



## ORIGINAL ARTICLE

# Synthesis, spectral linearity, antimicrobial, antioxidant and insect antifeedant activities of some 2,5-dimethyl-3-thienyl chalcones



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## KEYWORDS

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**Abstract** Twelve 2,5-dimethyl-3-thienyl chalcones [*E*-1-(2,5-dimethyl-3-thienyl)-3-(substituted phenyl)-2-propen-1-ones] have been synthesized by Claisen–Schmidt condensation of 3-acetyl-2,5-dimethyl furon and substituted benzaldehydes. Yields of the chalcones are more than 80%. These chalcones were characterized by their physical constants and spectral data. The group frequencies of infrared  $\nu(\text{cm}^{-1})$  of CO *s-cis* and *s-trans*, CH *in-plane* and *out of plane*, CH=CH *out of plane*, >C=C< *out of plane* modes, NMR chemical shifts  $\delta(\text{ppm})$  of H <sub>$\alpha$</sub> , H <sub>$\beta$</sub> , CO, C <sub>$\alpha$</sub>  and C <sub>$\beta$</sub>  of these chalcones were correlated with Hammett substituent constants, *F* and *R* parameters using single and multi-regression analyses. From the results of statistical analyses, the effects of substituents on the group frequencies are explained. Antibacterial, antifungal, antioxidant and insect antifeedant activities of these chalcones have been studied.

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## 1. Introduction

The QSAR, QPR and QSR of the organic substrates have been studied from the spectral data associated with their molecular equilibration (Thirunarayanan, 2007a,b). The Hammett corre-

lations of spectral data of organic compounds are useful for the prediction of their structure, stereo-chemical and physico-chemical properties (Ranganathan et al., 2011; Mulliken, 1939). The vibrational stretches of carbonyl groups gave two molecular conformers in unsaturated ketones such as *s-cis* and *s-trans* isomers. The *s-cis* carbonyl group stretches are higher than those of the *s-trans* carbonyl group. Based on this, the structure of molecular equilibration can be predicted in geometrical isomers, keto-enol tautomers in unsaturated carbonyl compounds (Thirunarayanan 2008a; Thirunarayanan and Ananthkrishna Nadar, 2002), alkenes, alkynes, styrenes, nitro-styrenes and naphthacyl ketones and their esters (Thirunarayanan et al., 2011). Nuclear magnetic resonance

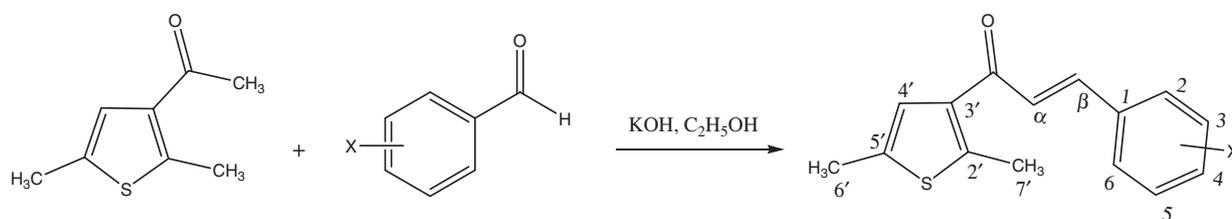
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X= H, 3-Br, 4-Br, 2-Cl, 3-Cl, 4-Cl, 3-OH, 4-OH, 3-OCH<sub>3</sub>, 4-CH<sub>3</sub>, 3-NO<sub>2</sub>, 4-NO<sub>2</sub>

**Scheme 1** Synthesis of substituted styryl 2,5-dimethyl-3-thienyl ketones.

spectroscopy provides the information about the number of protons present in the molecules and their categories either *E*- or *Z* in the above molecules. These categories of protons can be identified in the organic molecules, based on their coupling constants. If the molecules possess any substituent in the aromatic ring, corresponding absorption frequencies in IR and the chemical shift in NMR vary from ketone to ketone depending upon the type of substituents whether they are electron donating or electron withdrawing in nature. From these data the effect of substituents can be studied on the particular functional group of the molecule by means of regression analyses (Thirunarayanan and Ananthakrishna Nadar, 2006a,b). Further these data are employed for the study of transition state reaction mechanism (Dass, 2001), structure activity of biological potentials (Deiva et al., 1998), normal coordinate analysis (Sharma et al., 2002; Krishnakumar and Ramasamy, 2002), theoretical study of long range interactions in the beta sheet structures of oligo peptides (Horvath et al., 2005), enone-dienol tautomerism (Wang et al., 2005), density functional theory (Senthilkumar et al., 2006), rotational barriers in selenomides (Kaur et al., 2006) and gas phase reactivity of alkyl sulphides (Izadyar and Gholami 2006). The out of plane and in-plane deformation frequencies in fingerprint regions also used for QSAR and QPR studies (Vanangamudi and Thiruna-

rayanan, 2006). Generally chalcones possess various multi-pronged activities (Thirunarayanan, 2008b; Thirunarayanan et al., 2010) such as anticancer, antimicrobial (Sivakumar et al., 2007; Lahtchev, 2008), antioxidant (Weber et al., 2005), antiviral (Parmer et al., 1996), anti-aids (Deng et al., 2007), insect antifeedant (Thirunarayanan 2008b; Thirunarayanan et al., 2010), antimalarial (Dominguez et al., 2005), anti-plasmodial (Arulkumaran et al., 2008), and agrochemicals and drugs (Mirinda et al., 2000; Nowakowska, 2007; Majinda et al., 2001; Sitaram Kumar et al., 2007). These potential compounds are also applied in the study of structure activity relationships (Sung and Ananthakrishna Nadar, 2000). From a thorough literature survey it is observed that there is no report on the effect of substituents-QSAR or QPR study with these compounds, in the past. Therefore the authors have taken effort to synthesise some substituted styryl 2,5-methyl-3-thienyl ketones and study the correlation analysis with their IR and NMR data and their antimicrobial, antioxidant and insect antifeedant activities. (see Scheme 1)

## 2. Experimental

All chemicals used were procured from the Sigma–Aldrich and E-Merck chemical companies. Melting points of all chalcones

**Table 1** Analytical and mass spectral data of substituted styryl 2, 5-dimethyl-3-thienyl ketones.

Entry	Substituent	M.F.	F.W.	Yield (%)	M.P. (°C)	Mass (m/z)
1	H	C <sub>15</sub> H <sub>14</sub> OS	242	87	322–323 (323) <sup>a</sup>	242[M <sup>+</sup> ], 227, 213, 165, 139, 137, 131, 111, 103, 97, 82, 77, 55
2	2-Cl	C <sub>15</sub> H <sub>13</sub> ClOS	277	80	220–221	277[M <sup>+</sup> ], 279[M <sup>+</sup> 2], 241, 227, 152,139, 131, 111, 103, 77, 55
3	3-Cl	C <sub>15</sub> H <sub>13</sub> ClOS	277	83	142–143	277[M <sup>+</sup> ], 279[M <sup>+</sup> 2], 261, 241, 227, 152,139, 131, 111, 103, 77, 55, 35,15
4	4-Cl	C <sub>15</sub> H <sub>13</sub> ClOS	277	86	122–123	277[M <sup>+</sup> ], 279[M <sup>+</sup> 2], 261, 246, 241, 227, 165, 152,139, 137,124, 111, 103, 82, (122–124) <sup>b</sup> 77, 55, 35, 15
5	4-F	C <sub>15</sub> H <sub>13</sub> FOS	260	83	290–291	260[M <sup>+</sup> ], 262[M <sup>+</sup> 2], 245, 241, 231, 165, 152, 149, 139, 121, 111, 108, 95, 55, 47, 19,
6	2-OH	C <sub>15</sub> H <sub>14</sub> O <sub>2</sub> S	258	81	145–146 (145–146) <sup>c</sup>	258[M <sup>+</sup> ], 243, 241, 139, 147, 119, 113, 99, 95, 18, 15
7	3-OH	C <sub>15</sub> H <sub>14</sub> O <sub>2</sub> S	258	82	160–161	258[M <sup>+</sup> ], 243, 240, 165, 152, 139, 127, 121, 113, 99, 15
8	4-OH	C <sub>15</sub> H <sub>14</sub> O <sub>2</sub> S	258	83	140–141	258[M <sup>+</sup> ], 243, 241, 229, 165, 152, 147, 139, 119, 111, 106, 93, 77, 53, 17, 15
9	2-OCH <sub>3</sub>	C <sub>16</sub> H <sub>16</sub> O <sub>2</sub> S	272	86	91–92 (91–92) <sup>c</sup>	272[M <sup>+</sup> ], 257, 243, 241, 165, 161, 152, 139, 133, 120, 111, 107, 82, 77, 31, 15
10	4-CH <sub>3</sub>	C <sub>16</sub> H <sub>16</sub> OS	256	86	126–127	256[M <sup>+</sup> ], 241, 227, 213, 165, 152, 139, 131, 111, 103, 91, 90, 82, 15
11	3-NO <sub>2</sub>	C <sub>15</sub> H <sub>13</sub> NO <sub>3</sub> S	287	84	132–133	287[M <sup>+</sup> ], 272, 258, 241, 176, 139, 127, 111, 71, 27, 15
12	4-NO <sub>2</sub>	C <sub>15</sub> H <sub>13</sub> NO <sub>3</sub> S	287	84	210–211	287[M <sup>+</sup> ], 272, 258, 241, 176, 165, 152, 148, 139, 122, 111, 82, 77, 45, 27, 14.

