**CHAPTER 4**

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**Synthesis of Isoflavones and Flavones**

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<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1</td>
<td>INTRODUCTION</td>
<td>133</td>
</tr>
<tr>
<td>4.2</td>
<td>RESULTS AND DISCUSSION</td>
<td>142</td>
</tr>
<tr>
<td>4.2.A</td>
<td>Synthesis of Isoflavones</td>
<td>143</td>
</tr>
<tr>
<td>4.2.A.1</td>
<td>HTIB Mediated Synthesis of new 3-Aryl-1-(2-benzoyloxyphenyl)-2,3-bis(tosyloxy)propanones</td>
<td>143</td>
</tr>
<tr>
<td>4.2.A.2</td>
<td>Reaction of 3-Aryl-1-(2-benzoyloxyphenyl)-2,3-bis(tosyloxy)propanones with KOH/MeOH: Synthesis of isoflavones</td>
<td>149</td>
</tr>
<tr>
<td>4.2.B</td>
<td>Synthesis of Flavones</td>
<td>153</td>
</tr>
<tr>
<td>4.2.B.1</td>
<td>Chlorination of 3-Aryl-1-(2-benzoyloxyphenyl)prop-2-en-1-ones using dichlorodiiodobenzene (PhICl₂)</td>
<td>153</td>
</tr>
<tr>
<td>4.2.B.2</td>
<td>Reaction of 3-Aryl-1-(2-benzoyloxyphenyl)-2-chloroprop-2-en-1-ones with KOH/MeOH: Synthesis of Flavones</td>
<td>160</td>
</tr>
<tr>
<td>4.3</td>
<td>EXPERIMENTAL</td>
<td>163</td>
</tr>
<tr>
<td>4.4</td>
<td>REFERENCES</td>
<td>176</td>
</tr>
</tbody>
</table>
4.1 INTRODUCTION

Flavonoids are group of natural products that are widely present in plants. These are ingested by humans in their regular food and are commonly used as therapeutic agents. These compounds are generally distributed in nature exhibiting a wide range of biological activities like antibacterial, antiinflammatory, antiallergic, antiviral, antineoplastic, antifungal, antitumor, antiproliferative etc. Flavonoids are also very important for human health due to their activity as free radical acceptors. For example, 4′-hydroxy-3,5,6,7-tetramethoxyflavone which was isolated from the ethanol extract of the aerial parts of Varthemia iphionoides, has shown DPPH free radical-scavenging and cytotoxic activities. Some fully phosphorylated flavones act as potent pancreatic cholesterol esterase inhibitors.

Flavonoids which are characterised as natural aryl hydrocarbon receptors (AhR) are known to play a beneficial regulatory role in humans. Isoflavones such as daidzein and genistein (Chart 4.1) present in the herb contribute to the overall bioactivity of the herb. Daidzeins are phytoestrogens with weak oestrogenic activity. They are present in the human diet in soy beans and soy derived products. Genistein is a small, biologically active flavonoid that is also found in high amounts in soybean. This important compound possesses antioxidant and anti-photocarcinogenic properties. In particular, genistein has emerged as an important inhibitor of cancer metastasis. Isoflavones also act as apoptosis inducers in human heptoma HuH-7 cells. Some isoflavones are well-known tyrosine kinase inhibitors and studies also show that isoflavones bind to G-protein coupled receptors, including serotonin, dopamine, d-opiate, and benzodiazepine receptors.

Literature survey reveals that the flavonoids have been recognized as new therapeutics for hormone-dependent breast cancer, in which estrogens play a key role in growth and development of tumor. Various isoflavones were identified with potent aromatase inhibitory activities. A series of isoflavones contains an amine-bearing side chain, which is known to be essential for the tissue selectivity of many known selective estrogen receptor modulators (SERMs). Several compounds in this series were highly potent in inhibiting proliferation of human breast cancer cells. Flavonoids were shown to inhibit cytochrome P450 (P450) 2C9, particularly CYP1A1 and CYP1A2. Flavonoids can also participate in interactions with the drugs that act as substrates for CYP2C9 and provide a
possible molecular basis for understanding cooperativity in human P450-mediated drug-drug interactions.\(^\text{17}\)

For the nomenclature of flavonoids a separate, **Chart 4.1** is given.

**Chart 4.1 Nomenclature of Flavonoids**
In the recent years, the hypervalent iodine(III) reagents have shown wider applications in the synthesis of flavonoids\(^{18}\) possessing various biological activities as compared to that of other reagents like \(\text{TI(III)(NO}_3\text{)}_3 \cdot 3\text{H}_2\text{O}\), thallium(III) nitrate trihydrate (TTN). Such types of reagents are toxic and have adverse effects on the environment. Moreover, iodine(III) mediated approaches become more useful due to: (i) yields of the products are generally good or high, (ii) non-toxicity of the reagents, (iii) very simple experimentation and short time span. (iv) eco friendly. In continuation of our efforts to explore the utility of iodine(III) reagents in the synthesis of flavonoids, we herein discuss the synthesis of some isoflavones and flavones from new 3-aryl-1-(2-benzoyloxyphenyl)-2,3-bis(tosyloxy)propanones (45) and 3-aryl-1-(2-benzoyloxyphenyl)-2-chloroprop-2-en-1-ones (62), respectively. Before discussing the actual work done, it is significant to describe briefly some of the recently reported syntheses of flavonoids and related compounds using hypervalent iodine(III) reagents.

**Syntheses of Flavonoids and Related compounds with Hypervalent Iodine Reagents**

HTIB induced oxidation of flavanones (1) in methanol leads to dehydrogenation with the formation of flavones (2). This transformation can also be effected by using iodobenzene diacetate (IBD) in methanol or acetic acid or acetonitrile at room temperature (Scheme 4.1).\(^{19, 20}\)

![Scheme 4.1](image)

Recently, an alternative approach has also been developed for the oxidation of flavanones (3) to flavones (4) using hydroxy(tosyloxy)iodo]benzene in the presence of ionic liquid 1,3-di-\(n\)-butylimidazolium bromide ([bbim]\(^+\)Br\(^-\)) at room temperature (Scheme 4.2).\(^{21}\)
Various 3-haloflavones (5) have been prepared by the reaction of the corresponding flavone derivatives 6 with IBD and trimethylsilyl halide under mild reaction conditions. IBD can be replaced by the polymer supported iodobenzene diacetate without the decrease in activity (Scheme 4.3).\textsuperscript{22, 23}

A novel and convenient synthesis of isoflavones (8) has been reported from our laboratory by the oxidation of flavanones (7) with [hydroxy(tosyloxy)iodo]benzene (HTIB) in acetonitrile in the presence of methanesulphonic acid (CH\textsubscript{3}SO\textsubscript{3}H) or p-toluenesulphonic acid (p-TsOH). The oxidation of flavanones (7) with HTIB in boiling acetonitrile or propionitrile does not afford the expected α-functionalized products, 3-tosyloxyflavanones (9). Instead, 1,2-shift of C(2)-aryl group to C(3) occurs, thus providing a novel route for isoflavones (8) (Scheme 4.4).\textsuperscript{24}
Isoflavones (12) have also been synthesized in one-pot reaction by treating o-hydroxy/benzyloxylchalcones 10 with HTIB in methanol. A combined use of iodobenzene diacetate (IBD)/ p-toluenesulphonic acid (TsOH) has also been found to be effective for the same purpose (Scheme 4.5).²⁵

Oxidation of 3-cinnamoyl-4-hydroxy-6-methyl-2H-pyran-2-ones (13, chalcone analogs of DHA) with HTIB in CH₂Cl₂ leads to cyclization, thereby providing a new and convenient route for the synthesis of 3-aryl-7-methylpyrano[4,3-b]pyran-4H,5H-diones (14, isoflavone analogs of DHA) (Scheme 4.6).²⁶
Scheme 4.6

Dialkylchromanones (15) undergo rearrangement with HTIB in acetonitrile to yield the chromones of the type (17). In case of spirochromanones (16), oxidation with HTIB gives the dehydrotenoid core 18 (Scheme 4.7).²⁷,²⁸

