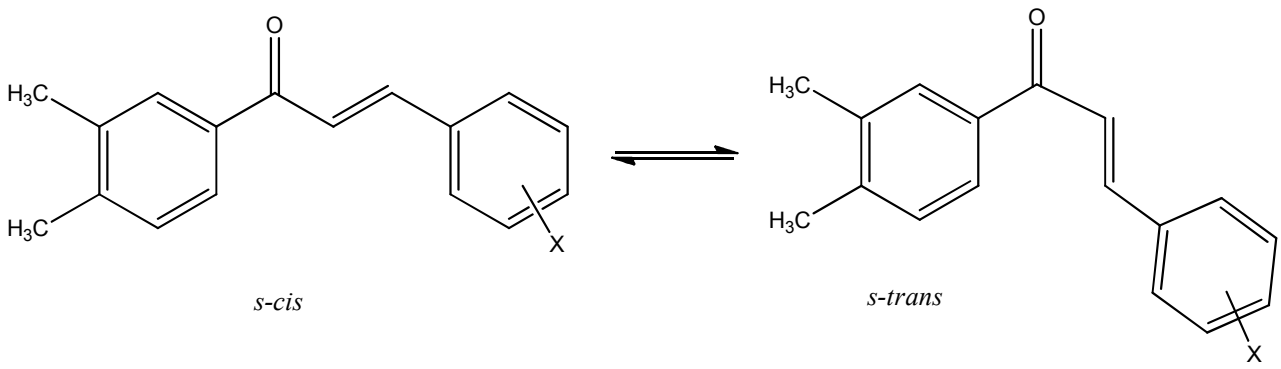


Fig. 2. The *s-cis* and *s-trans* con formers of 3,4-dimethoxy styryl phenyl chalcones

In this correlation the structure parameter Hammett equation employed is as shown in the following equation:

$$\nu = \rho\sigma + \nu_0 \quad (4)$$

Where ν is the carbonyl frequenciesof substituted system and υ_0 is the corresponding quantity of substituted system; σ is a Hammet 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. Hammett equation is one of the important tools for studying linear free energy relationships and it has been widely used in structures of the chemical reactivity of substituted aromatic system.

From **Table 3**, the s-*cis* conformer of the $\nu_{C=O}$ of satisfactory correlation with Hammett substituent constants and F parameter except resonance effect. And the s-*trans* conformer the $\nu_{C=O}$ of satisfactory correlation with Hammett substituent constants and F parameter except σ constant and resonance effect. All correlations gave positive ρ values and it implies that there is a normal substituent effect operates in all systems.

The correlations of CH *in-plane* modes have satisfactory correlation with Hammett constant σ_R. And other Hammett constants and F and R parameters have fails in correlation. All correlations gave negative ρ values and it implies that there is a reverse substituent effect operates in all systems.

All correlation has fails with CH *out of plane* modes with Hammett constants and F and R parameters. The CH *out of plane* modes gave positive ρ values in all correlations and it implies that there is a normal substituent effect operates in all systems.
All correlation were fails with CH=CH *out of plane* modes with Hammett constants andF and R parameters. All correlation gave negative ρ values and it implies that there is a reverse substituent effect operates in all systems.

The C=C *out of plane* modes have satisfactory correlation with Hammett constant σ_R. And other Hammett substituent constants and F and R parameters with C=C *out of plane* modes have fail in correlation. All correlation gave negative ρ values and it implies that there is a reverse substituent effect operates in all systems. The reasons for poor correlation was stated earlier and it is associated with the resonance conjugative structure as shown in Fig. 1. The multi regression analysis gave satisfactory correaltions. The correlated multi regression equations are given in (5) to(16).

$$\nu CO_{s\text{-}cis}(cm^{-1}) = 1643.71(\pm5.127) + 36.929(\pm10.202)\sigma_I + 11.856(\pm11.856)\,\sigma_R \quad (5)$$
(R = 0.978, n = 11, *P > 95%)*

$$\nu CO_{s\text{-}cis}(cm^{-1}) = 1646.57(\pm5.522) + 32.566(\pm11.009)F + 6.645(\pm11.216)R \quad (6)$$
(R = 0.972, n = 11, *P > 95%)*

$$\nu CO_{s\text{-}trans}(cm^{-1}) = 1588.41(\pm2.441) + 13.500(\pm4.8858)\sigma_I + 4.972(\pm5.646)\,\sigma_R \quad (7)$$
(R = 0.973, n = 11, *P > 95%*)

$$\nu CO_{s\text{-}trans}(cm^{-1}) = 1588.84(\pm2.341) + 13.198(\pm4.667)F + 5.996(\pm4.754)\,R \quad (8)$$
(R = 0.973, n = 11, *P > 95%*)

