

Synthesis, Structure-Parameter Correlation and Biological Evaluation of 1-(2-Chloro-5-Nitrophenyl)-3-Phenyl-2-Propenone Compounds

C. Balamurugan

PG & Research

Department of Chemistry

Govt Arts College, C.Mutlur, Chidambaram, Tamil Nadu - 608 102.

D. Kamalakkannan

PG & Research

Department of Chemistry

Govt Arts College, C.Mutlur, Chidambaram, Tamil Nadu - 608 102.

R. Suresh

PG & Research

Department of Chemistry

Govt Arts College, C.Mutlur, Chidambaram, Tamil Nadu - 608 102.

G. Vanangamudi

PG & Research

Department of Chemistry

Govt Arts College, C.Mutlur, Chidambaram, Tamil Nadu - 608 102.

G. Thirunarayanan

Department of Chemistry

Annamalai University, Annamalaiagar- 608 002

Abstract

A series of 1-(2-chloro-5-nitrophenyl)-3-phenyl-2-propenones were synthesized from 2-chloro-5-nitroacetophenone with various substituted benzaldehydes by crossed-Aldol condensation. The synthesized compounds have been characterized by their physical constants and spectral data. The antimicrobial activities of synthesized 1, 3-diphenyl-2-propenone compounds have been evaluated by Kirby-Baur disc diffusion method using their respective antibacterial and fungal strains.

Keywords: Crossed-Aldol condensation; 2-Chloro-5-nitrophenyl chalcones; IR and NMR spectra; Substituent effects; Antimicrobial activities

I. INTRODUCTION

Fundamental research plays an important role in medical field especially for synthesis of new drugs for curing particular disease. In this series ancient medicinal preparations containing active herbal plant extract plays the principal physiologically active constituents have been used to treat human diseases^[1]. Increasingly, this class of natural products is becoming the subject of anti-infective research^[2], and many groups have isolated and identified the structures of flavonoids possessing several anti-infective activities^[3]. However, several high-quality investigations have examined the relationship between flavonoid structure and anti-infective activities are in close agreement^[4]. In addition, numerous research groups have sought to elucidate the anti-infective mechanisms of action of selected flavonoids.

Aldol and Crossed-Aldol condensation^[5-12] were useful for synthesis of 1,3-diphenyl-2-propenones. Spectral data were useful for prediction of ground state molecular equilibration such as E s-cis, s-trans and Z s-cis and s-trans conformers^[13]. Chalcones are 1, 3-diphenyl-2-propenones which available in the flavonoids family contains medicinal effects like anti-microbial^[14], anti-inflammatory^[15], analgesic^[16], anti-ulcerative^[17], immune-modulatory^[18], anti-malarial^[19], anti-cancer^[20], anti-viral^[21], anti-leishmanial^[22], anti-oxidant^[23], anti-tubercular^[24], anti-hyperglycemic^[25], anti-oxidant activity^[26]. Presence of the reactive keto group and the ethylenic group in the 1, 3-diphenyl-2-propane compounds and their analogues possesses the antioxidant activity^[27]. 1,3-diphenyl-2-propenones having anti-oxidant activity prevents and counter acts the damage of the human tissue by the normal effects of physiological oxidation^[28].

Correlation analysis have been applied for studying the transition states of reaction mechanism^[29], electrochemical redox behaviour^[30], qualitative and quantitative analysis^[31-33], assessment of substituent effects in oligopeptides^[34], enol-enone tautomerism.

Recently Subramanian et. al.^[35] has studied the synthesis and spectral correlations of some heterocyclic 1, 3-diphenyl-2-propane compounds and they observed satisfactory correlations.

Vanangamudi et. al.^[36] has studied the Synthesis, spectral linearity, antimicrobial, antioxidant and insect antifeedant activities of some 2,5-dimethyl-3-thienyl chalcones.

Thirunarayanan et. al.^[37] has studied the synthesis and spectral correlations of some 1,3-oxazine-4-thione derivatives and observed satisfactory correlations.

Sathiyamoorthy et. al., [38] also studied the same with the some iodo and hydroxy substituted phenyl chalcones.

With a view to above, there is no report available for UV, IR and NMR spectral correlation analysis with Hammett substituent constants, F and R parameters and antimicrobial activities of 1-(2-chloro-5-nitrophenyl)-3-phenyl-2- propenone compounds.

II. EXPERIMENTAL

A. Materials and Methods

All the chemicals used were purchased from Sigma-Aldrich and E-Merck chemical company. Melting points of all compounds were determined in open glass capillaries on V-SCIENTIFIC MP-DS melting point apparatus and are uncorrected. UV spectra measured from ELICO BL-222 spectrophotometer. Infrared spectra (KBr, 4000-400cm⁻¹) were recorded SHIMADSU Fourier transform spectrophotometer. The NMR spectra of all chalcones were recorded from INSTRUM AV300 operating at 500MHz for ¹H spectra and 125.46 MHz for ¹³C spectra in CDCl₃ solvent using TMS as internal standard.

B. Synthesis of 1-(2-Chloro-5-Nitrophenyl)-3-Phenyl-2-Propenone Compounds

A mixture of equimolar quantities of substituted benzaldehydes (0.01mol) and 2-chloro-5-nitroacetophenone (0.01mol), sodium hydroxide (0.5 g) and 10 mL of ethanol were taken in 100 ml conical flask and shaken occasionally for 1 hour^[39-43] and finally warmed to 45 - 50°C (Scheme-I).

After the completion of the reaction, as monitored by TLC, the mixture was cooled to room temperature. The resulting precipitate was filtered and washed with cold water and dried. The product appeared as pale yellow solid and recrystallized using ethanol to obtain pale yellow glittering solid. The yield and physical constants of the synthesized 1,3-diphenyl-2-propenones were presented in table 1.