Scheme 4.7

Oxidation of flavanones (19) with IBD or HTIB in trimethyl orthoformate (TMOF) in the presence of an acid leads to the formation of methyl 2-aryl-2,3-dihydrobenzofuran-3-carboxylates (20) by the contraction of the pyran ring of flavanones (Scheme 4.8).²⁹
Oxidation of 6-hydroxyflavone (21) and 6-hydroxyflavanone (22) with IBD in acetic acid leads to regioselective acetyloxylation, thereby providing a novel and convenient route for the synthesis of 5-acetoxylated products 23 and 24, respectively (Scheme 4.9).^{30}

![Scheme 4.9](image_url)

Oxidation of flavonols (25) with HTIB or IBD in methanol results in the introduction of two methoxy groups to the carbon-carbon double bond, thus generating 2,3-dimethoxy-3-hydroxyflavanones (26) (Scheme 4.10).^{31,32}

![Scheme 4.10](image_url)

Some new 2,3-dimethoxy-3-hydroxy-2-(1-phenyl-3-aryl-4-pyrazolyl)chromanones (28) have been synthesized by the oxidation of 3-hydroxy-2-(1-phenyl-3-aryl-4-pyrazolyl)chromones (27) with iodobenzene diacetate in methanol (Scheme 4.11).^{33} These compounds show potent antibacterial activities.
Scheme 4.11

The microwave-activated reactions of HTIB with various chromanones, thiochromanones and dihydroquinolones under solvent-free conditions have also been studied. In addition to the common dehydrogenation reaction, 2,3-migration has also been observed in the case of flavanones (29) and 2,2-disubstituted chromanones (30 and 31) (Scheme 4.12).34

Scheme 4.12
Attack at the nucleophilic heteroatom has also been observed in the reactions of 1-thiochromanones (32) and 2-phenyl-2,3-dihydro-4-quinolone (33). Treatment of 1-thiochromanones (32) with HTIB under MW irradiation affords the corresponding sulfoxide 35, accompanied by a small amount of 1-thiochromone (36). The substitution on the nitrogen plays a decisive role since 2-phenyl-2,3-dihydro-4-quinolone (33) gives the dehydrogenated 2-phenyl-4-quinolone (37) as the sole product while 1-acetyl-2-phenyl-2,3-dihydro-4-quinolone (34) yields the migrated 3-phenyl-4-quinolone (38) (Scheme 4.13).
4.2 RESULTS AND DISCUSSION

It is evident from the short review on the use of iodine(III) reagents in the synthesis of flavonoids that organoiodine(III) reagents such as HTIB, IBD find significant use in offering alternatives to the conventional approaches for the synthesis of a wide variety of flavonoids and related compounds.

The research work discussed in the Chapter is aimed at the following objectives:

(a) To explore the utility of hypervalent iodine(III) reagents for tosyloxylation and halogenations of carbon-carbon double bond in 2'-substituted chalcones.

(b) To examine the comparative reactivity pattern of α,β-dihaloketones and α,β-ditosyloxyketones with an emphasis on the synthesis of flavones and isoflavones by alkaline induced cyclization of α,β-dihaloketones.

The results accomplished during this work have been discussed in two parts as follows:

4.2.A: Synthesis of isoflavones

4.2.A.1: HTIB mediated synthesis of new 3-aryl-1-(2-benzoyloxyphenyl)-2,3-bis(tosyloxy)propanones

4.2.A.2: Reaction of 3-aryl-1-(2-benzoyloxyphenyl)-2,3-bis(tosyloxy)propanones with KOH/MeOH: Synthesis of isoflavones

4.2.B: Synthesis of flavones

4.2.B.1: Chlorination of 3-aryl-1-(2-benzoyloxyphenyl)prop-2-en-1-ones using dichloroiodobenzene (PhICl₂)

4.2.B.2: Reaction of 3-aryl-1-(2-benzoyloxyphenyl)-2-chloroprop-2-en-1-ones with KOH/MeOH: Synthesis of flavones
4.2.A: SYNTHESIS OF ISOFLAVONES

4.2.A.1 HTIB mediated synthesis of new 3-aryl-1-(2-benzoyloxyphenyl)-2,3-bis(tosyloxy)propanones

In the present study, an effort has been made to extend the utility of HTIB for the synthesis of 3-aryl-1-(2-benzoyloxyphenyl)-2,3-bis(tosyloxy)propanones (45) from 3-aryl-1-(2-benzoyloxyphenyl)prop-2-en-1-ones (44). The reaction of newly synthesized compounds has been investigated with KOH/ MeOH with a view to compare the results with previous studies on α,β-ditosyloxyketones and their α,β-dibromo analogs.

The following description summarizes important chemical transformations of α,β-dibromoketones and α,β-ditosyloxyketones.

α,β-Dibromoketones

The chemistry of α,β-chalcone dibromides (39), which are readily accessible by bromination of chalcones is well explored. α,β-Chalcone dibromides (39) serve as valuable substrates to bring about a variety of chemical transformations. A number of heterocyclic compounds (including flavonoids) as well as acyclic moieties have been prepared from α,β-chalcone dibromides (39). Some of the important transformations are outlined in Chart 4.2. 35-53
Chart 4.2 Some important chemical transformations of α,β-chalcone dibromides
\textit{α,β-Ditosyloxyketones}

There is a considerable research interest in studying the reactivity of \(\alpha,\beta\)-ditosyloxyketones (40) to explore their potential in organic synthesis with particular emphasis on comparison with their \(\alpha,\beta\)-dibromo analogs. The synthesis of \(\alpha,\beta\)-ditosyloxyketones (40) has been carried out by the stereospecific \textit{syn}-1,2-ditosyloxilation of chalcones using HTIB which has already been discussed in the first part of Chapter 2 of this thesis. Some of our recent reports have focussed on the reactivity mode of \(\alpha,\beta\)-ditosyloxyketones (40). Consequently, some novel synthetic routes have been developed (Chart 4.3).\textsuperscript{54-56}

\begin{center}
\textbf{Chart 4.3 Some important chemical transformations of \(\alpha,\beta\)-chalcone ditosylates}
\end{center}

Encouraged by our previous results on hypervalent iodine(III) mediated oxidation and due to the increasing importance of organoiodine(III) reagents we have undertaken the oxidation of 3-aryl-1-(2-benzoyloxyphenyl)prop-2-en-1-ones (44) with HTIB in dichloromethane. The study has led to ditosyloxilation of double bond with the formation of 3-aryl-1-(2-benzoyloxyphenyl)-2,3-bis(tosyloxy)propanones (45) which are hitherto unknown.
It is reported earlier from our research group that 2'-hydroxychalcones (41) with HTIB undergo tosyloxylation regioselectively in the phenyl ring (A) to give 5-tosyloxy-2'-hydroxychalcones (42) rather than corresponding ditosylates 43 (by ditosyloxylation of double bond) (Scheme 4.14). 

\[
\begin{align*}
\text{Scheme 4.14} \\
\end{align*}
\]

The mechanistic pathway of the reaction probably involves the participation of the phenolic group (Scheme 4.15).

\[
\begin{align*}
\text{Scheme 4.15} \\
\end{align*}
\]

Thus, it became necessary to protect the phenolic group to achieve selective synthesis of titled ditosylstes 45. The free hydroxyl group of the 2'-hydroxychalcones (41) was protected
by benzoyl group using standard procedure involving the reaction of 2'-hydroxychalcones (41) with benzoyl chloride in anhydrous pyridine. The benzoyloxy derivatives, 2'-bezoyloxychalcones (44) were obtained in good yields (Scheme 4.16).

To carry out the ditosyloxylation of 44, initially, the reaction of 2'-bezoyloxychalcone (44a) was performed according to the procedure reported in literature using two equivalents of [hydroxy(tosyloxy)iodo]benzene in dichloromethane at room temperature. Under these conditions, the reaction did not occur and mostly unchanged starting material was recovered. Further experimentation by changing the reaction conditions revealed that chalcone ditosylate can be obtained by refluxing the mixture of 2'-bezoyloxychalcones (44) with two equivalents of HTIB in dichloromethane for about two days. Thus obtained crude chalcone ditosylate was crystallized with acetonitrile to give pure 45a in 76% yield.

Prompted by this result, the generality of this facile transformation was tested by treating other 2'-benzoyloxychalcones (44b-44f) with HTIB under similar conditions. The reaction, indeed, afforded the corresponding α,β-chalcone ditosylates 45b-45f in good yields (Scheme 4.16).