<sup>a</sup> Dhar and Gupta, 1971.

<sup>b</sup> Hassan et al., 2006.

<sup>c</sup> Asiri et al., 2010a,b.

**Table 2** Infrared spectral data  $\nu(\text{cm}^{-1})$  of  $\text{CO}_{s\text{-}cis}$  and  $s\text{-}trans$  stretches,  $\text{CH}_{ip}$  and  $op$ ,  $\text{CH}=\text{CH}_{op}$  and  $>\text{C}=\text{C} <_{op}$  modes of substituted styryl 2,5-dimethyl-3-thienyl ketones.

Entry	Substituent	$\text{CO}_{s\text{-}cis}$	$\text{CO}_{s\text{-}trans}$	$\text{CH}_{op}$	$\text{CH}_{ip}$	$\text{CH}=\text{CH}_{op}$	$>\text{C}=\text{C} <_{op}$
1	H	1646.91	1561.00	1178.08	785.62	1019.56	663.01
2	2-Cl	1648.80	1565.48	1134.80	750.53	1021.60	669.51
3	3-Cl	1665.75	1589.62	1141.66	756.04	1075.53	674.12
4	4-Cl	1656.00	1596.11	1136.52	747.42	1092.25	649.05
5	4-F	1652.29	1605.78	1136.72	789.15	1000.79	613.65
6	2-OH	1640.39	1600.00	1161.64	775.45	1021.18	668.91
7	3-OH	1647.98	1584.28	1142.13	780.86	1065.23	678.67
8	4-OH	1667.15	1595.62	1160.92	788.57	1020.11	694.75
9	2-OCH <sub>3</sub>	1651.17	1569.12	1171.83	778.08	1020.71	668.22
10	4-CH <sub>3</sub>	1654.79	1595.44	1123.29	769.68	1019.39	649.55
11	3-NO <sub>2</sub>	1655.47	1598.21	1135.19	731.71	1084.93	685.93
12	4-NO <sub>2</sub>	1652.63	1595.03	1138.19	743.52	1020.35	671.55

have been determined in open glass capillaries on Mettler FP51 melting point apparatus and are uncorrected. Infrared spectra (KBr, 4000–400  $\text{cm}^{-1}$ ) have been recorded on AVATAR-300 Fourier transform spectrophotometer. The nuclear magnetic resonance spectra are recorded in INSTRUM AV300 NMR spectrometer operating at 300 MHz which has been utilized for recording  $^1\text{H}$  spectra and 75.46 MHz for  $^{13}\text{C}$  spectra in  $\text{CDCl}_3$  solvent using TMS as the internal standard. Electron impact (EI) (70 eV) and chemical ionization mode  $\text{FAB}^+$  mass spectra have been recorded with a JEOL JMS600H spectrometer.

### 2.1. Synthesis of substituted styryl 2,5-dimethyl-3-thienyl ketones

An appropriate equimolar quantity of 3-acetyl-2,5-methylthiophene (0.01 mol), various substituted benzaldehydes (0.01 mol), 0.5 g of potassium hydroxide and 20 ml of ethanol were warmed in a 50 ml corning conical flask and shaken occasionally (Nayak et al., 1964). The obtained solid was filtered at the pump, washed with cold water and crystallized from ethanol to afford the respective chalcones as a glittering pale yellow solid. The synthesized chalcones are characterized by their physical constants, IR,  $^1\text{H}$  and  $^{13}\text{C}$  NMR and Mass spectral data. Analytical and Mass spectral data are presented in Table 1. Infrared spectral data are given in Table 2. The  $^1\text{H}$  chemical shifts (ppm)  $\delta\text{H}_\alpha$ ,  $\delta\text{H}_\beta$ ,  $^{13}\text{C}$  chemical shifts (ppm) of  $\delta\text{CO}$ ,  $\delta\text{C}_\alpha$  and  $\delta\text{C}_\beta$  of ketones are presented in Table 3.

## 3. Results and discussion

### 3.1. Infrared spectral study

In the present study, the synthesized substituted styryl 2,5-dimethyl-3-thienyl ketones exist as  $s\text{-}cis$  and  $s\text{-}trans$  conformers. These conformers are confirmed by the carbonyl group doublets obtained in the range of 1600–1700  $\text{cm}^{-1}$ . They are shown in (Fig. 1.) and the corresponding carbonyl frequencies ( $\text{cm}^{-1}$ ) of the conformers are presented in Table 2. The  $s\text{-}cis$

conformers absorb at higher vibrational frequencies than  $s\text{-}trans$  conformers. Generally carbonyl doublets are obtained at lower absorption frequencies for the electron donating substituents in the chalcones whereas the electron withdrawing substituents absorb their doublets at higher frequencies in both the conformers. In this present study also, the same trend was observed. These frequencies are correlated with various Hammett  $\sigma$  constants and Swain–Lupton's parameters (Swain and Lupton, 1968) by single and multi linear regression analysis. While seeking Hammett correlation involving group frequencies, the form of the Hammett equation employed is

$$\nu = \rho\sigma + \nu_0 \quad (1)$$

where  $\nu_0$  is the frequency for the parent member of the series.

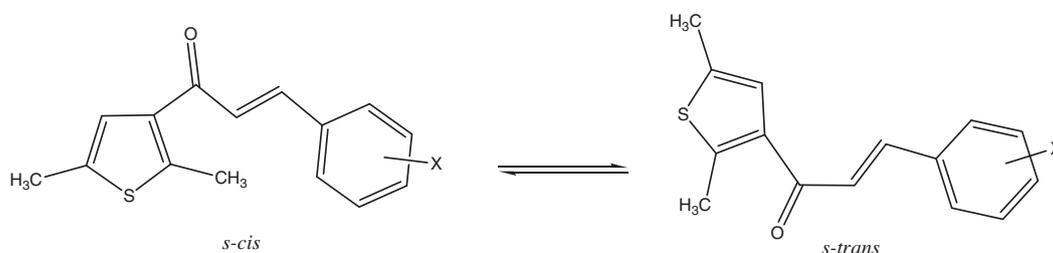
The results of single parameter statistical analyses of carbonyl frequencies with substituent constants are presented in Table 4. From Table 4, the stretching frequencies of both the conformers show no correlation with Hammett sigma constants and  $F$  and  $R$  parameters. This is due to the incapability of the substituents to transmit their effect from the phenyl ring to the thienyl ring across four or more carbon atoms as per the conjugative structure (Fig. 2). Both carbonyl frequencies show positive  $\rho$  values in the correlation. This means that there is normal substituent effect operating in all ketones.

