



H₄SiW₁₂O₄₀ Catalyzed One-Pot Synthesis of 12-Aryl-8,9,10,12-tetrahydrobenzo[*a*] Xanthen-11-ones Under Solvent-Free Conditions

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Received 21 September 2011; Accepted 13 November 2011

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 $H_4SiW_{12}O_{40}$ (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 view¹.

Xanthenes and benzoxanthenes are important biologically active heterocyclic compounds, which possess antiviral², anti-inflammatory³ and antibacterial⁴ activities. These are being utilized as antagonists for paralyzing action of zoxazolamine⁵ and in photodynamic therapy⁶. Furthermore, these compounds can be used as dyes⁷ in laser technologies⁸ and as pH sensitive fluorescent materials for visualization of biomolecules⁹.

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 NaHSO₄.SiO₂¹⁰, Strontium triflate¹¹, pTSA¹², Indium(III) chloride or $P_2O_5^{13}$, Dodecatungstophosphoric acid¹⁴, Iodine¹⁵, HBF₄/SiO₂¹⁶, HCIO₄-SiO₂¹⁷, Sulfamic acid¹⁸, Cyanuric chloride¹⁹, Zr(HSO₄)₄²⁰, Cu/SiO₂²¹,

Ruthenium chloride²², Caro's acid–silicagel²³, Surfactant²⁴, Scandium triflate/MW²⁵ and Camphor sulphonic acid²⁶. 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 $H_4SiW_{12}O_{40}$ (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 strength²⁷. Moreover, solvent-free reactions often provide clean, efficient and high-yielding organic processes in heterocyclic synthesis²⁸. In continuation of our efforts to develop new, green chemistry methods²⁹⁻³¹, 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

Experimental

Melting points recorded on an open capillary and IR spectra were measured on a Shimadzu IR-470 spectrophotometer. The ¹H 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 **4***a*

A mixture of 4-chlorobenzaldehyde (2 mmol), dimedone (2 mmol), 2-naphthol (2 mmol) and $H_4SiW_{12}O_{40}$ (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 samples¹⁰⁻²⁶.

Results and Discussion

Aromatic aldehydes **1a-1**, 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-I** (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.

| Product | Ar | Time (min) | Yield, % ^a |
|------------|--------------------------------------|------------|-----------------------------|
| 4a | $4-Cl-C_6H_4$ | 15 | 89, 87, 86, 83 ^b |
| 4b | $4-Br-C_6H_4$ | 20 | 91 |
| 4 c | 2,4-Cl-C ₆ H ₃ | 20 | 90 |
| 4d | C_6H_5 | 15 | 89 |
| 4e | $4-H_3C-C_6H_4$ | 30 | 85 |
| 4 f | $4-CH_3O-C_6H_4$ | 15 | 83 |
| 4 g | $3-CH_3O-C_6H_4$ | 15 | 87 |
| 4h | $4-O_2N-C_6H_4$ | 15 | 82 |
| 4i | $3-O_2N-C_6H_4$ | 15 | 87 |
| 4j | $2-O_2N-C_6H_4$ | 15 | 85 |
| 4k | $2-Cl-C_6H_4$ | 30 | 88 |
| 41 | $2-CH_3O-C_6H_4$ | 40 | 91 |

Table 1. $H_4SiW_{12}O_{40}$ catalyzed synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[*a*] xanthen-11-ones.

^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**.



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

We thank the International Center for Science, High Technology & Environmental Sciences, for financial support of this investigation.

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