![Scheme 4.16](image-url)
The physical data of 45a-45f are summarized in Table 4.1.

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Ar</th>
<th>M.p. (°C)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>45a</td>
<td>C₆H₅</td>
<td>99-100</td>
<td>76</td>
</tr>
<tr>
<td>45b</td>
<td>4-CH₃C₆H₄</td>
<td>104-105</td>
<td>75</td>
</tr>
<tr>
<td>45c</td>
<td>4-OCH₃C₆H₄</td>
<td>107-109</td>
<td>73</td>
</tr>
<tr>
<td>45d</td>
<td>4-BrC₆H₄</td>
<td>114-115</td>
<td>73</td>
</tr>
<tr>
<td>45e</td>
<td>4-ClC₆H₄</td>
<td>103-104</td>
<td>72</td>
</tr>
<tr>
<td>45f</td>
<td>4-NO₂C₆H₄</td>
<td>128-130</td>
<td>75</td>
</tr>
</tbody>
</table>

Table 4.1: Physical data of 3-aryl-1-(2-benzoyloxyphenyl)-2,3-bis(tosyloxy)propanones (45a-45f)

*Yields of the isolated products 45 w.r.t. 44

The benzoylated ditosylates 45 synthesized in this study are new compounds and were fully characterized through their spectral and elemental data. The IR spectrum of 45a showed two strong bands at approximately 1692 cm⁻¹ and 1743 cm⁻¹ due to carbonyl stretching. The ¹H NMR of the new ditosylate 45a showed two distinct singlets at δ 2.35 and δ 2.38 due to two p-methyl group protons of two tosylates groups. The rest of the protons appeared in the aromatic region. The structure of the product was also confirmed by ¹³C NMR.

Various 2'-hydroxychalcones (41) needed for this study were prepared by the condensation of 2'-hydroxyacetophenone (46) with different substituted aromatic aldehydes 47 (Scheme 4.17).[^58]

![Scheme 4.17](image)

[^58]: Ar = C₆H₅, 4-CH₃C₆H₄, 4-OCH₃C₆H₄, 4-BrC₆H₄, 4-ClC₆H₄, 4-NO₂C₆H₄
4.2.A.2 Reaction of 3-aryl-1-(2-benzoyloxyphenyl)-2,3-bis(tosyloxy)propanone with KOH/MeOH: Synthesis of isoflavones

Isoflavones (49) represent a large class of natural products and exhibit remarkably diverse biological properties. In the present investigation, a new method for the synthesis of isoflavones (49) has been developed. The new synthesis involves one-step starting from 3-aryl-1-(2-benzoyloxyphenyl)-2,3-bis(tosyloxy)propanones (45) which have been discussed in previous section (4.2.A.1).

In an earlier report from our laboratory, dealing with the chemistry of α,β-chalcone ditosylates, it has been shown that the reaction of 1,3-diaaryl-2,3-ditosyloxypropanones (40) with KOH/MeOH offers a novel route for the synthesis of desoxybenzoins (48) by 1,2-aryl shift and carbon-carbon bond cleavage (Scheme 4.18).56

![Scheme 4.18](image)

In continuation of these studies, now it was thought of significant interest to examine the reactivity of newly synthesized 3-aryl-1-(2-benzoyloxyphenyl)-2,3-bis(tosyloxy)propanones (45) with KOH/MeOH. The objective was to ascertain whether reaction occurs analogous to previous results or takes different course due to the presence of benzoyl group.

Thus, the reaction of 1-(2-benzoyloxyphenyl)-2,3-bis(tosyloxy)-3-phenylpropanone (45a) was carried out with KOH/MeOH according to the conditions described in our previous report.56 The crude product was purified by column chromatography. The m.p. and spectral data of the product did not show any indication of the formation of the corresponding desoxybenzoin. Instead, the product was identified as isoflavone (49a) on the basis of comparison of its m.p. and spectral data with those reported in literature59 (Scheme 4.19, Table 4.2).
Using similar conditions, the other α,β-ditosylates 45b-f, also gave the corresponding isoflavones 49b-f in good yields (60-70%). The physical data are summarized in Table 4.2.

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Ar</th>
<th>M.p. (°C)</th>
<th>Lit. m.p. (°C)</th>
<th>Yield(^a) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>49a</td>
<td>C(_6)H(_5)</td>
<td>129-130</td>
<td>131-132(^{59})</td>
<td>69</td>
</tr>
<tr>
<td>49b</td>
<td>4-CH(_3)C(_6)H(_4)</td>
<td>144-145</td>
<td>146-147(^{60})</td>
<td>70</td>
</tr>
<tr>
<td>49c</td>
<td>4-OCH(_3)C(_6)H(_4)</td>
<td>137-138</td>
<td>138-139(^{61})</td>
<td>67</td>
</tr>
<tr>
<td>49d</td>
<td>4-BrC(_6)H(_4)</td>
<td>183-184</td>
<td>182-184(^{61})</td>
<td>66</td>
</tr>
<tr>
<td>49e</td>
<td>4-ClC(_6)H(_4)</td>
<td>184-186</td>
<td>186-188(^{61})</td>
<td>69</td>
</tr>
<tr>
<td>49f</td>
<td>4-NO(_2)C(_6)H(_4)</td>
<td>201-202</td>
<td>202-204(^{60})</td>
<td>60</td>
</tr>
</tbody>
</table>

\(^a\)Yields of the isolated products 49 w.r.t. 45
Mechanism

The plausible mechanism for the conversion 45 $\rightarrow$ 49 has been outlined in Scheme 4.20.

The mechanism of the reaction is not certain and needs more investigations. It is obvious from the results that the conversion 45 $\rightarrow$ 49 involves the following three major steps:

(i) rearrangement of ditosylates to dimethylacetals
(ii) cleavage of benzoyloxy group to phenoxide ion
(iii) cyclization followed by aromatization

However, it is not certain what is the sequence of the occurrence of the above three steps. Since rearrangement of 2'-hydroxy/benzyloxychalcones (10) with HTIB in MeOH is known to give acetals 10. It seems likely that first step of the conversion 45 $\rightarrow$ 49 under study is the rearrangement of ditosylates to acetals F. Since it is also known that alkaline induced cyclization of 2'-hydroxy/benzyloxyacetals gives isoflavones, it is reasonable to propose the mechanistic pathways as shown in Scheme 4.20.

It is noteworthy that the rearranged product F or G could undergo C-C cleavage to give corresponding desoxybenzoin H analogous to our previous report. Apparently, the presence of phenoxide at the ortho position shows preference for intermolecular participation leading to cyclic intermediate I, which subsequently undergoes elimination of a molecule of MeOH to yield the aromatic product isoflavones (49).
In conclusion, the significant features of the present study are:

- A successful synthesis of 3-aryl-1-(2-benzoyloxyphenyl)-2,3-bis(tosyloxy)propanones (11) further illustrates the utility of HTIB.
- It provides a facile and convenient route for the synthesis of isoflavones.
- The benzyolated chalcone ditosylates are potential precursors for the synthesis of some useful heterocyclic compounds such as pyrazoles, isoxazoles, etc.
- More detailed investigations dealing with the synthetic scope of ditosylates based reactions and their mechanisms are desirable for future work.
4.2.B: SYNTHESIS OF FLAVONES

4.2.B.1 Chlorination of 3-aryl-1-(2-benzoyloxyphenyl)prop-2-en-1-ones using dichloroiodobenzene (PhICl₂)

The chemistry of α,β-chalcone dichlorides is relatively less explored as compared to the chemistry of α,β-chalcone dibromides. In continuation of our ongoing research program in exploring the applicability of iodine(III) reagents for the synthesis of new compounds, we decided to investigate the reaction of 2'-benzoyloxychalcones (44) with (dichloroiodo)benzene in dichloromethane with the hope to effect chlorination of double bond.