The study of substituent effects on the deformation modes of  $\text{CH}_{op/ip}$ ,  $\text{CH}=\text{CH}$  and  $\text{C}=\text{C}_{op}$  of vinyl parts of substituted styryl 2,5-dimethyl-3-thienyl ketones has been done based on the work of Thirunarayanan and Jaishankar (2003). The larger value of deformation mode frequency for the system is due to the low mobility of electrons between the  $>\text{C}=\text{C} <$  and the  $-\text{CH}=\text{CH}-$  frame work. The observed  $-\text{CH}$  out of plane,  $-\text{CH}$  in-plane and  $-\text{CH}=\text{CH}-$  out of plane frequencies in the present study are given in Table 2. All the deformation modes of stretching frequencies of substituted styryl 2,5-dimethyl-3-thienyl ketones have been correlated with different substituent constants according to John Shorter (1973). The results of statistical analysis are shown in Table 4.

From Table 4, the regression analysis of  $\text{CH}_{ip}$  modes with Hammett  $\sigma$ ,  $\sigma^+$ ,  $\sigma_R$  constants and  $F$  and  $R$  parameters produced no correlation. The inductive effects of the substituents failed in the correlation. A satisfactory correlation has been

**Table 3** The NMR chemical shifts (ppm) of  $\delta H_{\alpha}$ ,  $\delta H_{\beta}$ ,  $\delta CO$ ,  $\delta C_{\alpha}$ ,  $\delta C_{\beta}$  and ring carbons of 2,5-dimethyl-3-thienyl ketones.

Entry	X	H $\alpha$ (1H, <i>d</i> )	H $\beta$ (1H, <i>d</i> )	Ring protons	X	CO	C $_{\alpha}$	C $_{\beta}$	C $_1$	C $_2$	C $_3$	C $_4$	C $_5$
1	H	7.252	7.488	7.343–7.376 (6H, <i>m</i> )	–	185.78	125.29	141.78	136.24	126.35	128.56	128.08	128.56
2	2-Cl	7.187	7.389	7.225–7.302 (5H, <i>m</i> )	–	186.34	126.64	142.01	134.69	126.65	135.81	128.02	130.92
3	3-Cl	7.187	7.481	7.325–7.412 (5H, <i>m</i> )	–	186.03	125.97	141.48	135.69	126.49	134.65	129.84	129.91
4	4-Cl	7.241	7.645	7.468–7.623 (5H, <i>m</i> )	–	184.67	124.87	141.32	134.25	127.25	128.36	138.29	128.36
5	4-F	7.196	7.613	7.248–7.532 (5H, <i>m</i> )	–	186.10	124.69	141.45	130.35	130.05	116.85	165.52	116.85
6	2-OH	6.926	7.801	7.015–7.623 (5H, <i>m</i> )	–	186.92	124.74	141.64	117.56	157.14	115.86	128.99	122.36
7	3-OH	7.101	7.615	7.207–7.598 (5H, <i>m</i> )	–	187.12	120.70	136.57	135.45	115.09	57.76	115.05	130.11
8	4-OH	6.801	7.332	6.914–7.303 (5H, <i>m</i> )	–	181.99	122.67	142.74	128.23	127.13	115.36	157.25	115.36
9	2-OCH $_3$	6.759	7.614	6.761–7.561 (5H, <i>m</i> )	3.68 (3H, <i>s</i> )	186.66	122.93	141.78	116.32	158.19	114.23	129.95	122.30
10	4-CH $_3$	7.112	7.681	7.287–7.344 (5H, <i>m</i> )	2.35 (3H, <i>s</i> )	186.21	122.90	141.70	132.65	126.54	130.04	137.21	130.04
11	3-NO $_2$	7.345	8.474	7.495–8.356 (5H, <i>m</i> )	–	186.87	125.56	141.44	136.51	123.26	148.67	121.58	130.25
12	4-NO $_2$	7.307	7.723	7.339–7.704 (5H, <i>m</i> )	–	185.07	125.57	139.99	141.20	128.61	120.22	148.33	120.22
Entry	X	C $_6$	X	C $_2'$	C $_3'$	C $_4'$	C $_5'$	C $_6'$	C $_7'$				
1	H	126.35	–	151.25	125.65	107.15	151.35	15.31	9.32				
2	2-Cl	123.89	–	150.14	142.36	125.49	139.57	15.36	9.15				
3	3-Cl	125.62	–	150.44	141.48	125.62	139.23	15.69	8.73				
4	4-Cl	127.25	–	151.92	140.12	124.67	137.91	15.83	9.05				
5	4-F	130.05	–	153.73	139.82	126.74	136.73	15.79	9.76				
6	2-OH	127.65	–	152.67	139.52	123.98	138.12	15.32	9.88				
7	3-OH	117.57	–	156.31	138.41	125.05	136.50	15.93	10.36				
8	4-OH	127.13	–	152.41	142.38	123.56	137.29	15.16	11.03				
9	2-OCH $_3$	127.19	57.21	153.15	141.08	126.21	137.92	15.90	10.36				
10	4-CH $_3$	126.57	27.13	152.33	141.27	125.16	137.25	15.64	8.92				
11	3-NO $_2$	132.07	–	151.28	142.08	126.18	139.27	15.29	10.27				
12	4-NO $_2$	128.61	–	153.33	142.08	125.82	140.23	15.73	11.58				



**Figure 1** The *s-cis* and *s-trans* conformers of substituted styryl 2,5-dimethyl-3-thienyl chalcones.

**Table 4** Results of statistical analysis of infrared  $\nu(\text{cm}^{-1})$   $\text{CO}_{s-cis}$  and  $\text{CO}_{s-trans}$ ,  $\text{CH}_{ip}$  and  $op$ ,  $\text{CH}=\text{CH}_{op}$  and  $>\text{C}=\text{C}<_{op}$  modes of substituted styryl 2,5-dimethyl-3-thienyl ketones with Hammett  $\sigma$ ,  $\sigma^+$ ,  $\sigma_I$ ,  $\sigma_R$  constants and  $F$  and  $R$  parameters.

Frequency	Constants	$r$	$I$	$\rho$	$s$	$n$	Correlated derivatives
$\text{CO}_{s-cis}$	$\sigma$	0.806	1653.14	1.287	7.87	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.805	1653.30	1.824	7.87	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.814	1651.50	4.978	7.80	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.812	1654.13	3.529	7.83	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$F$	0.812	1651.74	4.042	7.83	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$R$	0.830	1655.32	5.651	7.51	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
$\text{CO}_{s-trans}$	$\sigma$	0.828	1587.05	9.165	15.05	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.807	1587.91	-1.908	15.45	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.830	1580.44	20.036	14.76	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.808	1589.14	4.791	15.44	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$F$	0.844	1577.04	28.767	13.84	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$R$	0.819	1588.48	-6.896	15.21	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
$\text{CH}_{ip}$	$\sigma$	0.833	1148.22	-14.757	16.82	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.829	1146.44	-8.968	17.07	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.810	1143.93	7.899	17.75	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.849	1138.96	-31.863	15.50	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$F$	0.802	1146.16	1.536	17.84	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$R$	0.847	1139.65	-19.601	15.74	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
$\text{CH}_{op}$	$\sigma$	0.975	770.24	-38.581	13.57	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.968	765.56	-24.306	15.09	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.829	775.51	-25.641	19.74	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.984	750.99	-63.037	10.97	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$F$	0.972	753.76	-34.893	14.23	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$R$	0.913	748.44	-24.336	13.25	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
$\text{CH}=\text{CH}_{op}$	$\sigma$	0.830	1035.36	31.071	30.45	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.835	1039.14	20.146	30.79	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.829	1023.62	41.714	31.42	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.823	1045.23	27.725	32.02	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$F$	0.816	1029.69	22.369	32.48	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$R$	0.831	1046.83	23.120	31.40	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
$\text{C}=\text{C}_{op}$	$\sigma$	0.804	665.35	2.265	21.91	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.805	665.50	-2.078	21.90	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.804	667.14	-4.410	21.91	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.814	668.41	11.605	21.69	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$F$	0.819	672.24	-17.538	21.52	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$R$	0.817	652.66	-16.498	25.37	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>

$r$  = Correlation co-efficient;  $\rho$  = Slope;  $I$  = Intercept;  $s$  = Standard deviation;  $n$  = Number of substituents.

observed for  $\text{CH}_{op}$  modes with Hammett  $\sigma$ ,  $\sigma^+$  constants and  $F$  and  $R$  parameters except for 2-Cl, 4-F and 2-OH substituents. When these constants are included in the regression, the correlation decreases considerably. This is due to the reason stated earlier with the conjugative structure as in Fig. 2. The ability of transmission of electronic effects of the substituents on  $\text{CH}_{op}$  is higher than that of  $\text{CH}_{ip}$  modes.

