Tetrahydronaphthalene as a precursor of new series of chalcones, flavanones, and flavones

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Abstract: An efficient synthetic route for a novel series of chalcones 2a–2d as well as for the corresponding flavanones 3a–3d and flavones 4a–4d, using functionalized tetrahydronaphthalene (THN), is described herein. The Claisen–Schmidt condensation of such THN and aromatic aldehydes, in the presence of an aqueous solution of KOH (40%), selectively gives the expected chalcones 2a–2d, which may further undergo an intramolecular oxa-Michael addition using piperidine, affording the corresponding flavanones 3a–3d in high yields. Alternatively, treatment of such chalcones 2a–2d with \textit{I}_2/DMSO provides rapidly, in a one-pot oxidative cyclization, a series of flavones 4a–4d in excellent yields ranging from 85% to 90%.

Key words: Morita–Baylis–Hillman, tetrahydronaphthalene, chalcone, flvanone, flavone

1. Introduction

Chalcones and flvanoids such as flavones and flvanones are natural products that have been isolated from a wide range of vascular plants.\textsuperscript{1} Their extensive spectrum of biological activities has attracted considerable interest in medicinal chemistry and in organic synthesis. Indeed, chalcones have been shown to exhibit anticancer,\textsuperscript{1–3} antiinflammatory,\textsuperscript{4} antioxidant,\textsuperscript{5} antifungal,\textsuperscript{6} and antibacterial\textsuperscript{7} activities. Therefore, a number of synthetic methods have been reported for the synthesis of these valuable derivatives, among which aldol and Claisen–Schmidt condensations are currently the common and simple protocols toward chalcones. On the other hand, the common synthetic methods for flvanones and flavones involve chalcones as substrates. Indeed, their oxidative cyclization or intramolecular oxa-Michael addition with various bases,\textsuperscript{8–10} acids,\textsuperscript{11,12} and others\textsuperscript{13} provides the corresponding flavones.

Other methods are also available for the synthesis of flvanones in a one-pot procedure including condensation between 2-hydroxyacetophenone and benzaldehyde derivatives in the presence of acids\textsuperscript{14} or bases,\textsuperscript{15,16} Mannich-type reactions,\textsuperscript{17} Mitsunobu reactions,\textsuperscript{18} Julia–Kocienski olefination,\textsuperscript{19} and others.\textsuperscript{20} Recently, Chen\textsuperscript{18} and co-workers described an environmentally friendly method using tertiary amines as bases in water or ethanol as solvents, directly affording the desired flvanones.

Numerous methods have been developed for flavones synthesis, including Baker–Venkataraman rearrangement,\textsuperscript{21,22} the Allan–Robinson protocol,\textsuperscript{23} and the reaction of oxidative cyclization of chalcones using numerous oxidizing agents such as DDQ,\textsuperscript{24} Ph-S-S-Ph,\textsuperscript{25,26} \textit{I}_2-DMSO,\textsuperscript{27} \textit{I}_2-SiO\textsubscript{2},\textsuperscript{28} \textit{I}_2-Al\textsubscript{2}O\textsubscript{3},\textsuperscript{29} NH\textsubscript{4}I,\textsuperscript{30} and InBr\textsubscript{3}.\textsuperscript{31}

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In our previous reports on the chemistry of Morita–Baylis–Hillman, we described the synthesis of a series of functionalized THN, and currently we are interested in their further synthetic applications. In this paper, we wish to report our results dealing with the conversion of these derivatives into new chalcones that may further undergo an intramolecular oxa-Michael addition, yielding the corresponding flavanones. Alternatively, a one-pot oxidative cyclization of these chalcones may afford the corresponding flavones.

2. Results and discussion

In our first attempt, we observed that, on treatment of a mixture of THN (1 equiv.) and benzaldehyde (1 equiv.) with DABCO (3 equiv.) in water at reflux for 24 h, no reaction occurred and the starting materials were recovered. Under the same conditions but in refluxing ethanol, the conversion of the starting materials still remained incomplete even after a longer reaction time (48 h) and unfortunately gave a mixture of chalcone 2a and the corresponding flavanone 3a.

Therefore, we decided to first establish the suitable conditions for a total and selective conversion of THN into chalcones 2, and then their further cyclization into flavanones 3 or, alternatively, their tandem cyclization-oxidation into flavones 4.

In order to first synthesize chalcone 2a, a mixture of THN (1 equiv.) and benzaldehyde (1 equiv.) in ethanol was treated with a 40% KOH aqueous solution (1 equiv.) at room temperature. Interestingly, the conversion of the starting materials was complete within 24 h and chalcone 2a was selectively obtained and isolated in 90% yield (Table 1, entry 1).

Table 1. Synthesis of (E)–chalcones 2a–2d from THN 1.

<table>
<thead>
<tr>
<th>Entry</th>
<th>ArCHO</th>
<th>Chalcone 2</th>
<th>t (h)</th>
<th>Yield 2 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C=O</td>
<td>(E)-2a :</td>
<td>24</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>Cl=C</td>
<td>(E)-2b :</td>
<td>24</td>
<td>83</td>
</tr>
<tr>
<td>3</td>
<td>Br=C</td>
<td>(E)-2c :</td>
<td>24</td>
<td>83</td>
</tr>
<tr>
<td>4</td>
<td>MeC=O</td>
<td>(E)-2d :</td>
<td>24</td>
<td>90</td>
</tr>
</tbody>
</table>

Encouraged by this clean Claisen–Schmidt condensation of THN with benzaldehyde, we attempted to further investigate this aldol reaction with various aromatic aldehydes. Under the previous conditions, the desired chalcones 2b–2d were therefore obtained in 83%–90% yields (Table 1, entries 2–4).
Below, we present the whole $^1$H NMR spectrum of chalcone ($E$–2d) (Figure 1), the structure of chalcone ($E$)-2d (Figure 2a), and only the region of the eight ethyleneic and aromatic protons (Figure 2b). The analysis of the latter shows one singlet for 1.00 H(d), an $A_2B_2$ system for 2.00 H (proton h) coupled with 2.00 H (proton g), another AB system for 1.00 H (proton e) coupled with 1.00 H (proton f), and, finally, one singlet for 1.00 H (proton c) (Figure 2b).

In addition, we did not observe any resonance signal in the region ranging from 6 to 8 ppm, corresponding to ethyleneic protons of chalcone ($Z$–2d). Moreover, the higher value of the coupling constants ($^3J_{H(e)–H(f)} = 15.6$ Hz) between the ethyleneic protons is in favor of ($E$–2d) (Figure 2b).