Literature survey reveals that dichloroiodobenzene has been used for chlorination of various organic compounds. Some of the applications of PhICl₂ in chlorinations are as follow:

The reaction of chalcones (51) with PhICl₂ in dichloroiodobenzene gives erythro 2,3-dichloro-1,3-diarylpropan-1-ones (52) (Scheme 4.21).⁶² The reaction offers an alternative to the method involving Cl₂ gas for such chlorinations.⁶³

Scheme 4.21

In a recent report from our laboratory, it has been shown that chlorination of 2-aryl-2,3-dihydro-4(1H)-quinolones (53) with PhICl₂ gives 6-chloro-2-aryl-2,3-dihydro-4(1H)-quinolones (54). (Scheme 4.22).⁶³ These results have also been compared by performing chlorination of a representative case with Cl₂. Surprisingly, the reaction leads to substitution at all the positions without any selectivity affording 2-(4-bromophenyl)-5,6,7,8-tetrachloro-4-hydroxyquinoline (55) (Scheme 4.22).⁶⁴
An alternative synthesis of 6-chloro-2-aryl-2,3-dihydro-4(1H)-quinolones (59) has also been effected using dichloroiodobenzene. Starting from o-aminoacetophenone (56) which is chlorinated with PhICl₂ to give 2-amino-5-chloroacetophenone (57). The synthesis of 6-chloro-2-aryl-2,3-dihydro-4(1H)-quinolones (59) is completed by carrying out condensation of 57 with aldehydes in EtOH/NaOH followed by cyclization of the resultant 2-amino-5-chloroaldehydes (58) using H₃PO₄-AcOH (Scheme 4.23).
(Dichloroiodo)benzene has also been employed for carrying out chlorination of 1-aryl-3-(3-aryl-1-phenyl-4-pyrazolyl)prop-2-en-1-ones (Chalcone Analogs) \((60)\). The reaction affords 1-aryl-3-(3-aryl-1-phenyl-4-pyrazolyl)-2-chloroprop-2-en-1-ones \((61)\) without isolation of addition product (Scheme 4.24).\(^{65}\)

In view of these observations, we became interested to examine the reaction of 2'-hydroxychalcones \((41)\) with (dichloroiodo)benzene in dichloromethane with a view to prepare chalcone dichlorides. To initiate this investigation 2'-hydroxychalcone \((41a)\) was treated with 1.5 equivalents of \(\text{PhICl}_2\) in DCM. But the reaction did not take place and most of the starting material was recovered. Further experimentation by changing the conditions did not give any significant improvement in the results (Scheme 4.25).
Recovery of the starting chalcone in these experiments led us to propose that probably 2’-hydroxy group makes hydrogen bonding with the carbonyl group of 41, therefore preventing the complex formation of O-I(III) species.

Thus, it became necessary to carry out the reaction starting with protected phenolic derivative, 2’-benzoyloxychalcone (44a). Accordingly, 44a was subjected to chlorination using 1.5 equivalents of PhICl₂ in DCM at room temperature. The progress of the reaction was monitored by TLC. Usual work-up followed by purification of the crude product by column chromatography showed the exclusive formation of single product (Scheme 4.23). The pure product obtained from this reaction was characterized as 1-(2-benzoyloxyphenyl)-2-chloro-3-phenylprop-2-en-1-one (62a, on the basis of spectral and analytical data) rather than the expected dichloride 63. Similar reaction conditions smoothly converted other protected chalcone derivatives 41b-41f into the corresponding 3-aryl-1-(2-benzoyloxyphenyl)-2-chloroprop-2-en-1-ones (62b-62f) in good yields (Scheme 4.26).
The physical data of the newly synthesized compounds 62b-62f are given in Table 4.3.

Table 4.3: Physical data 3-aryl-1-(2-benzyloxyphenyl)-2-chloroprop-2-en-1-ones (62a-62f)

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Ar</th>
<th>M.p. (°C)</th>
<th>Yield(^a) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>62a</td>
<td>C(_6)H(_5)</td>
<td>155</td>
<td>74</td>
</tr>
<tr>
<td>62b</td>
<td>4-CH(_3)C(_6)H(_4)</td>
<td>143-144</td>
<td>72</td>
</tr>
<tr>
<td>62c</td>
<td>4-OC(_6)H(_4)</td>
<td>137-138</td>
<td>70</td>
</tr>
<tr>
<td>62d</td>
<td>4-BrC(_6)H(_4)</td>
<td>99-100</td>
<td>71</td>
</tr>
<tr>
<td>62e</td>
<td>4-ClC(_6)H(_4)</td>
<td>95-96</td>
<td>72</td>
</tr>
<tr>
<td>62f</td>
<td>4-NO(_2)C(_6)H(_4)</td>
<td>124-125</td>
<td>70</td>
</tr>
</tbody>
</table>

\(^a\)Yields of the isolated products 62 w.r.t. 44

The IR spectrum of 62a displayed carbonyl stretch at 1666 cm\(^{-1}\) and 1720 cm\(^{-1}\). The \(^1\)H NMR spectrum showed a characteristic singlet at δ 7.50 that can be ascribed to C\(_3\)-proton (β-H). The rest of the protons appeared in the aromatic region. The structure of the product was also confirmed by \(^{13}\)C NMR. \(^{13}\)C NMR spectrum of 62a showed signals at δ 123.49-133.80 (aromatic carbons), 140.72 (C\(_3\)-H), 148.41 (C\(_2\)), 164.69 (C=O), 189.43 (C=O). The structures of the products were further confirmed by DEPT-135 experiments. The peaks at δ 148.41 (C\(_3\)), 164.69 and 189.43 (C=O) were disappeared on DEPT-135. Mass spectrum of 62a showed peaks at 362 (M\(^+\)) and 364 (M\(^+\)+2) in relative abundance of 3:1. The ratio of relative abundance of these peaks clearly confirmed the presence of one chlorine atom in the structure of the product. The complete \(^1\)H and \(^{13}\)C NMR assignment of 62a is shown in Figure 4.1.
$^1$H NMR

![Figure 4.1](image)

$^13$C NMR

![Figure 4.2](image)

**Figure 4.1** $^1$H and $^{13}$C NMR chemical shifts of compound 62a (in ppm on $\delta$ scale)

It is to be noted that the product 62 obtained from this reaction can exist in two diastereomeric forms E or Z forms (geometrical isomers). However, $^1$H NMR spectral data (singlet at $\delta$ 7.50, Figure 4.1) supported the formation of (Z)-isomer. The corresponding (E)-isomer is expected to show a singlet at slightly lower $\delta$ value than $\delta$ 7.50.53
It is also noteworthy that the present study involving the reaction between 2'-benzoyloxychalcones (44) and PhICl₂ does not give the expected dichloride 63. Instead, the products obtained from the reaction are probably the resultant of elimination of one molecule of HCl from these dichlorides 63 (Scheme 4.27).

Scheme 4.27

The actual reason for this observation is not clear. This, in fact, is in contrast to the previous reports on chlorination/bromination⁵³ and tosyloxylation (discussed in the section 4.2.A.1 of this Chapter) of 2'-substituted chalcones. Similarly it is also not clear whether chlorination involves the reaction between 2'-benzoyloxychalcone (44) and PhICl₂ or Cl₂ which is generated by the decomposition of PhICl₂.⁶⁶,⁶⁷ More detailed investigations are required to explain the above observations.
4.2.B.2 Reaction of 3-Aryl-1-(2-benzoyloxyphenyl)-2-chloroprop-2-en-1-ones with KOH/MeOH: Synthesis of Flavones

Flavones are widespread phenolic compounds which are originated from plants. As stated in the introduction of this Chapter flavones are important due to not only determining the beautiful plant colours but also because of remarkable biological activities. In recent years, flavones intake in the form of dietary supplements and plant extracts has been increasing. In the present investigation, we made an attempt to synthesize flavones by carrying out the reaction of 3-aryl-1-(2-benzoyloxyphenyl)-2-chloroprop-2-en-1-ones (62) with KOH/MeOH.

3-aryl-1-(2-benzoyloxyphenyl)-2-chloroprop-2-en-1-ones (62a) was reacted with KOH in methanol. The crude product was purified by column chromatography using silica gel. The product was identified as flavone 64a on the basis of comparison of its m.p. and spectral data with those reported in the literature (Scheme 4.28).