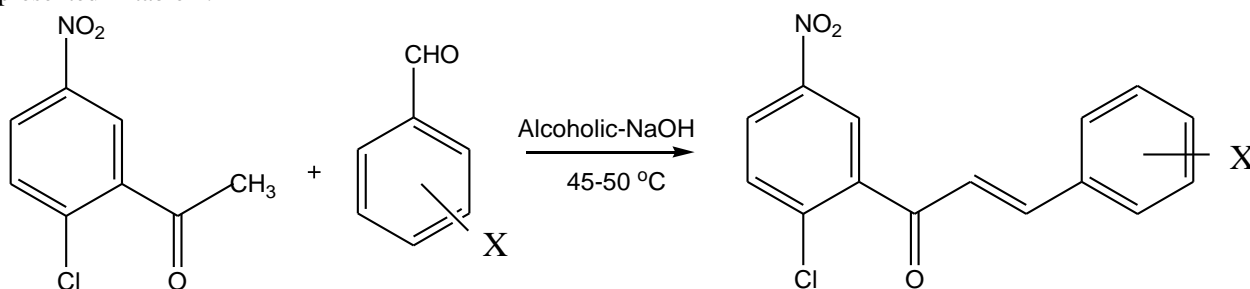


Fig. 1: Scheme-I

Where X = H, 3-Br, 4-Br, 4-NO₂, 3-Cl, 4-Cl, 4-F, 2-OCH₃, 4-OCH₃, 4-CH₃
Synthesis of 1-(2-chloro-5-nitrophenyl)-3-phenyl-2-propenones

Table- 1:

The yield, physical constants and analytical data of 1-(2-chloro-5-nitrophenyl)-3-phenyl-2-propenones

S.NO.	Substitution	Molecular Formula	Molecular Weight	Yield %	Melting Point °C
1	H	C ₁₅ H ₁₀ O ₃ NCl	287.5	80	116
2	3-Br	C ₁₅ H ₉ O ₃ NBrCl	366.5	76	136
3	4-Br	C ₁₅ H ₉ O ₃ NBrCl	366.5	79	139
4	4-NO ₂	C ₁₅ H ₉ O ₅ N ₂ Cl	302.5	76	130
5	3-Cl	C ₁₅ H ₉ O ₃ NCl ₂	322	83	128
6	4-Cl	C ₁₅ H ₉ O ₃ NCl ₂	322	80	143
7	4-F	C ₁₅ H ₉ O ₃ NFCl	305.5	78	109
8	2-OCH ₃	C ₁₆ H ₁₂ O ₄ NCl	317.5	80	121
9	4-OCH ₃	C ₁₆ H ₁₂ O ₄ NCl	317.5	80	124
10	4-CH ₃	C ₁₆ H ₁₂ O ₃ NCl	301.5	75	129

III. RESULT AND DISCUSSION

A. Spectral Linearity

In the present investigation the Hammett spectral linearity of synthesized 1, 3-diphenyl-2-propanone compounds has been studied by evaluating the substituent effects on the group frequencies. The assigned spectroscopic data of all 1, 3-diphenyl-2-propanone compounds such as absorption maximum λ_{max} (nm) of carbonyl groups, infrared carbonyl stretches of ν_{CO} -cis and s-trans, the deformation modes of vinyl part CH out of plane, in-plane, CH=CH and $>C=C<$ out of planes (cm^{-1}) and the NMR chemical shifts δ (ppm) of H_{α} , H_{β} , C_{α} , C_{β} , CO have been correlated with various Hammett substituent constants and F and R parameters.

B. UV Spectral Study

The measured absorption maxima (λ_{max} nm) of synthesized 1-(2-chloro-5-nitrophenyl)-3-phenyl-2-propanone compounds were presented in Table-2. These absorption maxima (λ_{max} nm) of these compounds have been correlated with Hammett substituent constants, F and R parameters using single and multi-linear regression analysis^[10, 11, 35-38, 45-50]. Hammett correlation involving the group frequencies and absorption maxima, the form of the Hammett equation employed is

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

Where λ_0 is the frequency for the parent member of the series.

Table- 2: The ultraviolet absorption maxima (λ_{max} nm), Infrared absorptions (ν cm^{-1}), 1H -NMR and ^{13}C -NMR spectral data of 1-(2-chloro-5-nitrophenyl)-3-phenyl-2-propanone compounds.

S.No	Substituents	UV nm	CO s-cis cm^{-1}	CO s-trans cm^{-1}	CH _{ip} cm^{-1}	CH _{op} cm^{-1}	CH=CH _{op} cm^{-1}	C=C _{pp} cm^{-1}	H _α (ppm)	H _β (ppm)	δC _α (ppm)	δC _β (ppm)	δCO (ppm)
1	H	302.0	1683.60	1602.80	1242.00	835.18	1045.00	615.29	7.477	7.700	121.28	134.03	194.53
2	3-Br	340.0	1674.21	1597.06	1193.90	835.18	1047.35	671.20	7.731	7.916	120.13	134.19	186.83
3	4-Br	342.2	1660.71	1598.99	1220.90	823.60	1041.56	678.94	7.506	7.827	120.94	134.27	189.56
4	4-NO ₂	329.3	1608.63	1570.06	1222.87	827.46	1022.70	673.16	7.503	8.307	122.90	142.85	186.88
5	3-Cl	333.0	1662.84	1604.77	1238.30	853.32	1093.63	599.00	7.476	7.820	121.28	145.32	194.53
6	4-Cl	338.0	1658.78	1589.34	1211.30	817.82	1080.14	690.52	7.471	7.810	125.39	144.22	186.53
7	4-F	329.0	1658.78	1591.06	1220.94	821.68	1029.99	678.94	7.717	8.170	126.12	145.87	189.57
8	2-OCH ₃	323.5	1656.85	1593.20	1201.65	827.46	1049.28	673.16	7.830	8.450	126.96	137.94	190.16
9	4-OCH ₃	326.0	1685.78	1598.93	1222.87	825.53	1024.20	677.01	7.820	8.506	125.10	134.19	189.56
10	4-CH ₃	320.5	1679.22	1585.56	1213.23	812.03	1026.13	692.44	7.484	7.872	126.09	145.85	186.87

The results of statistical analysis^[10, 11, 35-38, 45-50] of these UV absorption maxima (λ_{max} , nm) data with Hammett substituent constants and F and R parameters are presented in Table-3. The Hammett constants σ , σ^+ , σ_I , σ_R constants and F and R parameters produced poor correlations.