Some of the single parameter correlations failed with the infrared frequencies  $\text{CO}_{s-cis}$ ,  $\text{CH}_{ip}$ ,  $\text{CH}_{op}$ ,  $\text{CH}=\text{CH}_{op}$  and  $\text{C}=\text{C}_{op}$  with Hammett sigma constants and  $F$  and  $R$  parameters. While seeking the multi-regression analysis, satisfactorily correlations are obtained for these stretches with Swain-Lupton and  $F$  and  $R$  parameters (Swain and Lupton, 1968). The correlated multi regression equations are given in Eqs. (2)–(13).

$$\nu\text{CO}_{s-cis}(\text{cm}^{-1}) = 1652.42(\pm 5.624) + 4.241(\pm 1.129)\sigma_I + 2.689(\pm 0.960)\sigma_R \quad (R = 0.917, n = 12, P > 90\%) \quad (2)$$

$$\nu\text{CO}_{s-cis}(\text{cm}^{-1}) = 1654.13(\pm 5.215) + 2.943(\pm 1.041)F + 5.464(\pm 0.585)R \quad (R = 0.931, n = 12, P > 90\%) \quad (3)$$

$$\nu\text{CO}_{s-trans}(\text{cm}^{-1}) = 1581.14(\pm 10.068) + 19.798(\pm 2.144)\sigma_I + 0.870(\pm 0.182)\sigma_R \quad (R = 0.930, n = 12, P > 90\%) \quad (4)$$

$$\nu\text{CO}_{s-trans}(\text{cm}^{-1}) = 1573.17(\pm 9.302) + 30.543(\pm 1.856)F - 8.837(\pm 1.043)R \quad (R = 0.950, n = 12, P > 95\%) \quad (5)$$

$$\nu\text{CH}_{ip}(\text{cm}^{-1}) = 1131.85(\pm 10.833) + 17.588(\pm 2.175)\sigma_I - 35.346(\pm 1.849)\sigma_R \quad (R = 0.954, n = 12, P > 95\%) \quad (6)$$

$$\nu\text{CH}_{ip}(\text{cm}^{-1}) = 1137.42(\pm 10.941) + 5.543(\pm 2.183)F - 19.954(\pm 1.625)R \quad (R = 0.947, n = 12, P > 90\%) \quad (7)$$

$$\nu\text{CH}_{op}(\text{cm}^{-1}) = 754.56(\pm 7.802) - 8.844(\pm 1.566)\sigma_I - 61.285(\pm 13.319)\sigma_R \quad (R = 0.985, n = 12, P > 95\%) \quad (8)$$

$$\nu\text{CH}_{op}(\text{cm}^{-1}) = 755.50(\pm 9.897) - 4.311(\pm 1.978)F - 34.691(\pm 11.107)R \quad (R = 0.972, n = 12, P > 90\%) \quad (9)$$

$$\nu\text{CH} = \text{CH}_{op}(\text{cm}^{-1}) = 1030.65(\pm 22.386) + 36.078(\pm 4.495)\sigma_I + 20.579(\pm 3.821)\sigma_R \quad (R = 0.934, n = 12, P > 92\%) \quad (10)$$

$$\nu\text{CH} = \text{CH}_{op}(\text{cm}^{-1}) = 1039.59(\pm 21.694) + 17.949(\pm 4.330)F + 21.980(\pm 2.434)R \quad (R = 0.932, n = 12, P > 90\%) \quad (11)$$

$$\nu\text{C} = \text{C}_{op}(\text{cm}^{-1}) = 671.65(\pm 15.643) - 8.027(\pm 3.140)\sigma_I + 13.195(\pm 2.670)\sigma_R \quad (R = 0.916, n = 12, P > 90\%) \quad (12)$$

$$\nu\text{C} = \text{C}_{op}(\text{cm}^{-1}) = 673.78(\pm 14.973) - 18.246(\pm 2.988)F + 3.519(\pm 1.680)R \quad (R = 0.920, n = 12, P > 90\%) \quad (13)$$

### 3.2. <sup>1</sup>H Spectral study

The <sup>1</sup>H NMR spectra of twelve 2,5-dimethyl-3-thienyl chalcones under investigation are recorded in deuterated dimethyl sulphoxide employing tetramethylsilane (TMS) as the internal standard. The signals of the ethylenic protons were assigned. They are confirmed as AB or AA' BB' systems, respectively (Laturber, 1961; Solconiova and Toma, 1980; Solconiova et al., 1976). The chemical shifts of H<sub>α</sub> are at higher field than those of H<sub>β</sub> in this series of ketones. The ethylenic protons give an AB pattern and the β-proton doublet in most cases is well separated from the signals of the aromatic protons. The assigned chemical shifts of the ethylenic protons are presented in Table 3.

$$\delta\text{H}_\alpha(\text{ppm}) = 7.168(\pm 0.093) + 0.172(\pm 0.018)\sigma_I + 0.468(\pm 0.157)\sigma_R \quad (R = 0.976, n = 12, P > 95\%) \quad (15)$$

$$\delta\text{H}_\alpha(\text{ppm}) = 7.142(\pm 0.090) + 0.214(\pm 0.017)F + 0.321(\pm 0.010)R \quad (R = 0.966, n = 12, P > 95\%) \quad (16)$$

$$\delta\text{H}_\beta(\text{ppm}) = 7.614(\pm 0.222) + 0.305(\pm 0.044)\sigma_I + 0.415(\pm 0.038)\sigma_R \quad (R = 0.943, n = 12, P > 90\%) \quad (17)$$

$$\delta\text{H}_\beta(\text{ppm}) = 7.506(\pm 0.090) + 0.415(\pm 0.041)F + 0.116(\pm 0.020)R \quad (R = 0.946, n = 12, P > 90\%) \quad (18)$$

In nuclear magnetic resonance spectra, the proton chemical shifts δ(ppm) depend on the electronic environment of the nuclei concerned. These shifts can be correlated with reactivity parameters. Thus the Hammett equation may be used in the form as

$$\text{Log } \delta = \text{Log } \delta_0 + \rho\sigma \quad (14)$$

where δ<sub>0</sub> is the chemical shift in the corresponding parent compound.

The assigned <sup>1</sup>H NMR chemical shifts (ppm) of δH<sub>α</sub> and δH<sub>β</sub> of substituted styryl 2,5-dimethyl-3-thienyl ketones are presented in Table 3. These chemical shifts are correlated with Hammett substituent constants and *F* and *R* parameters. The results of statistical analyses of these chemical shifts (ppm) are shown in Table 5. From the Table 5, Hammett σ<sup>+</sup>, σ<sub>I</sub>, σ<sub>R</sub> and *F* and *R* parameters gave satisfactory correlations with H<sub>α</sub> chemical shifts except for H, 4-F, 2-OH, 2-OCH<sub>3</sub> and 4-CH<sub>3</sub> substituents. All correlations gave positive ρ values. This shows that the normal substituent effects operate in all

ketones. Hammett σ<sup>+</sup> constant only produces satisfactory correlation only with H<sub>β</sub> chemical shifts (ppm) of these ketones. Inductive, resonance and field effects failed in correlations. This is due to the incapability of predicting the substituent effects on the vinyl protons by the substituents along with the conjugative structure as in Fig. 2. The degree of transmission of substituent effects on H<sub>α</sub> is higher than H<sub>β</sub> chemical shifts.

