Microwave assisted green synthesis of pharmaceutically potent benzoxanthone analogues employing biodegradable oxalic acid as ecofriendly catalyst

Pooja Bedi 1, Goutam Pramanik 2, Tanay Pramanik 1,3,*

1Department of Chemistry, School of Chemical Engineering and Physical Science, Faculty of Technology and Sciences, Lovely Professional University, Phagwara, P.O.Box 144411, India
2Institute of Organic Chemistry and Biochemistry of the CAS, Flemingovo nam. 2, 166 10 Prague 6, Czech Republic
3Department of Chemistry, University of Engineering and Management, University Area, Action Area III, B/5, Newtown, Kolkata-700156, India

*corresponding author e-mail address: tanay.pramanik@gmail.com | Scopus ID 55681424100

ABSTRACT
The aim of the present research work is to develop an efficient and ecofriendly methodology to synthesize benzoxanthone analogues by employing oxalic acid as nontoxic, biodegradable catalyst in water medium. The reactions were carried out under microwave irradiations. Thus hereby a series of benzoxanthone were synthesized from various aromatic aldehydes of varying electronic natures via a complete green approach where microwave irradiation was used as an efficient green source of energy, oxalic acid was employed as green catalyst and water were used as green solvent in all the reactions. The synthesized compounds have given a good percentage of yield of all the products and they were characterized by melting point, FT-IR, H\(^1\)-NMR C\(^13\)-NMR and mass spectroscopic techniques.

Keywords: Green Synthesis, Microwave, Benzoxanthone, Oxalic acid, Aqueous phase synthesis.

1. INTRODUCTION
Benzoxanthones are important oxygen containing heterocyclic molecules. These are generally considered as benzofused analogs of xanthones which is a well-known secondary metabolite naturally occurring in plant body. These are represented by the general structure as shown in Figure 1:

![Figure 1. General structure of Benzoxanthone.](image1)

The synthesis of benzoxanthone has attracted considerable interest from the researchers because of their wide range of applications in various fields of chemistry. They have been used as antibacterial, antiviral, anti-inflammatory, antimalarial, anti-HIV, antiallergic, antioxidant, antiplatelet, anticarcinogenic, antiabetic, antiviral, anti-inflammatory, antimalarial, and as antagonist for photodynamic therapy, as dyes, in laser technology, as fluorescent materials having sensitivity to pH change for visualization of biomolecules and as antagonist for paralyzing action of zoxalolamine [12-16].

Benzoxanthones are generally synthesized by acid catalysed condensation of \(\beta\)-napthol, dimidone and aromatic aldehydes Scheme 1. The Mechanism of the reaction is shown in Scheme 2.

![Scheme 1. General reaction Scheme.](image2)

![Scheme 2. Mechanism of the reaction.](image3)

The synthesis of benzoxanthone has been reported in the presence of strontium trflate [17], InCl\(_3\), P\(_2\)O\(_5\) [18], NaHSO\(_4\)-SiO\(_2\) [19], HClO\(_4\) [20], pTSA [21], Cu-SiO\(_2\) [22], Caro acid [23], Cyanouric chloride [24] (2,4,6-trichloro-1,3,5-trizaine), Camphor sulphonic acid [25], Dodecatungstophosphoric acid [26], iodine [27], RuCl\(_3\), nH\(_2\)O [28], Calix-4-arene sulphonic acid [29], Sulfamic acid [30], CISOH[31], Silica-sulphuric acid [32], TBAF [33], Proline triflate [34], Zr(HSO\(_4\))\(_2\) [35], ZnO(NPs) [36], SiWA [37], HBF\(_4\)/SiO\(_2\) [38] [bmim][BF\(_4\)] [39],Ceric ammonium nitrate (CAN)[40].

However, all the methodologies mentioned above suffer from one or more shortcomings such as the use of toxic and hazardous...
catalysts, solvents, harsh reaction conditions, prolonged reaction time, high temperature, low yield and so on. In addition to the above mentioned methodologies, several environmentally friendly synthetic protocols involving the use of PEG-400 [41], TTAB [42] are also documented in literature. But till now, no one has carried out synthesis of benzoxanthone by using biodegradable catalyst using efficient ecofriendly energy source. Oxalic acid being a completely biodegradable and strong acid, has a great potentiality to be used as green catalyst for synthesis of Benzoxanthone but to the best of our knowledge, oxalic acid has never been used as catalyst for the said purpose by any researcher till date. So our research group has synthesized a series of benzoaxanthone by using aqueous solution of oxalic acid under microwave irradiations for the very first time ever. Oxalic acid is a completely biodegradable and non-toxic compound having very high acidity which accelerates the rate of the reaction. Microwave irradiation on the other hand is a well-known ecofriendly source of energy. Thus microwave assisted synthesis of benzoxanthones in water medium, using biodegradable oxalic acid as catalyst can surely be considered as a completely new and total green approach from all aspect.

