Synthesis and Characterization of Some Novel Chalcone Derivatives: An Intermediate for Various Heterocyclics Compounds

Singhal Manmohan*1, Paul Arindam 2, Singh Hemendra Pratap3

1School of Pharmaceutical Science, Jaipur National University, Jaipur, Rajasthan, India
2GD Memorial College of Pharmacy, Jodhpur, Rajasthan, India
3B N College of Pharmacy, Udaipur, Rajasthan, India

Abstract:
1, 3-diphenyl-2-propenones (Chalcone) are the important constituents of many natural sources, having various desired biological activities. A series of 1,3-diphenyl-2-propenone derivatives were synthesized and their structure were confirmed by IR and NMR spectroscopy. The compounds were synthesized by Claisen-Shimidt base catalyzed condensation of substituted acetophenones with substituted benzaldehydes.

Keywords: Chalcone, flavanone, Claisen-Shimidt reaction, benzaldehyde

Introduction
1, 3-diaryl-2-propen-1-ones (chalcones), constitutes an important class of natural products belonging to the flavonoid family, having various important biological activities. Additionally, some of chalcone derivatives have been found to inhibit several important enzymes in cellular systems, such as xanthine oxidase and protein tyrosine kinase. The evidences that these biological activities would be closely correlated to their antioxidant potential have been emerged in recent reports. [1] The antioxidant properties of chalcones are known to be influenced to a great extent by the two aryl structures, i.e. the substituent’s on two aryl rings of chalcone molecule and their substitution patterns. Especially, the hydroxyl substituent is one of the key groups to enhance greatly the antioxidant activity of chalcone mainly due to its easy conversion to phenoxy radicals through the hydrogen atom transfer mechanism. This phenoxy radical formation may be central to the antioxidant properties which are assessed primarily as radical scavenging potential of phenolic chalcones. [2] In fact, the hydroxyl substitutents are widespread among chalcones from natural sources. [3] There by, a number of structurally diverse chalcones including phenolic chalcones have been prepared and evaluated for their activities. Although some sporadic structure activity relationships (SAR) of some phenolic chalcone derivatives have been reported in the recent literature, it is fairly rare to find the systematic study on the

*Corresponding Author:
Manmohan Singhal
Email: manu_mpharm@yahoo.co.
relationships between structural derivatizations and antioxidant activity of structurally distinguishable polyphenolic chalcone derivatives. [4]

The chalcones are α-β unsaturated ketones containing the reactive keto ethylenic group – CO–CH=CH–. Presence of α-β-unsaturated carbonyl system in chalcone makes it biologically active. Some substituted chalcones and their derivatives have been reported to possess some interesting biological properties such as antibacterial, insecticidal, anaesthetic, analgesic, ulcerogenic, anti-inflammatory, antiplatelet, antiallergic, antimalarial, antiparkinsonian, antiviral etc. [5-8]

Chemistry of Chalcones
In claisen-Schmidt condensation reaction for synthesizing chalcones, aromatic aldehydes can be condensed with aliphatic or aromatic ketones in the presence of aqueous alkali to form α, β- unsaturated ketones called chalcones. In this mechanism, the first step is condensation of the aldol type involving the nucleophilic addition of carbanion derived from the aryl ketones to carbonyl carbon of the aromatic aldehydes. Dehydration of hydroxyl ketones forms the conjugated α, β- unsaturated ketones or chalcones. The structure of parent molecules of chalcones consist of two phenyl rings (A and B) and one α, β unsaturated double bond. The ring A must contain an electron deficient moiety like ethyl, methyl or alkyl groups for better activity. The unsaturated double bond plays an important role for the activity but marginal modifications in this double bond don’t have much effect on the activity. para position of the ring B is important for the activity. The ortho position of ring B also enhances the activity but in comparison with position it is low. 3D QSAR and in house QSPR studies of chalcones have para proved all these facts.