Some of the single parameter correlations failed with the <sup>1</sup>H NMR of δH<sub>α</sub> and δH<sub>β</sub> chemical shifts with Hammett sigma constants and *F* and *R* parameters. While seeking the multi regression analysis of these frequencies, satisfactory correlations were obtained with Swain–Lupton, *F* and *R* parameters (Swain and Lupton, 1968). The correlated multi regression equations are, (Eqs. (15)–(18))

### 3.3. <sup>13</sup>C NMR spectral study

The assigned carbonyl carbon chemical shifts (ppm) of δCO, δC<sub>α</sub> and δC<sub>β</sub> of substituted styryl 2,5-dimethyl-3-thienyl ketones are presented in Table 3 and these chemical shifts are correlated with Hammett sigma constants and *F* and *R* parameters. The results of statistical analysis are shown in Table 5. From the Table 5, chemical shifts (ppm) of CO carbon, correlated satisfactorily with Hammett σ, σ<sup>+</sup>, σ<sub>R</sub> and *R* parameters

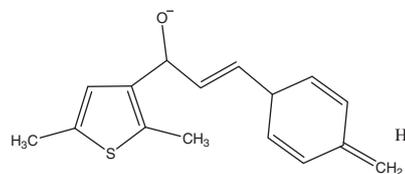


Figure 2 Resonance conjugative structure.

**Table 5** Results of statistical analysis of  $^1\text{H}$  chemical shifts(ppm)of  $\delta\text{H}_\alpha$ ,  $\delta\text{H}_\beta$  protons,  $^{13}\text{C}$  chemical shifts of  $\delta\text{CO}$ ,  $\delta\text{C}_\alpha$  and  $\delta\text{C}_\beta$  carbons of substituted styryl 2,5-dimethyl-3-thienyl ketones with Hammett  $\sigma$ ,  $\sigma^+$ ,  $\sigma_I$ ,  $\sigma_R$  constants and  $F$  and  $R$  parameters.

$\delta(\text{ppm})$	Constants	$r$	$\rho$	$I$	$s$	$n$	Correlated derivatives
$\text{H}_\alpha$	$\sigma$	0.871	0.228	7.092	0.30	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.906	0.277	7.117	0.06	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.956	0.308	6.998	0.18	10	2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-NO <sub>2</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.927	0.530	7.233	0.13	10	H, 2-Cl, 3-Cl, 4-Cl, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$F$	0.903	0.278	7.002	0.18	10	2-Cl, 3-Cl, 4-Cl, 4-F, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 2-NO <sub>2</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$R$	0.917	0.334	7.229	0.13	10	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 2-OCH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
$\text{H}_\beta$	$\sigma$	0.871	0.362	7.586	0.31	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.903	-0.151	7.625	0.30	9	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub>
	$\sigma_I$	0.801	0.419	7.479	0.32	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.814	0.475	7.738	0.34	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$F$	0.803	0.431	7.455	0.32	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$R$	0.800	0.142	7.637	0.33	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
CO	$\sigma$	0.913	0.490	186.76	1.46	10	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.902	0.611	185.83	1.43	10	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 4NO <sub>2</sub>
	$\sigma_I$	0.800	0.016	185.13	1.47	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.903	-0.193	185.76	1.47	10	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 4NO <sub>2</sub>
	$F$	0.771	0.041	185.81	1.47	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$R$	0.903	-0.139	185.76	1.08	10	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
$\text{C}_\alpha$	$\sigma$	0.957	3.199	124.05	1.25	10	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub>
	$\sigma^+$	0.907	2.196	124.45	1.27	11	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.949	3.795	123.02	1.54	10	2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.963	4.125	125.38	1.39	9	2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-NO <sub>2</sub>
	$F$	0.834	2.570	123.40	1.69	12	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$R$	0.946	1.958	125.08	1.95	11	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
$\text{C}_\beta$	$\sigma$	0.940	-0.171	141.17	1.64	11	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.907	-0.201	141.15	1.64	11	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.904	-3.110	141.27	1.64	11	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.921	-1.256	141.46	1.61	11	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$F$	0.911	-0.791	141.46	1.63	11	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$R$	0.906	-0.263	141.25	1.64	11	H, 2-Cl, 3-Cl, 4-Cl, 4-F, 3-OH, 4-OH, 2-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>

$r$  = Correlation co-efficient;  $\rho$  = Slope;  $I$  = Intercept;  $s$  = Standard deviation;  $n$  = Number of substituents.

producing positive  $\rho$  values except for 4-OH and 3-NO<sub>2</sub> substituents. This shows that the normal substituent effects operate in all ketones. The inductive and field effects failed in correlation. This is due to the incapability of substituents predicting their reactivity on carbonyl carbons along with the conjugated structure given in Fig. 2.

The assigned chemical shifts(ppm) of  $\text{C}_\alpha$  and  $\text{C}_\beta$  vinyl carbons in substituted styryl 2,5-dimethyl-3-thienyl ketones were correlated with Hammett sigma constants and  $F$  and  $R$  parameters. The  $\text{C}_\alpha$  chemical shifts correlated satisfactorily with Hammett sigma constants and  $R$  parameters except for 2-OH, 3-OH, 4-CH<sub>3</sub>, 3-NO<sub>2</sub> and 4-NO<sub>2</sub> substituents by showing positive  $\rho$  values. This shows that the normal substituent effects operate in all ketones. The field effects of the substituents

failed in correlation. This is due to the reason stated earlier and is associated with the conjugated structure as shown in Fig. 2.

The  $\text{C}_\beta$  chemical shifts(ppm) of substituted styryl 2,5-dimethyl-3-thienyl ketones were correlated with Hammett sigma constants and  $F$  and  $R$  parameters except for 2-OH substituent, showing negative  $\rho$  values. This shows that the reversal substituent effects operate in all ketones.

Single parameter correlations fails with the  $^{13}\text{C}$  NMR of  $\delta\text{C}_\alpha$  and  $\delta\text{C}_\beta$  chemical shifts(ppm) with Hammett sigma constants and  $F$  and  $R$  parameters. While seeking the multi-regression analysis of these frequencies, there are satisfactory correlations obtained with Swain-Lupton,  $F$  and  $R$  parameters (Swain and Lupton, 1968). The correlated multi regression equations are in Eqs. (19)–(24).

$$\delta\text{CO}(\text{ppm}) = 185.74(\pm 1.06) + 0.569(\pm 0.021)\sigma_I - 201(\pm 0.187)\sigma_R \quad (R = 0.903, n = 12, P > 90\%) \quad (19)$$

$$\delta\text{CO}(\text{ppm}) = 185.75(\pm 0.127) + 0.310(\pm 0.020)F - 0.134(\pm 0.013)R \quad (R = 0.932, n = 12, P > 90\%) \quad (20)$$

$$\delta\text{C}_\alpha(\text{ppm}) = 124.24(\pm 0.891) + 2.817(\pm 1.251)\sigma_I + 3.562(\pm 1.522)\sigma_R \quad (R = 0.972, n = 12, P > 95\%) \quad (21)$$

$$\delta\text{C}_\alpha(\text{ppm}) = 124.19(\pm 1.107) + 2.208(\pm 0.028)F + 1.818(\pm 0.177)R \quad (R = 0.955, n = 12, P > 95\%) \quad (22)$$

$$\delta\text{C}_\beta(\text{ppm}) = 141.74(\pm 1.115) - 0.693(\pm 0.023)\sigma_I + 1.393(\pm 0.199)\sigma_R \quad (R = 0.923, n = 12, P > 90\%) \quad (23)$$

$$\delta\text{C}_\beta(\text{ppm}) = 141.59(\pm 1.137) - 0.854(\pm 0.022)F + 0.316(\pm 0.170)R \quad (R = 0.914, n = 12, P > 90\%) \quad (24)$$

### 3.4. Microbial activities

Chalcones possess a wide range of biological activities such as antibacterial, antifungal (Sivakumar et al., 2007; Lahtchev, 2008), antiviral (Parmer et al., 1996), antifeedant (Thirunarayanan 2008b; Thirunarayanan et al., 2010), anticancer (Sivakumar et al., 2007; Lahtchev, 2008), antimalarial (Dominguez et al., 2005), antituberculosis (Weber et al., 2005), antiAIDS (Deng et al., 2007) and antioxidant (Weber et al., 2005) activities. These multipronged activities present in different chalcones are examined against bacteria, fungi, and insects.

