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## Synthesis, Study of Substituent Effect and Evaluation of Biological Activities of (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones

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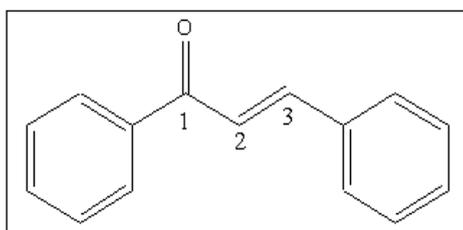
### ABSTRACT

In the present study, nine number of different substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds were synthesized by the condensation reaction of 3,4,5-trimethoxy acetophenone with different substituted benzaldehyde in alcoholic base (sodium hydroxide in ethanol). The yields of the products have been obtained above 80%. The formations of all the (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones have been confirmed by analytical and spectroscopic data. All the assigned spectral values of substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds are correlated by single and multi-correlation analyses with Hammett sigma constants and *F* & *R* parameters. From the regression analyses result, the electronic effects of the substituent were discussed. The evaluation of antimicrobial activity of synthesized chalcones has been screened using Kirby-Bauer method.

**Keywords:** 3,4,5-trimethoxyphenyl chalcones, Biological activities, Hammett correlation analysis, Substituent effect, UV, IR, NMR spectra

### INTRODUCTION

The chemistry of  $\alpha,\beta$ -unsaturated ketones has generated intensive scientific studies throughout the world. Especially interest has been focused on the synthesis and biodynamic activities of  $\alpha,\beta$ -unsaturated ketones. The name "Chalcone" was first named by Kostanecki and Tambor [1]. These compounds are also known as benzalacetophenone or benzylideneacetophenone. In chalcones compounds, two aromatic rings are linked at position 1 and 3 in a aliphatic 3 carbon chain as shown in Scheme 1. These,  $\alpha,\beta$ -unsaturated ketone act as very good synthon in the synthesis of novel heterocycles. The highly reactive keto-ethylenic ( $-\text{CO}-\text{CH}=\text{CH}-$ ) group in chalcone compounds responses various chemical properties. These are colored compounds because of the presence of the chromophore  $-\text{CO}-\text{CH}=\text{CH}-$  and their intensity of color is depends on the presence of other auxochromes.



Scheme 1: In chalcones compounds

Chalcone compounds are very important compounds especially they act as precursors for other organic compounds synthesized by researchers [2]. Recently, chalcones doped polymers [3-5] have gained more attention by the researchers because of their potential applications.

These  $\alpha,\beta$ -unsaturated ketones are the class of natural products and are abundant in vegetables (e.g., tomatoes, potatoes, etc.), fruits (e.g., apples, citrus, etc.) and many plants and spices (e.g., licorice) [6]. These are the major content in citrus fruits and various plants. They have been applied as very good synthons in the synthesis of five and six-membered ring systems namely, pyrazoles [7], pyrazolines [8], isoxazolines [9], aurones [10], flavanones [11] and di-aryl cyclohexenones [12] and so on.

These  $\alpha,\beta$ -unsaturated ketones are flavonoids family which contains medicinal effect like anti-microbial [13], anti-inflammatory [14], analgesic [15], anti-ulcerative[16], immune-modulatory [17], anti-malarial [18], anticancer [19], antiviral [20], antileishmanial [21], antioxidant [22], antitubercular [23], antihyperglycemic [24] etc., Hydroxy and phenyl substituted chalcone compounds have shown good anti-oxidant properties [25,26].

Nowadays, researchers have paid more attention to the study of correlation analysis of Ultra-Violet, Infra-Red and  $^1\text{H}$  &  $^{13}\text{C}$ -NMR spectral data with Hammett constants ( $\sigma$ ,  $\sigma^+$ ,  $\sigma_p$ ,  $\sigma_R$ ) in order to study their effect of substituents of chalcones [27], keto-oxiranes [28], pyrazolines [29], Schiff bases [30,31] and hydrazones [32]. However, limited number of investigations had been previously reported regarding the effect of the substituents with the help of the UV, IR and  $^1\text{H}$  and  $^{13}\text{C}$ -NMR spectral data in substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds.

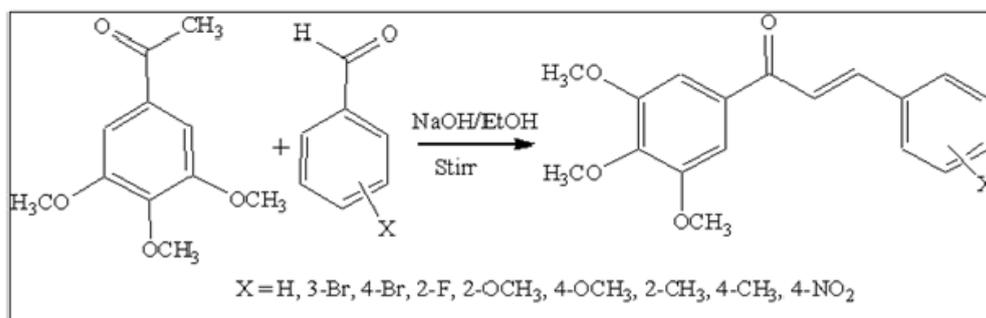
In the present study, the authors have prepared nine number substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds by the condensation of 3',4',5'-trimethoxyacetophenone with different substituted benzaldehyde. Their UV, IR and NMR spectra of these substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds have been recorded and their spectral data have been utilized for the study of substituent effects. Also the authors have evaluated the antimicrobial activities of these ketones by Bauer-Kirby[33] disc diffusion method against their microbial strains.