![Scheme 4.28](image)

Using similar conditions, the other chloro derivatives 62b-62f, also gave the corresponding flavones 64b-64f in good yields (65-71%); the physical data are summarized in Table 4.4.
Table 4.4: Physical data of flavones (64a-f)

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Ar</th>
<th>M.p. (°C)</th>
<th>Lit. m.p. (°C)</th>
<th>Yield(^a) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>64a</td>
<td>C(_6)H(_5)</td>
<td>95-96</td>
<td>97(^{68, 69})</td>
<td>71</td>
</tr>
<tr>
<td>64b</td>
<td>4-CH(_3)C(_6)H(_4)</td>
<td>77-79</td>
<td>78-80(^{70})</td>
<td>68</td>
</tr>
<tr>
<td>64c</td>
<td>4-OCH(_3)C(_6)H(_4)</td>
<td>154-155</td>
<td>155-156(^{68, 69})</td>
<td>70</td>
</tr>
<tr>
<td>64d</td>
<td>4-ClC(_6)H(_4)</td>
<td>174-176</td>
<td>176-178(^{71})</td>
<td>65</td>
</tr>
<tr>
<td>64e</td>
<td>4-BrC(_6)H(_4)</td>
<td>183-185</td>
<td>185-187(^{69, 70})</td>
<td>66</td>
</tr>
<tr>
<td>64f</td>
<td>4-NO(_2)C(_6)H(_4)</td>
<td>273-275</td>
<td>276-278(^{70})</td>
<td>67</td>
</tr>
</tbody>
</table>

\(^a\)Yields of the isolated products 64 w.r.t. 62

Mechanism

The plausible mechanism for the conversion of 62 → 64 outlined in Scheme 4.29 is analogous to the reported base induced cyclization/pyrolytic dehydrohalogenation of 2' substituted chalcone dihalides\(^{53}\). The transformation probably involves the formation of phenoxide ion J by cleavage of benzoyloxy group followed by intramolecular participation of phenoxide ion leading to cyclic intermediate K. The latter (K) gives product 64 with simultaneous elimination of a molecule of hydrogen chloride.

![Scheme 4.29](image-url)
It is relevant to mention that synthesis of flavones from such $\alpha$-haloalketones has earlier been reported by thermal and alkaline induced cyclization of $2'$-hydroxy (or protected) chalcone dihalides. These methods suffer from several drawbacks. For example, alkaline cyclization of these dihaloketones are claimed to give aurones (66) frequently rather than flavones (67). On the other hand, pyrolytic dehydrohalogenation of $2'$-hydroxychalcone dibromides (65) give a mixture of products like 6-bromoflavones (68), flavanones (69) and $2'$-hydroxychalcones (70) along with the product flavones (70) (Scheme 4.30).

![Scheme 4.30](image)

**Conclusion**

- Synthesis of flavones from 3-aryl-1-(2-benzoyloxyphenyl)-2-chloroprop-2-en-1-ones (62) is superior alternative than earlier reported synthesis in terms of yields, time and selectivity.
- The compounds synthesized in the present study *i.e.*, 3-aryl-1-(2-benzoyloxyphenyl)-2-chloroprop-2-en-1-ones (62) are new compounds.
- The experimental procedure involves mild and facile way to synthesize flavones (64).
- 3-Aryl-1-(2-benzoyloxyphenyl)-2-chloroprop-2-en-1-ones (62) can also serve as important precursors for the synthesis of other heterocyclic compounds like pyrazoles, oxazoles, etc.
4.3 EXPERIMENTAL

Melting points were taken in open capillaries and are uncorrected. IR spectra were recorded on Perkin-Elmer IR spectrophotometer. The $^1$H NMR spectra were recorded on Brucker 300 MHz instrument. The chemical shifts are expressed in ppm units downfield from an internal TMS standard. $o$-Hydroxyacetophenone, substituted aldehydes, benzoylchloride, pyridine etc. were obtained from commercial suppliers.

[Hydroxy(tosyloxy)iodo]benzene (HTIB)

HTIB needed for the study was prepared according to literature procedure as described previously in Experimental section of Chapter 2 of this thesis.

3-ARYL-1-(2-HYDROXYPHENYL)PROP-2-EN-1-ONES (41)

Typical procedure

To a solution of NaOH (0.8 g, 0.02 mol) in methanol (50 ml) was added 2'-hydroxyacetophenone (46, 1.36 g, 0.01 mol) and benzaldehyde (47a 1.06 g, 0.01 mol) at 0-5 °C. The reaction mixture was stirred overnight at room temperature. Then, this reaction mixture was poured over crushed ice and acidified with dil. HCl. The yellow solid thus obtained was filtered, washed with water and dried. The crude product was crystallized with ethanol to afford pure 2'-hydroxychalcone 41a (1.51 g, 67%).

Other derivatives of 2'-hydroxychalcones 41b-41f were synthesized in a similar manner. 2'-hydroxychalcones (41a-41h) are known in literature and their melting points and yields are given in Table 4.5.
Table 4.5: Physical data of 3-aryl-1-(2-hydroxyphenyl)prop-2-en-1-ones (chalcones, 41) prepared according to Scheme 4.17

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Ar</th>
<th>M.p. (lit. m.p.) (°C)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>41a</td>
<td>C₆H₅</td>
<td>77-78 (78)</td>
<td>67</td>
</tr>
<tr>
<td>41b</td>
<td>4-CH₃C₆H₄</td>
<td>120 (120-121)</td>
<td>70</td>
</tr>
<tr>
<td>41c</td>
<td>4-OCH₃C₆H₄</td>
<td>94 (94)</td>
<td>71</td>
</tr>
<tr>
<td>41d</td>
<td>4-BrC₆H₄</td>
<td>145 (146-147)</td>
<td>65</td>
</tr>
<tr>
<td>41e</td>
<td>4-ClC₆H₄</td>
<td>138-139 (139)</td>
<td>72</td>
</tr>
<tr>
<td>41f</td>
<td>4-NO₂C₆H₄</td>
<td>140-141 (141)</td>
<td>62</td>
</tr>
</tbody>
</table>

aYields of the isolated products 41 w.r.t. 46

3-ARYL-1-(2-BENZOYLOXYPHENYL)PROP-2-EN-1-ONES (44)

Typical procedure

To a solution of 2'-hydroxychalcone (41a, 2.24 g, 0.01 mol) in pyridine (40 mL) was added benzoyl chloride (1.28 g, 0.01 mol). The resulting mixture was refluxed for about 4-5 hours. Then, the reaction mixture was poured over crushed ice. The solid thus obtained was filtered, washed with water and dried. The crude product was purified by column chromatography using EtOAc-petroleum ether as eluent to afford pure 2'-benzoyloxychalcone (44a, 2.36 g, 72%).

Other 44b-44f derivatives were synthesized in a similar manner.
Table 4.6: Physical data of 3-aryl-1-(2-benzoyloxyphenyl)prop-2-en-1-ones (44a-44f)

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Ar</th>
<th>M.p. (°C)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>44a</td>
<td>C₆H₅</td>
<td>83-84</td>
<td>72</td>
</tr>
<tr>
<td>44b</td>
<td>4-CH₃C₆H₄</td>
<td>Oil</td>
<td>70</td>
</tr>
<tr>
<td>44c</td>
<td>4-OCH₃C₆H₄</td>
<td>Oil</td>
<td>66</td>
</tr>
<tr>
<td>44d</td>
<td>4-BrC₆H₄</td>
<td>Oil</td>
<td>68</td>
</tr>
<tr>
<td>44e</td>
<td>4-ClC₆H₄</td>
<td>Oil</td>
<td>69</td>
</tr>
<tr>
<td>44f</td>
<td>4-NO₂C₆H₄</td>
<td>110-112</td>
<td>71</td>
</tr>
</tbody>
</table>

*a*Yields of the isolated products 44 w.r.t. 41

1-(2-Benzoyloxyphenyl)-3-phenylprop-2-en-1-one (44a)

![Diagram of 1-(2-Benzoyloxyphenyl)-3-phenylprop-2-en-1-one (44a)](image)

M.p. 83-84 °C; Yield: 72%;
IR (ν<sub>max</sub>, in KBr): 1689 cm<sup>-1</sup> and 1737 cm<sup>-1</sup> (C=O stretch);
<sup>1</sup>H NMR (CDCl₃, 300 MHz, δ): 7.20 (d, 1H, J = 16.5 Hz), 7.32-7.45 (m, 7H, Ar-H, C₂-H, C₃-H), 7.55-7.64 (m, 4H, Ar-H), 7.79 (d, 2H, J = 7.5 Hz), 8.15 (d, 2H, J = 7.5 Hz).

