Ultrasound-Promoted Synthesis of 9-Aryl-1,8-dioxo-octahydroxanthenes Using TiO₂ as a Cheap and Reusable Catalyst

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Abstract: Reaction of aromatic aldehydes and dimedone was efficiently promoted by the TiO₂ as a catalyst in acetonitrile at room temperature under ultrasonic irradiation to afford the corresponding 9-aryl-1,8-dioxo-octahydroxanthene in excellent yields within minutes. However, the same reaction, without catalyst, yielded the corresponding 2,2'-arylmethylenebis(3-hydroxy-5,5-dimethyl-2-cycloexene-1-one). Study with various aldehydes and dimedone reveals that ultrasound and TiO₂ plays a key role in the synthesis of 9-aryl-1,8-dioxo-octahydroxanthene.

Keywords: Aldehydes, Dimedone, Ultrasound, Xanthene derivatives, TiO₂

Introduction

In recent years sonochemistry has been widely used in organic syntheses as it offers a versatile and facile pathway for a bewildering range of organic reactions. Sonochemistry involves the use of ultrasound technique to promote organic reactions. A large number of ultrasonic reactions can be carried out in higher yield, shorter reaction time or under milder conditions. Ultrasound irradiation has been demonstrated as an alternative energy source for organic reactions which can be ordinarily accomplished by heating. Due to the thermal effect of ultrasound wave, larger amount of molecules can meet the demand for the active energy in a given reaction, leading to the apparent improvement of the reaction efficiency with increased rates and reduced reaction time. It is also observed that reactions performed under ultrasound irradiation are commonly easier to work-up as compared to the conventional reactions. In recent time, the use of TiO₂ as catalyst has received a considerable attention in organic synthesis due to its environmental compatibility, ease of handling, non-toxic nature, low cost, chemical stability even under irradiation, ease of separation from the reaction mixture and above all its reusability protocol. TiO₂ finds diverse industrial applications such as whitener in paint, UV absorbers in sunscreen lotions and additives in food. Besides these industrial applications, commercially available TiO₂
has invoked an interest as a green, inexpensive, mild and recyclable heterogeneous Lewis acid catalyst in numerous organic transformations such as Biginelli condensation\textsuperscript{9}, Friedel-Crafts acylation\textsuperscript{10}, Beckmann rearrangement\textsuperscript{11} and also in the synthesis of dihydropyrazines\textsuperscript{12}. Xanthene derivatives are parent compounds of a large number of naturally occurring as well as synthetic derivatives and occupy a prominent position in medicinal chemistry, such as antiviral, antibacterial, anti-inflammatory agents, novel CCR1 receptor antagonists, anticancer agents and antinociceptive\textsuperscript{13}. Xanthene derivatives are also used as dyes, fluorescent materials and in laser technologies, due to their useful properties\textsuperscript{14}. A literature survey indicates that 9-aryl-1,8-dioxo-octahydroxanthene can be synthesized from aromatic aldehydes and dimedone in the presence of a number of catalysts, such as CaCl\textsubscript{2},\textsuperscript{15} SbCl\textsubscript{3}/SiO\textsubscript{2},\textsuperscript{16} HClO\textsubscript{4}/SiO\textsubscript{2},\textsuperscript{17} FeCl\textsubscript{3}/SiO\textsubscript{2},\textsuperscript{18} silica sulfuric acid\textsuperscript{19}, Dowex-50w\textsuperscript{20}, Amberlyst-15\textsuperscript{21}, [Hbim]BF\textsubscript{4}\textsuperscript{22} and TMSCl\textsuperscript{23}. However, many of these reported synthetic protocols suffer from one or more disadvantages, such as long reaction time, moderate yields, the use of expensive catalyst, strongly acidic conditions, tedious work-up and formation of by-products. We herein report the TiO\textsubscript{2} promoted synthesis of 9-aryl-1,8-dioxo-octahydroxanthene from corresponding aldehydes and dimedone in acetonitrile at a room temperature under ultrasound. However, the same reaction, in absence of the catalyst, yielded the corresponding 2,2'-arylmethylenebis(3-hydroxy-5,5-dimethyl-2-cycloexene-1-one) (Scheme 1).