## MATERIALS AND METHODS

All the used chemicals were bought from Sigma-Aldrich, E-Merck and Himedia chemical companies. The melting point of prepared (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones have been obtained in open glass capillaries on Mettler FP51 apparatus. The UV spectra of all compounds were recorded using Shimadzu-1650 ultraviolet spectrophotometer in spectral grade methanol. Avatar-Nicolet 330 FT spectrometer has been utilized for recording infrared spectra (KBr, 4000-400  $\text{cm}^{-1}$ ). The Bruker AV400 NMR spectrometer was utilized for recording nuclear magnetic resonance spectra of all substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones operating at 400 MHz and at 500 MHz for  $^1\text{H}$  NMR spectra and 100 MHz for  $^{13}\text{C}$  spectra in  $\text{CDCl}_3$  solvent using TMS as internal standard.

### General procedure for preparation of (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones

In a 250 ml round bottom flask, a mixture of 3,4,5-trimethoxy acetophenone (0.05 mol), unsubstituted and substituted benzaldehydes (0.05 mol) were taken and stirred with a magnetic stirrer. To this solution, 50 ml sodium hydroxide solution has been added in drop wise and continued the stirring for 30 min [34]. Then 0.1 N hydrochloric acid was added in order to neutralization and the precipitated is formed. The crude (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones were obtained after filtration, dried in air-oven and recrystallized using ethanol. The general reaction scheme for the synthesis of (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones is shown in Scheme 2. The yield, physical constants and the analytical data of (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones are presented in Table 1.



Scheme 2: Synthesis of substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds

Table 1: Physical constants of substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds

Entry	Substituent (X)	Molecular formula	Molecular weight	Yield (%)	Melting point (°C)
1	H	C <sub>18</sub> H <sub>18</sub> O <sub>4</sub>	298	87	83-85
2	3-Br	C <sub>18</sub> H <sub>17</sub> BrO <sub>4</sub>	377	82	110-112
3	4-Br	C <sub>18</sub> H <sub>17</sub> BrO <sub>4</sub>	377	86	114-116
4	2-F	C <sub>18</sub> H <sub>17</sub> FO <sub>4</sub>	316	88	142-143
5	2-OCH <sub>3</sub>	C <sub>19</sub> H <sub>20</sub> O <sub>5</sub>	328	93	127-129
6	4-OCH <sub>3</sub>	C <sub>19</sub> H <sub>20</sub> O <sub>5</sub>	328	87	110-112
7	2-CH <sub>3</sub>	C <sub>19</sub> H <sub>20</sub> O <sub>4</sub>	312	88	109-111
8	4-CH <sub>3</sub>	C <sub>19</sub> H <sub>20</sub> O <sub>4</sub>	312	92	119-121
9	4-NO <sub>2</sub>	C <sub>18</sub> H <sub>17</sub> NO <sub>6</sub>	343	84	143-145

## RESULTS AND DISCUSSION

### Spectral linearity

The spectral correlation analyses of substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds has been done for evaluating the effect of substituents [34] by utilizing their spectral data. These UV  $\lambda_{\text{max}}$  (nm), IR frequencies of  $\nu\text{CO}_{s\text{-cis}}$  and  $\nu\text{CO}_{s\text{-trans}}$  and deformation modes of CH *ip*, *op*, CH=CH and >C=C< *op* ( $\text{cm}^{-1}$ ), NMR chemical shifts  $\delta$  (ppm) of H $_{\alpha}$ , H $_{\beta}$ , C $_{\alpha}$ , C $_{\beta}$  and CO have been assigned and are tabulated in Table 2. These data are correlated with various substituent constants.

**Table 2: The ultraviolet absorption maxima ( $\lambda_{max}$ , nm), infrared absorptions ( $\nu$ ,  $\text{cm}^{-1}$ ) and NMR chemical shifts ( $\delta$ , ppm) spectral data of substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds**

Entry	X	UV ( $\lambda_{max}$ )	Infrared red ( $\nu$ , $\text{cm}^{-1}$ )						$^1\text{H-NMR}$ ( $\delta$ , ppm)		$^{13}\text{C-NMR}$ ( $\delta$ , ppm)		
			CO ( <i>s-cis</i> )	CO ( <i>s-trans</i> )	CH <i>ip</i>	CH <i>op</i>	CH=CH <i>op</i>	C=C <i>op</i>	H <sub>a</sub>	H <sub>β</sub>	CO	C <sub>α</sub>	C <sub>β</sub>
1	H	357.0	1647.21	1597.06	1192.01	769.60	1035.77	509.21	7.582	7.819	188.15	121.99	121.99
2	3-Br	369.5	1649.14	1597.06	1193.94	759.95	1037.70	518.85	7.473	8.162	187.97	124.81	124.81
3	4-Br	370.5	1649.14	1598.99	1192.01	752.24	1031.92	511.14	7.564	7.730	187.63	123.20	123.20
4	2-F	358.5	1647.21	1598.99	1193.94	759.95	1028.06	513.07	7.499	7.773	187.88	121.69	121.69
5	2-OCH <sub>3</sub>	367.5	1653.00	1597.06	1193.94	796.60	1031.92	513.07	7.559	7.755	187.71	123.16	123.16
6	4-OCH <sub>3</sub>	353.5	1651.07	1598.99	1195.87	788.89	1029.99	513.07	7.544	7.754	187.79	122.4	122.40
7	2-CH <sub>3</sub>	369.5	1649.14	1598.99	1197.79	763.81	1031.92	514.99	7.461	7.789	188.21	119.66	119.66
8	4-CH <sub>3</sub>	351.0	1647.21	1595.13	1186.22	783.10	1037.70	516.92	7.537	7.798	188.26	120.99	120.99
9	4-NO <sub>2</sub>	326.5	1653.00	1598.99	1193.94	817.82	1041.56	514.99	7.684	7.961	187.12	122.09	122.09

**UV spectral study**

The measured the UV absorption maximum ( $\lambda_{max}$  nm) values of substitute (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds have been presented in In Table 2. These values have been utilized to correlate them against substituent constants derived from Hammett ( $\sigma$ ,  $\sigma^+$ ,  $\sigma_I$ ,  $\sigma_R$ ) [35,36] and Swain-Lupton's parameters [37] using both single and multi-linear regression analyses. The Hammett equation used for these UV correlations is given in equation (1):

$$\lambda = \rho\sigma + \lambda_0 \quad (1)$$

Where,  $\lambda_0$  is the UV absorption maximum value  $\lambda_{max}$  (nm) of the unsubstituted compound. These observed UV absorption maximum ( $\lambda_{max}$  nm) values all the substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds have been correlated with Hammett substituent constants and *F* & *R* parameters and the results are shown in Table 3.