1-(2-Benzoyloxyphenyl)-3-(4'-methylphenyl)prop-2-en-1-one (44b)

![Diagram of 1-(2-Benzoyloxyphenyl)-3-(4'-methylphenyl)prop-2-en-1-one (44b)](image)

Oil; Yield: 70%;
IR (ν<sub>max</sub>, in KBr): 1685 cm<sup>-1</sup> and 1738 cm<sup>-1</sup> (C=O stretch);
\(^1\)H NMR (CDCl\(_3\), 300 MHz, \(\delta\)): 2.41 (s, 3H, CH\(_3\)), 7.16 (d, 1H, \(J = 16.5\) Hz), 7.23-7.58 (m, 8H, Ar-H, C\(_2\)-H, C\(_3\)-H), 7.67-7.81 (m, 4H, Ar-H), 8.23 (d, 2H, \(J = 7.8\) Hz).

1-(2-Benzoyloxyphenyl)-3-(4'-methoxyphenyl)prop-2-en-1-one (44c)

\[
\begin{array}{c}
\text{OCPh} \\
\text{O} \\
\text{OCH}_3
\end{array}
\]

Oil; Yield: 66%;
IR (\(\nu\text{max}, \text{in KBr}\)): 1687 cm\(^{-1}\) and 1740 cm\(^{-1}\)(C=O stretch);
\(^1\)H NMR (CDCl\(_3\), 300 MHz, \(\delta\)): 3.84 (s, 3H, OCH\(_3\)), 7.15 (d, 1H, \(J = 15.9\) Hz), 7.35-7.69 (m, 10H, Ar-H, C\(_2\)-H, C\(_3\)-H), 7.80 (d, 2H, \(J = 7.5\) Hz), 8.16 (d, 2H, \(J = 8.1\) Hz).

1-(2-Benzoyloxyphenyl)-3-(4'-bromophenyl)prop-2-en-1-one (44d)

\[
\begin{array}{c}
\text{OCPh} \\
\text{O} \\
\text{Br}
\end{array}
\]

Oil; Yield: 68%;
IR (\(\nu\text{max}, \text{in KBr}\)): 1689 cm\(^{-1}\) and 1739 cm\(^{-1}\)(C=O stretch);
\(^1\)H NMR (CDCl\(_3\), 300 MHz, \(\delta\)): 7.20 (d, 1H, \(J = 16.5\) Hz), 7.32-7.45 (m, 7H, Ar-H, C\(_2\)-H, C\(_3\)-H), 7.55-7.64 (m, 4H, Ar-H), 7.79 (d, 2H, \(J = 7.5\) Hz), 8.15 (d, 2H, \(J = 7.5\) Hz).

1-(2-Benzoyloxyphenyl)-3-(4'-chlorophenyl)prop-2-en-1-one (44e)

\[
\begin{array}{c}
\text{OCPh} \\
\text{O} \\
\text{Cl}
\end{array}
\]

Oil; Yield: 69%;
IR (\(\nu\text{max}, \text{in KBr}\)): 1688 cm\(^{-1}\) and 1739 cm\(^{-1}\)(C=O stretch);
1H NMR (CDCl₃, 300 MHz, δ): 7.14 (d, 1H, J = 15.9 Hz), 7.22-7.56 (m, 6H, Ar-H, C₂-H, C₃-H), 7.34 (d, 2H, J = 8.1 Hz), 7.60 (d, 2H, J = 8.1 Hz), 7.79 (d, 2H, J = 7.8 Hz), 8.14 (d, 2H, J = 7.8 Hz).

1-(2-Benzoyloxyphenyl)-3-(4'-nitrophenyl)prop-2-en-1-one (44f)

![Chemical Structure](image)

M.p. 110-112 °C; Yield: 71%;
IR (νmax. in KBr): 1680 cm⁻¹ and 1736 cm⁻¹ (C=O stretch);
1H NMR (CDCl₃, 300 MHz, δ): 7.09 (d, 1H, J = 15.9 Hz), 7.25-7.77 (m, 10H, Ar-H, C₂-H, C₃-H), 7.64 (d, 2H, J = 8.4 Hz), 8.12 (d, 2H, J = 8.4 Hz).

3-ARYL-1-(2-BENZOLOXYPHENYL)-2,3-BIS(TOSYLOXY)PROPANONES (45)

![Chemical Structure](image)

**Typical procedure**

To a solution of 2'-benzoyloxychalcone (44a, 1.3g, 10 mmol) in dichloromethane was added HTIB (3.1g, 20 mmol). The resulting mixture was allowed to stir at 40-42 °C. HTIB was highly insoluble in dichloromethane, but gradually disappeared as the reaction proceeded. The stirring was allowed to continue for about 16-18 h. The solvent was evaporated in vacuo. The gummy mass so obtained was triturated with pet ether (60-80 °C) to remove iodobenzene. The colorless solid obtained was thoroughly washed with water to remove p-toluenesulphonic acid formed as byproduct. The solid was recrystallized with acetonitrile to give the pure chalcone ditosylate 45a (2.01 g, 76%).

Other 45b-45f derivatives were prepared in a similar manner.
1-(2-Benzoyloxyphenyl)-2,3-bis(tosyloxy)-3-phenylpropanone (45a)

\[
\begin{array}{c}
\text{OCOPh} \\
\text{CH-CH} \\
\text{O} \\
\text{OTs} \quad \text{OTs}
\end{array}
\]

M.p. 99-100 °C; Yield: 76%;

IR ($\nu_{\text{max}}$, in KBr): 1692 cm$^{-1}$ and 1743 cm$^{-1}$ (C=O stretch);

$^1$H NMR (CDCl$_3$, 300 MHz, $\delta$): 2.35 (s, 3H, CH$_3$), 2.38 (s, 3H, CH$_3$), 4.98 (d, 1H, $J = 7.8$ Hz), 6.89 (d, 1H, $J = 7.8$ Hz), 7.03-7.05 (m, 4H), 7.17-7.21 (m, 6H), 7.33 (d, 2H, $J = 8.3$ Hz), 7.43-7.55 (m, 6H), 7.71 (d, 2H, $J = 8.4$ Hz), 8.17 (d, 2H, $J = 8.3$ Hz);

Elemental analysis: Calculated for C$_{36}$H$_{30}$O$_9$S$_2$: C, 64.46; H, 4.51; Found: C, 64.39; H, 4.47.

1-(2-Benzoyloxyphenyl)-2,3-bis(tosyloxy)-3-(4'-methylphenyl)propanone (45b)

\[
\begin{array}{c}
\text{OCOPh} \\
\text{CH-CH} \\
\text{O} \\
\text{OTs} \quad \text{OTs}
\end{array}
\]

M.p. 104-105 °C; Yield: 75%;

IR ($\nu_{\text{max}}$, in KBr): 1695 cm$^{-1}$ and 1745 cm$^{-1}$ (C=O stretch);

$^1$H NMR (CDCl$_3$, 300 MHz, $\delta$): 2.21 (s, 3H, CH$_3$), 2.36 (s, 3H, CH$_3$), 2.38 (s, 3H, CH$_3$), 4.92 (d, 1H, $J = 7.8$ Hz), 6.83 (m, 3H), 6.86 (d, 2H, $J = 8.1$ Hz), 6.92 (d, 2H, $J = 8.1$ Hz), 7.03 (d, 1H, $J = 7.8$ Hz), 7.17-7.20 (m, 3H), 7.33 (d, 2H, $J = 8.4$ Hz), 7.43-7.53 (m, 4H), 7.66 (d, 1H, $J = 7.5$ Hz), 7.72 (d, 2H, $J = 8.4$ Hz), 8.12 (d, 2H, $J = 8.4$ Hz);

$^{13}$C NMR (CDCl$_3$, 100 MHz, $\delta$): 21.67, 22.91, 83.93, 69.70, 124.10, 125.66, 126.90, 127.88, 128.32, 128.55, 129.28, 129.53, 129.91, 130.47, 130.76, 131.34, 135.45, 136.49, 142.56, 148.72, 167.32, 189.56;

Elemental analysis: Calculated for C$_{37}$H$_{32}$O$_9$S$_2$: C, 64.90; H, 4.71; Found: C, 64.83; H, 4.64;

Mass (m/z): 684 (M$^+$).
1-(2-Benzoyloxyphenyl)-2,3-bis(tosyloxy)-3-(4'-methoxyphenyl)propanone (45c)

M.p. 107-109 °C; Yield: 73%;
IR (ν max, in KBr): 1697 cm⁻¹ and 1746 cm⁻¹ (C=O stretch);
¹H NMR (CDCl₃, 300 MHz, δ): 2.36 (s, 3H, CH₃), 2.38 (s, 3H, CH₃), 3.70 (s, 3H, OCH₃), 4.89 (d, 1H, J = 7.8 Hz), 6.52 (d, 2H, J = 8.7 Hz), 6.83 (d, 1H, J = 7.8 Hz), 6.94 (d, 2H, J = 8.9 Hz), 7.03 (d, 2H, J = 8.1 Hz), 7.13 (d, 1H, J = 8.1 Hz), 7.21 (d, 2H, J = 8.1 Hz), 7.34 (d, 2H, J = 8.4 Hz), 7.44-7.51 (m, 5H), 7.66 (d, 1H, J = 7.5 Hz), 7.72 (d, 2H, J = 8.4 Hz), 8.12 (d, 2H, J = 8.4 Hz);
Elemental analysis: Calculated for C₃₇H₃₂O₁₀S₂: C, 63.41; H, 4.60; Found: C, 63.35; H, 4.58.