It is noteworthy that the chemical shifts of vinylic protons of all chalcones 2b–2d ranged from 7.45 to 7.54 ppm and the values of the coupling constants between them are still higher ($^3J_{H(e)–H(f)} = 15.4–15.6$ Hz), suggesting again the stereoselective formation of ($E$)-2b–2d (Table 2).

All these $^3J_{H(e)–H(f)}$ values are in agreement with those of other ($E$)–chalcones previously described in the literature.34

Next, we focused our attention on the cyclization of chalcones 2a–2d into flavanones 3a–2d by an intramolecular oxa-Michael addition, using common tertiary amines as bases18 including 1,4-diazabicyclo[2.2.2]
Table 2. Chemical shifts and $^3 J_{H(e)-H(f)}$ for chalcones (E)-2a–2d.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Chalcones 2</th>
<th>$\delta_{H(e)}$ (ppm)</th>
<th>$\delta_{H(f)}$ (ppm)</th>
<th>$^3 J_{H(e)-H(f)}$ (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(E)-2a</td>
<td>7.52</td>
<td>7.85</td>
<td>15.6</td>
</tr>
<tr>
<td>2</td>
<td>(E)-2b</td>
<td>7.54</td>
<td>8.23</td>
<td>15.6</td>
</tr>
<tr>
<td>3</td>
<td>(E)-2c</td>
<td>7.49</td>
<td>8.16</td>
<td>15.6</td>
</tr>
<tr>
<td>4</td>
<td>(E)-2d</td>
<td>7.45</td>
<td>7.83</td>
<td>15.4</td>
</tr>
</tbody>
</table>

octane (DABCO), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 4-dimethylaminopyridine (DMAP), and imidazole in water or ethanol as solvents (Table 3, entries 1–5).

Table 3. Optimization of the reaction conditions for the conversion of 2a into 3a.