The failure in correlation is due to the incapable of inductive and resonance effects of substituents on the absorption and is associated with the resonance-conjugative structure shown in Fig-2.

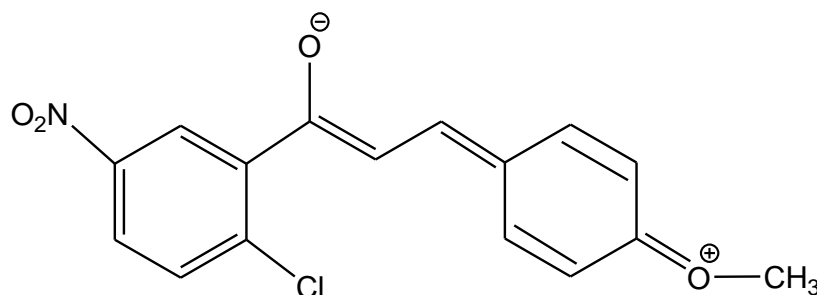


Fig. 2: Resonance conjugative structure of 1-(2-chloro-5-nitrophenyl)-3-(4-methoxyphenyl)-2-propenone compounds

The multi regression analysis of these frequencies of all ketones with inductive, resonance and Swain–Lupton's^[49] constants produce satisfactory correlations as evident in equations (2) and (3).

$$UV(\lambda_{max}) = 310.097 (\pm 6.638) + 30.003 (\pm 14.139) \sigma_I - 7.375 (\pm 11.497) \sigma_R \dots (2)$$

(R = 0.963, n = 10, P > 95%)

$$UV(\lambda_{max}) = 315.377 (\pm 6.956) + 17.937 (\pm 14.181) F - 2.0051 (\pm 10.682) R \dots (3)$$

(R = 0.944, n = 10, P > 95%)

C. IR Spectral Study

The measured carbonyl stretching frequencies (cm^{-1}) of *s-cis* and *s-trans* conformers of present study are presented in Table-2 and the corresponding conformers are shown in Fig-2. The stretching frequencies for carbonyl absorption are assigned based on the assignments made by Hays and Timmons^[50] for *s-cis* and *s-trans* conformers at 1690 and 1670 cm^{-1} , respectively. These data have been correlated with Hammett substituent constants and Swain-Lupton's constants^[49] and are presented in Table-3. In this correlation the structure parameter Hammett equation employed is as shown in the following equation:

$$\nu = \rho\sigma + \nu_o \dots (4)$$

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

The results of single parameter statistical analysis of carbonyl frequencies of *s-trans* conformers gave satisfactory correlation Hammett substituent constants σ and σ^+ with all the substituents.

The results of single parameter statistical analysis of carbonyl frequencies of $\nu_{\text{CH}=\text{CH}_{\text{op}}}$ deformation mode gave satisfactory correlation with Hammett substituent constants σ and σ^+ except 3-Br, 4-Br and 4-Cl substituents. If these substituents given exceptions were included in the correlation, they reduced the correlation significantly.

The remaining Hammett substituent constants, F and R parameters have shown poor correlation with remaining conformers.

The failure in correlation is due the conjugation between the substituent and the carbonyl group in 1-(2-chloro-5-nitrophenyl)-3-phenyl-2-propenone compounds and is associated with the resonance conjugative structure as shown in Figure 3.

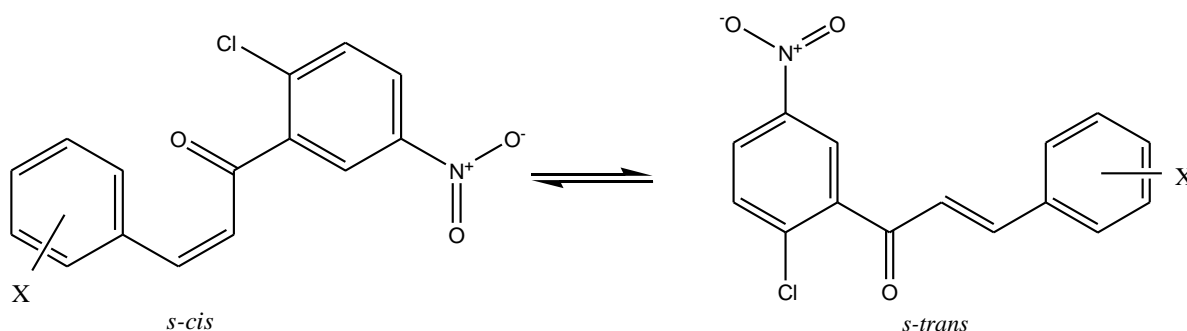


Fig. 3: *s-cis* and *s-trans* conformers of 1-(2-chloro-5-nitrophenyl)-3-phenyl-2-propenone compounds

In view of the inability of some of the σ constants to produce satisfactory correlations individually, it was thought that worthwhile to seek multiple correlations involving either σ_I and σ_R constants or Swain-Lupton's^[49] F and R parameters. The correlation equations for *s-cis*, *s-trans* and deformation modes are given in equations (5) – (16).

$$CO_{s-cis}(\text{cm}^{-1}) = 1598.235 (\pm 9.751) - 7.458 (\pm 20.771) \sigma_I + 0.504 (\pm 16.890) \sigma_R \dots (5)$$

(R = 0.913, n = 10, P > 90%)

$$CO_{s-cis}(\text{cm}^{-1}) = 1596.119 (\pm 8.847) - 2.271 (\pm 18.036) F - 0.642 (\pm 13.585) R \dots (6)$$

(R = 0.904, n = 10, P > 90%)

$$CO_{s-trans}(\text{cm}^{-1}) = 1523.525 (\pm 28.564) - 3.061 (\pm 60.805) \sigma_I + 4.188 (\pm 49.443) \sigma_R \dots (7)$$

(R = 0.913, n = 10 P > 90%)

$$\text{CO}_{s\text{-trans}}(\text{cm}^{-1}) = 1530.817(\pm 25.276) - 6.229(\pm 51.525)F + 18.189(\pm 38.810)R \quad \dots(8)$$