$\nu CH_{ip}^{(cm-1)} = 1176.43(\pm15.669) + 53.651(\pm31.180)\sigma_I + 21.174(\pm36.235)\ \sigma_R$ (9)
(R = 0.952, n = 11, *P > 95%)*

$\nu CHip(cm^{-1}) = 1171.54(\pm15.808) - 45.634(\pm31.513)F + 5.254(\pm32.105)R$ (10)
(R = 0.945, n = 11, *P > 90%*)

$\nu CHop(cm^{-1}) = 756.28(\pm12.873) + 11.535(\pm25.617)\sigma_I + 23.108(\pm29.771)\ \sigma_R$ (11)
(R = 0.934, n = 11, *P > 90%*)

$\nu CHop(cm^{-1}) = 761.30(\pm12.465) + 1.476(\pm24.8488)F + 22.772(\pm25.315)\ R$ (12)
(R = 0.934, n = 11, *P > 90%)*

$\nu CH{=}CHop(cm^{-1}) = 1051.84(\pm7.328) - 14.881(\pm14.582)\sigma_I - 5.381(\pm16.946)\ \sigma_R$ (13)
(r = 0.936, n = 11, *P > 90%)*

$\nu CH{=}CHop(cm^{-1}) = 1052.19(\pm6.992) - 15.937(\pm13.937)F - 5.245(\pm14.199)\ R$ (14)
(R = 0.934, n = 11, *P > 90%)*

$\nu C{=}Cop(cm^{-1}) = 547.40(\pm11.340) + 17.195(\pm22.565)\sigma_I - 43.372(\pm26.224)\ \sigma_R$ (15)
(R= 0.952, n = 11, *P > 95%)*

$\nu C{=}Cop(cm^{-1}) = 551.14(\pm11.776) + 10.460(\pm23.475)F - 27.247(\pm23.910)\ R$ (16)
(R= 0.949, n = 11, *P > 90%)*

NMR spectral study

^{1}H NMR study

From the ^{1}H NMR spectra of synthesized 3′, 4′-dimethylphenyl chalcones the chemical shift (δ, ppm) values of Hα and Hβ are assigned and tabulated in **Table 2**. These chemical shifts were correlated with Hammett substituent constants and F and R parameters. The statistical analysis1[18]of these chemical shifts is presented in **Table 3**. From **Table 3**, the Hα chemical shifts (δ, ppm) have shown satisfactory correlations with Hammett σ_R constant and R parameter. The remaining Hammett substituent constants and F parameter have shown poor correlations. The Hβ chemical shifts (δ, ppm) of these chalcones were fail in correlations with Hammett substituent constants and F and R parameters. The reasons for the failure in correlation are stated earlier and associated with the resonance – conjugated structure shown in **Fig. 1.**

Some of the single parameter correlations with Hammett substituent constants are not obeyed in the regression. While seeking these parameters in multi-regression, with F and R Swain-Lupton's[14]constants, they are found to show satisfactory correlations. The multi correlation equations are given in (17)-(20).

$\delta H_\alpha(ppm) = 7.537(\pm0.054) - 0.109(\pm0.107)\sigma_I + 0.024(\pm0.125)\ \sigma_R$ (17)
(R = 0.933, n = 11, *P > 90%)*

$\delta H_\alpha(ppm) = 7.538(\pm0.052) - 0.103(\pm0.103)F + 0.0238(\pm0.105)R$ (18)
(R = 0.934, n = 11, *P > 90%)*

$\delta H_\beta(ppm) = 7.810(\pm0.098) + 0.026\pm0.195)\sigma_I - 0.032(\pm0.226)\ \sigma_R$ (19)
(R = 0.906, n = 11, *P > 90%)*

$H_\beta(ppm) = 7.829(\pm0.094) + 0.003(\pm0.188)F + 0.025(\pm0.192)R$ (20)
(R = 0.905, n = 11, *P > 90%)*

^{13}C NMR spectra

The chemical shift (δ, ppm) values of carbonyl carbon, Cα and Cβ of 3′, 4′-dimethylphenyl chalcones are assigned and tabulated in **Table 2**. These chemical shifts are correlated[18]with Hammett substituent constants, F and R parameters. The results of statistical analysis are shown in **Table 3**. From **Table 3**, it is evident that the Hammett substituent constants, σ, σ^+, and σ_I have shown satisfactory correlations with Carbonyl carbon chemical shifts of these chalcones.