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\[ \text{(E)-2a-d} \xrightarrow{\text{Piperidine, CHCl\textsubscript{3}, reflux}} \text{3a-d} \]
```

<table>
<thead>
<tr>
<th>Entry</th>
<th>Chalcone 2</th>
<th>Solvent</th>
<th>Amine</th>
<th>t (h)</th>
<th>Flavanone 3</th>
<th>Yield 3 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2a</td>
<td>H\textsubscript{2}O</td>
<td>DABCO (3 equiv.)</td>
<td>48</td>
<td>N.R.</td>
<td>N.R.</td>
</tr>
<tr>
<td>2</td>
<td>2a</td>
<td>EtOH</td>
<td>DABCO (3 equiv.)</td>
<td>48</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>2a</td>
<td>EtOH</td>
<td>DBU (3 equiv.)</td>
<td>48</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>2a</td>
<td>EtOH</td>
<td>DMAP (3 equiv.)</td>
<td>48</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>2a</td>
<td>EtOH</td>
<td>Imidazole (3 equiv.)</td>
<td>48</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>2a</td>
<td>H\textsubscript{2}O</td>
<td>Piperidine (6 mL)</td>
<td>48</td>
<td>3a</td>
<td>40</td>
</tr>
<tr>
<td>7</td>
<td>2a</td>
<td>EtOH</td>
<td>Piperidine (6 mL)</td>
<td>48</td>
<td>3a</td>
<td>40</td>
</tr>
<tr>
<td>8</td>
<td>2a</td>
<td>Et\textsubscript{2}O</td>
<td>Piperidine (6 mL)</td>
<td>48</td>
<td>3a</td>
<td>40</td>
</tr>
<tr>
<td>9</td>
<td>2a</td>
<td>CH\textsubscript{2}Cl\textsubscript{2}</td>
<td>Piperidine (6 mL)</td>
<td>48</td>
<td>3a</td>
<td>40</td>
</tr>
<tr>
<td>10</td>
<td>2a</td>
<td>CHCl\textsubscript{3}</td>
<td>Piperidine (6 mL)</td>
<td>48</td>
<td>3a</td>
<td>75</td>
</tr>
</tbody>
</table>

In all these cases, heating at reflux a mixture of chalcone 2a and 3 equiv. of each of these bases, in water or ethanol as solvents, was unsuccessful and the starting materials were completely recovered after 48 h (Table 3, entries 1–5).

After that, we followed a previous report on the cyclization of a variety chalcones into the corresponding flavanones,\textsuperscript{35} using a piperidine excess in water, but unfortunately the conversion of 2a into 3a did not occur, presumably because we had observed that chalcone 2a was not soluble in such a solvent (Table 2, entry 6).

Therefore, we investigated the cyclization of compound 2a into flavanone 3a in the presence of an excess of piperidine in various organic solvents (EtOH, Et\textsubscript{2}O, CH\textsubscript{2}Cl\textsubscript{2}, and CHCl\textsubscript{3}) (Table 2, entries 7–10).

Interestingly, the reaction worked in all these solvents, affording 2a, and the best yield (75%) was obtained when the title reaction was carried out in refluxing chloroform for 48 h (Table 3, entry 10).

Following the same protocol and involving piperidine in refluxing chloroform, a new series of flavanones 3b–3d were successfully synthesized in 82%–84% yields (Table 4, entries 2–4).

Below are listed the chemical shifts of protons H-2 and H-3 of flavanones 3a–3d as well as the values of the coupling constants, either $^3 J$ between protons H-2 and H-3 or $^2 J$ between the diastereotopic protons H-3a and H-3b (Table 5).

We summarized the $^1$H NMR data for H-2, H-3a, and H-3b in the following triangle. Indeed, the vertices of the triangle represent these protons and their chemical shifts, and the three sides give all the coupling
Table 4. Piperidine-promoted cyclization reaction of chalcones 2a–2d into flavanones 3a–3d in refluxing chloroform.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Chalcone 2</th>
<th>Flavanone 3</th>
<th>t (h)</th>
<th>Yield 3 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(E)-2a:</td>
<td>3a:</td>
<td>48</td>
<td>75</td>
</tr>
<tr>
<td>2</td>
<td>(E)-2b:</td>
<td>3b:</td>
<td>48</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>(E)-2c:</td>
<td>3c:</td>
<td>48</td>
<td>82</td>
</tr>
<tr>
<td>4</td>
<td>(E)-2d:</td>
<td>3d:</td>
<td>48</td>
<td>84</td>
</tr>
</tbody>
</table>

Table 5. $^1$H NMR data for protons H-2 and H-3 of flavanones 3a–3d.

<table>
<thead>
<tr>
<th>Flavanone 3</th>
<th>H-2: $\delta$ ppm ($^3$$J_{\text{anti}}$, $^3$$J_{\text{syn}}$Hz)</th>
<th>H-3: $\delta$ ppm ($^2$$J$, $^3$$J$Hz)</th>
<th>H$_\beta$-3: $\delta$ ppm ($^2$$J$, $^3$$J$Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>5.39 (13.1, 3.1)</td>
<td>2.82 (16.9, 3.1)</td>
<td>3.01 (16.9, 13.1)</td>
</tr>
<tr>
<td>3b</td>
<td>5.80 (13.2, 2.6)</td>
<td>2.84 (16.9, 2.6)</td>
<td>2.98 (16.9, 13.2)</td>
</tr>
<tr>
<td>3c</td>
<td>5.76 (13.3, 2.8)</td>
<td>2.83 (16.9, 2.8)</td>
<td>3.01 (16.9, 13.3)</td>
</tr>
<tr>
<td>3d</td>
<td>5.36 (13.0, 2.9)</td>
<td>2.82 (16.9, 2.9)</td>
<td>3.03 (16.9, 13.0)</td>
</tr>
</tbody>
</table>

Constants values of $^3$$J_{\text{syn}}$, $^3$$J_{\text{anti}}$, and $^2$$J_{\text{gem}}$ (Figure 3). It is noteworthy that all these data are in agreement with those of the literature (Figure 3).$^{34}$

Alternatively, we next attempted the direct conversion of chalcones 2a–2d into the corresponding flavones 4a–4d, using a tandem oxidative cyclization approach. Successfully, upon treatment of chalcones 2a–2d with iodine (10 mol%) as the catalyst in DMSO at 80 °C, a novel series of flavones 4a–4d were prepared within 5 min, in 85%–90% yields (Scheme 3; Table 6). The possible mechanism is in agreement with the literature.$^{36}$

In conclusion, we have developed an efficient synthetic route for the preparation of a series of chalcones, using a Claisen–Schmidt condensation at room temperature, between THN and aromatic aldehydes in an aqueous solution of KOH (40%) in ethanol.
