Synthesis and Substituent Effects in Substituted Styryl 4-Methoxy-1-Naphthyl Ketones

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ABSTRACT. A series of substituted styryl 4-methoxy-1-naphthyl ketones [(2E)-1-(4-methoxy-1-naphthyl)-3-phenyl-2-propen-1-ones] were synthesized using facile method of microwave assisted condensation reaction. The yield of chalcones is more than 90%. They are characterized by their physical constants, micro analysis, infrared (KBr, 4000-400 cm⁻¹) and NMR both ¹H and ¹³C spectral data. From infrared spectra, the s-cis and s-trans C=O stretching modes are assigned. All spectral data are correlated with various Hammett substituent constants. From the results of statistical analysis the effect of substituents on CO, α and β protons and carbons are explained.

Keywords: Synthesis, Substituent Effects, Infrared Spectroscopy, NMR Spectroscopy, Naphthyl Chalcones

INTRODUCTION

With microwave irradiation of substituted benzaldehyde and aromatic ketones in presence of anhydrous zinc chloride gave exclusively high yield of substituted styryl chalcones.¹ Their basic skeletons of chalcones are widely figured in natural products and are known to have multi pronged activity.² Many of the chalcones are used as agrochemical and drugs.³ Recently much attention has paid on the synthesis of chalcones mainly from acetophenone analogs⁴ with various aromatic benzaldehydes. Several catalysis⁵ such as basic alumina, Al₂O₃-AlPO₄₅ P₃O₅-piperidone ultrasonic rays using C-200 and Lewis acids have been used for knovenogal condensation and bases or quaternary ammonium salts have also been employed. Further studies on the efficient synthesis of chalcones are of current interest because of their wide range of application. Thus the author to report here the first time a simple fac-

요약
초음파를 이용한 응축반응을 이용하여 다양한 치환기가 붙은 4-methoxy-1-naphthyl ketone화합물들을 90% 이상의 수율로 합성하였으며, 생성된 화합물들을 미세 분석법, IR, ¹H, ¹³C NMR 분석법 등을 이용하여 확인하였다. IR 스펙트럼에서 s-cis와 s-trans C=O stretching 모드를 확인하였으며, NMR 데이터로부터 아를렌의 탄소와 수소에 대한 화학 무게를 확인하였다. 이러한 분광데이터를 이용하여 여러 분자들에 대한 Hammet 치환기 상수 값을 얻었으며, 이들로부터 가용매 분해반응에 미치는 치환기 효과를 해석할 수 있었다.

주제어: 합성, 치환기 효과, 적외선 분광법, 핵자기공명 분광법, 나프틸 칼콘
ile approach to synthesis high yield of substituted styryl 4-methoxy-1-naphthyl chalcones and investigate the substituent effects from infrared and nuclear magnetic resonance spectra were recorded.

**EXPERIMENTAL SECTION**

A mixture of substituted benzaldehydes (0.01 mol) and 4-methoxy-1-naphthyl ketones (0.01 mol) and anhydrous zinc chloride (0.001 mol) was taken in ACE tube and flushed with Argon and tightly capped. The mixture is subjected to microwave oven heating for 5-8 minutes in a domestic microwave oven (LG Microwave Oven MG-395WA) and then it is allowed to reach to room temperature. The reaction mixture was treated with ethanol and the separated solid was filtered, washed with n-Hexane and dried. The solid was recrystallised by benzene-hexane mixture. The reaction is shown in Scheme 1. Compounds a-f and h are unknown and the remaining compounds are known.

Melting points were determined in open glass capillaries on Mettler FP51 melting point apparatus and are uncorrected. Infrared spectra (KBr, 4000-400 cm$^{-1}$) were recorded on JASCO IR-700 Japan model spectrophotometer. The nuclear magnetic resonance spectra both $^1$H and $^{13}$C of chalcones were recorded using UNITYPLUS-300 “KIBSIPS” 300 MHz spectrometer, operating at 200MHz frequency for recording $^{13}$C NMR Spectra. The micro analysis of the chalcones were performed in Perkin Elmer 240C Analyzer.