From **Table 3**, it is evident that the Hammett substituent constants σ and σ^+ have shown satisfactory correlations with Cα chemical shifts of these chalcones. The Cβ chemical shifts (δ, ppm) have shown satisfactory correlations with the Hammett σ, σ^+, σ_I constants and F parameter.

The failure in correlations of σ_R and F and R parameters with carbonyl carbon chemical shifts, and failure in correlations of σ_I and σ_R and F and R parameters with Cα chemical shifts, and failure in correlations of σ_R and R parameter with Cβ chemical shifts, is due to the reasons stated in earlier and associated with the resonance conjugative structure shown in Figure 1.

The multi regression analysis shows that the carbonyl carbon, Cα and Cβ chemical shift (δ, ppm) values of 3′, 4′-dimethylphenyl chalcones have been satisfactorily correlated with σ_I , $\sigma_R$and Swain-Lupton's[14]andF and R parameters. The multi-regression equations are given in (21)-(26).

$\delta CO(ppm) = 190.40(\pm1.553) -0.397(\pm3.091)\sigma_I -1.344(\pm3.592)\ \sigma_R$ (21)
(R = 0.914, n = 11, *P > 90%)*

$\delta CO\ (ppm) = 190.49(\pm1.486) -0.802(\pm2.962)F -1.437(\pm3.018)R$ (22)
(R = 0.918, n = 11, *P > 90%)*

$\delta C_\alpha\ (ppm) =122.15\ (\pm0.956) + 0.600(\pm1.903)\sigma_I - 3.856(\pm2.211)\ \sigma_R$ (23)
(r = 0.955, n = 11, *P > 95%)*

$\delta C_\alpha\ (ppm) =122.57\ (\pm0.949) -0.047(\pm1.892)F -2.977(\pm1.928)\ R$ (24)
(R = 0.948, n = 11, *P > 90%)*

$\delta C_\beta(ppm) =144.30\ (\pm0.692) -3.271(\pm1.378)\sigma_I +1.161(\pm1.602)\ \sigma_R$ (25)
(R = 0.964, n = 11, *P > 95%)*

$\delta C_\beta\ (ppm)=143.898(\pm0.743) - 2.639(\pm1.489)F -0.054(\pm1.509)\ R$ (26)
(R = 0.953, n = 11, *P > 95%)*

Antimicrobial activities

Chalcones possess a wide range of biological activities such as antibacterial, antifungal, antiviral, antifeedant, antimalarial, antituberculosis, and antioxidantactivities. These multipronged activities present in different chalcones are examined against respective microbes-bacteria's and fungi.

Antibacterial sensitivity assay

Antibacterial sensitivity assay was performed using Kirby-Bauer[19] disc diffusion technique. In each Petri plate about 0.5 ml of the test bacterial sample was spread uniformly over the solidified Mueller Hinton agar using sterile glass spreader. Then the discs with 5mm diameter made up of Whatman No.1 filter paper, impregnated with the solution of the compound were placed on the medium using sterile forceps. The plates were incubated for 24 hours at 37^{o}C by keeping the plates upside down to prevent the collection of water droplets over the medium. After 24 hours, the plates were visually examined and the diameter values of the zone of inhibition were measured. Triplicate results were recorded by repeating the same procedure.

The antibacterial screening effect of synthesized chalcones is shown in **Fig. 3 (Plates 1 - 12).** The zone of inhibition is compared using **Table 4**and the Clustered column Chart is shown in **Fig. 4.** A very good antibacterial activity was possessed by all substituents on the microorganisms in general.