**Table 3: Results of statistical analysis of UV absorption maxima ( $\lambda_{max}$ , nm), IR frequencies ( $\nu$ ,  $\text{cm}^{-1}$ ) and NMR chemical shifts ( $\delta$ , ppm) of substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds with Hammett  $\sigma$ ,  $\sigma^+$ ,  $\sigma_I$ ,  $\sigma_R$  and *F* and *R* parameters**

Frequency	Constant	r	I	$\rho$	s	n	Correlated derivatives
$\lambda_{max}$	$\sigma$	0.771	318.97	-55.62	17.26	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.907	319.58	-40.17	6.33	8	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.866	331.36	-65.88	20.26	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.847	301.74	-50.88	23.82	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	<i>F</i>	0.767	332.32	-61.57	20.06	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	<i>R</i>	0.740	301.91	-40.06	24.78	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
CO <i>s-cis</i>	$\sigma$	0.977	1662.95	8.62	1.61	7	H, 3-Br, 4-Br, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.980	1662.69	07.10	1.45	8	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.966	1661.05	10.12	1.11	7	H, 3-Br, 4-Br, 2-F, 4-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.819	1664.61	3.14	4.08	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	<i>F</i>	0.974	1660.61	10.39	0.80	7	H, 3-Br, 4-Br, 2-F, 4-OCH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	<i>R</i>	0.809	1664.31	01.36	4.15	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
CO <i>s-trans</i>	$\sigma$	0.648	1598.62	06.89	4.71	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.723	1598.85	03.21	5.16	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.749	1597.73	05.89	5.13	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.766	1602.41	14.12	3.99	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	<i>F</i>	0.817	1598.40	03.15	5.29	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	<i>R</i>	0.867	1602.89	13.08	3.99	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
CH <sub>ip</sub>	$\sigma$	0.756	1166.00	8.99	4.95	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.933	1166.30	3.92	1.71	8	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub>

	$\sigma_I$	0.748	1164.00	10.52	5.26	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.749	1169.50	11.68	5.21	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$F$	0.738	1164.50	7.89	5.23	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$R$	0.855	1170.21	12.02	5.01	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
CH <sub>op</sub>	$\sigma$	0.764	787.85	42.52	19.13	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.735	787.79	28.4	20.99	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.764	775.92	59.06	18.98	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.824	797.93	24.33	24.16	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$F$	0.876	776.48	50.73	19.89	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$R$	0.821	797.98	19.63	24.35	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
CH=CH <sub>op</sub>	$\sigma$	0.703	991.11	1.65	19.51	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.712	992.20	-5.13	19.37	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.831	984.82	22.70	18.50	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.804	990.49	-3.79	19.49	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$F$	0.820	986.91	13.67	19.09	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$R$	0.809	993.07	6.65	19.43	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
C=C <sub>op</sub>	$\sigma$	0.862	510.33	84.69	42.34	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.842	511.82	47.43	47.99	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.844	495.50	86.22	47.44	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.845	540.33	95.21	47.11	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$F$	0.831	502.14	56.02	50.32	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$R$	0.847	544.58	92.10	46.53	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
H <sub>α</sub>	$\sigma$	0.934	7.221	0.231	0.131	6	H, 3-Br, 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.914	7.230	0.081	0.150	6	H, 3-Br, 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.810	7.291	0.190	0.241	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.906	7.384	0.665	0.184	6	H, 3-Br, 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$F$	0.823	7.323	0.255	0.243	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$R$	0.963	7.398	0.577	0.198	6	H, 3-Br, 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
H <sub>β</sub>	$\sigma$	0.807	7.756	-0.022	0.146	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.815	7.761	-0.051	0.142	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.646	7.825	-0.251	0.133	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.735	7.793	-0.271	0.142	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$F$	0.748	7.831	-0.248	0.132	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$R$	0.735	7.800	-0.199	0.141	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
CO	$\sigma$	0.907	189.14	-1.540	0.53	7	H, 3-Br, 4-Br, 2-F, 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.974	189.15	-1.071	0.60	7	H, 3-Br, 4-Br, 2-F, 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.907	189.56	-2.091	0.53	8	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.838	188.71	-1.188	0.73	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$F$	0.868	189.55	-1.872	0.57	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$R$	0.832	188.72	-0.922	0.74	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
C <sub>α</sub>	$\sigma$	0.719	122.33	1.150	2.15	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> ,

	$\sigma^+$	0.908	122.39	0.391	2.19	6	4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub> H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.804	122.57	0.363	2.19	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.836	123.13	3.132	2.04	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$F$	0.705	122.34	0.393	2.19	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$R$	0.732	123.15	2.571	2.08	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
$C_\beta$	$\sigma$	0.726	144.36	-1.731	2.34	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.702	144.18	-0.120	2.42	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.704	144.28	-0.412	2.42	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.659	142.83	-6.284	1.82	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$F$	0.721	143.61	1.743	2.37	9	H, 3-Br, 4-Br, 2-F, 2-OCH <sub>3</sub> , 4-OCH <sub>3</sub> , 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>
	$R$	0.906	142.53	-6.141	1.74	7	H, 3-Br, 4-Br, 2-F, 2-CH <sub>3</sub> , 4-CH <sub>3</sub> , 4-NO <sub>2</sub>

r=Correlation coefficient; I=Intercept; p=Slope; s=Standard deviation; n=Number of correlated derivatives

From the Table 3, the Hammett constant  $\sigma^+$  ( $r=0.907$ ) has shown fair correlation with UV spectral values of all the substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds with the exception of 4-OCH<sub>3</sub> substituent. This 4-OCH<sub>3</sub> substituent has reduced the correlation when it has been included in regression analysis.