Pyrazole belongs to the family of azoles i.e. five-membered ring containing nitrogen and carbon atom. The dihydro pyrazoles are called pyrazolines. Some substituted pyrazolines and their derivatives have been reported to possess some interesting biological activities such as anticancer, insecticidal etc. The replacement of two -CH units in benzene by nitrogen atoms gives pyrimidines. Some substituted pyrimidines and their derivatives have been reported to possess antimicrobial, antitumour and antifungal activities. It has incidental antiviral activity against herpes and vaccinia infections. So on the bases of above findings, In the present investigation we are attempted to synthesis some 1, 3-diaryl-2-propen-1-ones derivatives, which are important for the synthesis of other important heterocyclic nucleus, as well as of biological importance. [9-10]

Material and methods
All the compounds were measured synthesized according to the given synthetic scheme figure 1. Melting points were in open capillary tubes on a Buchi 530 melting point apparatus and were uncorrected. Infrared (IR) and proton nuclear magnetic resonance (1H NMR) spectra were recorded for the compounds on Jasco IR Report 100 (KBr) and Brucker Advance (300 MHz) instruments, respectively. Chemical shifts are reported in parts per million (ppm) using
tetramethylsilane (TMS) as an internal standard. The homogeneity of the compounds was monitored by ascending thin-layer chromatography (TLC) on silica gel G (Merck) coated aluminum plates, visualized by iodine vapor and UV light.

**Synthesis of Substituted Chalcones:**
Substituted benzaldehydes (0.012mol) were added to a mixture of substituted acetophenones (0.01mol) in 25 ml of ethanol in a 200 ml beaker. The content of the beaker was mixed well and to that 10 ml of 10% potassium hydroxide solution was added and stirred vigorously at 25 °C until the mixture was so thick that stirring was no longer effective (3-4 h). After the completion of the stirring, the reaction mixture was kept in a refrigerator overnight. The reaction mixture was then diluted with ice-cold water (50 ml), acidified with 10% aqueous hydrochloric acid to precipitate the chalcones. The product was filtered with suction on a Buchner funnel, washed with cold water until the washings were neutral to litmus and then washed with 10 ml of ice-cold rectified spirit. The dried product was recrystallized from chloroform.

**Result and discussion:**
The synthesis of the Chalone is single step method. Structure of synthesized Chalcones is given in figure 2. The synthesized chalcone derivatives were undergone physiochemical characterization and the obtained results are given in table 1. The yields of the synthesized compounds were found to be significant. The structure of the synthesized compounds was confirmed by IR and NMR spectroscopy as shown in table 2. All the compounds give the characteristic IR peak that proved that the presence of particular functional groups and NMR spectroscopy helps to find the presence of specific type of protons present in the synthesized compounds.

These synthesized derivatives may be used for synthesizing the some other important heterocyclic nucleus as pyrazole, oxazole, semicarbazones etc. these compounds are also of biological importance

**Conclusion:**
The synthesized compounds were characterized by TLC, melting point, IR spectroscopy, and NMR spectroscopy. The results obtained from this study confirmed that the product has formed. Henceforth viewing these characteristic properties more compounds can be synthesized and subjected to pharmacological evaluation. These Chalone derivatives may have variety of biological activities viz. antitubercular, analgesic, anti-inflammatory, antipyretic, antioxidant, anticonvulsant, lishmanicidal, anticancer activity, etc. and may be a pavement for synthesis of and characterization of some new chalcone derivatives.

**References**


Figure: 1 Synthetic scheme for chalcone derivatives
Figure 2: Structure of chalcone derivatives