Figure 3. Chemical shifts and coupling constants values $^2J$ and $^3J$ between H-2 and H-3.

Table 6. Straightforward conversion of chalcones 2a–2d into flavones 4a–4d.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Chalcone 2</th>
<th>Flavone 4</th>
<th>t (min)</th>
<th>Yield 4 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(E)-2a</td>
<td>4a</td>
<td>5</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>(E)-2d</td>
<td>4b</td>
<td>5</td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td>(E)-2c</td>
<td>4c</td>
<td>5</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>(E)-2d</td>
<td>4d</td>
<td>5</td>
<td>85</td>
</tr>
</tbody>
</table>

Their further intramolecular cyclization into flavanones was performed in high yields, in refluxing chloroform, using piperidine. Alternatively, a tandem cyclization-oxidation of these chalcones using $I_2$/DMSO afforded the corresponding flavones.

All the newly synthesized chalcones, flavanones, and flavones were isolated in high yields of 80%–90% and their antimicrobial, antioxidant, and antiinflammatory activities are being evaluated.
3. Experimental

3.1. General

$^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker AC-300 spectrometer (300 MHz for $^1$H and 75 MHz for $^{13}$C) in CDCl$_3$, using TMS as an internal standard (chemical shifts in $\delta$ values, $J$ in Hz). Resolution mass spectra (MS) were recorded on a mass spectrometer. High resolution mass spectra (HRMS) were recorded as ESI-MS. Analytical thin-layer chromatography (TLC) was performed using Fluka Kieselgel 60 F$_{254}$ precoated silica gel plates. Visualization was achieved by UV light (254 nm). Flash chromatography was performed using Merck silica gel 60 and a gradient solvent system (pet-ether/ether as eluents). Please see the Supplementary material for full experimental details, $^1$H and $^{13}$C NMR spectra, and MS.

3.1.1. General procedure for the synthesis of chalcones (2a–2d)

A mixture of tetrahydronaphthalene 1 (0.01 mol) and aromatic aldehyde (0.01 mol) was stirred in ethanol (5 mL) and then an aqueous solution of KOH (40%, 1 mL) was added. The mixture was kept overnight at room temperature, and then was acidified with an aqueous solution of 2 M HCl. The separated solid was filtered and crystallized from ethanol, affording the pure chalcone 2a.

(E)-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthalene-2-yl)-3-phenylprop-2-en-1-one (2a). Yellow solid; yield: 90%; mp 138–140 C. $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 1.81–1.74 (m, 4H), 2.78–2.72 (m, 4H), 6.71 (s, 1H, ArH), 7.45–7.39 (m, 4H, ArH), 7.58 (d, $J_\alpha$ = 15.6 Hz, 1H), 7.55–7.39 (m, 2H, ArH), 7.85 (d, $J_\beta$ = 15.6 Hz, 1H), 12.37 (s, 1H, ArOH).

$^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 22.8, 23.4, 28.8, 30.0, 118.0, 118.6, 121.0, 127.9, 128.6, 129.1, 129.7, 130.6, 135.2, 144.7, 147.6, 161.4, 193.3. MS (m/z) (rel intensity, %) 278 (M$^+$, 78), 261 (9), 201 (99), 174 (100), 77 (64). HRMS (ES$^+$): m/z calcd for C$_{19}$H$_{19}$O$_2$ [M+H]$^+$ 279.1385, found 279.1385.

(E)-3-(2-Chlorophenyl)-1-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)prop-2-en-1-one (2b). Yellow solid, yield: 83%; mp 134–136 C. $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 1.81–1.74 (m, 4H), 2.78–2.72 (m, 4H), 6.71 (s, 1H, ArH), 7.52–7.28 (m, 4H, ArH), 7.54 (d, $J_\alpha$ = 15.6 Hz, 1H), 7.73–7.70 (m, 1H, ArH), 8.23 (d, $J_\beta$ = 15.6 Hz, 1H), 12.28 (s, 1H, ArOH).

$^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 22.6, 23.2, 28.6, 30.0, 117.9, 118.3, 123.6, 127.0, 127.9, 129.7, 130.3, 131.1, 133.4, 135.5, 140.3, 147.7, 161.3, 193.0. MS (m/z) (rel intensity, %) 312 (M$^+$, 35), 277 (98), 201 (34), 174 (100), 117 (1), 77 (21). HRMS (ES$^+$): m/z calcd for C$_{19}$H$_{18}$ClO$_2$ [M+H]$^+$ 313.0995, found 313.1007.

(E)-3-(2-Bromophenyl)-1-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)prop-2-en-1-one (2c). Yellow solid, yield: 83%; mp 140–142 C. $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 1.82–1.76 (m, 4H), 2.79–2.71 (m, 4H), 6.71 (s, 1H), 7.36–7.19 (m, 2H, ArH), 7.49 (d, $J_\alpha$ = 15.6 Hz, 1H), 7.52–7.60 (m, 2H, ArH); 8.16 (d, $J_\beta$ = 15.6, 1H), 12.27 (s, 1H, ArOH).

$^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 22.6, 23.2, 28.6, 30.0, 117.9, 118.3, 123.8, 125.8, 127.6, 127.9, 128.0, 129.7, 131.2, 133.5, 133.5, 142.8, 147.7, 161.3, 192.9. MS (m/z) (rel intensity, %) 356 (M$^+$, 11), 277 (100), 201 (47), 174 (23), 77 (12). HRMS (ES$^+$): m/z calcd for C$_{19}$H$_{18}$BrO$_2$ [M+H]$^+$ 357.0490, found 357.0482, found C$_{19}$H$_{18}$BrO$_2$ [M+H]$^+$ 359.0475, found 359.0475.

(E)-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthalene-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (2d). Yellow solid, yield: 90%; mp 100–102 C. $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 1.82–1.76 (m, 4H), 2.79–2.73 (m, 4H), 3.84 (s, 3H), 6.71 (s, 1H) 6.94–6.91 (m, 2H, ArH), 7.45 (d, $J_\alpha$ = 15.4 Hz, 1H), 7.6–7.54 (m, 3H, ArH), 7.83 (d, $J_\beta$ = 15.4 Hz, 1H), 12.50 (s, 1H, ArOH).

$^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 22.8, 23.2, 28.6, 30.0, 55.5.
3.1.2. General procedure for the synthesis of flavanones (3a–3d)