\begin{center}
\begin{tikzpicture}
\node (a) at (0,0) {CHO};
\node (b) at (1,0) {O}
\node (c) at (2,0) {O}
\node (d) at (3,0) {O}
\node (e) at (4,0) {OH}
\node (f) at (5,0) {OH}
\node (g) at (6,0) {R
\begin{center}
\begin{tikzpicture}
\node (a) at (0,0) {CHO};
\node (b) at (1,0) {O}
\node (c) at (2,0) {O}
\node (d) at (3,0) {O}
\node (e) at (4,0) {OH}
\node (f) at (5,0) {OH}
\node (g) at (6,0) {R

\textbf{Scheme 1. Two-component synthesis of Xanthene derivatives}

\section*{Experimental}
All chemicals were purchased from commercial suppliers, such as Sigma-Aldrich and Merck. Reactions were carried out in a Rivotek (25±1 °C) ultrasonic cleaning bath at 50 kHz. The ultrasonic cleaner had an output power of 120W and a power supply of 450W. The tank dimensions were 290: 240:150 mm with a liquid holding capacity of 9.5 L. The reactions were carried out in a RB flask of 10 mL capacity suspended at the center of the cleaning bath, 5 cm below the surface of the liquid. The melting points of the products were recorded on a Bruker instrument and compared with the reported literature values.\textsuperscript{1}H and \textsuperscript{13}C NMR spectra were obtained on a 400 MHz NMR spectrometers Bruker Maldi-TOF. Chemical shifts are indicated in parts per million with respect to TMS. The IR spectra were recorded in the range of 4000-400 cm\textsuperscript{-1} on an FTIR Perkin 2000 Model spectrometer using...
KBr disk. Mass spectra were recorded on a High resolution mass spectrometer (UPLCMS) Bruker. Purity of the compounds was checked by TLC on a silica gel alumina sheet using n-hexane and ethylacetate as eluent. The visualization was accomplished with UV lamps at 254 nm.

**General procedure for the synthesis of the synthesis of 2,2′-arylmethylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexane-1-one) 3(a-i)**

A 10 mL round-bottomed flask containing an aldehyde (1 mmol), dimedone, (2 mmol), in acetonitrile (2 mL) was placed in an ultrasonic bath for 5 to 15 minute at room temperature. After completion, the reaction mixture was analyzed by TLC. The reaction mixture was treated with water, aqueous phase was extracted with ethylacetate (2x10 mL) and the organic layers was washed with water, saturated brine solution and dried over anhydrous Na₂SO₄. The combined organic layers were evaporated under reduced pressure and the resulting crude product was purified by column chromatography with ethylacetate and n-hexane. The products were characterized by ¹H NMR spectra. The spectroscopic data obtained on the synthesized compounds are given in spectral section.

**General procedure for the synthesis of the synthesis of 9-Aryl-1,8-dioxo-octahydroxanthene derivatives 4(a-s)**

A 10 mL round-bottomed flask containing an aldehyde (1 mmol), dimedone, (2 mmol) and 5 mol % of TiO₂ in acetonitrile (2 mL) was placed in an ultrasonic bath for 5 to 15 minute at room temperature. The product was isolated with ethylacetate (3x5 mL) and the combined layer was filtered to separate out TiO₂ and residue washed with ethylacetate. The solid residue of TiO₂ was further washed with acetone (10 mL) and then dried up; this recovered TiO₂ is reusable. After removal of solvent from the combined filtrate under reduced pressure, the organic residue was subjected to column chromatography to obtain pure 9-aryl-1,8-dioxo-octahydroxanthene compound. The identity of the product was confirmed by IR, ¹H and ¹³C{¹H} NMR and Mass spectra. The spectroscopic data obtained on the synthesized compounds are given in below.

**Spectral data for selected compounds**

**Compound 3a**

White solid; Analytical TLC (silica gel 60) (30% EtOAc in hexane) R_f = 0.3; ¹H NMR (CDCl₃, 400 MHz): δ 1.09 (s, 6H, 2 × CH₃), 1.22 (s, 6H, 2 × CH₃), 2.27-2.47 (m, 8H, 4 × CH₂), 5.53 (s, 1H, CH), 7.07-7.27 (m, 5H, Ar), 11.88 (s, 1H, OH).