Based on Hays and Timmons’ infrared carbonyl stretching frequencies of $s$-cis and $s$-trans conformers are assigned. The NMR chemical shifts (ppm) of ethylene $\alpha$, $\beta$ protons and carbons are assigned based on reported in earlier literature. The Physical constants, micro analysis and spectral data of all chalcones are summarized in Table 1.

**Substituent effects**

Correlation study involves the prediction of ground state molecular equilibriums of organic substrates such as $s$-cis and $s$-trans isomers of alkenes, alkynes, benzoylchlorides, styrenes and $\alpha$, $\beta$-unsaturated ketones from spectral data. Their use in structure parameter correlations has now becomes popular for studying transition state study of reaction mechanisms, biological activities and normal coordinate analysis. Dhami and Stothers have extensively studied the $^1$H NMR spectra of a large number of acetophenones and styrenes with a view to establish the validity of the additivity of substituent effects in aromatic shielings, first observed by Lauterber. Savin and coworkers obtained the NMR spectra of unsaturated ketones of the type RC$_6$H$_4$-CH=CH-CO-CMe$_3$ and sought Hammett correlations for the ethylenic protons. Solc\’anovi\’a and coworkers have measured $^1$H and $^{13}$C NMR spectra of substituted phenyl sty-
Hence the authors have synthesized thirteen chalcones of the above type using microwave irradiation technique. And the substituent effects of above compounds are investigated from infrared and NMR spectra were made.

**Substituent Effects from infrared spectra**

The carbonyl stretching frequencies (cm$^{-1}$) of $s$-$cis$ and $s$-$trans$ isomers of present study are shown in Table 1 and the corresponding conformers are shown in (I).

The infrared spectra were all recorded on the KBr disc in order to avoid the shoulder formation on carbonyl doublets. The $s$-$cis$ conformers exhibit higher frequencies than the $s$-$trans$ conformers due to the bulkier naphthalene group causes greater strain and they enhance the higher absorption of carbonyl group of $s$-$cis$ isomer than the $s$-$trans$ isomer. These frequencies are separately analyzed through various Hammett sigma constants.

From the statistical analysis, there is no significant correlation obtained with Hammett sigma constants in $s$-$cis$ conformers. This is the conjugation between the C=O and the -CH=CH- part is less important due to non-co-planarity arising out of non bonded repulsion between naphthalene and styryl parts in the systems. In $s$-$cis$ conformers there is significant correlation is obtained ($r=0.995$) with $\sigma_R$ constants. Further no significant correlations are obtained for both conformers with $\sigma_I$, $\sigma_I$ and $\sigma_R$ parameters except $s$-$trans$ with $\sigma_R$ constants. This is due to the cross conjugation of methoxy substituent in fourth position of naphthyl ring as shown in (II).

In view of the inability of some $\sigma$ constants to produce individually satisfactory correlations, it was thought worthwhile to seek multiple correlations involving either $\sigma_I$ and $\sigma_R$ constants or Swain-Lupton’s F and R parameters. The correlation equations (1,2) generated are

\[ \nu_{C=O} (s\text{-}cis) \,(\text{cm}^{-1}) = 1669 + 17.660F + 11.697R \, (r=0.939, \, n=13, \, P > 90\%) \quad (1) \]

\[ \nu_{C=O} (s\text{-}trans) \,(\text{cm}^{-1}) = 1638.8 - 2.769\sigma_I + 29.893\sigma_R \]
Some cases where both the group parameters were fail to predict collectively the substituent effects. This may treated exceptional and by large it is to be realized that the collective participation of either $\sigma_I$ and $\sigma_R$ parameters or $F$ and $R$ parameters is more dependent than that of any single parameters role to predict the substituent effects. A good single parameter correlation is shown in Fig. 1.