A mixture of 2'-hydroxychalcone (0.01 mol) 2a and piperidine (6 mL) was stirred for 48 h in chloroform (5 mL) at reflux. Then the reaction mixture was acidified with an aqueous solution of 2 M HCl and was extracted with CH₂Cl₂ (3 × 5 mL). The resulting extracts were combined, washed with brine, and dried over anhydrous MgSO₄. The residue, obtained after solvent evaporation, was purified by silica-gel column chromatography (5% ether/petroleum ether), affording the pure flavanone 3a.

2-Phenyl-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3a). Pale yellow solid, yield: 75%; mp 90–92 C. ¹H NMR (CDCl₃, 300 MHz) δ 1.79–1.74 (m, 4H), 2.75–2.73 (m, 4H), 2.82 (dd, J = 16.9, 3.1 Hz, 1H), 3.01 (dd, J = 16.9, 13.1 Hz, 1H), 5.39 (dd, J = 13.1, 3.1 Hz, 1H), 6.74 (s, 1H), 7.47–7.35 (m, 5H, ArH), 7.62 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 22.6, 23.1, 28.5, 29.7, 44.7, 79.4, 117.4, 118.8, 126.1, 126.8, 128.6, 128.7, 130.9, 139.1, 147.2, 159.1, 192. MS (m/z) (rel intensity, %) 278 (M⁺, 57), 201 (49), 174 (100), 77 (22). HRMS (EI⁺): m/z calcd for C₁₉H₁₈O₂ [M+H]⁺ 313.0989, found 313.0995.

2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3b). Pale yellow solid, yield: 82%; mp 124–126 C. ¹H NMR (CDCl₃, 300 MHz) δ 1.81–1.74 (m, 4H), 2.81–2.74 (m, 4H), 2.84 (dd, J = 13.2, 16.9 Hz, 1H), 2.98 (dd, J = 16.9, 2.6 Hz, 1H), 5.80 (dd, J = 13.2, 2.6 Hz, 1H), 6.77 (s, 1H), 7.42–7.23 (m, 3H, ArH), 7.65 (s, 1H), 7.74–7.72 (m, 1H, ArH). ¹³C NMR (CDCl₃, 75 MHz) δ 22.6, 23.05, 28.5, 30.1, 43.6, 76.3, 118.9, 126.9, 127.2, 127.4, 129.5, 129.7, 131.2, 131.6, 137.0, 147.2, 159.2, 191.6. MS (m/z) (rel intensity, %) 312 (M⁺, 31), 277 (90), 201 (32), 174 (100), 117(47), 77 (23). HRMS (ES⁺): m/z calcd for C₁₉H₃₅ClO₂ [M+H]⁺ 357.0490, found 357.0496, calcd for C₁₉H₈₁BrO₂ [M+H]⁺ 359.0470, found 359.0474.

2-(2-Bromophenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3c). Pale yellow solid, yield: 82%; mp 139–141 C. ¹H NMR (CDCl₃, 300 MHz) δ 1.82–1.75 (m, 4H), 2.81–2.73 (m, 4H), 2.83 (dd, J = 13.3, 16.9 Hz, 1H), 3.01 (dd, J = 16.9, 2.8 Hz, 1H), 7.56 (dd, J = 13.3, 2.8 Hz, 1H), 6.78 (s, 1H), 7.26–7.20 (m, 1H, ArH), 7.45–7.38 (m, 1H, ArH), 7.59–7.57 (m, 1H, ArH), 7.65 (s, 1H), 7.74–7.70 (m, 1H, ArH). ¹³C NMR (CDCl₃, 75 MHz) δ 22.7, 23.06, 28.5, 30.1, 43.7, 78.6, 117.4 118.9, 121.5, 126.9, 127.5, 128.01, 129.8, 131.2, 132.9, 138.6, 147.3, 159.2, 191.6. MS (m/z) (rel intensity, %) 356 (M⁺, 7), 277 (100), 201 (45), 174 (25), 77 (18). HRMS (ES⁺): m/z calcd for C₁₉H₇₉BrO₂ [M+H]⁺ 357.0490, found 357.0496, calcd for C₁₉H₇ₙBrO₂ [M+H]⁺ 359.0470, found 359.0474.

2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3d). Pale yellow solid, yield: 84%; mp 100–102 C. ¹H NMR (CDCl₃, 300 MHz) δ 1.82–1.75 (m, 4H), 2.78–2.70 (m, 4H), 2.80 (dd, J = 16.9, 2.9 Hz, 1H), 3.03 (dd, J = 16.9, 13.0 Hz, 1H), 3.82 (s, 3H), 5.36 (dd, J = 13.0, 2.9 Hz, 1H), 6.73 (s, 1H, ArH), 6.96–6.91 (m, 2H, ArH), 7.40–7.37 (m, 2H, ArH), 7.62 (s, 1H, ArH). ¹³C NMR (CDCl₃, 75 MHz) δ 22.7, 23.08, 28.5, 30.09, 44.6, 55.3, 79.2, 114.1, 117.5, 118.8, 126.8, 127.7, 131, 131.1, 147.1, 159.3, 160, 192.2. MS (m/z) (rel intensity, %) 308 (M⁺, 1), 201 (6), 174 (37), 134 (100), 117 (20), 77 (9). HRMS (ES⁺): m/z calcd for C₂₀H₂₁O₄ [M+H]⁺ 309.1491, found 309.1491.
3.1.3. General procedure for the synthesis of flavones (4a–4d)

To a solution of 2'-hydroxychalcone 2a (0.01 mol) in DMSO (5 mL) was added iodine (10%) and the reaction mixture was heated at 80 °C for 5 min. After cooling, the reaction mixture was diluted with water and the iodine was removed by washing with a saturated solution of sodium thiosulfate. The product 4a was then extracted with CH₂Cl₂ (3 × 5 mL). The resulting extracts were combined, washed with brine, and dried over anhydrous MgSO₄, and the residue was purified by silica-gel column chromatography (20% ether/petroleum ether), affording pure flavone 4a.

2-Phenyl-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4a). Pale yellow solid, yield: 90%; mp 147–149 C. ¹H NMR (CDCl₃, 300 MHz) δ 1.87–1.81 (m, 4H), 2.85–2.94 (m, 4H), 6.77 (s, 1H), 7.27 (s, 1H), 117.4, 121.7, 125.07, 126.2, 129.0, 131.4, 132.1, 135.1, 144.7, 154.4, 163.1, 178.6. MS (m/z) (rel intensity, %) 276 (M⁺, 100), 261 (2), 174 (18), 117 (24), 77 (14). HRMS (ES⁺): m/z calcd for C₁₉H₁₇O₂ [M+H]+ 277.1229, found 277.1237.

2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4b). Pale yellow solid, yield: 85%; mp 90–92 C. ¹H NMR (CDCl₃, 300 MHz) δ 1.85–1.80 (m, 4H), 2.92–2.83 (m, 4H), 6.60 (s, 1H), 7.19 (s, 1H), 7.63–7.46 (m, 3H, ArH), 7.62–7.60 (m, 1H, ArH), 7.92 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 22.57, 22.8, 28.9, 29.9, 112.5, 117.4–112.5, 121.5, 127.03, 130.6, 130.7, 131.6, 132.8, 135.2, 144.9, 154.6, 154.8, 162.3, 178.2. MS (m/z) (rel intensity, %) 310 (M⁺, 7), 174 (24), 117 (26). HRMS (ES⁺): m/z calcd for C₁₉H₁₆ClO₂ [M+H]+ 311.0839, found 311.0844.

2-(2-Bromophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4c). Pale yellow solid, yield: 85%; mp 99–101 C. ¹H NMR (CDCl₃, 300 MHz) δ 1.87–1.81 (m, 4H), 2.92–2.88 (m, 4H), 6.51 (s, 1H), 7.19 (s, 1H), 112.3, 117.4, 121.6, 121.8, 125.1, 127.6, 130.8, 131.7, 133.9, 134.3, 135.3, 145.0, 154.6, 154.8, 162.3, 178.3. MS (m/z) (rel intensity, %) 354 (M⁺, 100), 207 (48), 174 (49); HRMS (ES⁺): m/z calcd for C₁₉H₁₇BrO₂ [M+H]+ 355.0334, found 355.0331; calcd for C₁₉H₁₇BrO₂ [M+H]+ 357.0313, found 357.0314.