**Compound 3b**

White solid; Analytical TLC (silica gel 60) (30% EtOAc in hexane) R_f = 0.3; ¹H NMR (CDCl₃, 400 MHz): δ 1.09 (s, 6H, 2 × CH₃), 1.22 (s, 6H, 2 × CH₃), 2.27-2.47 (m, 8H, 4 × CH₂), 5.53 (s, 1H, CH), 7.07-7.27 (m, 5H, Ar), 11.88 (s, 1H, OH).

**Compound 3d**

White solid; Analytical TLC (silica gel 60) (30% EtOAc in hexane) R_f = 0.3; ¹H NMR (CDCl₃, 400 MHz): δ 1.05 (s, 6H, 2 × CH₃), 1.19 (s, 6H, 2 × CH₃), 2.20-2.39 (m, 8H, 4 × CH₂), 5.32 (s, 1H, CH), 7.18-7.20 (m, 4H, Ar), 11.71 (s, 1H, OH).

**Compound 3e**

White solid; Analytical TLC (silica gel 60) (30% EtOAc in hexane) R_f = 0.3; ¹H NMR (CDCl₃, 400 MHz): δ 1.00 (s, 6H, 2 × CH₃), 1.10 (s, 6H, 2 × CH₃), 2.19-2.35 (m, 8H, 4 × CH₂), 5.45 (s, 1H, CH), 6.90-6.97 (m, 4H, Ar), 11.80 (s, 1H, OH).
**Compound 3g**

White solid; Analytical TLC (silica gel 60) (30% EtOAc in hexane) R<sub>f</sub> = 0.3; ¹H NMR (CDCl<sub>3</sub>, 400 MHz): δ 1.02 (s, 6H, 2 × CH₃), 1.12 (s, 6H, 2 × CH₃), 2.22-2.43 (m, 8H, 4 × CH₂), 3.45 (s,3H, OCH₃), 5.50 (s, 1H, CH), 6.78-7.84 (2H, Ar), 6.92-7.00 (2H, Ar), 11.79 (s, 1H, OH).

**Compound 3h**

White solid; Analytical TLC (silica gel 60) (30% EtOAc in hexane) R<sub>f</sub> = 0.3; ¹H NMR (CDCl<sub>3</sub>, 400 MHz): δ 1.02 (s, 6H, 2 × CH₃), 1.12 (s, 6H, 2 × CH₃), 2.22-2.43 (m, 8H, 4 × CH₂), 3.45 (s,3H, OCH₃), 5.50 (s, 1H, CH), 6.80-6.89 (2H, Ar), 6.90-7.19 (2H, Ar), 11.84 (s, 1H, OH).

**Compound 3i**

White solid; Analytical TLC (silica gel 60) (30% EtOAc in hexane) R<sub>f</sub> = 0.3; ¹H NMR (CDCl<sub>3</sub>, 400 MHz): δ 1.04 (s, 6H, 2 × CH₃), 1.15 (s, 6H, 2 × CH₃), 2.27-2.47 (m, 8H, 4 × CH₂), 5.53 (s, 1H, CH), 6.72-7.89 (2H, Ar), 6.90-7.00 (2H, Ar), 11.88 (s, 1H, OH).

**Compound 4a**

White solid; Analytical TLC (silica gel 60) (25% EtOAc in hexane) R<sub>f</sub> = 0.25; ¹H NMR (CDCl<sub>3</sub>, 400 MHz): δ 0.99 (s, 6H, 2 × CH₃), 1.12 (s, 6H, 2 × CH₃), 2.14-2.47 (m, 8H, 4 × CH₂), 4.53 (s, 1H, CH), 7.07-7.27 (m, 5H, Ar); ¹³C NMR (CDCl<sub>3</sub>): δ 27.33, 29.27, 31.83, 32.2, 40.87, 50.74, 115.67, 126.36, 128.04, 128.37, 144.08, 162.24, 196.37. LC–MS: 367 [M+17].