1-(2-Benzoyloxyphenyl)-2,3-bis(tosyloxy)-3-(4'-bromophenyl)propanone (45d)

M.p. 114-115 °C; Yield: 73%;
IR (ν max, in KBr): 1703 cm⁻¹ and 1741 cm⁻¹ (C=O stretch);
¹H NMR (CDCl₃, 300 MHz, δ): 2.36 (s, 3H, CH₃), 2.39 (s, 3H, CH₃), 4.96 (d, 1H, J = 7.8 Hz), 6.74 (d, 1H, J = 7.8 Hz), 7.08 (d, 2H, J = 8.7 Hz), 7.16 (d, 2H, J = 8.4 Hz), 7.28-7.41 (m, 4H), 7.49 (d, 2H, J = 8.1 Hz), 7.52-7.61 (m, 5H), 7.71 (d, 2H, J = 8.1 Hz), 7.83 (d, 2H, J = 8.7 Hz), 8.05 (d, 2H, J = 8.4 Hz);
Elemental analysis: Calculated for C₃₆H₂₉BrO₉S₂: C, 57.68; H, 3.90; Found: C, 57.60; H, 3.85.
1-(2-Benzoyloxyphenyl)-2,3-bis(tosyloxy)-3-(4'-chlorophenyl)propanone (45e)

\[
\begin{align*}
\text{OCOPh} & \quad \text{CH–CH} \\
\text{O} & \quad \text{OTs} \\
\text{Cl} &
\end{align*}
\]

M.p. 103-104 °C; Yield: 72%.
IR (ν_{max} in KBr): 1691 cm\(^{-1}\) and 1743 cm\(^{-1}\) (C=O stretch);
\(^1\)H NMR (CDCl\(_3\), 300 MHz, δ): 2.34 (s, 3H, CH\(_3\)), 2.37 (s, 3H, CH\(_3\)), 5.10 (d, 1H, J = 7.8 Hz), 6.81 (d, 1H, J = 7.8 Hz), 7.07 (d, 2H, J = 8.1 Hz), 7.19 (d, 2H, J = 8.7 Hz), 7.25 (d, 2H, J = 8.1 Hz), 7.34 (d, 2H, J = 8.4 Hz), 7.37-7.46 (m, 4H), 7.50-7.58 (m, 5H), 7.73 (d, 2H, J = 8.4 Hz), 7.87 (d, 2H, J = 8.7 Hz), 7.92 (d, 2H, J = 8.1 Hz);
Elemental analysis: Calculated for C\(_{36}\)H\(_{29}\)ClO\(_9\)S\(_2\): C, 61.31; H, 4.14; Found: C, 61.24; H, 4.11.

1-(2-Benzoyloxyphenyl)-2,3-bis(tosyloxy)-3-(4'-nitrophenyl)propanone (45f)

\[
\begin{align*}
\text{OCOPh} & \quad \text{CH–CH} \\
\text{O} & \quad \text{OTs} \\
\text{NO}_2 &
\end{align*}
\]

M.p. 128-130 °C; Yield: 75%.
IR (ν_{max} in KBr): 1703 cm\(^{-1}\) and 1739 cm\(^{-1}\) (C=O stretch);
\(^1\)H NMR (CDCl\(_3\), 300 MHz, δ): 2.33 (s, 3H, CH\(_3\)), 2.37 (s, 3H, CH\(_3\)), 4.92 (d, 1H, J = 7.8 Hz), 6.78 (d, 1H, J = 7.8 Hz), 7.07 (d, 2H, J = 8.1 Hz), 7.21-7.36 (m, 4H), 7.49-7.52 (m, 5H), 7.69 (d, 2H, J = 8.4 Hz), 7.56-7.64 (m, 4H), 7.72 (d, 2H, J = 8.1 Hz), 8.31 (d, 2H, J = 8.4 Hz);
Elemental analysis: Calculated for C\(_{36}\)H\(_{29}\)NO\(_{11}\)S\(_2\): C, 60.41; H, 4.08; Found: C, 60.36; H, 4.03.
3-ARYL-4H-CHROMEN-4-ONES (49)

Typical procedure: To a solution of α,β-ditosylate of 2'-benzoyloxychalcone (45a, 0.670 g, 0.001 mol) in ethanol was added KOH (0.112 g, 0.002 mol). The resulting mixture was refluxed for about 2-3 hours. Then, the reaction mixture was poured over crushed ice. The solid thus obtained was filtered, washed with water and dried. The crude product was purified by column chromatography using EtOAc-petroleum ether as eluent to afford white coloured pure isoflavone (49a, 0.15 g, 69%).

Other derivatives (49b-49f) were prepared in a similar manner. 3-aryl-4H-chromen-4-ones (Isoflavones, 49a-49h) are known in literature and their melting points and yields are given in Table 4.2.

3-ARYL-1-(2-BENZOYLOXYPHENYL)-2-CHLOROPROP-2-EN-1-ONES (62)

(Dichloroiodo)benzene (PhICl₂)

PhICl₂ needed for the study was prepared according to the literature procedure as described previously in Experimental section of Chapter 2 of this thesis.

Synthesis of 3-aryl-1-(2-benzoyloxyphenyl)-2-chloroprop-2-en-1-ones (62)

Typical procedure: To a solution of 2'-benzoyloxychalcone (44a, 0.66 g, 2 mmol) in dichloromethane was added PhICl₂ (0.57 g, 2.1 mmol). The resulting mixture was allowed to stir at room temperature. The stirring was allowed to continue for about 6-7 h. The solvent was distilled off and the gummy mass so obtained was triturated with pet ether to remove
iodobenzene. The crude product was purified by column chromatography using EtOAc-petroleum ether as eluent to afford pure 62a (0.55 g, 76%).

Other 62b-62f derivatives were prepared in similar manner.

1-(2-Benzoyloxyphenyl)-2-chloro-3-phenylprop-2-en-1-one (62a)

\[ \text{OCOPh} \quad \text{C} = \text{CH} \quad \text{Cl} \]

M.p. 155 °C; Yield: 74%.
IR (\( \nu_{\text{max}} \), in KBr): 1666 cm\(^{-1}\) and 1720 cm\(^{-1}\) (C=O stretch);
\(^1\)H NMR (CDCl\(_3\), 300 MHz, \( \delta \)): 7.33-7.42 (m, 7H, Ar-H), 7.50 (s, 1H, C\(_3\)-H), 7.53-7.64 (m, 3H, Ar-H), 6.86 (d, 2H, \( J = 8.1 \) Hz);
\(^{13}\)C NMR (CDCl\(_3\), 100 MHz, \( \delta \)): 123.49, 126.02, 128.46, 128.52, 128.68, 129.82, 130.24, 130.55, 130.81, 131.00, 131.20, 132.23, 132.68, 133.80, 140.72, 148.41, 164.69, 189.43;
Elemental analysis: Calculated for C\(_{22}\)H\(_{15}\)ClO\(_3\): C, 72.83; H, 4.17; Found: C, 72.75; H, 4.12;
Mass (m/z): 362 (M\(^+\)), 364 (M\(^+\)+2).