The remaining Hammett substituent constants  $\sigma$ ,  $\sigma_I$ ,  $\sigma_R$  and  $F$  &  $R$  parameters were failed ( $r < 0.900$ ) for producing satisfactory correlations with UV maximum absorptions of all substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds. The failing in correlation indicates that polar, inductive, field and resonance effect of the substituents are not able to transmit their electronic effects through resonance. The resonance conjugative structure is shown in Figure 1.

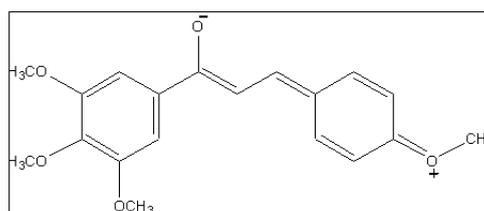


Figure 1: Resonance conjugative structure

All the correlations have produced negative  $\rho$  value and it shows that reverse substituent effect have been operated with respect to UV absorption maximum  $\lambda_{max}$  (nm) values. Since most of the single regression analyses have been failed with sigma constants of Hammett and  $F$  &  $R$  parameters. Hence, the author has opted to go for multi regression analyses [37]. The multi regression analyses have shown satisfactory correlations as shown in the following equations (2) and (3).

$$\lambda_{max}(\text{nm}) = 320.541 (\pm 10.002) - 66.445 (\pm 22.935) \sigma_I - 51.722 (\pm 18.642) \sigma_R \quad (2)$$

$(R=0.982, n=9, P>95\%)$

$$\lambda_{max}(\text{nm}) = 320.864 (\pm 8.534) - 72.392 (\pm 18.523) F - 56.201 (\pm 19.947) R \quad (3)$$

$(R=0.987, n=9, P>95\%)$

### IR spectral correlation analysis

In the present study, the synthesized  $\alpha,\beta$ -unsaturated ketones are expected to exist as *s-cis* and *s-trans* conformations as shown in Figure 2. The infrared frequency values of these *s-cis* and *s-trans* conformations are presented in Table 2.

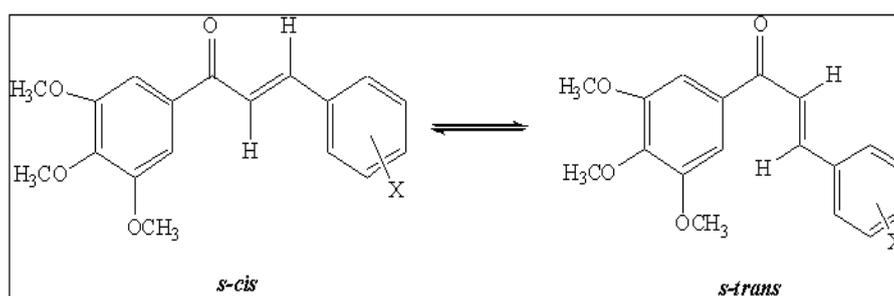


Figure 2: The *s-cis* and *s-trans* conformers of (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones

All the recorded infrared frequencies ( $\text{cm}^{-1}$ ) such as  $\nu\text{CO}_{s-cis}$  and  $\nu\text{CO}_{s-trans}$  and deformation modes of  $\text{CH}_{ip}$ ,  $op$ ,  $\text{CH}=\text{CH}$  and  $>\text{C}=\text{C}<$   $op$  have been adopted to correlation analysis [36,37]. For this correlation analysis, the following equation (4) has been utilized.

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

Where,  $\nu_0$  is the infrared frequency  $\nu$  ( $\text{cm}^{-1}$ ) value of the unsubstituted compound.

#### IR spectral correlation analysis of $\nu\text{CO}_{s-cis}$ ( $\text{cm}^{-1}$ ) frequencies

The observed infrared frequency of  $\nu\text{CO}_{s-cis}$  ( $\text{cm}^{-1}$ ) values have been incorporated in single regression analysis and multi regression analyses. The results of regression analysis are shown in Table 3. During single correlation analysis, all the substituents except 2-F and 2- $\text{CH}_3$  substituents have shown satisfactory correlation with Hammett constant  $\sigma$  ( $r=0.977$ ) only. The Hammett constant  $\sigma^+$  ( $r=0.980$ ) has also produced satisfactory correlation with all substituents (except 2- $\text{CH}_3$ ) and  $\sigma_I$  ( $r=0.906$ ) and  $F$  parameter ( $r=0.974$ ) have also produced satisfactory correlations with the exemption of 2- $\text{OCH}_3$  and 2- $\text{CH}_3$  substituents.

These exempted substituents are decreasing the correlation co-efficient value significantly when they are incorporated in correlation analysis. The resonance factors of the both Hammett and Swain-Lupton's parameters have failed in correlations ( $r<0.900$ ). This is due to the reason stated earlier. All the correlations (except  $\sigma_R$  and  $R$ ) found to show positive  $\rho$  values which displays that normal effect has been operated.

#### IR spectral correlation analysis of $\nu\text{CO}_{s-trans}$ ( $\text{cm}^{-1}$ ) frequencies

The IR frequency of carbonyl group of *s-trans* conformers of all substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds have been failed to producing satisfactory correlations ( $r<0.900$ ) with positive  $\rho$  value. This indicates the operation of normal substituent effect with respect to IR frequency  $\nu\text{CO}_{s-trans}$  ( $\text{cm}^{-1}$ ) values in all substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones.