**Compound 4b**

White solid; Analytical TLC (silica gel 60) (25% EtOAc in hexane) R<sub>f</sub> = 0.25; IR (CHCl₃, cm⁻¹): 3020, 2961, 1720, 1667, 1592, 1530, 1352, 1198, 1000; ¹H NMR (CDCl<sub>3</sub>, 400 MHz): δ 1.19 (s, 6H, 2 × CH₃), 1.24 (s, 6H, 2 × CH₃), 2.37-2.57 (m, 8H, 4 × CH₂), 4.86 (s, 1H, CH), 7.27 (d, 2H, Ar), 8.14 (d, 2H, Ar); ¹³C NMR (CDCl<sub>3</sub>): δ 27.14, 29.60, 32.72, 50.16, 56.85, 60.19, 106.20, 115.10, 136.85, 140.78, 153.68, 173.93, 197.17. LC–MS: 412 [M+17].

**Compound 4e**

White solid; Analytical TLC (silica gel 60) (25% EtOAc in hexane) R<sub>f</sub> = 0.25; ¹H NMR (CDCl<sub>3</sub>, 400 MHz): δ 1.08 (s, 6H, 2 × CH₃), 1.20 (s, 6H, 2 × CH₃), 2.27-2.47 (m, 8H, 4 × CH₂), 5.43 (s, 1H, CH), 6.93-6.95 (d, 2H, Ar), 7.35-7.37 (d, 2H, Ar); ¹³C NMR (CDCl<sub>3</sub>): δ 27.43, 29.53, 31.43, 32.48, 46.43, 47.05, 115.26, 119.64, 128.61, 131.26, 137.31, 189.41, 190.64; LC–MS: 445 [M+17].

**Compound 4h**

White solid; Analytical TLC (silica gel 60) (25% EtOAc in hexane) R<sub>f</sub> = 0.25; IR (CHCl₃, cm⁻¹): 3392, 3064, 2960, 2929, 2253,1719, 1667, 1595, 1380,1166; ¹H NMR (CDCl<sub>3</sub>, 400 MHz): δ 1.08 (s, 6H, 2 × CH₃), 1.20 (s, 6H, 2 × CH₃), 2.27-2.47 (m, 8H, 4 × CH₂), 4.51 (s, 1H, CH), 6.90-7.0 (d, 2H, Ar), 7.22-7.24 (d, 2H, Ar); ¹³C NMR (CDCl<sub>3</sub>): δ 27.70, 29.72, 31.80, 32.60, 41.37, 51.11, 115.60, 128.60, 130.20, 132.40, 143.11, 162.80, 196.70; LC–MS: 401 [M+17].
**Compound 4n**

White solid; Analytical TLC (silica gel 60) (25% EtOAc in hexane) R_f = 0.25; IR (CHCl_3, cm\(^{-1}\)): 3148, 2958, 1720, 1590, 1378, 1192, 1081; \(^1\)H NMR (CDCl_3, 400 MHz): d 0.99 (s, 6H, 2 x CH\(_3\)), 1.09 (s, 6H, 2 x CH\(_3\)), 2.14-2.20 (d, 4H), 2.24 (s, 3H), 2.45 (s, 4H), 4.78 (s, 1H, CH), 6.77-7.27 (4H, Ar); LC–MS: 387 [M+17].

**Results and Discussion**

We investigated the TiO\(_2\) catalyzed, ultrasound promoted two-component synthesis of 9-aryl-1,8-dioxo-octahydroxanthene from various aldehydes and dimedone in acetonitrile at room temperature. Initially, the reaction of 4-nitrobenzaldehyde (1 mmol), dimedone (2 mmol) was chosen as a model reaction to optimize the reaction conditions, with or without catalyst. To our surprise the reaction proceeded efficiently in presence of TiO\(_2\) (5 mol %) as catalyst to the afford the corresponding 9-aryl-1,8-dioxo-octahydroxanthene 4b (95% yields) in dramatically 5 min at room temperature under sonication (Table 1, entry 5). However the same reaction under the same reaction conditions, but without catalyst, yielded the corresponding open chain analogue of 9-aryl-1,8-dioxo-octahydroxanthene 3b (90%) (Table 1, entry 6).

