H$_4$SiW$_{12}$O$_{40}$ Catalyzed One-Pot Synthesis of 12-Aryl-8,9,10,12-tetrahydrobenzo[\(a\)] Xanthen-11-ones Under Solvent-Free Conditions

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Abstract: An efficient and environmentally benign protocol for the one-pot, three-component synthesis of 12-aryl-8,9,10,12-tetrahydro-benzo[\(a\)]xanthen-11-one derivatives by condensation of aryl aldehydes, 2-naphthol and dimedone using H$_4$SiW$_{12}$O$_{40}$ (SiWA) as a reusable catalyst with high catalytic activity was reported. The reaction was carried out at 100 °C under solvent-free conditions within 15-40 min in 82-91% yield.

Keywords: 12-Aryl-8,9,10,12-tetrahydrobenzo[\(a\)]xanthen-11-ones, Dimedone, 2-Naphthol, Aldehyde, Tungstosilicic acid, Multicomponent reaction.

Introduction

Organic reactions under green media have attracted much interest from chemists, particularly from the viewpoints of green chemistry. Green chemistry approaches are significant due to the reduction in byproducts and waste chemicals and lowering of energy costs. The possibility of performing multi-component reactions (MCRs) under green media could enhance their ability from the economical aspect as well as ecological point of view.$^1$

Xanthenes and benzoxanthenes are important biologically active heterocyclic compounds, which possess antiviral$^2$, anti-inflammatory$^3$ and antibacterial$^4$ activities. These are being utilized as antagonists for paralyzing action of zoxazolamine$^5$ and in photodynamic therapy$^6$. Furthermore, these compounds can be used as dyes$^7$ in laser technologies$^8$ and as pH sensitive fluorescent materials for visualization of biomolecules$^9$.

Tetrahydroxanthenone derivatives are generally synthesized by the three-component condensation of 2-naphthol, aryl aldehydes and cyclic 1,3-dicarbonyl compounds under different conditions. There are several reports for the synthesis of 12-aryl-8,9,10,12-Tetrahydrobenzo[\(a\)]xanthen-11-ones using catalysts such as NaHSO$_4$/SiO$_2$$^{10}$, Strontium triflate$^{11}$, pTSA$^{12}$, Indium(III) chloride or P$_2$O$_5$$^{13}$, Dodecatungstophosphoric acid$^{14}$, Iodine$^{15}$, HBF$_4$/SiO$_2$$^{16}$, HClO$_4$/SiO$_2$$^{17}$, Sulfamic acid$^{18}$, Cyanuric chloride$^{19}$, Zr(HSO$_4$)$_4$$^{20}$, Cu/SiO$_2$$^{21}$,
H$_4$SiW$_{12}$O$_{40}$ Catalyzed One-Pot Synthesis of Conditions

Ruthenium chloride$^{22}$, Caro's acid–silicagel$^{23}$, Surfactam$^{24}$, Scandium triflate/MW$^{25}$ and Camphor sulphonic acid$^{26}$. However, in spite of their potential utility, some of these methods suffer drawbacks such as the use of toxic and hazardous solvents, unsatisfactory product yields, expensive catalyst, requirement of huge amounts of catalyst, purification of the products by column chromatography and prolonged reaction times. So the development of a clean, high yielding and ecofriendly approach is still desirable. In this regard, a simple and efficient method for the one-pot synthesis of 12-aryl-8,9,10,12-tetrahydro-benzo[a]xanthen-11-one derivatives using H$_4$SiW$_{12}$O$_{40}$ (SiWA) is reported herein.

In recent years, solid acids have found increased application in organic synthesis, as they may be easily recovered and recycled. Heteropolyacids are strong solid acids, harmless to the environment, and highly stable toward humidity, with flexibility in modifying acid strength$^{27}$. Moreover, solvent-free reactions often provide clean, efficient and high-yielding organic processes in heterocyclic synthesis$^{28}$. In continuation of our efforts to develop new, green chemistry methods$^{29-31}$, we describe herein a clean and convenient synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a] xanthen-11-ones by three-component condensation reaction of 2-naphthol, aromatic aldehydes, and dimedone using catalytic amount of tungstosilicic acid as a recyclable catalyst under solvent-free conventional heating conditions (Scheme 1) 15-40 min.

![Scheme 1](image)

**Experimental**

Melting points recorded on an open capillary and IR spectra were measured on a Shimadzu IR-470 spectrophotometer. The $^1$H NMR spectra were recorded on a Bruker-400 MHz. All of the products are known and were characterized by their spectral and physical data. The monitoring of the progress of all reactions was carried out by TLC. TLC was runned using TLC aluminum sheets silica gel 60 F$_{254}$ (Merck).