#### IR spectral correlation analysis of $\nu\text{CH}_{ip}$ ( $\text{cm}^{-1}$ ) frequencies

The IR frequency of  $\nu\text{CH}_{ip}$  ( $\text{cm}^{-1}$ ) deformation modes of all substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds (except 4- $\text{NO}_2$  substituent) produced satisfactory correlation with Hammett constant  $\sigma^+$  ( $r=0.905$ ). If the 4- $\text{NO}_2$  substituent is incorporated in regression, it diminishes the correlations significantly. These IR frequency  $\nu\text{CH}_{ip}$  ( $\text{cm}^{-1}$ ) deformation modes produced poor correlations. All the correlations have shown positive  $\rho$  values. This shows that normal substituent effect has been operated with respect to IR frequency  $\nu\text{CH}_{ip}$  ( $\text{cm}^{-1}$ ) values in substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds.

#### IR spectral correlation analysis of $\nu\text{CH}_{op}$ ( $\text{cm}^{-1}$ ) frequencies

The deformation modes of infrared frequency  $\nu\text{CH}_{op}$  ( $\text{cm}^{-1}$ ) values of (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones shows poor correlations ( $r<0.900$ ) with all Hammett substituent constants ( $\sigma$ ,  $\sigma^+$ ,  $\sigma_I$ ,  $\sigma_R$ ) and  $F$  and  $R$  parameters. All the correlations have shown positive  $\rho$  values. This indicates the operation of normal substituent effect with respect to IR frequency  $\nu\text{CO}_{s-trans}$  ( $\text{cm}^{-1}$ ) values in all substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones.

#### IR spectral correlation analysis of $\nu\text{CH}=\text{CH}_{op}$ ( $\text{cm}^{-1}$ ) frequencies

The IR frequency  $\nu\text{CH}_{op}$  ( $\text{cm}^{-1}$ ) values of all substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds have shown poor correlations ( $r<0.900$ ) with all Hammett substituent constants ( $\sigma$ ,  $\sigma^+$ ,  $\sigma_I$ ,  $\sigma_R$ ) and  $F$  and  $R$  parameters. The positive  $\rho$  value has been obtained in all correlations. This indicates the operation of normal substituent effect with respect to IR frequency  $\nu\text{CO}_{s-trans}$  ( $\text{cm}^{-1}$ ) values in all substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones.

#### IR spectral correlation analysis of $\nu\text{C}=\text{C}_{op}$ ( $\text{cm}^{-1}$ ) frequencies

In single regression analysis, the poor correlation co-efficient values ( $r<0.900$ ) have been obtained for out of plane deformation modes of  $\nu\text{C}=\text{C}_{op}$  ( $\text{cm}^{-1}$ ) frequencies of (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones with all Hammett substituent constants ( $\sigma$ ,  $\sigma^+$ ,  $\sigma_I$ ,  $\sigma_R$ ) and  $F$  and  $R$  parameters. All the correlations (except  $\sigma^+$ ,  $\sigma_R$ ) have shown positive  $\rho$  values. This indicates the operation of normal substituent effect with respect to IR frequency  $\nu\text{C}=\text{C}_{op}$  ( $\text{cm}^{-1}$ ) values in all substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones.

In single correlation analysis, most of them failed to produce good correlations. So we have planned to go for multi correlation analyses. The multi-regression analyses have produced good correlation co-efficient values with Hammett substituent constants ( $\sigma_I$ ,  $\sigma_R$ ) and  $F$  and  $R$  parameters [37]. The multi correlation analyses equations are given in the following equations (5)-(16).

$$\nu\text{CO}_{s-cis} (\text{cm}^{-1}) = 1661.714 (\pm 1.953) + 10.165 (\pm 3.465)\sigma + 3.276 (\pm 1.794) \sigma_R \quad (5)$$

$(R=0.969, n=9, P>95\%)$

$$\nu\text{CO}_{s-cis} (\text{cm}^{-1}) = 1661.393 (\pm 1.692) + 11.136 (\pm 3.666)F + 3.852 (\pm 1.946)R \quad (6)$$

$(R=0.978, n=9, P>95\%)$

$$\nu\text{CO}_{s-trans} (\text{cm}^{-1}) = 1600.702 (\pm 2.373) + 6.043 (\pm 2.425)\sigma_I + 14.195 (\pm 3.835)\sigma_R \quad (7)$$

$(R=0.973, n=9, P>95\%)$

$$\nu\text{CO}_{s-trans} (\text{cm}^{-1}) = 1601.341 (\pm 2.374) + 5.915 (\pm 2.078)F + 14.417 (\pm 4.465)R \quad (8)$$

$(R=0.974, n=9, P>95\%)$

$$\nu\text{CH}_{ip} (\text{cm}^{-1}) = 1166.499 (\pm 2.815) + 10.6541 (\pm 3.432)\sigma_I + 11.813 (\pm 3.913)\sigma_R \quad (9)$$

$(R=0.969, n=9, P>95\%)$

$$\nu\text{CH}_{ip} (\text{cm}^{-1}) = 1167.434 (\pm 2.556) + 10.662 (\pm 3.547)F + 14.395 (\pm 3.964)R \quad (10)$$

$(R=0.975, n=9, P>95\%)$

$$\nu_{\text{CHop}} (\text{cm}^{-1}) = 781.152 (\pm 11.635) + 59.337 (\pm 16.653) \sigma_{\text{I}} + 25.089 (\pm 8.648) \sigma_{\text{R}} \quad (11)$$

$$(R=0.969, n=9, P>95\%)$$

$$\nu_{\text{CHop}} (\text{cm}^{-1}) = 783.07 (\pm 11.594) + 56.95 (\pm 15.173) F + 32.33 (\pm 11.094) R \quad (12)$$

$$(R=0.932, n=9, P>90\%)$$

$$\nu_{\text{CH=CHop}} (\text{cm}^{-1}) = 984.081 (\pm 12.024) + 22.664 (\pm 8.553) \sigma_{\text{I}} - 3.508 (\pm 1.604) \sigma_{\text{R}} \quad (13)$$

$$(R=0.969, n=9, P>95\%)$$

$$\nu_{\text{CH=CHop}} (\text{cm}^{-1}) = 988.986 (\pm 12.258) + 15.622 (\pm 5.593) F + 10.134 (\pm 2.634) R \quad (14)$$