**Table 1.** Reaction of 4-nitrobenzaldehyde and dimedone under different reaction conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Condition</th>
<th>Catalyst/No Catalyst</th>
<th>Solvent</th>
<th>Time</th>
<th>Product 3 Yield, %</th>
<th>Product 4 Yield, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30 °C without sonication</td>
<td>TiO(_2)</td>
<td>Acetonitrile</td>
<td>24 h</td>
<td>Trace</td>
<td>Trace</td>
</tr>
<tr>
<td>2</td>
<td>30 °C without sonication</td>
<td>No Catalyst</td>
<td>Acetonitrile</td>
<td>24 h</td>
<td>Trace</td>
<td>Nil</td>
</tr>
<tr>
<td>3</td>
<td>30 °C without sonication</td>
<td>TiO(_2)</td>
<td>No solvent</td>
<td>24 h</td>
<td>Nil</td>
<td>Trace</td>
</tr>
<tr>
<td>4</td>
<td>30 °C without sonication</td>
<td>No Catalyst</td>
<td>No solvent</td>
<td>24 h</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>5</td>
<td>30 °C with sonication</td>
<td>TiO(_2)</td>
<td>Acetonitrile</td>
<td>5 min</td>
<td>Nil</td>
<td>95</td>
</tr>
<tr>
<td>6</td>
<td>30 °C with sonication</td>
<td>No Catalyst</td>
<td>Acetonitrile</td>
<td>5 min</td>
<td>90</td>
<td>Trace</td>
</tr>
<tr>
<td>7</td>
<td>30 °C with sonication</td>
<td>TiO(_2)</td>
<td>No Solvent</td>
<td>5 min</td>
<td>Nil</td>
<td>58</td>
</tr>
<tr>
<td>8</td>
<td>30 °C with sonication</td>
<td>No Catalyst</td>
<td>No Solvent</td>
<td>5 min</td>
<td>28</td>
<td>Trace</td>
</tr>
<tr>
<td>9</td>
<td>Reflux without sonication</td>
<td>TiO(_2)</td>
<td>Acetonitrile</td>
<td>24 h</td>
<td>Trace</td>
<td>Trace</td>
</tr>
<tr>
<td>10</td>
<td>Reflux without sonication</td>
<td>No Catalyst</td>
<td>Acetonitrile</td>
<td>24 h</td>
<td>Trace</td>
<td>Trace</td>
</tr>
</tbody>
</table>

\(^{a,b}\) Isolated yield

When the reaction was carried out with and without solvents at room temperature without ultrasonic radiations, merely traces of the product were observed even after 24 h. (Table 1, entry 1–4). Only traces of product were obtained when the reaction was carried out at elevated temperature in the absence of ultrasound radiations (Table 1, entry 9-10). The mechanism of the reaction between aldehyde and dimedone has been described in literature\(^{24}\). First, intermediate 3 was formed through Knoevenagel addition between dimedone and aldehyde and subsequently, water elimination from intermediate 3 resulted in the formation of desired 4. In these processes, TiO\(_2\) plays a crucial role in accelerating the reaction, especially for water elimination of intermediate 3. It can be verified by the fact that the reaction under catalyst-free condition only yielded the product 3. Ultrasonic effect also plays an important role in accelerating the reaction, presumably by cavitations\(^{25}\).

In addition to TiO\(_2\), the reaction was also carried out in the presence of other catalyst, i.e. ZnO, CuO and SiO\(_2\) and the results are summarized in Table 2. As evident from Table 2, TiO\(_2\) proved to be the best catalyst for the reaction of 4-nitrobenzaldehyde and dimedone under ultrasonic irradiation, in acetonitrile at room temperature (Table 2, entry 1).
Table 2. Scanning of catalysts, using reaction between 4-nitrobenzaldehyde and dimedone under ultrasonication

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst, 5 mol %</th>
<th>Time, min</th>
<th>Product 4, %, Yield&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TiO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>5</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>ZnO</td>
<td>5</td>
<td>45</td>
</tr>
<tr>
<td>3</td>
<td>CuO</td>
<td>5</td>
<td>36</td>
</tr>
<tr>
<td>4</td>
<td>SiO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>5</td>
<td>52</td>
</tr>
</tbody>
</table>

<sup>a</sup>Isolated yield

With the best catalyst in hand, we moved to study the effect of catalyst loading on the model reaction and the result was listed in Table 3.