**Substituent effects from NMR Spectra**

**$^1$H NMR Spectra**

The $^1$H NMR spectral signals of ethylenic pro-

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**Table 1. Physical constants, micro analysis and spectral data of substituted styryl 4-methoxy-1-naphthyl ketones.**

<table>
<thead>
<tr>
<th>No.</th>
<th>Molecular formula</th>
<th>m.p. °C</th>
<th>%C (Required)</th>
<th>%H (Required)</th>
<th>%N (Required)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>C$<em>{20}$H$</em>{16}$O$_3$</td>
<td>113-114(113)$^\circ$</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>b</td>
<td>C$<em>{20}$H$</em>{16}$NO$_2$</td>
<td>99-100</td>
<td>79.13(79.19)</td>
<td>5.46(5.65)</td>
<td>4.60(4.62)</td>
</tr>
<tr>
<td>c</td>
<td>C$<em>{20}$H$</em>{16}$NO$_2$</td>
<td>82-83</td>
<td>79.16(79.19)</td>
<td>5.50(5.65)</td>
<td>4.58(4.62)</td>
</tr>
<tr>
<td>d</td>
<td>C$<em>{20}$H$</em>{16}$BrO$_2$</td>
<td>78-79</td>
<td>65.36(65.41)</td>
<td>4.09(4.12)</td>
<td>--</td>
</tr>
<tr>
<td>e</td>
<td>C$<em>{20}$H$</em>{16}$ClO$_2$</td>
<td>120-121</td>
<td>74.38(74.42)</td>
<td>4.61(4.68)</td>
<td>--</td>
</tr>
<tr>
<td>f</td>
<td>C$<em>{20}$H$</em>{16}$ClO$_2$</td>
<td>137-138</td>
<td>74.40(74.42)</td>
<td>4.64(4.68)</td>
<td>--</td>
</tr>
<tr>
<td>g</td>
<td>C$<em>{20}$H$</em>{16}$NO$_3$</td>
<td>126-127(127)$^\circ$</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>h</td>
<td>C$<em>{20}$H$</em>{16}$O$_3$</td>
<td>113-114</td>
<td>78.19(78.93)</td>
<td>5.23(5.30)</td>
<td>--</td>
</tr>
<tr>
<td>i</td>
<td>C$<em>{20}$H$</em>{16}$O$_3$</td>
<td>88-89(88)$^\circ$</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>j</td>
<td>C$<em>{20}$H$</em>{16}$NO$_2$</td>
<td>114-115(115)$^\circ$</td>
<td>--</td>
<td>--</td>
<td>--</td>
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<tr>
<td>k</td>
<td>C$<em>{20}$H$</em>{16}$NO$_2$</td>
<td>106-107(106)$^\circ$</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>l</td>
<td>C$<em>{20}$H$</em>{16}$NO$_2$</td>
<td>113-114(114)$^\circ$</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>m</td>
<td>C$<em>{20}$H$</em>{16}$NO$_2$</td>
<td>141-142(142)$^\circ$</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

(±2.181) (±4.907) (±4.185)

(R=0.927, n=13, P > 90%)

Fig. 1. Plot of $\nu$C=O (s-trans) of substituted styryl 4-methoxy-1-naphthyl ketones versus $\sigma_R$. Some in all chalcone investigated are assigned. The chemical shifts of H$_\alpha$ protons are at higher field
Table 2. Results of statistical analysis of chemical shifts of $H_\alpha$ and $H_\beta$ protons of substituted styryl 4-methoxy-1-naphthyl ketones