$$(R=0.925, n=9, P>90\%)$$

$$\nu_{\text{C=Cop}} (\text{cm}^{-1}) = 515.642 (\pm 26.414) + 87.269 (\pm 25.528) \sigma_{\text{I}} + 96.302 (\pm 31.034) \sigma_{\text{R}} \quad (15)$$

$$(R=0.964, n=9, P>95\%)$$

$$\nu_{\text{C=Cop}} (\text{cm}^{-1}) = 524.407 (\pm 26.463) + 77.054 (\pm 27.427) F + 109.290 (\pm 31.828) R \quad (16)$$

$$(R=0.963, n=9, P>95\%)$$

### NMR spectral correlations

In NMR spectral correlation analyses of both  $^1\text{H}$  and  $^{13}\text{C}$ -NMR spectral values, the following Hammett equation (17) has been utilized.

$$\delta = \rho\sigma + \delta_0 \quad (17)$$

Where,  $\delta_0$  is the chemical shift value of parent compound.

### Correlation analysis with $^1\text{H}$ -NMR spectral vales

#### $^1\text{H}$ -NMR spectral correlation analysis of $\text{H}_\alpha$ (ppm) protons

The  $^1\text{H}$ -NMR chemical shift ( $\delta$ , ppm) values of  $\text{H}_\alpha$  protons of the synthesized (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones have been used for the single regression analysis with Hammett constants ( $\sigma$ ,  $\sigma^+$ ,  $\sigma_{\text{I}}$ ,  $\sigma_{\text{R}}$ ) [36] and *F* and *R* parameters. During the single correlation analyses, except 4-Br, 2-F, 2-OCH<sub>3</sub> substituents, all the substituents produced satisfactory correlations with  $\sigma$  ( $r=0.934$ ),  $\sigma^+$  ( $r=0.914$ ),  $\sigma_{\text{R}}$  ( $r=0.906$ ) and *R* parameter ( $r=0.963$ ). These exempted substituents decrease the correlations when they are incorporated in regression.

The remaining  $\sigma_{\text{I}}$  constant and *F* parameter [36] are failed in single regression. The inductive and field effects of the substituents are unable to predict their electronic effect from phenyl group to vinyl part as per the conjugative structure shown in Figure 1, which causes the fail in correlations.

#### $^1\text{H}$ -NMR spectral correlation analysis of $\text{H}_\beta$ (ppm) protons

In single regression analysis with  $\text{H}_\beta$  chemical shifts ( $\delta$ , ppm) values produced poor correlation with all Hammett's constants and *F* and *R* parameters. The fail in correlation is due to the incapability to the polar, inductive, resonance and field effect of the substituents. All the correlations have shown negative  $\rho$  values. It denotes the reverse substituent effect has been operated.

During the single regressions, several constants are failed. Hence, it is worthy to seek multi correlations [37]. The multi-regression analyses produced satisfactory correlations as shown in equations (18-21).

$$\delta_{\text{H}_\alpha} (\text{ppm}) = 7.442 (\pm 0.116) - 0.196 (\pm 0.264) \sigma_{\text{I}} + 0.665 (\pm 0.282) \sigma_{\text{R}} \quad (18)$$

$$(R=0.971, n=9, P>95\%)$$

$$\delta_{\text{H}_\alpha} (\text{ppm}) = 7.433 (\pm 0.121) - 0.145 (\pm 0.262) F + 0.541 (\pm 0.287) R \quad (19)$$

$$(R=0.965, n=9, P>95\%)$$

$$\delta_{\text{H}_\beta} (\text{ppm}) = 7.865 (\pm 0.084) - 0.242 (\pm 0.186) \sigma_{\text{I}} + 0.205 (\pm 0.198) \sigma_{\text{R}} \quad (20)$$

$$(R=0.958, n=9, P>90\%)$$

$$\delta_{\text{H}_\beta} (\text{ppm}) = 7.864 (\pm 0.087) - 0.215 (\pm 0.175) F + 0.147 (\pm 0.184) R \quad (21)$$

$$(R=0.954, n=9, P>90\%)$$

### $^{13}\text{C}$ -NMR spectral correlation analysis

#### $^{13}\text{C}$ -NMR spectral correlation analysis of $\delta_{\text{C}_\alpha}$ carbons

The  $^{13}\text{C}$ -NMR chemical shifts ( $\delta$ , ppm) of  $\text{C}_\alpha$  carbons have shown satisfactory correlation coefficient value with constant  $\sigma^+$  ( $r=0.907$ ) with the exception of 4-OCH<sub>3</sub>, 2-CH<sub>3</sub> and 4-CH<sub>3</sub> substituents. The remaining substituent constants have shown poor correlations ( $r<0.900$ ). This is attributed to the inductive effects and resonance effects and field effect of the substituent. All the correlations have shown negative  $\rho$  values. This indicates the operation of reverse substituent effect.

#### $^{13}\text{C}$ -NMR spectral correlation analysis of $\delta_{\text{C}_\beta}$ carbons

All the substituents expect those with 2-OCH<sub>3</sub> and 4-OCH<sub>3</sub> substituents have shown satisfactory correlation with *R* parameter ( $r=0.906$ ). The remaining constants and *F* parameter [36] have shown poor correlations ( $r<0.900$ ). This is attributed to the resonance effect of the substituents. All the correlations (except *F* parameter) have shown negative  $\rho$  values. This indicates the operation of reverse substituent effect.