2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4d). Pale yellow solid, yield: 85%; mp 135–137 C. ¹H NMR (CDCl₃, 300 MHz) δ 1.86–1.82 (m, 4H), 2.92–2.86 (m, 4H), 3.88 (s, 3H), 6.70 (s, 1H), 7.02 (s, 1H), 7.35–7.1 (m, 2H, ArH), 7.88–7.84 (m, 2H, ArH), 7.90 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 22.6, 23.1, 28.9, 30.0, 55.5, 105.8, 114.4, 117.3, 121.6, 124.0, 125.0, 127.9, 134.9, 144.5, 154.3, 162.3, 163.1, 178.6. MS (m/z) (rel intensity, %) 306 (M⁺, 100), 207 (3), 174. HRMS (ES⁺): m/z calcd for C₂₀H₁₉O₃ [M+H]+ 307.1334, found 307.1335.

Acknowledgment

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References

Supplementary material

1. General

$^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker AC-300 spectrometer (300 MHz for $^1$H and 75 MHz for $^{13}$C) in CDCl$_3$, using TMS as an internal standard (chemical shifts in $\delta$ values, $J$ in Hz). Resolution mass spectra (MS) were recorded on a mass spectrometer. High resolution mass spectra (HRMS) were recorded as ESI-MS. Analytical thin layer chromatography (TLC) was performed using Fluka Kieselgel 60 F$^{254}$ precoated silica gel plates. Visualization was achieved by UV light (254 nm). Flash chromatography was performed using Merck silica gel 60 and a gradient solvent system (pet-ether/ether as eluents).

2. General procedure for the synthesis of chalcones (2a–2d)

A mixture of tetrahydronaphthalene 1 (0.01 mol) and aromatic aldehyde (0.01 mol) was stirred in ethanol (5 mL) and then an aqueous solution of KOH (40%, 1 mL) was added. The mixture was kept overnight, at room temperature, and then was acidified with an aqueous solution of 2M HCl. The separated solid was filtered and crystallized from ethanol, affording the pure chalcone 2a.

3. General procedure for the synthesis of flavanones (3a–3d)

A mixture of 2'-hydroxychalcone (0.01 mol) 2a and piperidine (6 mL) was stirred for 48 h in chloroform (5 mL) at reflux. The reaction mixture was then acidified with an aqueous solution of 2 M HCl and was extracted with CH$_2$Cl$_2$ (3 × 5 mL). The resulting extracts were combined, washed with brine, and dried over anhydrous MgSO$_4$. The residue obtained after solvent evaporation was purified by silica-gel column chromatography (5% ether/petroleum ether), affording the pure flavanone 3a.

4. General procedure for the synthesis of flavones (4a–4d)

To a solution of 2'-hydroxychalcone 2a (0.01 mol) in DMSO (5 mL) was added iodine (10%)
and the reaction mixture was heated at 80 °C for 5 min. After cooling, the reaction mixture was diluted with water and the iodine was removed by washing with a saturated solution of sodium thiosulfate. The product 4a was then extracted with CH₂Cl₂ (3 × 5 mL). The resulting extracts were combined, washed with brine, and dried over anhydrous MgSO₄ and the residue was purified by silica-gel column chromatography (20% ether/petroleum ether), affording the pure flavone 4a.

5. Characterization data of chalcones (2a–2d)

(E)-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthale-2-yl)-3-phenylprop-2-en-1-one (2a)

Yield (90%); yellow solid; mp = 138–140 °C; ¹H NMR (CDCl₃, 300 MHz) δ 1.81–1.74 (m, 4H), 2.78–2.72 (m, 4H), 6.71 (s, 1H, ArH), 7.45–7.39 (m, 4H, ArH), 7.58 (d, Jₐ = 15.6 Hz, 1H), 7.55–7.39 (m, 2H, ArH), 7.85 (d, Jₐ = 15.6 Hz, 1H), 12.37 (s, 1H, ArOH); ¹³C NMR (CDCl₃, 75 MHz) δ 22.8, 23.4, 28.8, 30.0, 118.0, 118.6, 121.0, 127.9, 128.6, 129.1, 129.7, 130.6, 135.2, 144.7, 147.6, 161.4, 193.3; MS (m/z) (rel intensity, %) 278 (M⁺, 78), 261 (9), 201 (99), 174 (100), 77 (64); HRMS (ES⁺): m/z calcd for C₁₉H₁₉O₂ [M+H]⁺ 279.1385, found 279.1385.

(E)-3-(2-Chlorophenyl)-1-(3-hydroxy-5,6,7,8-tetrahy-dronaphthalen-2-yl)prop-2-en-1-one (2b)

Yield (83%); yellow solid; mp = 134–136 °C; ¹H NMR (CDCl₃, 300 MHz) δ 1.81–1.74 (m, 4H), 2.78–2.72 (m, 4H), 6.71 (s, 1H, ArH), 7.52–7.28 (m, 4H, ArH), 7.54 (d, Jₐ = 15.6 Hz, 1H), 7.73–7.70 (m, 1H, ArH), 8.23 (d, Jₐ = 15.6 Hz, 1H), 12.28 (s, 1H, ArOH); ¹³C NMR (CDCl₃, 75 MHz) δ 22.6, 23.2, 28.6, 30.0, 117.90–118.3, 123.6, 127.0, 127.9, 127.99, 129.7, 130.3, 131.1, 133.4, 135.5, 140.3, 147.7, 161.3, 193.0; MS (m/z) (rel intensity, %) 312 (M⁺, 35), 277 (98), 201 (34), 174 (100), 117 (1), 77 (21); HRMS (ES⁺): m/z calcd for C₁₉H₁₈ClO₂ [M+H]⁺ 313.0995, found 313.1007.
(E)-3-(2-Bromophenyl)-1-(3-hydroxy-5,6,7,8-tetray-dronaphthalen-2-yl)prop-2-en-1-one (2c)

Yield (83%); yellow solid; mp = 140–142 °C; $^1$H NMR (CDCl$_3$, 300 MHz) δ 1.82–1.76 (m, 4H), 2.79–2.71 (m, 4H), 6.71 (s, 1H), 7.36–7.19 (m, 2H, ArH), 7.49 (d, $J_a$ = 15.6 Hz, 1H), 7.52 (s, 1H, ArH), 7.72–7.60 (m, 2H, ArH); 8.16 (d, $J_b$ = 15.6, 1H), 12.27 (s, 1H, ArOH); $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 22.6, 23.2, 29.9, 30.5, 117.8, 118.3, 123.8, 125.8, 127.6, 127.9, 128.0, 129.7, 131.2, 133.5, 135.2, 142.8, 147.7, 161.3, 192.9; MS (m/z) (rel intensity, %) 356 (M$^+$, 11), 277 (100), 201 (47), 174 (23), 77 (12); HRMS (ES$^+$): m/z calcd for C$_{19}$H$_{18}$BrO$_2$ [M+H]$^+$ 357.0490, found 357.0482.

(E)-1-(3-Hydroxy-5,6,7,8-tetrahydrodronaphthalen-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (2d)

Yield (90%); yellow solid; mp = 100–102 °C; $^1$H NMR (CDCl$_3$, 300 MHz) δ 1.82–1.76 (m, 4H), 2.79–2.73 (m, 4H), 3.84 (s, 3H), 6.71 (s, 1H) 6.94–6.91 (m, 2H, ArH), 7.49 (d, $J_a$ = 15.4 Hz, 1H), 7.6–7.54 (m, 3H, ArH), 7.83 (d, $J_b$ = 15.4 Hz, 1H), 12.50 (s, 1H, ArOH); $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 22.6, 23.2, 28.6, 30.0, 55.5, 114.7, 117.5, 117.9, 118.5, 127.6, 127.9, 129.6, 130.4, 144.6, 147.2, 161.3, 162.1, 193.3; MS (m/z) (rel intensity, %) 308 (M$^+$, 37), 277 (8), 174 (41), 134 (100), 77 (19); HRMS (ES$^+$): m/z calcd for C$_{20}$H$_{21}$O$_3$ [M+H]$^+$ 309.1491, found 309.1492.