Table 3. Effect of catalyst loading on the reaction of 4-nitrobenzaldehyde and dimedone under ultrasonication

<table>
<thead>
<tr>
<th>Entry</th>
<th>TiO&lt;sub&gt;2&lt;/sub&gt; mol %</th>
<th>Time min</th>
<th>Product 4 %, Yield&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>5</td>
<td>63</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>5</td>
<td>95</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>5</td>
<td>95</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>5</td>
<td>95</td>
</tr>
</tbody>
</table>

<sup>a</sup>Isolated yield

After optimization of the catalyst loading, the reaction was also performed in various solvents such as, water, ethanol, methanol, dichloromethane, ethyl acetate, toluene and acetonitrile for the both type of reaction (with/without catalyst). As evident from Table 4, the acetonitrile was found to be the best solvent for the reaction (Table 4, entry 1-6).

Table 4. Effect of solvents on the reaction of 4-nitrobenzaldehyde, and dimedone under ultrasonication

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time min</th>
<th>Product 3 %, Yield&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Product 4 %, Yield&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dichloromethane</td>
<td>5</td>
<td>82</td>
<td>89</td>
</tr>
<tr>
<td>2</td>
<td>Acetonitrile</td>
<td>5</td>
<td>90</td>
<td>95</td>
</tr>
<tr>
<td>3</td>
<td>Water</td>
<td>5</td>
<td>80</td>
<td>66</td>
</tr>
<tr>
<td>4</td>
<td>Ethanol</td>
<td>5</td>
<td>65</td>
<td>71</td>
</tr>
<tr>
<td>5</td>
<td>Methanol</td>
<td>5</td>
<td>54</td>
<td>79</td>
</tr>
<tr>
<td>6</td>
<td>Toluene</td>
<td>5</td>
<td>61</td>
<td>76</td>
</tr>
</tbody>
</table>

<sup>a,b</sup>Isolated yield

After the optimization of catalyst and other reactions conditions, we investigated the reaction of other benzaldehydes having electron-donating and electron-withdrawing group with dimedone under ultrasonic conditions. The results are given in Table 5 and Table 6 which shows that all the reactions preceded clean, to give the corresponding 2,2'-arylmethylenes(3-hydroxy-5,5-dimethyl-2-cycloexene-1-one) 3 and 9-aryl-1,8-dioxo-octahydroxanthene 4 respectively.

Table 5. Synthesis of 2,2'-arylmethylenes(3-hydroxy-5,5-dimethyl-2-cyclohexane-1-one) derivatives

![Chemical reaction diagram]
<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehyde</th>
<th>Product&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Time, min</th>
<th>% Yield&lt;sup&gt;b&lt;/sup&gt;</th>
<th>m.p. °C</th>
<th>m.p.°C&lt;sup&gt;lit&lt;/sup&gt;</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>CHO</td>
<td><img src="image" alt="3a" /></td>
<td>6</td>
<td>88</td>
<td>190-191</td>
<td>192-194&lt;sup&gt;22&lt;/sup&gt;</td>
</tr>
<tr>
<td>2</td>
<td>CHO</td>
<td><img src="image" alt="3b" /></td>
<td>5</td>
<td>90</td>
<td>194-197</td>
<td>195-197&lt;sup&gt;22&lt;/sup&gt;</td>
</tr>
<tr>
<td>3</td>
<td>CHO</td>
<td><img src="image" alt="3c" /></td>
<td>8</td>
<td>86</td>
<td>200-202</td>
<td>201-203&lt;sup&gt;22&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>CHO</td>
<td><img src="image" alt="3d" /></td>
<td>8</td>
<td>73</td>
<td>236-238</td>
<td>241-243&lt;sup&gt;22&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>CHO</td>
<td><img src="image" alt="3e" /></td>
<td>13</td>
<td>85</td>
<td>141-144</td>
<td>145-147&lt;sup&gt;22&lt;/sup&gt;</td>
</tr>
<tr>
<td>6</td>
<td>CHO</td>
<td><img src="image" alt="3f" /></td>
<td>14</td>
<td>79</td>
<td>199-201</td>
<td>202-204&lt;sup&gt;22&lt;/sup&gt;</td>
</tr>
<tr>
<td>7</td>
<td>CHO</td>
<td><img src="image" alt="3g" /></td>
<td>10</td>
<td>84</td>
<td>148-149</td>
<td>146-148&lt;sup&gt;22&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Contd...
Table 6. Synthesis of 9-aryl-1,8-dioxo-octahydroxanthen derivatives