<sup>13</sup>C-NMR spectral correlation analysis of  $\delta$ CO carbons

The <sup>13</sup>C-NMR chemical shifts ( $\delta$ , ppm) of carbonyl carbons with Hammett constants ( $\sigma$ ,  $\sigma^+$ ,  $\sigma_I$ ,  $\sigma_R$ ) [36] and  $F$  and  $R$  parameters, except that with 2-OCH<sub>3</sub> and 4-CH<sub>3</sub> substituents produced satisfactory correlation with Hammett constants  $\sigma$  ( $r=0.907$ ) and  $\sigma^+$  ( $r=0.974$ ). Except that with 4-CH<sub>3</sub> substituent, all the substituents produced satisfactory correlation with Hammett constant  $\sigma_I$  ( $r=0.907$ ). The remaining constant  $\sigma_R$  and  $F$  and  $R$  parameters are failed in correlations ( $r<0.900$ ). This is attributed to inductive resonance and field effects of the substituents are unable to transit their electronic effects through resonance. All the correlations have shown negative  $\rho$  values. This indicates the operation of reverse substituent effect.

Only few of the single regression analyses are failed in single correlation analysis. So the author has opted to multi-regression [37], the multi-regression analyses produced satisfactory correlations with the chemical shifts of ( $\delta$ , ppm) C <sub>$\alpha$</sub> , C <sub>$\beta$</sub>  and CO. The multi correlation equations are given in equations (22-27).

$$\Delta\text{co (ppm)}=189.312 (\pm 0.293) - 2.117 (\pm 0.662) \sigma_I - 6.028 (\pm 0.718) \sigma_R \quad (22)$$

$(R=0.982, n=9, P>95\%)$

$$\delta\text{CO (ppm)}=189.276 (\pm 0.281) - 2.091 (\pm 0.615) F - 1.398 (\pm 0.653) R \quad (23)$$

$(R=0.983, n=9, P>95\%)$

$$\delta\text{C}_\alpha \text{ (ppm)}=123.233 (\pm 0.1.334) - 0.034 (\pm 0.043) \sigma_I + 3.131 (\pm 1.275) \sigma_R \quad (24)$$

$(R=0.936, n=9, P>90\%)$

$$\delta\text{C}_\alpha \text{ (ppm)}=122.918 (\pm 1.340) + 0.934 (\pm 0.894) F + 2.779 (\pm 1.127) R \quad (25)$$

$(R=0.934, n=9, P>90\%)$

$$\delta\text{C}_\beta \text{ (ppm)}=142.978 (\pm 1.182) - 0.421 (\pm 0.701) \sigma_I - 6.284 (\pm 2.913) \sigma_R \quad (26)$$

$(R=0.966, n=9, P>95\%)$

$$\delta\text{C}_\beta \text{ (ppm)}=142.384 (\pm 1.127) + 0.582 (\pm 0.433) F - 6.027 (\pm 2.628) R \quad (27)$$

$(R=0.970, n=9, P>95\%)$

## Antibacterial sensitivity assay

Using the standard Kirby-Bauer disc diffusion method [33], the antibacterial sensitivity assay of all synthesized substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds have been performed against three gram positive pathogenic strains *Bacillus subtilis*, *Micrococcus luteus*, *Staphylococcus aureus* and 2 g negative strains *Escherichia coli*, *Pseudomonas* with ampicillin as standard.

The antibacterial activities of substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones are displayed in Figure 3 (Plates 1-10). The zone of inhibition values are measured and given in Table 4 and their corresponding clustered column chart is displayed in Figure 4. The zone of inhibition (mm) values of substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds reveals that most of the compounds have shown moderate, (some of the poor) activity against all the five microorganisms evaluated in the present investigation. It reveals that all the compounds have shown moderate antibacterial activities against *Pseudomonas*. The compound with substituent 3-Br has shown improved activity against *E. coli*. The compound with substituent 4-Br has shown excellent activity compared to other compounds against *Pseudomonas*. The parent compound and the compound with substituent 4-OCH<sub>3</sub> have shown only fair antibacterial activity against all the bacteria.

**Table 4: Zone of inhibition (mm) values of antibacterial activity of substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds**

Entry	X	Zone of inhibition (mm)				
		Gram positive bacteria			Gram negative bacteria	
		<i>Bacillus subtilis</i>	<i>Micrococcus</i>	<i>Staphylococcus aureus</i>	<i>Escherichia coli</i>	<i>Pseudomonas</i>
1	H	7	7	7	8	7
2	3-Br	0	7	6	10	8
3	4-Br	7	7	0	9	12
4	2-F	0	8	6	8	7
5	2-OCH <sub>3</sub>	6	7	0	7	7
6	4-OCH <sub>3</sub>	7	9	7	8	6
7	2-CH <sub>3</sub>	8	0	7	7	8
8	4-CH <sub>3</sub>	0	8	8	7	8
9	4-NO <sub>2</sub>	6	9	6	0	6
Std: Ampicillin		9	11	15	18	14
Control: DMSO		0	0	0	0	0

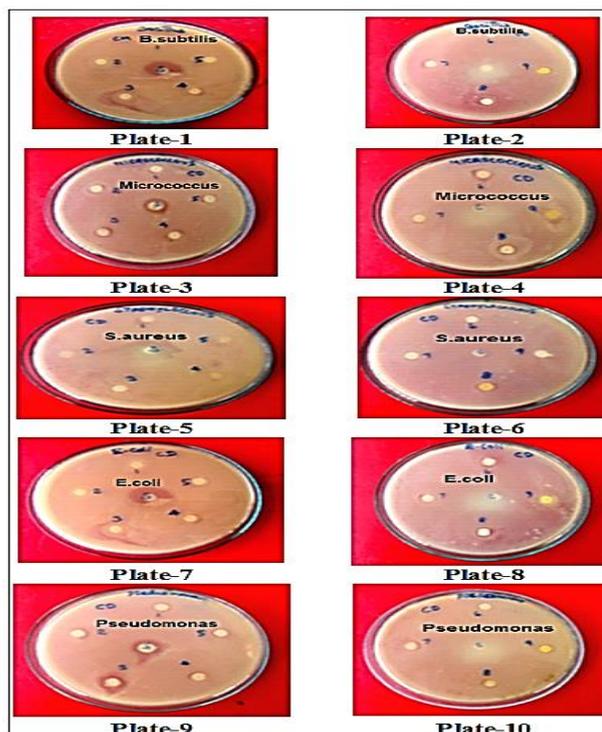


Figure 3: Antibacterial activity of substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds (petri plates)