6. Characterization data of flavanones (3a–3d)

2-Phenyl-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4 3H)-one (3a)

Yield (75%); pale yellow solid; mp = 90–92 °C; $^1$H NMR (CDCl$_3$, 300 MHz) δ 1.79–1.74 (m, 4H), 2.75–2.73 (m, 4H), 2.82 (dd, $J = 16.9$, 3.1 Hz, 1H), 3.01 (dd, $J = 16.9$, 13.1 Hz, 1H), 5.39 (dd, $J = 13.1$, 3.1 Hz, 1H), 6.74 (s, 1H), 7.47–7.35 (m, 5H, ArH), 7.62 (s, 1H); $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 22.6, 23.1, 28.5, 29.7, 44.7, 79.4, 117.4, 118.8, 126.1, 126.8, 128.6,
128.7, 130.9, 139.1, 147.2, 159.1, 192. **MS (m/z)** (rel intensity, %) 278 (M+, 57), 201 (49), 174 (100), 77 (22); HRMS (EI+): m/z calcd for C\textsubscript{10}H\textsubscript{18}O\textsubscript{2} 278.13068, found 278.13029.

**2-(2-Chlorophenyl)-6,7,8,9-tetrahydro 2Hbenzo[g] chromen-4(3H)-one (3b)**

Yield (82%); pale yellow solid; mp = 124–126 °C; \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 300 MHz) δ 1.81–1.74 (m, 4H), 2.81–2.74 (m, 4H), 2.84 (dd, J = 13.2, 16.9 Hz, 1H), 2.98 (dd, J = 16.9, 2.6 Hz, 1H), 5.80 (dd, J = 13.2, 2.6 Hz, 1H), 6.77 (s, 1H), 7.42–7.23 (m, 3H, ArH), 7.65 (s, 1H), 7.74–7.72 (m, 1H, ArH); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 75 MHz) δ 22.6, 23.05, 28.5, 30.1, 43.6, 76.3, 118.9, 126.9, 127.2, 127.4, 129.5, 129.7, 131.2, 131.6, 137.0, 147.2, 159.2, 191.6; \textbf{MS (m/z)} (rel intensity, %) 312 (M+, 31), 277 (90), 201 (32), 174 (100), 117(47), 77 (23); HRMS (ES+): m/z calcd for C\textsubscript{19}H\textsubscript{18}\textsubscript{35}ClO\textsubscript{2} [M+H]+ 313.0989, found 313.0995.

**2-(2-Bromophenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3c)**

Yield (82%); pale yellow solid; mp = 139–141 °C; \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 300 MHz) δ 1.82–1.75 (m, 4H), 2.81–2.73 (m, 4H), 2.83 (dd, J = 13.3, 16.9 Hz, 1H), 3.01 (dd, J = 16.9, 2.8 Hz, 1H), 5.76 (dd, J = 13.3, 2.8 Hz, 1H), 6.78 (s, 1H), 7.26–7.20 (m, 1H, ArH), 7.45–7.38 (m, 1H, ArH), 7.59–7.57 (m, 1H, ArH), 7.65 (s, 1H), 7.74–7.70 (m, 1H, ArH); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 75 MHz) δ 22.7, 23.06, 28.5, 30.1, 43.7, 78.6, 117.4, 118.9, 121.5, 126.9, 127.5, 128.01, 129.8, 131.2, 132.9, 138.6, 147.3, 159.2, 191.6; \textbf{MS (m/z)} (rel intensity, %) 356 (M+, 7), 277 (100), 201 (45), 174 (25), 77 (18); HRMS (ES+): m/z calcd for C\textsubscript{19}H\textsubscript{18}\textsubscript{81}BrO\textsubscript{2} [M+H]+ 357.0490, 359.0496, 357.0496, calculated for C\textsubscript{19}H\textsubscript{18}\textsubscript{81}BrO\textsubscript{2} [M+H]+ 357.0490, 359.0474.

**2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-2Hbenzo[g]chromen-4(3H)-one (3d)**

Yield (84%); pale yellow solid; mp = 100–102 °C; \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 300 MHz) δ 1.82–1.74 (m, 4H), 2.78–2.70 (m, 4H), 2.80 (dd, J = 16.9, 2.9 Hz, 1H), 3.03 (dd, J = 16.9, 13.0 Hz, 1H), 3.82 (s, 3H), 5.36 (dd, J = 13.0, 2.9 Hz, 1H), 6.73 (s, 1H, ArH), 6.96–6.91 (m, 2H, ArH), 7.40–7.37 (m, 2H, ArH), 7.62 (s, 1H, ArH); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 75 MHz) δ 22.7, 23.08, 28.5, 30.09, 44.6, 55.3, 79.2, 114.1, 117.5, 118.8, 126.8, 127.7, 131, 131.1, 147.1, 159.3, 160,
192.2; MS (m/z) (rel intensity, %) 308 (M⁺, 1), 201 (6), 174 (37), 134 (100), 117 (20), 77 (9); HRMS (ES⁺): m/z calcd for C₂₀H₂₁O₃ [M+H]⁺ 309.1491, found 309.1491.

7. Characterization data of flavones (4a–4d)

2-Phenyl-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4a)

Yield: (90%); pale yellow solid; mp = 147–149 °C; ¹H NMR (CDCl₃, 300 MHz) δ 1.87–1.81 (m, 4H), 2.85–2.94 (m, 4H), 6.77 (s, 1H), 7.27 (s, 1H), 7.68–7.53 (m, 3H, ArH), 7.94–7.94 (m, 3H, ArH); ¹³C NMR (CDCl₃, 75 MHz) δ 22.6, 2.9, 28.9, 30.0, 107.2, 117.4, 121.7, 125.07, 126.2, 129.0, 131.4, 132.1, 135.1, 144.7, 154.4, 163.1, 178.6; MS (m/z) (rel intensity, %) 276 (M⁺, 100), 261 (2), 174 (18), 117 (24), 77 (14); HRMS (ES⁺): m/z calcd for C₁₉H₁₇O₂ [M+H]⁺ 277.1229, found 277.1237.

2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4b)

Yield (85%); pale yellow solid; mp = 90–92 °C; ¹H NMR (CDCl₃, 300 MHz) δ 1.85–1.80 (m, 4H), 2.92–2.83 (m, 4H), 6.60 (s, 1H), 7.19 (s, 1H), 7.63–7.46 (m, 3H, ArH), 7.62–7.60 (m, 1H, ArH), 7.92 (s, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 22.57, 22.8, 28.9, 29.9, 112.5, 117.4–112.5, 121.5, 127.03, 130.6, 130.7, 131.6, 132.9, 132.8, 135.2, 144.9, 154.6, 162.3, 178.2; MS (m/z) (rel intensity, %) 310 (M⁺, 100), 261 (2), 174 (18), 117 (24), 77 (14); HRMS (ES⁺): m/z calcd for C₁₉H₁₆ClO₂ [M+H]⁺ 311.0839, found 311.0844.

2-(2-Bromophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4c)

Yield (85%); pale yellow solid; mp = 99–101 °C; ¹H NMR (CDCl₃, 300 MHz) δ 1.87–1.81 (m, 4H), 2.92–2.88 (m, 4H), 6.51 (s, 1H), 7.21 (s, 1H), 7.73–7.33 (m, 2H, ArH), 7.54–7.58 (m, 1H, ArH), 7.69–7.73 (m, 1H, ArH), 7.94 (s, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 22.6, 22.9, 28.9, 30.0, 112.3, 117.4, 121.6, 121.8, 125.1, 127.6, 130.8, 131.7, 133.9, 134.3, 135.3, 145.0, 154.6, 163.8, 178.3; MS (m/z) (rel intensity, %) 354 (M⁺, 100), 207 (48), 174 (44), 117 (49); HRMS (ES⁺): m/z calcd for C₁₉H₁₆⁷⁹BrO₂ [M+H]⁺ 355.0334, found 355.0331, calcd for C₁₉H₁₆⁸¹BrO₂ [M+H]⁺ 357.0313, found 357.0314.