(R = 0.918, n = 10, P > 90%)

$$\nu\text{CH}_{ip}(\text{cm}^{-1}) = 1219.134(\pm 7.004) - 6.446(\pm 58.99)\sigma_1 + 3.104(\pm 36.00)\sigma_R \quad \dots(9)$$

(R = 0.924, n = 10, P > 90%)

$$\nu\text{CH}_{ip}(\text{cm}^{-1}) = 1232.767(\pm 12.027) - 22.684(\pm 24.518)F + 14.583(\pm 18.469)R \quad \dots(10)$$

(R = 0.943, n = 10, P > 90%)

$$\nu\text{CH}_{op}(\text{cm}^{-1}) = 837.483(\pm 9.99) - 3.813(\pm 21.299)\sigma_1 + 25.343(\pm 17.319)\sigma_R \quad \dots(11)$$

(R = 0.948, n = 10, P > 95%)

$$\nu\text{CH}_{op}(\text{cm}^{-1}) = 836.497(\pm 9.352) - 4.770(\pm 19.064)F + 16.740(\pm 14.360)R \quad \dots(12)$$

(R = 0.941, n = 10, P > 95%)

$$\nu\text{CH}=\text{CH}_{op}(\text{cm}^{-1}) = 1048.783(\pm 19.053) + 44.386(\pm 40.585)\sigma_1 + 53.720(\pm 33.002)\sigma_R \quad \dots(13)$$

(R = 0.960, n = 10, P > 95%)

$$\nu\text{CH}=\text{CH}_{op}(\text{cm}^{-1}) = 1059.926(\pm 16.393) + 24.959(\pm 33.417)F + 55.071(\pm 25.170)R \quad \dots(14)$$

(R = 0.965, n = 10, P > 95%)

$$\nu\text{C}=\text{C}_{op}(\text{cm}^{-1}) = 621.742(\pm 25.117) + 51.536(\pm 53.500)\sigma_1 - 79.700(\pm 43.504)\sigma_R \quad \dots(15)$$

(R = 0.960, n = 10, P > 95%)

$$\nu\text{C}=\text{C}_{op}(\text{cm}^{-1}) = 626.729(\pm 23.004) + 40.574(\pm 46.894)F - 58.240(\pm 35.322)R \quad \dots(16)$$

(R = 0.985, n = 10, P > 90%)

Table – 3: Results of statistical analysis of UV, IR, ¹H-NMR, and ¹³C-NMR spectral values of 1-(2-chloro-5-nitrophenyl)-3-phenyl-2-propenone compounds with Hammett σ , σ^+ , σ_1 , σ_R constants and F and R parameters.

Absorption	Constants	r	I	ρ	s	n	Correlated derivatives
$\lambda_{max}(nm)$	σ	0.814	322.66	4.620	8.93	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ^+	0.819	323.01	2.819	8.93	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_1	0.860	312.69	29.457	7.22	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_R	0.815	320.56	-5.907	9.00	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	F	0.843	316.13	18.142	8.19	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	R	0.809	312.24	-3.471	9.05	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
Frequency	constant	r	I	ρ	s	n	Correlated derivatives
$\nu\text{CO}_{s\text{-cis}}(\text{cm}^{-1})$	σ	0.801	1595.40	-2.763	10.25	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ^+	0.800	1595.07	-2.763	10.26	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_1	0.812	1598.05	-7.421	10.31	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_R	0.800	1595.63	0.140	10.40	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	F	0.825	1596.36	-2.206	10.39	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	R	0.801	1595.37	-0.511	10.40	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
$\nu\text{CO}_{s\text{-trans}}(\text{cm}^{-1})$	σ	0.907	1521.33	5.484	30.12	8	H, 4-Br, 4-NO ₂ , 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ^+	0.905	1522.48	7.325	29.85	8	H, 4-Br, 4-NO ₂ , 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_1	0.871	1522.05	-2.751	30.19	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_R	0.810	1522.45	4.039	30.18	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	F	0.815	1523.97	-8.092	30.15	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	R	0.717	1528.77	18.551	29.71	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
$\nu\text{CH}_{ip}(\text{cm}^{-1})$	σ	0.803	1215.74	-1.54	15.64	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ^+	0.802	1218.67	-0.69	15.65	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_1	0.834	1228.49	-29.11	14.67	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_R	0.835	1226.74	24.32	14.61	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	F	0.833	1227.28	-24.18	14.74	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	R	0.829	1225.34	15.90	14.96	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃

$\nu\text{CH}_{op}(\text{cm}^{-1})$	σ	0.843	828.43	14.04	10.85	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ^+	0.835	829.18	6.88	11.30	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_I	0.848	749.77	-0.32	14.44	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_R	0.848	836.12	25.16	10.59	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	F	0.817	830.20	-6.48	12.00	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	R	0.840	834.93	17.02	11.03	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
$\nu\text{CH}=\text{CH}_{op}(\text{cm}^{-1})$	σ	0.907	1047.68	47.00	18.03	7	H, 4-NO ₂ , 3-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ^+	0.906	1050.82	26.33	19.36	8	H, 3-Br, 4-Br, 4-NO ₂ , 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_I	0.835	1029.89	48.36	23.65	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_R	0.850	1064.27	55.89	21.79	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	F	0.816	1039.21	19.32	24.98	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	R	0.861	1068.00	53.62	20.00	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
$\nu\text{C}=\text{C}_{op}(\text{cm}^{-1})$	σ	0.834	663.88	-30.11	34.41	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ^+	0.832	661.73	-17.62	31.57	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_I	0.825	649.76	45.63	32.30	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_R	0.853	639.72	-77.18	28.26	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	F	0.833	648.63	46.53	31.83	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	R	0.852	639.93	-60.59	28.42	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
Chemical shifts	Constants	r	I	ρ	s	n	Correlated derivatives
$\delta H_{\alpha}(\text{ppm})$	σ	0.811	7.599	-0.050	0.162	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ^+	0.821	7.591	-0.054	0.158	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_I	0.811	7.569	0.097	0.161	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_R	0.845	7.497	-0.317	0.144	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	F	0.834	7.510	0.259	0.152	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	R	0.853	7.477	-0.301	0.136	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
$\delta H_{\beta}(\text{ppm})$	σ	0.960	8.019	-0.515	0.243	7	3-Br, 4-Br, 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃
	σ^+	0.972	7.971	-0.363	0.215	7	3-Br, 4-Br, 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃
	σ_I	0.817	8.134	-0.290	0.307	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_R	0.907	7.116	-0.997	0.210	8	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃
	F	0.804	8.014	0.065	0.311	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	R	0.991	7.643	-0.957	0.142	8	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃
Chemical shifts	Constants	r	I	ρ	s	n	Correlated derivatives
$\delta\text{CO}(\text{ppm})$	σ	0.828	189.58	2.414	3.043	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ^+	0.831	189.79	1.611	3.016	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_I	0.824	190.88	-4.163	3.079	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_R	0.840	190.42	5.538	2.908	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	F	0.817	190.42	-2.619	3.125	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	R	0.841	191.37	4.543	2.891	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
$\delta\text{C}_{\alpha}(\text{ppm})$	σ	0.849	123.49	-3.541	2.378	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ^+	0.846	123.24	-2.048	2.416	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃

	σ_I	0.810	123.56	-0.166	2.730	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_R	0.840	120.55	-9.379	1.660	7	H, 4-Br, 3-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	F	0.822	122.61	2.847	2.659	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	R	0.809	121.00	-6.336	2.020	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
$\delta C_{\beta}(\text{ppm})$	σ	0.815	139.81	-1.746	5.695	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ^+	0.810	139.69	-0.991	5.700	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_I	0.831	136.81	9.168	5.468	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	σ_R	0.872	136.65	-9.838	5.263	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	F	0.822	137.17	7.678	5.482	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃
	R	0.824	137.91	-4.749	5.565	10	H, 3-Br, 4-Br, 4-NO ₂ , 3-Cl, 4-Cl, 4-F, 2-OCH ₃ , 4-OCH ₃ , 4-CH ₃

r = correlation co-efficient; ρ = slope; I = intercept; s = standard deviation; n = number of substituents

D. ¹H NMR Spectral Study:

The ¹H NMR spectra of synthesized 1-(2-chloro-5-nitrophenyl)-3-phenyl-2-propenone compounds have been recorded using deuteriochloroform (CDCl₃) as solvent and employing tetramethylsilane (TMS) as internal standard. The ethylenic protons signals of the 1, 3-diphenyl-2-propane compounds were assigned from their spectra. They were calculated as AB or AA' or BB' systems respectively. The lower chemical shifts (ppm) obtained for H_α and higher chemical shifts (ppm) obtained for H_β in this series of ketones. The vinyl protons give an AB pattern and the β-proton doublets were well separated from the signals of the aromatic protons. The assigned vinyl proton chemical shifts δ(ppm) of all ketones were presented in Table-2. In nuclear magnetic resonance spectra, the proton or the ¹³C chemical shifts (δ) depends on the electronic environment of the nuclei concerned. The assigned vinyl proton chemical shifts (ppm) have been correlated with reactivity parameters using Hammett equation in the form of

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

where δ_0 is the chemical shift of unsubstituted ketones.

The assigned H_α and H_β proton chemical shifts (ppm) are correlated with various Hammett sigma constants and Swain-Lupton's parameters. The results of statistical analysis^[10,11, 35-38, 45-50] were presented in Table-3. The obtained correlation was satisfactory for H_β with Hammett substituent constants σ , σ^+ , and σ_R also with R parameters excluding H, 4-NO₂ and 4-CH₃ substituents.

While seeking the multi-correlation by the application of Swain-Lupton's^[49] treatment to the relative chemical shifts of H_α and H_β with F and R values is successful with resonance, inductive effect generates the multi regression equations (18) – (21).

$$\delta H_{\alpha}(\text{ppm}) = 7.455(\pm 0.135) + 0.120(\pm 0.282)\sigma_I - 0.323(\pm 0.234)\sigma_R \quad \dots(18)$$

(R = 0.947, n = 10, P > 90%)

$$\delta H_{\alpha}(\text{ppm}) = 7.402(\pm 0.108) + 0.229(\pm 0.221)F - 0.287(\pm 0.166)R \quad \dots(19)$$

(R = 0.961, n = 10, P > 95%)

$$\delta H_{\beta}(\text{ppm}) = 7.787(\pm 0.195) - 0.217(\pm 0.415)\sigma_I - 0.986(\pm 0.338)\sigma_R \quad \dots(20)$$

(R = 0.975, n = 10, P > 95%)

$$\delta H_{\beta}(\text{ppm}) = 7.654(\pm 0.121) - 0.032(\pm 0.247)F - 0.959(\pm 0.186)R \quad \dots(21)$$

(R = 0.988, n = 10, P > 95%)

E. ¹³C NMR Spectral Study:

Scientists and physical organic chemists^[10, 11, 35-38, 45-50], have made extensive study of ¹³C NMR spectra for a large number of different ketones and styrenes. The assigned vinyl C_α, C_β and carbonyl carbon chemical shifts are presented in Table-2. The results of statistical analysis are given in Table-3. Both C_α and C_β chemical shifts (ppm) gave poor correlation with Hammett substituent constants and F and R parameters. This is due to the reason stated earlier and associated with resonance conjugative structure shown in Figure-2.