Analysis of the zone of inhibition (mm) values reveals that three chalcone compounds with 3-Br, 2-Cl and 3-NO_2 substituents have shown good antibacterial activityagainst *Bacillussubtilis.*

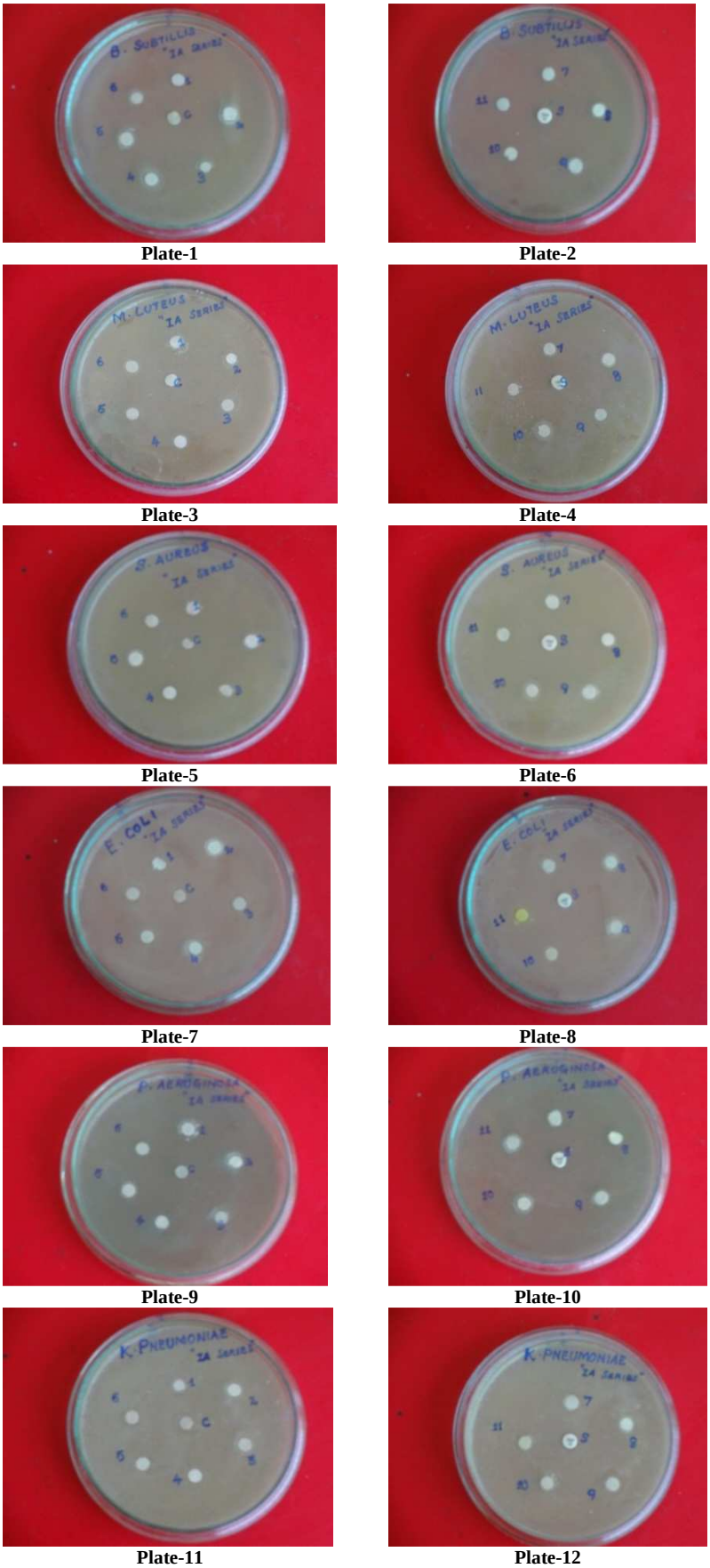


Fig. 3. Antibacterial activity of substitutedstyryl 3, 4-dimethyl phenyl ketones-petri dishes