Table 1: Physico-chemical properties of synthesized chalcone derivatives

<table>
<thead>
<tr>
<th>Component</th>
<th>R₁</th>
<th>R₂</th>
<th>Molecular formula</th>
<th>mp (°C)</th>
<th>Yield (%)</th>
<th>Rf value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>H</td>
<td>H</td>
<td>C₁₅H₁₂O₂</td>
<td>89</td>
<td>85</td>
<td>0.80</td>
</tr>
<tr>
<td>3b</td>
<td>H</td>
<td>4”-OH</td>
<td>C₁₅H₁₂O₃</td>
<td>164</td>
<td>85</td>
<td>0.83</td>
</tr>
<tr>
<td>3c</td>
<td>H</td>
<td>4”-OCH₃</td>
<td>C₁₆H₁₄O₃</td>
<td>135</td>
<td>85</td>
<td>0.82</td>
</tr>
<tr>
<td>3d</td>
<td>H</td>
<td>4”-N(CH₃)₂</td>
<td>C₁₇H₁₇NO₂</td>
<td>155</td>
<td>85</td>
<td>0.78</td>
</tr>
<tr>
<td>3e</td>
<td>4”-OH</td>
<td>6”-OH</td>
<td>C₁₅H₁₂O₄</td>
<td>216</td>
<td>90</td>
<td>0.85</td>
</tr>
<tr>
<td>3f</td>
<td>4”-OH</td>
<td>4”-N(CH₃)₂</td>
<td>C₁₇H₁₇NO₃</td>
<td>174</td>
<td>90</td>
<td>0.81</td>
</tr>
<tr>
<td>3g</td>
<td>H</td>
<td>6”-OH</td>
<td>C₁₅H₁₂O₃</td>
<td>166</td>
<td>85</td>
<td>0.86</td>
</tr>
<tr>
<td>3h</td>
<td>5’OH</td>
<td>6”-OH</td>
<td>C₁₅H₁₂O₄</td>
<td>218</td>
<td>85</td>
<td>0.84</td>
</tr>
<tr>
<td>3i</td>
<td>5’OH</td>
<td>4”-OH</td>
<td>C₁₅H₁₂O₄</td>
<td>208</td>
<td>85</td>
<td>0.87</td>
</tr>
<tr>
<td>3j</td>
<td>5’OH</td>
<td>4”-OCH₃</td>
<td>C₁₆H₁₄O₄</td>
<td>152</td>
<td>85</td>
<td>0.79</td>
</tr>
<tr>
<td>Comp code</td>
<td>Spectral Analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------</td>
<td>------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>IR (KBr) v cm(^{-1}) = 3480(–OH), 1748—1716 (–CO), 1670 (–CH=CH–), 1616, 1558 (aromatic), 754, 697 (monosubstituted benzene). (^1)H-NMR (δ/ppm in CDCl(_3)): 5.0 (s, 1H, 2’ -OH), 7.14 (dd, J= 7.9, 1.8 Hz, 1H, 4” -H), 7.21 (d, J= 7.9 Hz, 2H, 3”, 5” –H”), 7.30 (d, J= 7.9Hz, 2H, 2”, 6” -H), 7.56 (s, 1H, –CH= CH–), 7.64 (m, J= 8.3 Hz, 4H, Ar-H), 7.90 (s, 1H, –CH=CH–).</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>IR (KBr) v cm(^{-1}) = 3480, 3345 (–OH), 1771, 1732 (–CO), 1682 (–CH=CH–), 1603, 1575 (aromatic), 834 (p-disubstituted benzene). (^1)H-NMR (δ/ppm in CDCl(_3)): 5.0 (s, 1H, 2’ -OH), 5.1 (s, 1H, 4” -OH), 6.68 (d, J=7.9Hz, 2H, 3”, 5” -H), 7.13 (d, J=8.0Hz, 2H, 2”, 6” -H), 7.64—6.92 (m, J=8.3 Hz, 4H, Ar-H), 7.56 (s, 1H, –CH=CH–), 7.90 (s, 1H, –CH=CH–).</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3c</td>
<td>IR (KBr) v cm(^{-1}) = 3480, 3446 (–OH), 1748, 1716 (–CO), 1670 (–CH=CH–), 1605, 1575 (aromatic), 834 (p-disubstituted benzene). (^1)H-NMR (δ/ppm in CDCl(_3)): 3.73 (s, 3H, 4” -OCH(_3)), 5.0 (s, 1H, 2’ -OH), 6.72 (d, J=7.9Hz, 2H, 3”, 5” -H), 7.19 (d, J=7.9Hz, 2H, 2”, 6” -H), 7.56 (s, 1H, –CH=CH–), 7.64—6.92 (m, J=8.1 Hz, 4H, Ar-H), 7.90 (s, 1H, –CH=CH–).</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3d</td>
<td>IR (KBr) v cm(^{-1}) = 3480, 3446 (–OH), 1748, 1716 (–CO), 1670 (–CH=CH–), 1621, 1558, 1521 (aromatic), 1312 (C–N stretching in Ar amines), 835 (p-disubstituted benzene). (^1)H-NMR (δ/ppm in CDCl(_3)): 2.8 (s, 6H, 4” -NMe(_2)), 5.0 (s, 1H, 2’ -OH), 6.54 (d, J=7.9 Hz, 2H, 3”, 5” -H), 7.12 (d, J=8.0 Hz, 2H, 2”, 6” -H), 7.56 (s, 1H, –CH=CH–), 7.64—6.92 (m, J=7.9 Hz, 4H, Ar-H), 7.90 (s, 1H, –CH=CH–).</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3e</td>
<td>IR (KBr) v cm(^{-1}) = 3841 (–OH), 1732, 1698 (–CO), 1670 (–CH=CH–), 1616, 1558 (aromatic), 727, 652 (monosubstituted benzene). (^1)H-NMR (δ/ppm in CDCl(_3)): 5.0 (s, 3H, 2’, 4”, 6” -OH), 6.68 (d, J=7.9Hz, 2H, 3”, 5” -H), 7.13 (d, J=7.9Hz, 2H, 2”, 6” -H), 7.39 (s, 1H, –CH=CH–), 7.47—6.39 (m, J=8.2 Hz, 3H, Ar-H), 8.17 (s, 1H, –CH=CH–).</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3f</td>
<td>IR (KBr) v cm(^{-1}) = 3480 (–OH), 1748, 1697 (–CO), 1670 (–CH=CH–), 1616, 1540 (aromatic), 1316 (C–N stretching in Ar amines), 824 (p-disubstituted benzene). (^1)H-NMR (δ/ppm in CDCl(_3)): 2.85 (s, 6H, 4” -NMe(_2)), 5.0 (s, 2H, 2’, 4’ -OH), 6.54 (d, J=7.9Hz, 2H, 3”, 5” -H), 7.12 (d, J=7.9Hz, 2H, 2”, 6” -H), 7.56 (s, 1H, –CH=CH–), 7.47—6.39 (m, J=8.1 Hz, 3H, Ar-H), 7.90 (s, 1H, –CH=CH–).</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| 3g | IR (KBr) v cm\(^{-1}\) = 3391, 3209 (–OH), 1748, 1698 (–CO), 1653 (–CH=CH–), 1623, 1576 (aromatic), 728, 697 (monosubstituted benzene). \(^1\)H-NMR (δ/ppm in CDCl\(_3\)): 5.0 (s, 2H, 2’, 6” -OH), 7.11—6.75 (m, J=8.2 Hz, 4H, Ar-H), 7.14 (dd, J=7.9, 1.8Hz, 1H, 4” -H), 7.21 (d, J=7.9Hz, 2H, 3”, 5” -H), 7.30 (s, 1H, 2” -H), 7.56 (s,
1H, –CH=CH–, 7.90 (s, 1H, –CH=CH–).