While seeking the multi-regression analysis through Swain-Lupton's^[49] parameter correlations were satisfactorily obtained within these carbon chemical shifts and the regression equations are given in (22) – (27).

$$\delta \text{CO}(\text{ppm}) = 192.915(\pm 2.627) - 4.590(\pm 5.596)\sigma_I + 5.763(\pm 4.550)\sigma_R \quad \dots(22)$$

(R = 0.948, n = 10, P > 90%)

$$\delta \text{CO}(\text{ppm}) = 192.080(\pm 2.428) - 2.165(\pm 4.951)F + 4.417(\pm 3.729)R \quad \dots(23)$$

(R = 0.944, n = 10, P > 90%)

$$\delta C_{\alpha}(\text{ppm}) = 120.250 (\pm 1.563) + 0.863 (\pm 3.329) \sigma_1 - 9.421 (\pm 2.707) \sigma_R \dots (24)$$

$$(R = 0.914, n = 10, P > 90\%)$$

$$\delta C_{\alpha}(\text{ppm}) = 120.284 (\pm 1.673) + 2.212 (\pm 3.405) F - 6.207 (\pm 2.564) R \dots (25)$$

$$(R = 0.927, n = 10, P > 90\%)$$

$$\delta C_{\beta}(\text{ppm}) = 133.189 (\pm 4.655) + 9.932 (\pm 9.916) \sigma_1 - 10.324 (\pm 8.063) \sigma_R \dots (26)$$

$$(R = 0.951, n = 10, P > 95\%)$$

$$\delta C_{\beta}(\text{ppm}) = 135.549 (\pm 4.544) + 7.235 (\pm 9.264) F - 4.328 (\pm 6.978) R \dots (27)$$

$$(R = 0.936, n = 10, P > 90\%)$$

IV. ANTIMICROBIAL ACTIVITY

A. Antibacterial Activity:

The newly synthesized 1-(2-chloro-5-nitrophenyl)-3-phenyl-2-propenone compounds were subjected to evaluate their antibacterial activity against gram positive bacteria *Bacillus subtilis*, *M.luteus* and *S.aureus* gram negative bacteria *Escherichia coli*, *P.aeruginosa* and *k.pneumonias* by using Kirby Bauer^[51] disc diffusion method. The agar was purchased from HI MEDIA Laboratories Ltd, Mumbai, India. The agar medium prepared by dissolving 2.5 g of agar in 100 ml water at boiled condition as per standard procedure. The bubble free medium poured in to Petri dishes and allowed to cool under closed condition for gel formation. After streaking microorganism what man no-40 discs of 6.0 mm in diameter laid on the gel to identify the inhibition zones (plate 1-6). The test compounds were prepared by dissolving 10 mg each compound in 5 ml of dimethyl sulphoxide. The solution of each compound 0.1 ml were added on what man disc and incubated at 37°C for 24 Hour.

A reference standard drug of gram positive and gram negative bacteria was made by dissolving 10.0 mg of ampicillin in 5.0 ml of distilled water separately. All the experiments were carried out with duplicate to avoid error. Simultaneously reference were tested with 0.1 ml of dimethyl sulphoxide which not reveal any zone of inhibition. The zone of inhibition in diameter produced by each compound was measured in mm. The results are given in Table-4.

Table - 4:

Antibacterial activity of 1-(2-chloro-5-nitrophenyl)-3-phenyl-2-propenone compounds.

S.No	Substituents	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>P.aeruginosa</i>	<i>k.pneumonias</i>
1	H	6	-	-	6	6	6
2	3-Br	7	6	-	7	6	7
3	4-Br	7	6	6	-	7	-
4	4-NO ₂	7	7	6	7	7	-
5	3-Cl	-	6	6	8	-	-
6	4-Cl	-	-	-	7	6	6
7	4-F	6	6	6	6	8	7
8	2-OCH ₃	-	7	7	6	6	-
9	4-OCH ₃	6	6	-	6	6	-
10	4-CH ₃	6	6	7	-	7	6
Standard	Ampicillin	10	9	9	9	13	13
control	DMSO	-	-	-	-	-	-