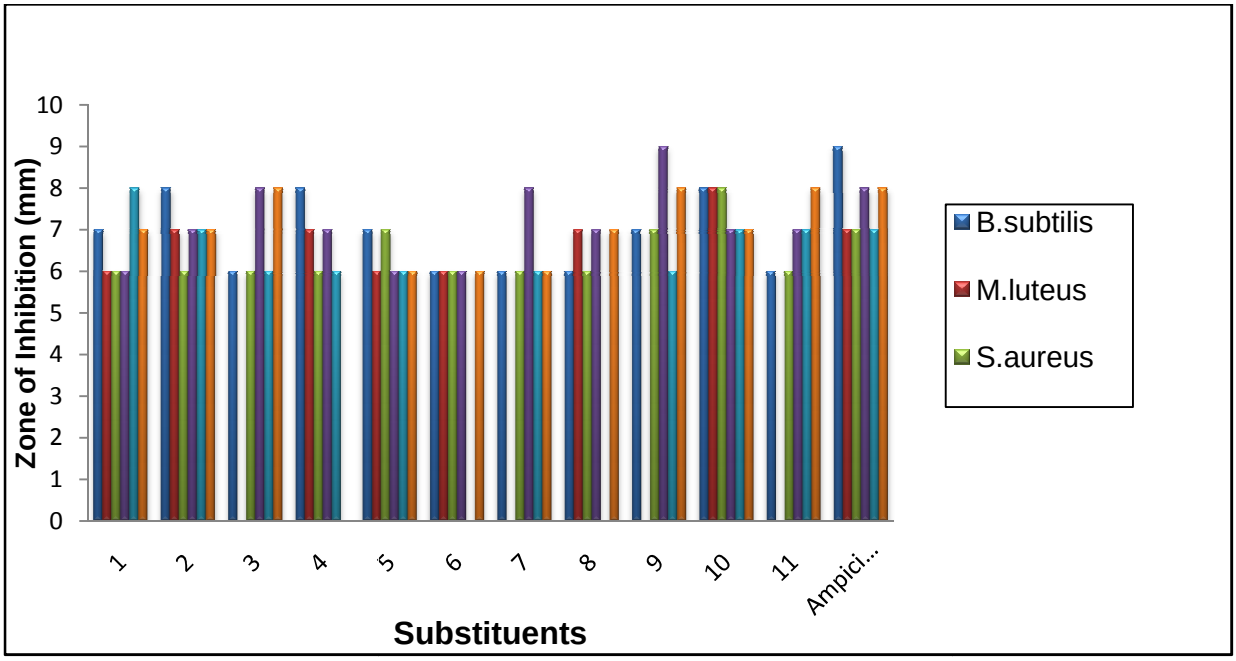


Fig.4. Antibacterial activity of substitutedstyryl 3, 4-dimethyl phenyl ketones-clustered column chart

Table 4.Antibacterial activity of substitutedstyryl 3, 4-dimethyl phenyl ketones

S.NO.	COMPOUND	Zone of Inhibition (mm)					
		Gram positive Bacteria			Gram negative Bacteria		
		B.subtilis	*M.luteus*	*S.aureus*	*E.coli*	*P.aeruginosa*	*K.pneumonia*
1	H	7	6	6	6	8	7
2	3-Br	8	7	6	7	7	7
3	4-Br	6	-	6	8	6	8
4	2-Cl	8	7	6	7	6	-
5	3-Cl	7	6	7	6	6	6
6	4-Cl	6	6	6	6	-	6
7	4-F	6	-	6	8	6	6
8	4-OCH_3	6	7	6	7	-	7
9	4-CH_3	7	-	7	9	6	8
10	3-NO_2	8	8	8	7	7	7
11	4-NO_2	6	-	6	7	7	8
Standard	Ampicillin	9	7	7	8	7	8
control	DMSO	-	-	-	-	-	-

All the remaining eight chalcones compounds withH(Parent), 4-Br, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3 and 4-NO_2 substituents have shown moderate antibacterial activity against *Bacillussubtilis*.

The only one chalcone compound with 3-NO_2 substituent has shown excellent antibacterial activity than standard ampicillin against *Micrococcus luteus*. Only six chalcones with H(Parent), 3-Br, 2-Cl, 3-Cl, 4-Cl and 4-OCH_3substituents have shown moderate antibacterial activity against *Micrococcus luteus*.

Only one chalcone compoundwith 3-NO_2 substituent has shown excellent antibacterial activity than standard ampicillin against *Staphylococcus aureus*. All the remaining 10 halcone compounds with H (parent), 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 4-F, 4-OCH_3, 4-CH_3 and 4-NO_2 substituents have shown moderate antibacterial activity against *Staphylococcus aureus*.

Only one chalcone compound with 4-CH_3substituent has shown excellent antibacterial activity against*Escherichia coli*. Only 2 chalcone compounds with 4-Br and 4-F substituents have shown good antibacterial activity against*Escherichia coli*.

Only one chalcone in series-A with H (Parent) compound has shown excellent antibacterial activity than standard ampicillin against*Pseudomonas aeruginosa*. Only 8 chalcones with 3-Br, 4-Br, 2-Cl, 3-Cl, 4-F, 4-Me, 3 NO_2, and 4-NO_2substituents have shown moderate antibacterial activity against*Pseudomonas aeruginosa*.