#### 3.4.1. Collection of microorganisms

*Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumonia*, *Micrococcus luteus*, *Pseudomonas aerogenosa*, *Staphylococcus aureus*, *Aspergillus niger*, *Mucor species* and *Trichoderma viride* were procured from the Research Department of Microbiology, Sengunthar Arts and Science College, Thiruchengode, Namakkal Dt., Tamilnadu.

#### 3.4.2. Inoculum preparation

The nutrient broth was procured from Himedia, Mumbai. The nutrient broth was prepared by weighing 1.3 g, of the broth and dissolved in 100 ml of sterile distilled water. The flask was swirled gently while adding the nutrient broth and the pH of the medium was adjusted to 7.0. The Erlenmeyer flask was plugged with non-adsorbent cotton and sterilized in an autoclave at 121 °C and 15 lbs/inc<sup>2</sup> pressure for 15 min. After cooling inside a laminar flow, a loopful of fresh bacterial sample was inoculated and incubated in an orbital shaker at 37 °C for 24 h. Then the cultures were diluted 1:50 with sterile physiological saline and 0.5 ml of the inoculum was used for the preparation of the spread plate. The same procedure has been adopted for all test bacterial samples.

#### 3.4.3. Preparation of agar slants

Nutrients agar medium was prepared and sterilized in an autoclave at 121 °C and 15 lbs/inc<sup>2</sup> pressure for 15 min. After sterilization the medium was dispensed into the test tubes. The test tubes were kept in the slanting position on a support. After complete solidification of the medium, streaking of the microorganism was done in the slant area using a sterile inoculation loop. After the streaking process, the test tubes were incubated at 37 °C for 24 h. After good growth, the slants have been stored in a deep freezer (2 °C) for further studies.

#### 3.4.4. Preparation of Mueller Hinton agar plates

The Mueller Hinton agar of weight 38 g was dissolved in 1000 ml of sterile distilled water. The pH of the medium was adjusted to 7.0. The flask was plugged with cotton and sterilized at 121 °C and 15 lbs/inc<sup>2</sup> pressure for 15 min. After sterilization, the medium was cooled to 45–47 °C, poured 15 ml of it on each sterile Petri-plate and allowed to solidify.

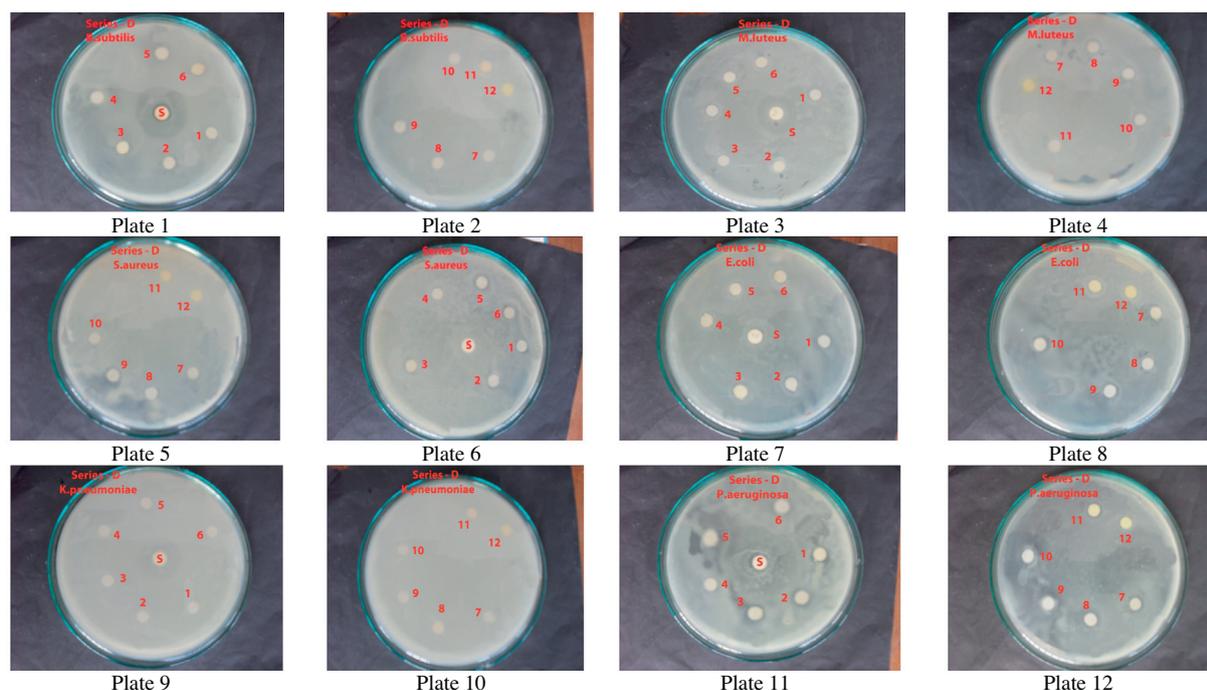
#### 3.4.5. Preparation of test compound

The newly synthesized 2,5-dimethyl-3-thienyl chalcones of weight 15 mg each were dissolved in 1 ml of DMSO solvent. Using 100 µl solution, the discs were impregnated and placed on the Mueller Hinton solidified Agar medium to find out the antimicrobial activity of the compounds on each organism.

By adopting the above procedure, the antimicrobial activity of the chalcones has been studied on six microorganisms and the results have been discussed.

#### 3.4.6. Antibacterial sensitivity assay

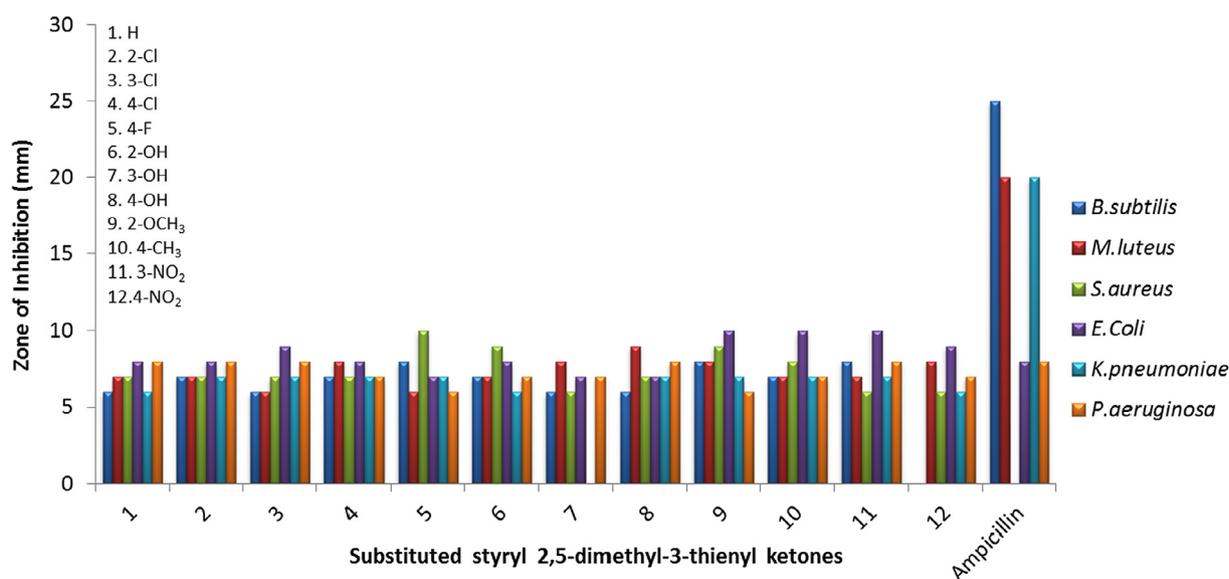
Antibacterial sensitivity assay was performed using Kirby-Bauer (Bauer et al., 1966) disc diffusion technique. In each Petri plate about 0.5 ml of the test bacterial sample was spread



**Figure 3** Antibacterial activities of substituted styryl 2,5-dimethyl-3-thienyl ketones-zone of inhibitions petri dishes.