1-(2-Benzoyloxyphenyl)-2-chloro-3-(4'-methylphenyl)prop-2-en-1-one (62b)

\[ \text{OCOPh} \quad \text{C} = \text{CH} \quad \text{Cl} \quad \text{CH}_3 \]

M.p. 143-144 °C; Yield: 72%.
IR (\( \nu_{\text{max}} \), in KBr): 1667 cm\(^{-1}\) and 1720 cm\(^{-1}\) (C=O stretch);
\(^1\)H NMR (CDCl\(_3\), 300 MHz, \( \delta \)): 2.43 (s, 3H, CH\(_3\)), 7.02-7.16 (m, 5H, Ar-H), 7.32 (d, 2H, \( J = 7.8 \) Hz), 7.35-7.46 (m, 4H, Ar-H), 7.50 (s, 1H, C\(_3\)-H), 7.73 (d, 2H, \( J = 7.8\)Hz);
\(^{13}\)C NMR (CDCl\(_3\), 100 MHz, \( \delta \)): 123.49, 126.02, 128.46, 128.52, 128.68, 129.82, 130.24, 130.55, 130.81, 131.00, 131.20, 132.23, 132.68, 133.80, 140.72, 148.41, 164.69, 189.43;
Elemental analysis: Calculated for C\(_{23}\)H\(_{17}\)ClO\(_3\): C, 73.31; H, 4.55; Found: C, 73.25; H, 4.50.
1-(2-Benzoyloxyphenyl)-2-chloro-3-(4'-methoxyphenyl)prop-2-en-1-one (62c)

\[
\begin{array}{c}
\text{O} \quad \text{O} \\
\text{C} \quad \text{P} \\
\text{H} \quad \text{C} \\
\text{O} \quad \text{C} \\
\text{H} \quad \text{Cl}
\end{array}
\]

M.p. 137-138 °C; Yield: 70%;
IR (v_{max} in KBr): 1665 cm\(^{-1}\) and 1723 cm\(^{-1}\) (C=O stretch);
\(^1\)H NMR (CDCl\(_3\), 300 MHz, δ): 3.83 (s, 3H, OCH\(_3\)), 6.90 (d, 2H, J = 8.7 Hz), 7.38-7.43 (m, 4H, Ar-H), 7.49 (s, 1H, C-H), 7.55-7.64 (m, 3H, Ar-H), 7.82 (d, 2H, J = 8.7 Hz), 8.04 (d, 2H, J = 7.5 Hz);
\(^13\)C NMR (CDCl\(_3\), 100 MHz, δ): 123.49, 126.02, 128.46, 128.52, 128.68, 129.82, 130.24, 130.55, 130.81, 131.00, 131.20, 132.23, 132.68, 133.80, 140.72, 148.41, 164.69, 189.43;
Elemental analysis: Calculated for C\(_{23}\)H\(_{17}\)ClO\(_4\): C, 70.32; H, 4.36; Found: C, 70.28; H, 4.30.

1-(2-Benzoyloxyphenyl)-2-chloro-3-(4'-bromophenyl)prop-2-en-1-one (62d)

\[
\begin{array}{c}
\text{O} \quad \text{O} \\
\text{C} \quad \text{P} \\
\text{H} \quad \text{C} \\
\text{O} \quad \text{C} \\
\text{H} \quad \text{Br}
\end{array}
\]

M.p. 99-100 °C; Yield: 71%;
IR (v_{max} in KBr): 1690 cm\(^{-1}\) and 1725 cm\(^{-1}\) (C=O stretch);
\(^1\)H NMR (CDCl\(_3\), 300 MHz, δ): 7.18-8.20 (m, 13H, Ar-H), 7.50 (s, 1H, C-H);
\(^13\)C NMR (CDCl\(_3\), 100 MHz, δ): 123.49, 126.02, 128.46, 128.52, 128.68, 129.82, 130.24, 130.55, 130.81, 131.00, 131.20, 132.23, 132.68, 133.80, 140.72, 148.41, 164.69, 189.43;
Elemental analysis: Calculated for C\(_{23}\)H\(_{17}\)BrClO\(_3\): C, 59.82; H, 3.19; Found: C, 59.78; H, 3.15.
1-(2-Benzoyloxyphenyl)-2-chloro-3-(4'-chlorophenyl)prop-2-en-1-one (62e)

\[
\text{O} \quad \text{C} \quad \text{O} \quad \text{P} \\
\text{H} \\
\text{C} \quad \text{O} \\
\text{C} \\
\text{H} \\
\text{C} \\
\text{O} \\
\text{C} \\
\text{H} \\
\text{C} \\
\text{C} \\
\text{H} \\
\text{O} \\
\text{C} \\
\text{C} \\
\text{H} \\
\text{C} \\
\text{Cl} \\
\text{Cl}
\]

M.p. 95-96 °C; Yield: 72%;
IR (\(\nu_{\text{max}}\), in KBr): 1695 cm\(^{-1}\) and 1724 cm\(^{-1}\) (C=O stretch);
\(^1\)H NMR (CDCl\(_3\), 300 MHz, \(\delta\)): 7.30-7.41 (m, 5H, Ar-H), 7.49 (s, 1H, C\(_3\)-H), 7.65 (d, 2H, \(J = 8.1\) Hz), 8.06 (d, 2H, \(J = 7.2\) Hz), 8.19 (d, 2H, \(J = 8.1\) Hz), 8.27 (d, 2H, \(J = 7.2\) Hz);
\(^13\)C NMR (CDCl\(_3\), 100 MHz, \(\delta\)): 123.49, 126.02, 128.46, 128.52, 128.68, 129.82, 130.24, 130.55, 130.81, 131.00, 131.20, 132.23, 132.68, 133.80, 140.72, 148.41, 164.69, 189.43;
Elemental analysis: Calculated for C\(_{22}\)H\(_{14}\)ClO\(_3\): C, 66.52; H, 3.55; Found: C, 66.46; H, 3.51.

1-(2-Benzoyloxyphenyl)-2-chloro-3-(4'-nitrophenyl)prop-2-en-1-one (62f)

\[
\text{O} \quad \text{C} \quad \text{O} \\
\text{C} \quad \text{H} \\
\text{C} \quad \text{Cl} \\
\text{H} \\
\text{Cl} \\
\text{N} \\
\text{O} \\
\text{2}
\]

M.p. 124-125 °C; Yield: 70%;
IR (\(\nu_{\text{max}}\), in KBr): 1690 cm\(^{-1}\) and 1728 cm\(^{-1}\) (C=O stretch);
\(^1\)H NMR (CDCl\(_3\), 300 MHz, \(\delta\)): 7.10-8.12 (m, 9H, Ar-H), 7.49 (s, 1H, C\(_3\)-H), 7.55 (d, 2H, \(J = 7.2\) Hz), 8.22 (d, 2H, \(J = 7.2\) Hz);
\(^13\)C NMR (CDCl\(_3\), 100 MHz, \(\delta\)): 123.49, 126.02, 128.46, 128.52, 128.68, 129.82, 130.24, 130.55, 130.81, 131.00, 131.20, 132.23, 132.68, 133.80, 140.72, 148.41, 164.69, 189.43;
Elemental analysis: Calculated for C\(_{22}\)H\(_{14}\)ClNO\(_5\): C, 64.79; H, 3.46; Found: C, 64.72; H, 3.40.
**2-ARYL-4H-CHROMEN-4-ONES (64)**

![Chemical structure](image)

**Typical procedure**

To a solution of 62a (0.362g, 0.001 mol) in ethanol was added KOH (0.112g, 0.002 mol). The resulting mixture was refluxed for about 2-3 hours. Then, the reaction mixture was poured over crushed ice. The solid thus obtained was filtered, washed with water and dried. The crude product was purified by column chromatography using EtOAc-petroleum ether as eluent to afford pure isoflavone (64a, 0.157 g, 71%).

Other 64b-64f derivatives were prepared in a similar manner. 2-aryl-4H-chromen-4-ones (Flavones, 64a-64f) are known in literature and their melting points and yields are given in Table 4.4.
4.4 REFERENCES


68. Sarda, S. R.; Pathan, M. Y.; Paike, V. V.; Pachmase, P. R.; Jadhav, W. N.; Pawar, R. P. *Arkivoc* 2006, 16, 43.