**General procedure for the preparation of 12-aryl-8,9,10,12-tetrahydrobenzo[a] xanthen-11-one 4a**

A mixture of 4-chlorobenzaldehyde (2 mmol), dimedone (2 mmol), 2-naphthol (2 mmol) and H$_4$SiW$_{12}$O$_{40}$ (3.5 mol%, ca. 0.2 g) was heated with stirring at 100 °C for an appropriate time (TLC). After completion of the reaction, the mixture was cooled to room temperature and washed with water. The solid product was purified by recrystallization from EtOH to afford the pure product. All compounds are known and their physical and spectroscopic data were in good agreement with those of authentic samples$^{10-26}$. 
Results and Discussion

Aromatic aldehydes 1a-l, 2-naphthol 2 and dimedone 3 in the presence of a catalytic amount of SiWA undergo a fast 1:1:1 addition reaction at 100 °C under solvent-free conditions for several minutes to produce 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones 4a-l (Table 1). The results were excellent in terms of yields and product purity in the presence of SiWA, while without it for long period of time (1-2 h), the yields of products were trace. Next, the optimum amount of SiWA was evaluated. The highest yield was obtained with 3.5 mol% of the catalyst. A further increase in the amount of SiWA did not have any significant effect on the product yield. The generality of this reaction was examined using different aldehydes having electron-donating as well as electron-withdrawing groups. In all cases, the reactions gave the corresponding products in good to excellent yields (Table 1) and in short reaction times. Substituent on the aromatic ring had no obvious effect on yield or reaction time under the above optimal conditions. This method offers significant improvements with regard to the scope of the transformation, simplicity and green aspects by avoiding toxic solvents.

Table 1. H₄SiW₁₂O₄₀ catalyzed synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a] xanthen-11-ones.

<table>
<thead>
<tr>
<th>Product</th>
<th>Ar</th>
<th>Time (min)</th>
<th>Yield, %a</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>4-Cl-C₆H₄</td>
<td>15</td>
<td>89, 87, 86, 83b</td>
</tr>
<tr>
<td>4b</td>
<td>4-Br-C₆H₄</td>
<td>20</td>
<td>91</td>
</tr>
<tr>
<td>4c</td>
<td>2,4-Cl-C₆H₃</td>
<td>20</td>
<td>90</td>
</tr>
<tr>
<td>4d</td>
<td>C₆H₅</td>
<td>15</td>
<td>89</td>
</tr>
<tr>
<td>4e</td>
<td>4-H₃C-C₆H₄</td>
<td>30</td>
<td>85</td>
</tr>
<tr>
<td>4f</td>
<td>4-CH₂O-C₆H₄</td>
<td>15</td>
<td>83</td>
</tr>
<tr>
<td>4g</td>
<td>3-CH₂O-C₆H₄</td>
<td>15</td>
<td>87</td>
</tr>
<tr>
<td>4h</td>
<td>4-O₂N-C₆H₄</td>
<td>15</td>
<td>82</td>
</tr>
<tr>
<td>4i</td>
<td>3-O₂N-C₆H₄</td>
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<td>87</td>
</tr>
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<td>4j</td>
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<tr>
<td>4k</td>
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<tr>
<td>4l</td>
<td>2-CH₂O-C₆H₄</td>
<td>40</td>
<td>91</td>
</tr>
</tbody>
</table>

aYield refers to isolated pure product. bCatalyst was reused three times after drying.

The recovery and reusability of the catalyst was examined in the synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a] xanthen-11-ones. When the reaction was completed, water was added and the product was filtered. The aqueous solution containing soluble catalyst was evaporated under reduced pressure, and the obtained powder was washed with diethyl ether, dried and reused for the same reaction again. It was found that the catalyst could be reused three times with slight decreasing in catalytic activity, 87, 86 and 83% (Table 1, entry 1).

A possible mechanism for the formation of the products is shown in Scheme 2. The reaction occurs via initial formation of the ortho-quinone methides intermediate, which was formed by the nucleophilic addition of 2-naphthol to aldehyde catalyzed by SiWA. Subsequent Michael addition of the o-QM with dimedone and followed by addition of the
phenolic hydroxyl moiety to the carbonyl of ketone provides cyclic hemiketal which on dehydration afforded 4.

**Scheme 2**

**Conclusion**

We have developed a simple, efficient, one-pot and green protocol for the synthesis of 12-aryl-8,9,10,12-tetrahydro-benzo[a]xanthen-11-ones using SiWA as a reusable heterogeneous catalyst under solvent-free conditions. The present approach offers several advantages such as high yields and purity, shorter reaction times and low cost.

**Acknowledgment**

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**References**