<table>
<thead>
<tr>
<th>Type of protons</th>
<th>Constants for correlation</th>
<th>$r$</th>
<th>$I$</th>
<th>$\rho$</th>
<th>$s$</th>
<th>$n$</th>
<th>Substituents in styryl part</th>
</tr>
</thead>
<tbody>
<tr>
<td>$H_\alpha$</td>
<td>$\sigma$</td>
<td>0.974</td>
<td>8.278</td>
<td>0.148</td>
<td>0.070</td>
<td>13</td>
<td>H$_m$-NH$_2$, $p$-NH$_2$, $m$-Br, $m$-Cl, $p$-Cl$_2$, $p$-CN, $p$-NO$_2$, $o$-NO$_2$, $m$-NO$_2$, $p$-NO$_2$, $p$-OCH$_3$, $o$-CH$_3$, $m$-CH$_3$, $o$-F, $p$-Cl, $m$-Br, $p$-OH, $m$-OH, $o$-OH, $m$-Br, $p$-B$_r$, $m$-Cl, $m$-Br, $o$-F, $p$-Cl, $m$-Cl, $p$-Br</td>
</tr>
<tr>
<td></td>
<td>$\sigma^+$</td>
<td>0.970</td>
<td>8.355</td>
<td>0.263</td>
<td>0.077</td>
<td>13</td>
<td>$m$-Br, $p$-Cl, $m$-Cl, $p$-Cl$_2$, $p$-CN, $p$-NO$_2$, $o$-NO$_2$, $m$-NO$_2$, $p$-NO$_2$, $p$-OCH$_3$, $o$-CH$_3$, $m$-CH$_3$, $o$-F, $p$-Cl, $m$-Br, $p$-OH, $m$-OH, $o$-OH, $m$-Br, $p$-B$_r$, $m$-Cl, $p$-Br, $m$-Cl, $p$-Br, $o$-F, $p$-Cl, $m$-Cl, $p$-Br</td>
</tr>
<tr>
<td></td>
<td>$\sigma_I$</td>
<td>0.878</td>
<td>8.096</td>
<td>0.687</td>
<td>0.150</td>
<td>13</td>
<td>$m$-Br, $p$-Cl, $m$-Cl, $p$-Cl$_2$, $p$-CN, $p$-NO$_2$, $o$-NO$_2$, $m$-NO$_2$, $p$-NO$_2$, $p$-OCH$_3$, $o$-CH$_3$, $m$-CH$_3$, $o$-F, $p$-Cl, $m$-Br, $p$-OH, $m$-OH, $o$-OH, $m$-Br, $p$-B$_r$, $m$-Cl, $p$-Br, $m$-Cl, $p$-Br, $o$-F, $p$-Cl, $m$-Cl, $p$-Br</td>
</tr>
<tr>
<td></td>
<td>$\sigma_R$</td>
<td>0.861</td>
<td>8.391</td>
<td>0.564</td>
<td>0.158</td>
<td>13</td>
<td>$m$-Br, $p$-Cl, $m$-Cl, $p$-Cl$_2$, $p$-CN, $p$-NO$_2$, $o$-NO$_2$, $m$-NO$_2$, $p$-NO$_2$, $p$-OCH$_3$, $o$-CH$_3$, $m$-CH$_3$, $o$-F, $p$-Cl, $m$-Br, $p$-OH, $m$-OH, $o$-OH, $m$-Br, $p$-B$_r$, $m$-Cl, $p$-Br, $m$-Cl, $p$-Br, $o$-F, $p$-Cl, $m$-Cl, $p$-Br</td>