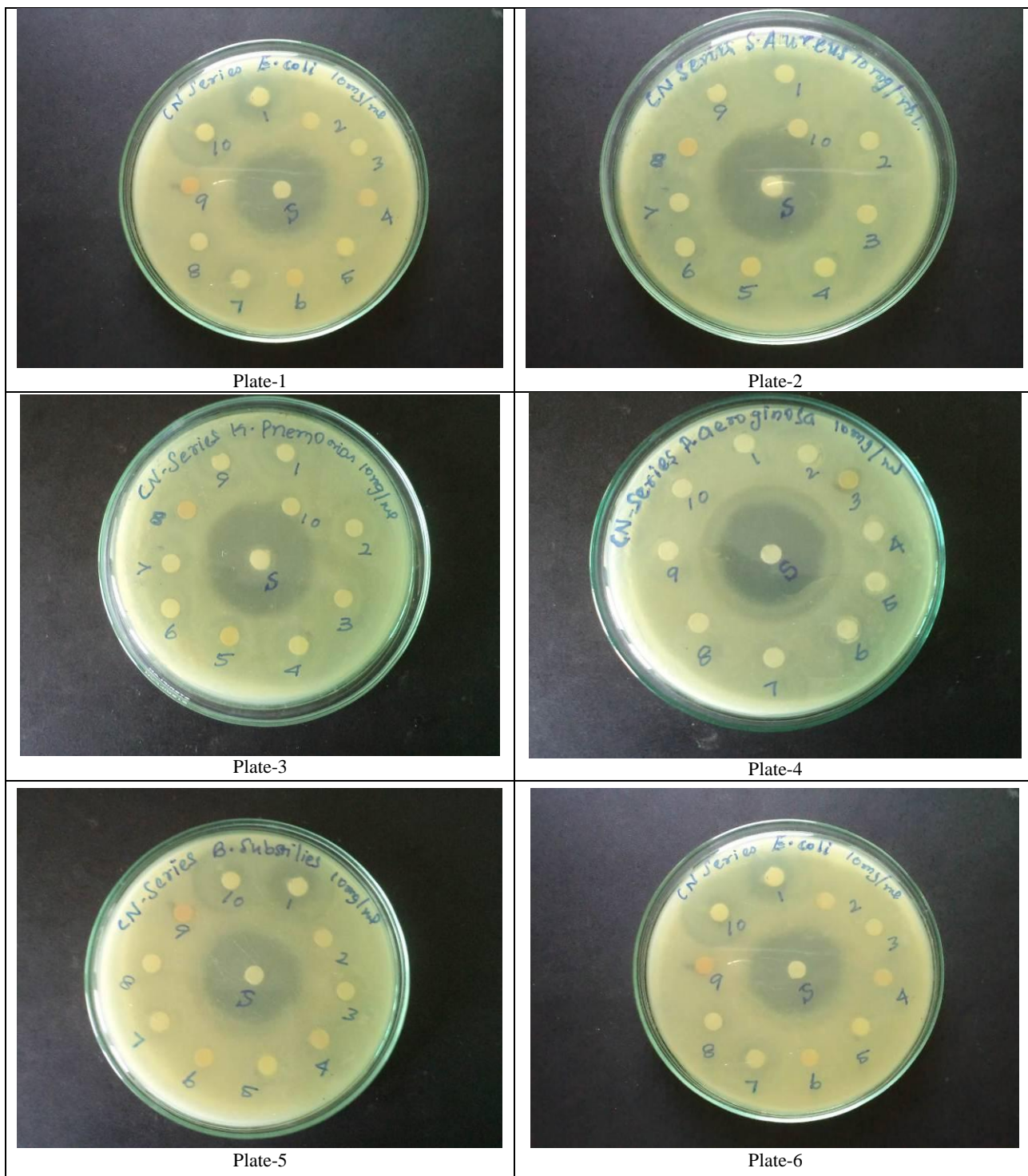


Fig. 4: Antibacterial activity of substituted (E)-1-(2-chloro-5-nitrophenyl)-3-phenylprop-2-en-1-one compounds (Plates 1-6)

Analysis of the zone of inhibition values reveals that the three 1,3-diphenyl-2-propenone compounds with H (parent), 4-NO₂ and 4-CH₃ substituents against *Bacillus subtilis* and 4-Br, 3-Cl, 4-F, 4-NO₂ substituents against *Micrococcus luteus* have shown good antibacterial activity. The 2-OCH₃ and 4-NO₂ substituents against *Staphylococcus aureus* and H (parent), 3-Cl, 4-CH₃, 4-F substituents against *Escherichia coli* have shown good antibacterial activity. 4-F substituent against *Pseudomonas aeruginosa* and 4-Cl substituent against *Klebsiella pneumoniae* have shown good antibacterial activity.

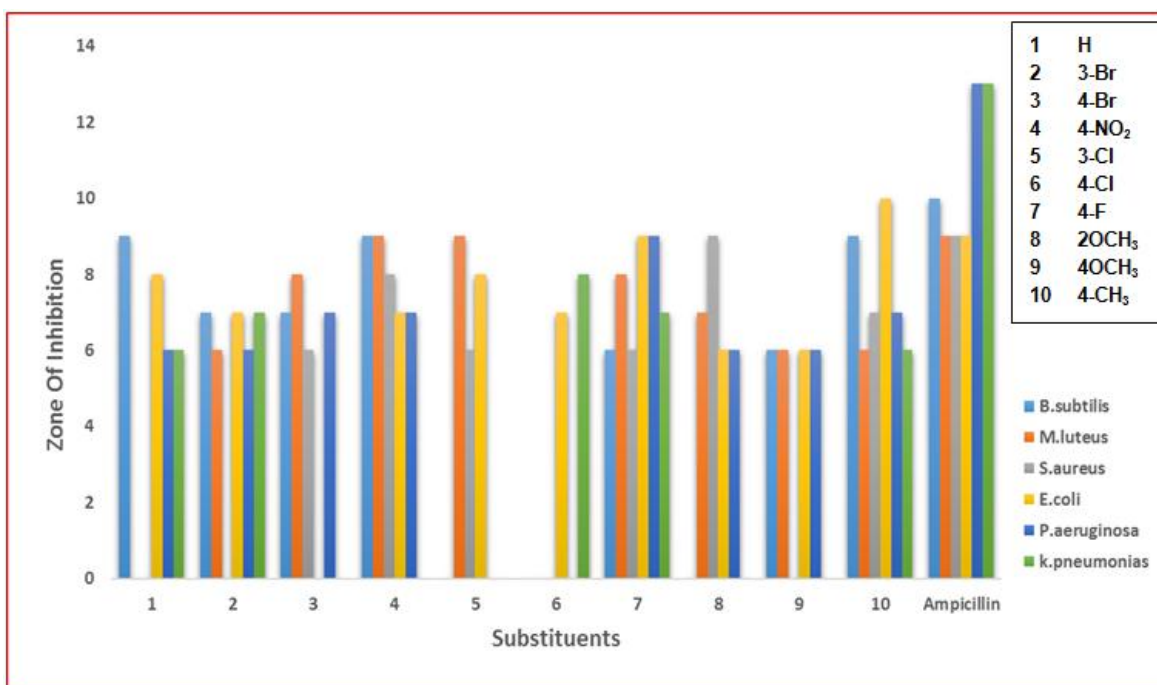


Fig. 5: The antibacterial-clustered column chart of 1-(2-chloro-5-nitrophenyl)-3-phenyl-2- propenone compounds.

B. Antifungal Activity

All the those compounds screened for antibacterial activity were also tested for antifungal activity using potato –dextrose-agar (PDA) medium same cup and plate method against *Aspergillus niger*, *Trichoderma viride* and *Mucor* species. Preparation of nutrient broths subculture base layer medium and PDA-medium was done as per the standard procedure (plate 7-9). A reference standard drug fluconazole 10 mg dissolved in 5ml of water 0.1 ml of solution used as a control which did not reveal any inhibition. The experiments were duplicated to minimize the error. The zone of inhibition in diameter produced by each compound was measured in mm and tabulated in table-5.

Table - 5:
Antifungal activity of 1-(2-chloro-5-nitrophenyl)-3-phenyl-2-propenone compounds.