3h | IR (KBr) ν cm⁻¹ = 3446 (–OH), 1748, 1698 (–CO), 1670, 1652 (–CH=CH–), 1616, 1540 (aromatic), 714, 673 (monosubstituted benzene). ¹H-NMR (δ/ppm in CDCl₃): 5.0 (s, 3H, 2’, 5’, 6”-OH), 6.68 (d, J=7.9Hz, 1H, 3’-H), 6.77 (dd, J=7.9, 1.8Hz, 1H, 6’-H), 6.97 (dd, J=7.9, 1.8Hz, 1H, 4’-H), 7.11—6.75 (m, J=8.3 Hz, 4H, Ar-H), 7.39 (s, 1H, –CH=CH–), 8.17 (s, 1H, –CH=CH–).

3i | IR (KBr) ν cm⁻¹ = 3244 (–OH), 1732, 1698 (–CO), 1683 (–CH=CH–), 1646, 1557 (aromatic), 834 (p-disubstituted benzene). ¹H-NMR (δ/ppm in CDCl₃): 5.0 (s, 3H, 2’, 5’, 4”-OH), 6.68 (d, J=7.9Hz, 2H, 3”, 5”-H), 7.11—6.75 (m, J=8.3 Hz, 3H, Ar-H), 7.13 (d, J=7.9Hz, 2H, 2”, 6”-H), 7.56 (s, 1H, –CH=CH–), 7.90 (s, 1H, –CH=CH–).

3j | IR (KBr) ν cm⁻¹ = 3244 (–OH), 1732, 1716 (–CO), 1683 (–CH=CH–), 1577, 1540 (aromatic), 834 (p-disubstituted benzene). ¹H-NMR (δ/ppm in CDCl₃): 3.73 (s, 3H, 4”-OCH₃), 5.0 (s, 2H, 2’, 5’-OH), 6.72 (d, J =7.9 Hz, 2H, 3”, 5”-H), 7.11—6.75 (m, J=8.3 Hz, 3H, Ar-H), 7.19 (d, J=7.9Hz, 2H, 2”, 6”-H), 7.56 (s, 1H, –CH=CH–), 7.90 (s, 1H, –CH=CH–).