Only three chalcones compounds with 4-Br, 4-CH_3 and 4-NO_2substituents have shown good antibacterial activity against*Klebsiella pneumonia*. Only 7 chalcone compounds with H (Parent), 3-Br, 3-Cl, 4-Cl, 4-F, 4-OCH_3, and 3-NO2substituents have shown moderate antibacterial activity against*Klebsiella pneumonia*.

Antifungal sensitivity assay

Antifungal sensitivity assay was performed using Kirby-Bauer[19] disc diffusion technique. PDA medium was prepared and sterilized as above. It was poured (ear bearing heating condition) in the Petri-plate which was already filled with 1 ml of the fungal species. The plate was rotated clockwise and counter clock-wise for uniform spreading of the species. The discs were impregnated with the test solution. The test solution was prepared by dissolving 15mg of the Chalcone in 1ml of DMSO solvent. The medium was allowed to solidify and kept for 24 hours. Then the plates were visually examined and the diameter values of zone of inhibition were measured. Triplicate results were recorded by repeating the same procedure.

Antifungal activity of substituted styryl 3, 4-dimethyl phenyl ketones

The observed antifungal activities of substitutedstyryl 3, 4-dimethyl phenyl ketones are shown in **Fig. 5 (Plates 1 - 6).** The zone of inhibition is compared using **Table 5**and the Clustered column Chart is shown in **Fig.6.**Analysis of the zone of inhibition (mm) values reveals that only five chalcone compounds with H (Parent), 3-Br, 2-Cl, 3-Cl and 4-Cl substituents have shown moderate antifungal activity against *Aspergillus Niger*. Only siix chalcone compounds with H (Parent), 3-Br, 3-Cl, 4-Cl, 4-CH_3 and 3-NO_2 substituents have shown moderate antifungal activity against*Mucor species*. Only seven chalcone compounds with H (Parent), 3-Cl, 4-Cl, 4-F, 4-OCH_3, 3-NO_2 and 4-NO_2 substituents have shown moderate antifungal activity against*Trichodermaviride*.

Table 5.Antifungal activity of substituted styryl 3, 4-dimethyl phenyl ketones

S.No.	Substituent	Zone of Inhibition (mm)		
		A.niger	*M.Species*	*T.viride*
1	H	6	6	6
2	3-Br	7	6	-
3	4-Br	-	-	-
4	2-Cl	6	-	-
5	3-Cl	6	6	6
6	4-Cl	7	6	6
7	4-F	-	-	6
8	4-OCH_3	-	-	6
9	4-CH_3	-	6	-
10	3-NO_2	-	6	7
11	4-NO_2	-	-	6
Standard	Miconazole	8	12	9
Control	DMSO	-	-	-