S.No	Substitution	Mean zone of inhibition (mm)		
		A. Niger	T. Viride	M. Species
1	H	6	8	6
2	3-Br	6	6	6
3	4-Br	-	6	6
4	4-NO ₂	6	-	7
5	3-Cl	7	6	6
6	4-Cl	6	7	-
7	4-F	-	-	-
8	2-OCH ₃	-	6	6
9	4-OCH ₃	6	7	6
10	4-CH ₃	6	-	-
11	DMF	-	-	-
12	Fluconazole	8	12	12

Analysis of the Zone of inhibition (mm) values reveals that the seven 1,3-diphenyl-2-propenone compound with H (parent), 4-Cl, 3-Br, 4-NO₂, 3-Cl, 4-OCH₃, 4-CH₃ substituents against *Aspergillus niger* and H (parent), 4-OCH₃ 3-Br, 4-Br, 3-Cl, 4-Cl, 2-OCH₃ substituents against *Trichoderma viride* has shown good antifungal activity. The seven 1,3-diphenyl-2-propenone

compounds with H (parent), 3-Br, 4-NO₂, 4-Br, 3-Cl, 2-OCH₃ and 4-OCH₃ substituents have shown good antifungal activity against Mucor Species.



Fig. 6: Plate – 7

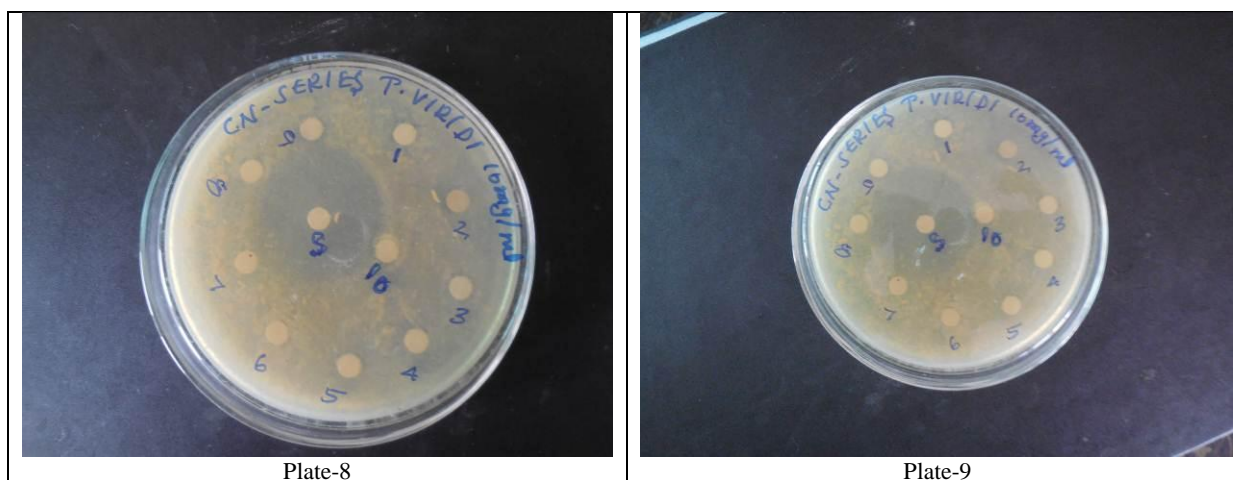


Plate-8

Plate-9

Fig. 7: plate- 8, Plate-9

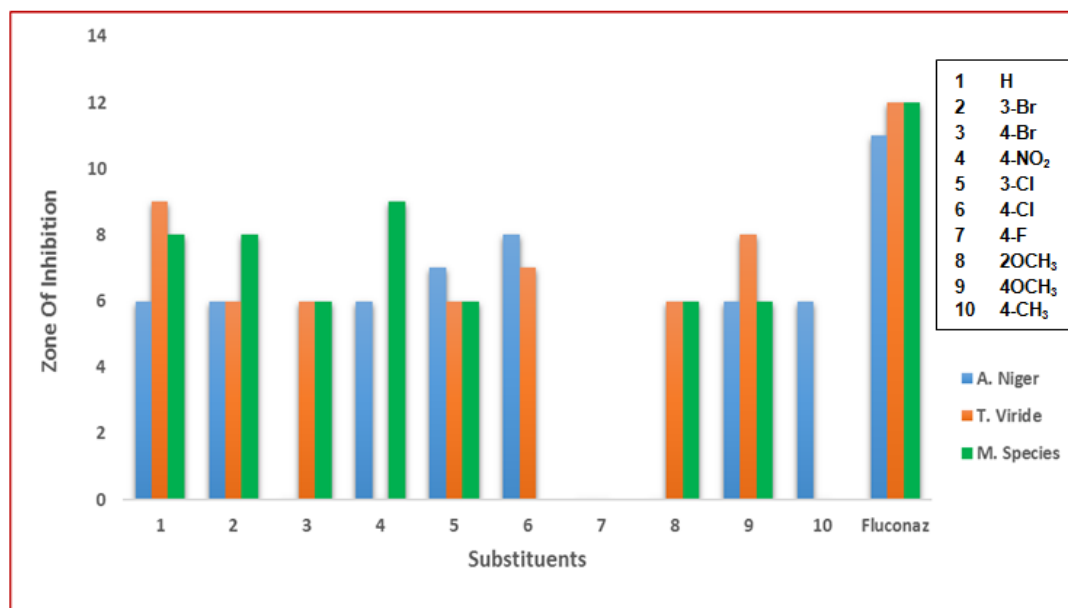


Fig. 6: The anti-fungal-clustered column chart of 1-(2-chloro-5-nitrophenyl)-3-phenyl -2-propenone compounds.

V. CONCLUSIONS

About ten 1-(2-chloro-5-nitrophenyl)-3-phenyl-2-propenone compounds have been synthesized by condensation of 2-chloro-5-nitroacetophenone and substituted benzaldehydes by Crossed-Aldol condensation. The 1-(2-chloro-5-nitrophenyl)-3-phenyl-2-propenone compounds have been characterized by their physical constants, spectral data. The UV, IR, NMR spectral data of these 1-(2-chloro-5-nitrophenyl)-3-phenyl-2-propenone compounds has been correlated with Hammett substituent constants, F and R parameters. From the results of statistical analysis the effects of substituent on the spectral data have been studied. The antimicrobial activities of all synthesized 1-(2-chloro-5-nitrophenyl)-3-phenyl-2-propenone compounds have been studied using Kirby- Bauer disc diffusion method. The screening results revealed that most of the compounds shown good antibacterial activity and moderate antifungal activities.

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