**Table 6** Antibacterial activity of substituted styryl 2,5-dimethyl-3-thienyl ketones.

Entry	Compound	X	Zone of inhibition (mm)					
			Gram positive Bacteria			Gram negative Bacteria		
			<i>B. subtilis</i>	<i>M. luteus</i>	<i>S. aureus</i>	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>P. aeruginosa</i>
1	D-1	H	6	7	7	8	6	8
2	D-2	2-Cl	7	7	7	8	7	8
3	D-3	3-Cl	6	6	7	9	7	8
4	D-4	4-Cl	7	8	7	8	7	7
5	D-5	4-F	8	6	10	7	7	6
6	D-6	2-OH	7	7	9	8	6	7
7	D-7	3-OH	6	8	6	7	–	7
8	D-8	4-OH	6	9	7	7	7	8
9	D-9	2-OCH <sub>3</sub>	8	8	9	10	7	6
10	D-10	4-CH <sub>3</sub>	7	7	8	10	7	7
11	D-11	3-NO <sub>2</sub>	8	7	6	10	7	8
12	D-12	4-NO <sub>2</sub>	–	8	6	9	6	7
	Standard	Ampicillin	25	20	–	8	20	8
	Control	DMSO	–	–	–	–	–	–

**Figure 4** Antibacterial activities of substituted styryl 2,5-dimethyl-3-thienyl ketones-zone of inhibitions chart.

uniformly over the solidified Mueller Hinton agar using a sterile glass spreader. Then the discs with 5 mm 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 h at 37 °C by keeping the plates upside down to prevent the collection of water droplets over the medium. After 24 h, 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.

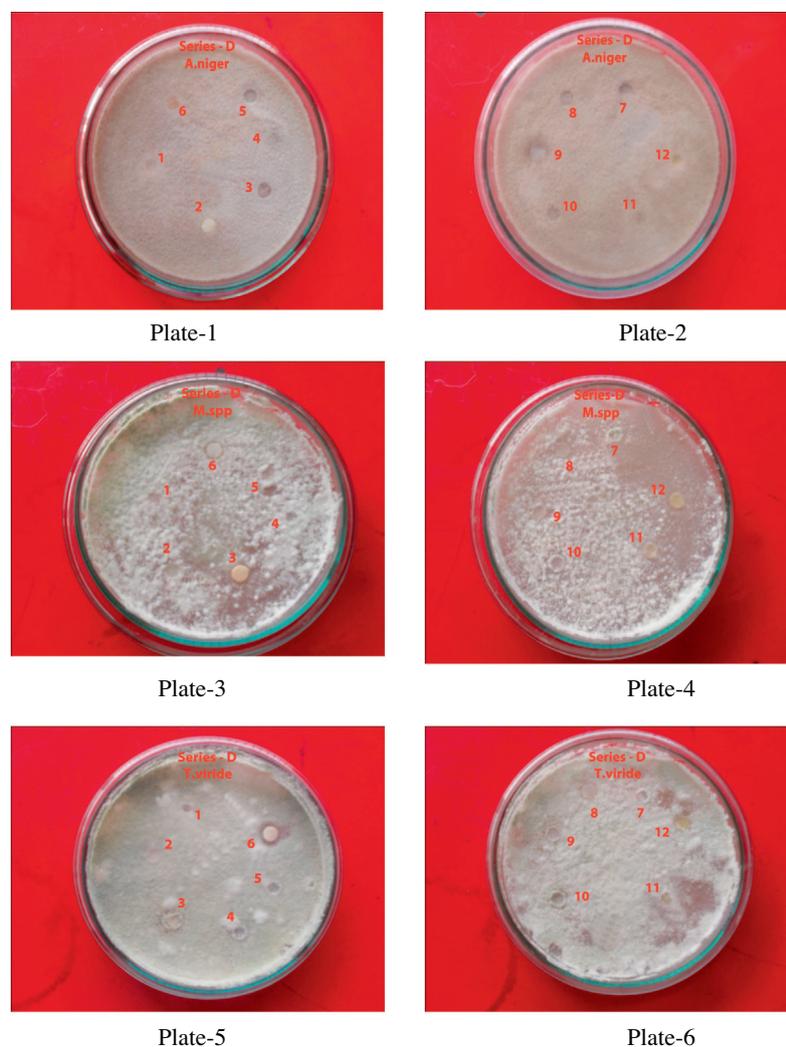
The satisfactory antibacterial effect of synthesized chalcones is shown in (Fig. 3.) (Plates 1–12). The zone of inhibition is compared using Table 6 and the Clustered column Chart is shown in (Fig. 4). From the chart, it is inferred that the chalcone with –OCH<sub>3</sub>, –CH<sub>3</sub> and –NO<sub>2</sub> at the 3rd position have excellent and improved antibacterial activity against the all the six microorganisms. This series showed very good activities against *S. aureus*, *E. coli* and *P. aeruginosa*.

### 3.4.7. Antifungal activity

**3.4.7.1. Preparation of the potato dextrose agar medium.** PDA agar medium was prepared in a conical flask by dissolving 3.9 g of the agar in 100 ml distilled water. It was sterilized in the autoclave for 15 min. at 121 °C and 15 lbs/inch<sup>2</sup> pressure. Then the medium was allowed for solidification for an hour. After that the fungal species was inoculated in the medium and kept for 5–7 days at room temperature.

**3.4.7.2. Preparation of the fungal inoculum.** About 20–25 ml of sterile water (after cooling) was mixed with the medium. The water over the medium was swirled and decanted with the fungal species. Tween-80(1–2 ml) has been added with this solution for uniform growth.

**3.4.7.3. Antifungal sensitivity assay.** Antifungal sensitivity assay was performed using Kirby–Bauer (Bauer et al., 1966) disc diffusion technique. PDA medium was prepared and sterilized as above. It was poured (ear bearing hot condition) on the



**Figure 5** Antifungal activities of 2,5-dimethyl-3-thienyl chalcones Petri-dishes.

Petri-plate which was already filled with 1 ml of the fungal species. The plate was rotated clockwise and counter clockwise for uniform spreading of the species. The discs were impregnated with the test solution. The test solution was prepared by dissolving 15 mg of the chalcone in 1 ml of DMSO solvent. The medium was allowed to solidify and kept for 24 h. Then 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 antifungal activities of substituted chalcones synthesized in the present study are shown in (Fig. 5). for plates (1–6) and the zone of inhibition values of the effect are given in Table 7. The clustered column chart, shown in (Fig. 6). With the analysis of the clustered column chart, by comparing the antifungal activity of this series, the substituents like 3-Cl, 2-OH and 4-Me, showed considerable antifungal activity. The substituents like 3-Cl, 2-OH, 4-OH and 4-NO<sub>2</sub> groups showed excellent antifungal activity on *M. spp*.

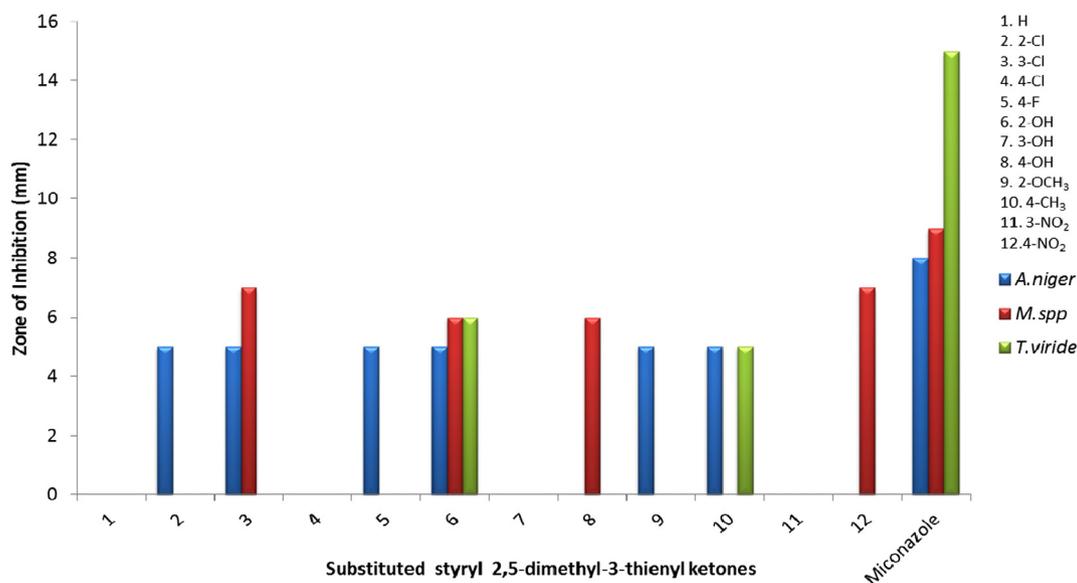
#### 3.4.8. Antioxidant activity

All synthesized 2,5-dimethyl-3-thienyl chalcones possess significant biological activities. The basic skeleton of enones, present widely in natural products are known to have multi-pronged