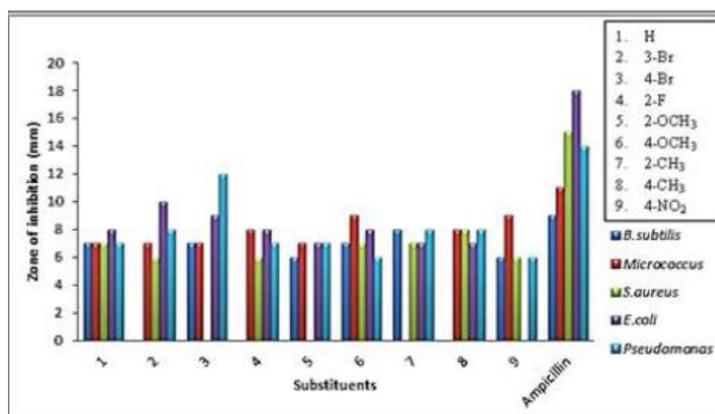


Figure 4: Antibacterial activity of substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds (clustered column chart)

**Antifungal activity**

The analyses of antifungal screening [33] of substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones are performed against 2 fungal species namely, *A. niger* and *Stenotomus chrysops* with miconazole as standard drug. The petri-plates for antifungal activities of substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones are displayed in Figure 5 (Plates 11–14). The measured zone of inhibition values are given in Table 5 and the corresponding clustered column chart is shown in Figure 6. This implies compounds with 3-Br, 4-Br, 2-CH<sub>3</sub> and 4-NO<sub>2</sub> substituted compounds have shown excellent activity against *S. chrysops* compared to *A. niger*. The compound with substituent 4-OCH<sub>3</sub> is biologically inactive against the two fungi namely *A. niger* and *S. chrysops*.

Table 5: Zone of inhibition (mm) values of antifungal activities of substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds

Entry	X	Zone of inhibition (mm)	
		<i>A. niger</i>	<i>S. chrysops</i>
1	H	8	8
2	3-Br	0	10
3	4-Br	6	8
4	2-F	7	7
5	2-OCH <sub>3</sub>	6	6
6	4-OCH <sub>3</sub>	0	0
7	2-CH <sub>3</sub>	7	8
8	4-CH <sub>3</sub>	6	7
9	4-NO <sub>2</sub>	7	9
Standard	Miconazole	14	12
Control	DMSO	0	0

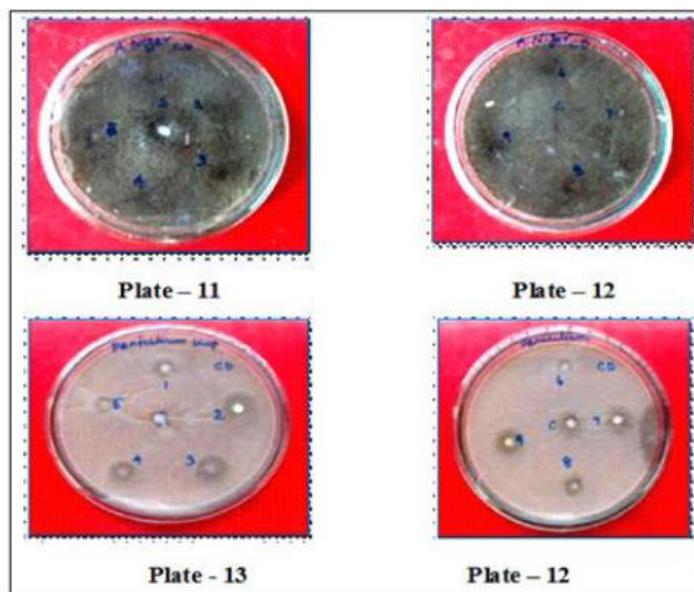


Figure 5: Antifungal activity of substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (petri plates)

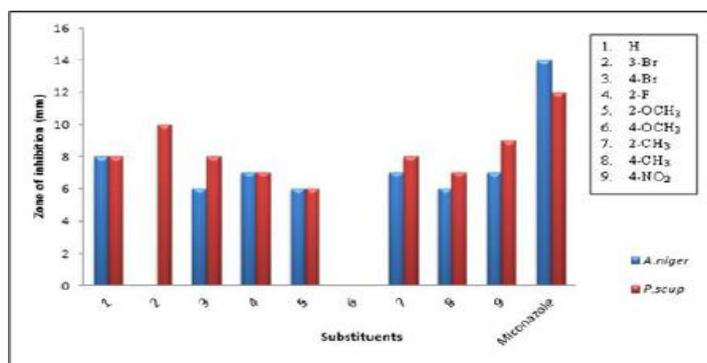


Figure 6: Antifungal activity of substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (clustered column chart)

## CONCLUSIONS

In the present research work, a series containing nine numbers of different substituted (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-ones are synthesized by the reaction of 3,4,5-trimethoxy acetophenone (0.05 mol) with various substituted and unsubstituted benzaldehydes. They are confirmed by their physical constants, UV-Vis, IR and NMR spectral data. These spectral data have been utilized to correlate them with Hammett substituent constants and *F* and *R* parameters by using both single and multi-linear regression analyses. From the correlation analyses, the effect of substituents has been studied. Most of the single correlations and all the multi-correlations are produced satisfactory correlations. The antimicrobial activity of the entire synthesized (*E*)-3-phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one compounds have been performed by using standard Kirby-Bauer method. The 2-CH<sub>3</sub> substituted compound has shown excellent activity against *B. subtilis*. The 4-OCH<sub>3</sub> and 4-NO<sub>2</sub> substituted compound have shown excellent activity against *Micrococcus*. The 4-Br substituted compound has also shown good activity against *Pseudomonas*. The 3-Br substituted compound found to shown excellent activity against *S. chrysops* species.

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