</tr>
<tr>
<td></td>
<td>$\sigma$</td>
<td>0.980</td>
<td>8.527</td>
<td>0.233</td>
<td>0.031</td>
<td>13</td>
<td>$m$-Br, $p$-Cl, $m$-Cl, $p$-Cl$_2$, $p$-CN, $p$-NO$_2$, $o$-NO$_2$, $m$-NO$_2$, $p$-NO$_2$, $p$-OCH$_3$, $o$-CH$_3$, $m$-CH$_3$, $o$-F, $p$-Cl, $m$-Br, $p$-OH, $m$-OH, $o$-OH, $m$-Br, $p$-B$_r$, $m$-Cl, $p$-Br, $m$-Cl, $p$-Br, $o$-F, $p$-Cl, $m$-Cl, $p$-Br</td>
</tr>
<tr>
<td></td>
<td>$\sigma^+$</td>
<td>0.983</td>
<td>8.570</td>
<td>0.149</td>
<td>0.030</td>
<td>13</td>
<td>$m$-Br, $p$-Cl, $m$-Cl, $p$-Cl$_2$, $p$-CN, $p$-NO$_2$, $o$-NO$_2$, $m$-NO$_2$, $p$-NO$_2$, $p$-OCH$_3$, $o$-CH$_3$, $m$-CH$_3$, $o$-F, $p$-Cl, $m$-Br, $p$-OH, $m$-OH, $o$-OH, $m$-Br, $p$-B$_r$, $m$-Cl, $p$-Br, $m$-Cl, $p$-Br, $o$-F, $p$-Cl, $m$-Cl, $p$-Br</td>
</tr>
<tr>
<td></td>
<td>$\sigma_I$</td>
<td>0.900</td>
<td>8.430</td>
<td>0.369</td>
<td>0.083</td>
<td>13</td>
<td>$m$-Br, $p$-Cl, $m$-Cl, $p$-Cl$_2$, $p$-CN, $p$-NO$_2$, $o$-NO$_2$, $m$-NO$_2$, $p$-NO$_2$, $p$-OCH$_3$, $o$-CH$_3$, $m$-CH$_3$, $o$-F, $p$-Cl, $m$-Br, $p$-OH, $m$-OH, $o$-OH, $m$-Br, $p$-B$_r$, $m$-Cl, $p$-Br, $m$-Cl, $p$-Br, $o$-F, $p$-Cl, $m$-Cl, $p$-Br</td>
</tr>
<tr>
<td></td>
<td>$\sigma_R$</td>
<td>0.766</td>
<td>8.547</td>
<td>0.247</td>
<td>1.105</td>
<td>13</td>
<td>$m$-Br, $p$-Cl, $m$-Cl, $p$-Cl$_2$, $p$-CN, $p$-NO$_2$, $o$-NO$_2$, $m$-NO$_2$, $p$-NO$_2$, $p$-OCH$_3$, $o$-CH$_3$, $m$-CH$_3$, $o$-F, $p$-Cl, $m$-Br, $p$-OH, $m$-OH, $o$-OH, $m$-Br, $p$-B$_r$, $m$-Cl, $p$-Br, $m$-Cl, $p$-Br, $o$-F, $p$-Cl, $m$-Cl, $p$-Br</td>
</tr>
</tbody>
</table>