\[
\begin{align*}
8 & \quad \text{CHO} & \quad \text{CH}_3 & \quad \text{OH} & \quad \text{OH} \\
& \quad \text{CH}_3 & \quad \text{OH} & \quad \text{OH} & \quad \text{OH} \\
& \quad \text{CHO} & \quad \text{CH}_3 & \quad \text{OH} & \quad \text{OH} \\
& \quad \text{CHO} & \quad \text{NO}_2 & \quad \text{OH} & \quad \text{OH} \\
& \quad \text{CHO} & \quad \text{NO}_2 & \quad \text{OH} & \quad \text{OH} \\
& \quad \text{CHO} & \quad \text{NO}_2 & \quad \text{OH} & \quad \text{OH} \\
& \quad \text{CHO} & \quad \text{NO}_2 & \quad \text{OH} & \quad \text{OH} \\
\end{align*}
\]

*Purity determined by TLC & $^1$H NMR. $^b$Isolated yield

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehyde</th>
<th>Product (^a)</th>
<th>Time min</th>
<th>% Yield (^b)</th>
<th>m.p. (^\circ\text{C})</th>
<th>m.p. (^\text{lit.}) (^\circ\text{C})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CHO</td>
<td>(4a)</td>
<td>6</td>
<td>90</td>
<td>204-206</td>
<td>205(^{24})</td>
</tr>
<tr>
<td>2</td>
<td>CHO</td>
<td>(4b)</td>
<td>5</td>
<td>95</td>
<td>221-223</td>
<td>222-224(^{24})</td>
</tr>
<tr>
<td>3</td>
<td>CHO</td>
<td>(4c)</td>
<td>8</td>
<td>93</td>
<td>164-166</td>
<td>165-166(^{24})</td>
</tr>
<tr>
<td>4</td>
<td>CHO</td>
<td>(4d)</td>
<td>7</td>
<td>87</td>
<td>250-252</td>
<td>252-254(^{24})</td>
</tr>
</tbody>
</table>

Contd...
5  
\[
\begin{align*}
\text{CHO} & \quad \text{Br} \\
\text{Br} & \\
\end{align*}
\]

5  91  240-243  240-242\textsuperscript{24}

4e

9  89  190-191  190-192\textsuperscript{24}

4f

8  93  226-227  226-229\textsuperscript{24}

4g

6  92  230-233  230-232\textsuperscript{24}

4h

8  94  184-185  183-185\textsuperscript{24}

4i

9  95  225-227  226-227\textsuperscript{24}

4j

10  93  241-242  242-243\textsuperscript{24}

4k

11  91  161-162  161-162\textsuperscript{24}

4l

Contd...
The products were obtained as colorless crystalline solids. All compounds were characterized by IR, $^1$H, $^{13}$C {$^1$H} NMR and Mass Spectra. The reaction between aldehyde and dimedone under ultrasonic irradiation in acetonitrile without catalyst gave only chain compound 3b as the major product which was confirmed by the presence of singlet at $\delta$ 11.77, and 5.52 corresponding to -OH and methyne protons, respectively in the $^1$H NMR spectrum. Similarly a singlet at $\delta$ 4.86, characteristic of the methyne proton was observed for the cyclized compound 4b. The spectra of synthesized compounds were compared with the literature Values.$^{17-25}$

All the spectroscopic data obtained were found to be in good agreement with the reported values. The recyclability of catalyst TiO$_2$ was also studied. The catalyst can be easily filtered out from the aqueous layer and dried for reuse. It is apparent from Figure 1 that the catalyst can be used up to five times without the significantly of catalytic activity.
Conclusion

Our studies clearly demonstrate that TiO$_2$ is a versatile, cheap, and reusable catalyst for the synthesis of 9-Aryl-1,8-dioxo-octahydroxanthene from aldehyde and didehdone under ultrasonic radiations.

References
25. Li X J Z, Xie L, Zhao Y and Wang T, Ultrason Sonochem., 2013, 20(6), 1384-1389; DOI:10.1016/j.ultsonch.2013.03.010