2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-4H benzo[g] chromen-4-one (4d)

Yield (85%); pale yellow solid; mp = 135–137 °C; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta\) 1.86–1.82 (m, 4H), 2.92–2.86 (m, 4H), 3.88 (s, 3H), 6.70 (s, 1H), 7.02 (s, 1H), 7.35–7.1 (m, 2H, ArH), 7.88–7.84 (m, 2H, ArH), 7.90 (s, 1H); \(^13\)C NMR (CDCl\(_3\), 75 MHz) \(\delta\) 22.6, 23.1, 28.9, 30.0, 55.5, 105.8, 114.4, 117.3, 121.6, 124.0, 125.0, 127.9, 134.9, 144.5, 154.3, 162.3, 163.1, 178.6; MS (m/z) (rel intensity, %) 306 (M\(^+\), 100), 207 (3), 174; HRMS (ES\(^+\)): m/z calcd for C\(_{20}\)H\(_{19}\)O\(_3\) [M+H]\(^+\) 307.1334, found 307.1335.

8. \(^1\)H and \(^{13}\)C NMR spectra of chalcones (2a–2d)

\((E)-1-(3-Hydroxy-5,6,7,8-tetrahydro-naphthalen-2-yl)-3-phenylprop-2-en-1-one (2a)
\(^1\)H NMR
E)-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-3-phenylprop-2-en-1-one (2a)

$^{13}$C NMR

![Diagram of the molecule 2a]
(E)-3-(2-Chlorophenyl)-1-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)prop-2-en-1-one (2b)

'H NMR
(E)-3-(2-Chlorophenyl)-1-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)prop-2-en-1-one (2b)

$^{13}$C NMR
(E)-3-(2-Bromophenyl)-1-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)prop-2-en-1-one (2c)

$^1$H NMR
(E)-3-(2-Bromophenyl)-1-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)prop-2-en-1-one (2c)

$^{13}$C NMR
(E)-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (2d)

$^1$H NMR
(E)-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (2d)

$^{13}$C NMR

2d
9. $^1$H and $^{13}$C NMR spectra of flavanones (3a–3d)

2-Phenyl-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3a)

$^1$H NMR
2-Phenyl-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3a)

$^{13}$C NMR

![Chemical Structure of 3a](image)

<table>
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<tr>
<th>ppm</th>
<th>147.16</th>
<th>139.96</th>
</tr>
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<tr>
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<td>128.75</td>
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<tr>
<td></td>
<td>128.85</td>
<td>126.10</td>
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<tr>
<td></td>
<td>117.44</td>
<td>79.39</td>
</tr>
</tbody>
</table>

$\text{mmol} \times 0.86 \times 937.76 \times 406.1 \times 123.1 \times (C) \times \text{species} \times 6$
2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3b)

$^1$H NMR
$3b$
2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3b)

$^{13}$C NMR

![Chemical structure of 3b](image)
$2\text{-}(2\text{-Bromophenyl})\text{-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one}$ (3c)

$^1\text{H NMR}$
2-(2-Bromophenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3c)

$^{13}$C NMR
2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3d)

$^1$H NMR
2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3d)

$^{13}$C NMR

Jun12-2015
612.28(C5186g7meddel/ome/cdcb)
ea_ct3qpd CDCl3 (C/Species) h=89.19

![Chemical Structure of 3d](image)

![NMR Spectrum](image)
10. $^1$H and $^{13}$C NMR spectra of flavones (4a–4d)
2-Phenyl-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4a)
$^1$H NMR
2-Phenyl-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4a)

$^{13}$C NMR

Jun25-2015
625.4(c520/1/)med/def/2ol/cdeB
e_c13epd CDOD (C2/predes) H2O

[Chemical structure diagram]
2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4b)

$^1$H NMR
2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4b)

$^{13}$C NMR

![Chemical Structure](image)

**13C NMR Spectra**

- **178.22**
- **142.29**
- **140.61**
- **127.42**
- **127.51**
- **125.07**
- **119.89**
- **117.57**
- **117.47**
- **2.96**
- **2.95**

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**References**

- md1
e_c3 궁 제5 (C): Spectrua H 15
2-(2-Bromophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4c)

$^1$H NMR
2-(2-Bromophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4c)

$^{13}$C NMR

\begin{verbatim}
mdl1
mdl1.16/c96412/t10med/oxbr/cdc3
a_ct3qpd CDC3 (C= Spectrum) 1t 16
\end{verbatim}

![Diagram of 4c molecule with labeled carbon peaks]
2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4d)

$^1$H NMR

![NMR Spectrum Image]
2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4d)

$^{13}$C NMR

![Chemical structure of 4d](image)
11. HRMS spectra of chalcones (2a–2d)

\((E)-1-(3\text{-Hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl})-3\text{-phenylprop-2-en-1-one} (2a)\)
(E)-3-(2-Chlorophenyl)-1-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)prop-2-en-1-one (2b)
(E)-3-(2-Bromophenyl)-1-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)prop-2-en-1-one (2c)
E)-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (2d)
12. GC/MS and HRMS spectra of flavanones (3a–3d)
2-Phenyl-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3a)
2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3b)
2-(2-Bromophenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3c)
2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3d)
13. GC/MS and HRMS spectra of flavonees (4a–4d)

2-Phenyl-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4a)
2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4b)
2-(2-Bromophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4c)
2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4d)