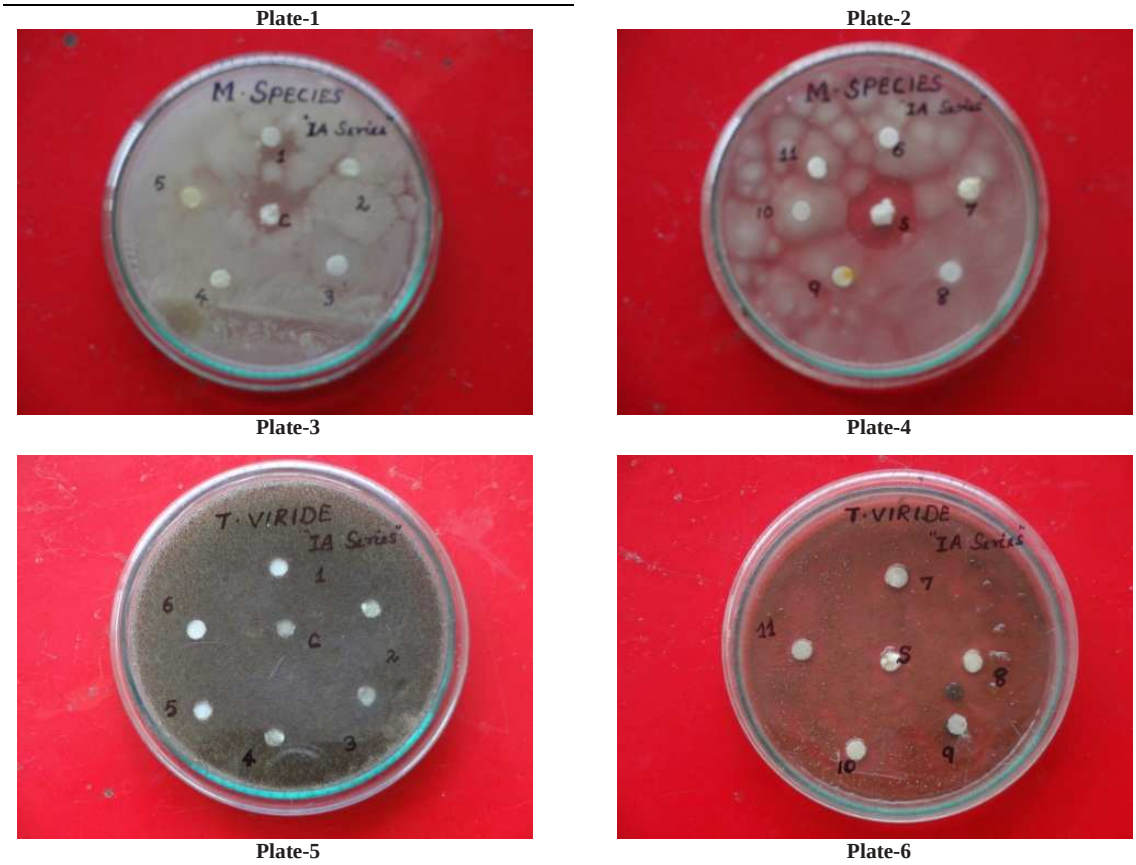


Fig. 5. Antifungal activity of substituted styryl 3, 4-dimethyl phenyl ketones

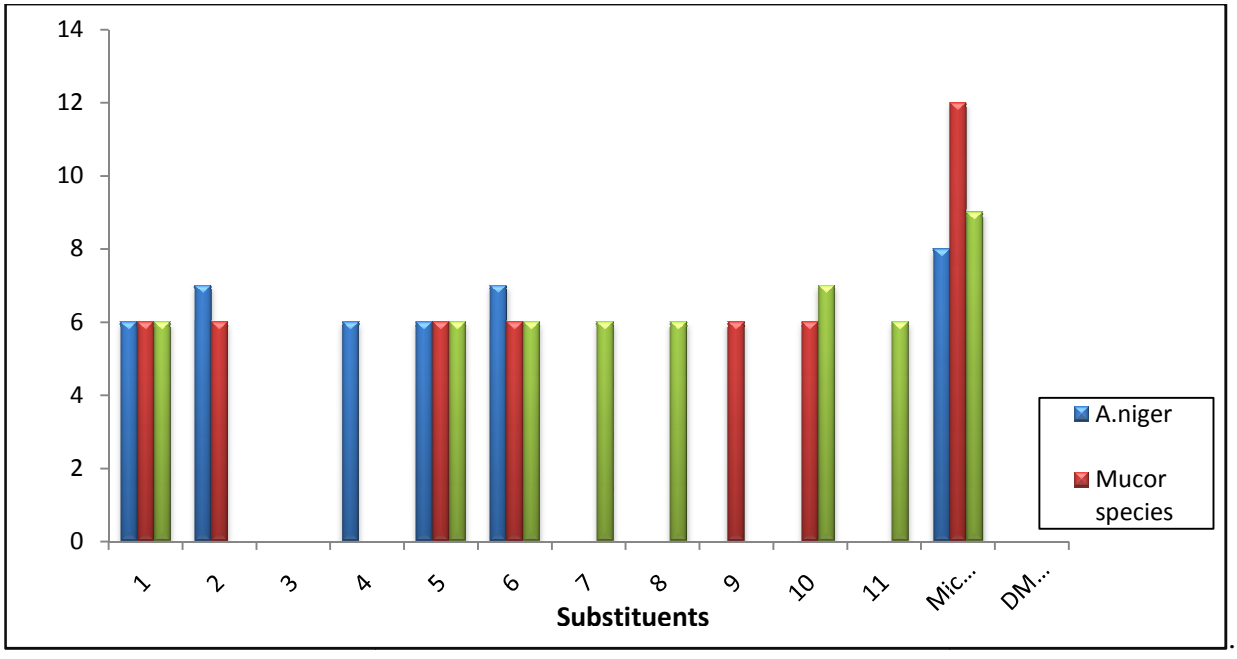


Fig. 6.Antifungal activity of substituted styryl 3, 4-dimethyl phenyl ketones-clustered column chart

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