**Table 7** Antifungal activities of substituted styryl 2, 5-dimethyl-3-thienyl ketones.

Entry	Compound	X	Zone of inhibition (mm)		
			<i>A. niger</i>	<i>M. spp</i>	<i>T. viride</i>
1	D-1	H	–	–	–
2	D-2	2-Cl	5	–	–
3	D-3	3-Cl	5	–	–
4	D-4	4-Cl	–	–	–
5	D-5	4-F	5	–	–
6	D-6	2-OH	5	6	6
7	D-7	3-OH	–	–	–
8	D-8	4-OH	–	6	–
9	D-9	2-OCH <sub>3</sub>	5	–	–
10	D-10	4-CH <sub>3</sub>	5	–	5
11	D-11	3-NO <sub>2</sub>	–	–	–
12	D-12	4-NO <sub>2</sub>	–	7	–
	Standard	Miconazole	8	9	15

activity(Thirunarayanan 2008b; Thirunarayanan et al., 2010; Sivakumar et al., 2007; Lahtchev, 2008; Weber et al., 2005).



**Figure 6** Antifungal activities of 2,5-dimethyl-3-thienyl ketones-zone of inhibition clustered chart.

Presence of polar functional groups, hydrophobic moiety and the absence of steric hindrance near the aryl ring are the important factors for the presence of biological activities of chalcones and their derivatives. In this present study it is observed that only two of the synthesized chalcones have fair antioxidant activity.

**3.4.8.1. Measurement of antioxidant activity of 2,5-dimethyl-3-thienyl chalcones.** Antioxidant activities of all synthesized 2,5-dimethyl-3-thienyl chalcones have been evaluated by the DPPH radical scavenging effect (Jayasinghe et al., 2006). 0.1 M acetate was prepared by dissolving 1.64 g of sodium acetate in 15 mL of water and 150  $\mu$ L of acetic acid. The final volume was adjusted to 20 mL by adding water. The 0.2 mmol of DPPH solution was prepared by dissolving 3.9 g of DPPH in 50 mL of ethanol.  $\alpha$ -Tocopherol (1 mg in 10 mL of ethanol) solution was prepared. A series of test tubes were arranged with 1.0 mL of buffer solution mixed with 0.5 mL of DPPH solution. A series of various concentrations of synthesized chalcones and  $\alpha$ -Tocopherol (1  $\mu$ g in 1 mL of ethanol) were added to each tube and mixed well. After 30 min at RT the absorbance of each solution is measured by UV-Vis spectro-

photometer at 517 nm. A mixture of buffer solution and ethanol were used as the reference for the spectrophotometer. A graph was plotted with the weight of the compound versus absorptions and  $IC_{50}$  values were determined. The antioxidant activity was expressed in terms of  $IC_{50}$  ( $\mu$ g/mL, concentration required to inhibit DPPH radical formation by 50%).  $\alpha$ -Tocopherol was used as a positive control. From this experiment the chalcones 6–9 were found to have a satisfactory antioxidant activity.

#### 3.4.9. Insect antifeedant activity

The multipronged activities present in different chalcones are intended to examine their insect antifeedant activities against castor *semilooper*. The larvae of *Achoea Janata* L were reared as described on the leaves of caster *Richnus communis* in the laboratory at the temperature range of  $26 \pm 1$  °C and a relative humidity of 75–85%. The leaf – disc bioassay method (Dasharathi et al., 2005; Dethler's, 1947) was used against the 4th instar larvae to measure the antifeedant activity. The 4th instar larvae were selected for testing because the larvae at this stage feed very voraciously.

**Table 8** Insect antifeedant activity of substituted styryl 2, 5-dimethyl-3-thienyl ketones.

Entry	X	4–6 pm	6–8 pm	8–10 pm	10–12 pm	12–6am	6–8 am	8am– 12Nn	12Nn– 2 pm	2–4 pm	Total leaf disc consumed in 24 h
1	H	1	1	0.5	0.5	0.5	1	1	1	1	8
2	2-Cl	0.5	0.25	0.25	0.5	0.5	0.5	1	1	0.5	0.5
3	3-Cl	0.5	0.25	0.25	0.5	0.5	0.5	1	1	0.5	0.5
4	4-Cl	0.5	0.5	0.25	1	0.5	0.5	0.25	0.25	0.25	0.4
5	4-F	0.25	0.25	0.25	0	0	0.25	0	0	0	0.1
6	2-OH	0.25	0	0	0.25	0	0	0.20	0.20	0	0.90
7	3-OH	1	3	2	2	1	4	0	1	1	15
8	4-OH	2	0	1	0	1	0	1	0	0	5
9	2-OCH <sub>3</sub>	1	0.5	0.5	1	1	0	1	1	1	9
10	4-CH <sub>3</sub>	0.5	0.5	0.5	2	2	1	1	1	1	9
11	3-NO <sub>2</sub>	2	3	3	1	1	1	0.5	1	0	12
12	4-NO <sub>2</sub>	1	2	2	2	1	0.5	0.5	1	0	10

Number of leaf discs consumed by the insect (values are mean + SE of five).

**Table 9** Insect antifeedant activity of compound **4** (*2E*)-1-(2,5-dimethyl-3-thienyl)-3-(4-chlorophenyl)-2-propen-1-one at four different concentrations – number of leaf discs consumed by the insect (values are mean + SE of five).

ppm	4–6 pm	6–8 pm	8–10 pm	10–12 pm	12–6am	6–8 am	8am–12Nn	12Nn–2 pm	2–4 pm	Total leaf disc consumed in 24 h
50	0	0.5	0.5	0	0	0	0	0	0	0.1
100	0	0.25	0	0.25	0	0	0	0	0	0.05
150	0	0	0	0	0	0	0	0	0	0

3.4.9.1. *Measurement of insect antifeedant activity of 2,5-dimethyl-3-thienyl chalcones.* Leaf discs with a diameter of 1.85 cm were punched from castor leaves with the petioles intact. All chalcones were dissolved in acetone at a concentration of 200 ppm dipped for 5 min. The leaf discs were air-dried and placed in a one litre beaker containing little water in order to facilitate translocation of water. Therefore the leaf discs remains fresh throughout the duration of the rest, 4th instar larvae of the test insect, which had been preserved on the leaf discs of all chalcones and allowed to feed on them for 24 h. The areas of the leaf discs consumed were measured by the Dethler's (Dethler's, 1947) method. The observed antifeedant activity of chalcones was presented in Table 8.

The results of the antifeedant activity of keto chalcones presented in Table 8 reveal that the compounds **2–5** are found to reflect remarkable antifeedant activity among all other chalcones. This test is performed with the insects which took only two-leaf discs soaked under the solution of this compound (Thirunarayanan 2008b; Thirunarayanan et al., 2010). Compounds **3–5** also showed enough antifeedant activity but their activities are lesser than **4**. Further, compound **4** was subjected to measure the antifeedant activity at different concentrations of 50, 100, 150 ppm and the observation reveals that as the concentrations decrease, the activity also decreases. From the results in Table 9, it is observed that the chalcone **4** showed an appreciable antifeedant activity at 200 ppm concentration.

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