Table 3. Results of statistical analysis of chemical shifts of $H_\alpha$ and $H_\beta$ protons of substituted styryl 4-methoxy-1-naphthyl ketones with $\sigma_I$ and $\sigma_R$ or F and R parameters

| Correlation equations for $H_\alpha$ protons | $\delta_{\alpha}^{\text{corr}}=8.213+0.481\sigma_I+0.368\sigma_R$ | $R=0.978, n=13, P>95\%$ |
| Correlation Equations for $H_\beta$ protons | $\delta_{\beta}^{\text{corr}}=8.566+0.166F+0.224R$ | $R=0.955, n=13, P>90\%$ |

than those of $H_\beta$ protons in all chalcones. The ethylenic proton signals give an AB pattern and the $\beta$ protons doublet in most cases is well separated from the signals of the aromatic protons. The chemical shifts of $\alpha$, $\beta$ protons are given in Table 1. The observation that $H_\beta$ protons appear at higher field than that of $H_\alpha$ protons makes the subject very interesting. This may possibly due to the polarization of $C=C$ double bond in the system being predominantly caused by the carbonyl group so as to make electron density greater at the $\alpha$ position than that of $\beta$ position.

The results of statistical analysis are presented in Table 2. All the attempted correlations involving substituent parameters gave only positive $\rho$ values. This shows normal substituent effects is operates in all the chalcones. The Chemical shifts observed for $H_\alpha$ and $H_\beta$ protons in the present investigation are correlated satisfactorily with Hammett sigma constants. In some cases correlation of $H_\alpha$ with $\sigma$ values is slightly better. By and large the necessity of enhanced $\sigma$ values for correlation is not demanded by substituents. That the correlation with $\sigma_I$ and $\sigma_R$ parameters is not satisfactory in $H_\alpha$ implies that such $\sigma$ values are incapable of predicting chemical shifts individually due to the domination of cross conjugation between carbonyl group and methoxy group in naphthyl ring. In Table 3 the multiple correlations involving either $\sigma_I$ and $\sigma_R$ or F and R values for these ketones are presented. It is indeed satisfactory that in most cases the multiple correlations are successful. Some of the single parameter
correlations are shown in Fig. 2, 3.

\( ^{13} \)C NMR Spectra

From \( ^{13} \)C NMR spectra the observed \( ^{13} \)C Chemical shifts of \( C_a \) and the \( C_b \) carbons are presented in Table 1. These chemical shifts are correlated with various Hammett substituent constants. The results of statistical analysis of substituent effects on \( C_a \) and \( C_b \) carbons are shown in Table 4. There is a fair degree of correlation obtained for \( C_a \) and the \( C_b \) carbon chemical shifts with Hammett sigma constants. The degree of transmission of electronic effects is found to be higher with \( C_a \) carbon than \( C_b \) carbon. Uniformly \( \sigma_I \) and \( \sigma_R \) parameters or \( F \) and \( R \) values are adequately explain the substituent effects in all chalcones are evidenced from the correlation equations which are given in Table 5.

In single parameter correlations, there are satisfactory correlations obtained with \( \sigma \) values for \( C_a \)

\begin{table}
\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
Type of carbon & Constants for correlation & \( \sigma \) & \( \sigma^+ \) & \( \sigma_I \) & \( \sigma_R \) & \( \sigma_s \) & \( \sigma_n \) & Substituents in styryl part \\
\hline
\( C_a \) & & 0.927 & 119.421 & 0.813 & 0.393 & 13 & H, m-NH, & \\
& & 0.880 & 119.563 & 0.457 & 0.435 & 13 & p-NH, m-Br, & \\
& & 0.907 & 118.915 & 1.819 & 0.333 & 13 & m-Cl, p-Cl, & \\
& & 0.768 & 119.670 & 1.265 & 0.439 & 13 & m-OH, & \\
& & 0.990 & 140.397 & 2.906 & 1.118 & 13 & p-CH\textsubscript{3}, & \\
& & 0.937 & 140.854 & 1.875 & 1.096 & 13 & p-CH\textsubscript{3}, & \\
& & 0.937 & 139.137 & 4.756 & 1.459 & 13 & p-NO\textsubscript{2}, & \\
& & 0.724 & 141.144 & 3.574 & 2.501 & 13 & p-NO\textsubscript{2}, & \\
\hline
\end{tabular}
\end{table}

\begin{table}
\begin{tabular}{|c|c|c|c|c|c|c|c|}
\hline
Type of carbon & Constants for correlation & \( \sigma \) & \( \sigma^+ \) & \( \sigma_I \) & \( \sigma_R \) & \( \sigma_s \) & \( \sigma_n \) & Substituents in styryl part \\
\hline
\( C_a \) & & 189.130 & 1.439 & 0.679 & 0.319 & 0.166 & 0.374 & 0.319 & (R = 0.914, n = 13, P > 90\%) \\
& & 188.967 & 1.788 & 0.154 & 0.313 & 0.250 & 0.495 & 0.313 & (R = 0.914, n = 13, P > 90\%) \\
\hline
\( C_b \) & & 139.8 & 3.548 & 0.936 & 1.548 & 0.807 & 1.815 & 1.548 & (R = 0.994, n = 13, P > 90\%) \\
& & 140.849 & 2.464 & 2.716 & 2.716 & 0.988 & 1.240 & 1.240 & (R = 0.994, n = 13, P > 90\%) \\
\hline
\end{tabular}
\end{table}
and C₆ carbons. This implies that one need not attach any significance to the correlations involving \( \sigma \) values. A good single parameter correlation is shown in Fig. 4.

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REFERENCES