2. MATERIALS AND METHODS

2.1. General.

1-H and 13-C NMR spectra were recorded with Bruker AC/F300 or DPX 300 or DPX 500 spectrometer in CDCl3 solvent. The characterization of synthesized compounds was done by determining melting point, by recording IR, 1H, 13C nuclear magnetic resonance (NMR) and mass spectra. All the commercially available reactants and chemicals were used directly without doing further purification as they were obtained from the suppliers. The synthesized compounds are not entirely new compounds, they are the compounds which are already reported in the literature, the synthesized compounds are characterized by melting point, IR, H and 13C-NMR, direct mass analysis and by HRMS, the obtained results are verified by comparing the same with literature reported characterizations. The melting point, IR, and NMR spectra of the prepared compounds were identical to those of reported ones. All the reactions were carried out using microwave reactor with power 560W.

2.2. General Procedure for Synthesis.

In a conical flask 0.015 moles of each of β-napthol, dimidone and desired aldehyde were taken. Then the flask was charged with 10 ml of aqueous solution of 2M oxalic acid. The reaction mixture was exposed to microwave irradiation for specific time at 560 W microwave reactors. The reaction mixture was cooled down to room temperature after every 1 min of the exposure under MW irradiation. The progress of reaction was continuously monitored by checking thin-layer chromatography (TLC). After the completion of reaction (indicated by TLC), the reaction was quenched by pouring the reaction mixture into crushed ice. The solid crude product that was precipitated in water medium was separated out by filtration. The crude product was recrystallized from hot ethanol (two times). Finally, it was washed with hexane to remove any non-polar impurities and to get pure benzoxanthone. The obtained pure products were characterized by melting point, FT-IR, NMR and mass spectra.

3. RESULTS

A simple and efficient method is hereby developed for one pot synthesis of 12-aryl-8, 9, 10, 12-tetrahydrobenzo[a]-xanthen-11-one derivatives by condensation of various substituted benzaldehydes, β-napthol and dimidone using oxalic acid as biodegradable catalyst under microwave irradiation. After various attempts of synthesis of our target compound with various amounts of solvents and catalysts, it was found that 10mL aqueous solution of 2M oxalic acid was the most suitable one for carrying out our reactions. After carrying out the given reaction for several times by varying the power of microwave reactor, 560 W powers were found to be the most optimized and effective power of MW irradiation which was allowing the reaction to be completed within stipulated time duration and giving a considerably good percentage of yield of the desired product. The purification of the compound was a challenging job. As all the crude products were obtained in solid form and we wanted to minimize the usage of solvent for the purpose of purification, the purification of the crude compounds was carried out via recrystallization instead of doing the same via column chromatography. The purity of the compound was not up to the mark after first time recrystallization from hot ethanol. Thus a 2nd time recrystallization was carried out from hot ethanol to obtain compound with enough purity. Finally a hexane wash was given to remove the non-polar impurities from the compound. The compound was pure enough only after giving the final round of hexane wash, as seen from their spectroscopic data analysis. The obtained results are summarized in table -1. As observed from table-1, aromatic aldehydes substituted with either electron-donating or electron-withdrawing groups underwent the reaction smoothly and all of them have given the products with good to an excellent percentage of yields. It was worthy to note that all the reactions were completed within time duration of 25 to 44 minutes. It was interesting to note that 3-NO2 benzaldehyde took maximum time to go for completion of reaction when it was made to react with beta napthol and dimidone whereas the reaction took minimum time to go for completion with 4-NO2 benzaldehyde. Thus the position of the functional group of aromatic aldehyde plays an important role while the rate of reaction is considered. In general, it was an electron withdrawing group of aromatic aldehyde which makes the reaction to become more feasible. The mechanism of the reaction also justifies the same observation as an electron withdrawing group increases the electrophilicity of aromatic aldehyde.
Microwave assisted green synthesis of pharmaceutically potent benzoxanthone analogues employing biodegradable oxalic acid as ecofriendly catalyst

Table 1. MW assisted synthesis of benzoxanthones with different aldehydes in aqueous Solution of oxalic acid.

| Entry | X         | Time (Min) | % Yield | Observed M. P of product (°C) |
|-------|-----------|------------|---------|------------------------------|
| 1     | 4-Cl      | 33         | 81      | 180-182                      |
| 2     | 4-Br      | 30         | 72      | 185-186                      |
| 3     | 4-F       | 27         | 84      | 176-178                      |
| 4     | 2-NO₂     | 30         | 78      | 216-218                      |
| 5     | 3-NO₂     | 44         | 71      | 167-168                      |
| 6     | 4- NO₂    | 25         | 81      | 174-176                      |
| 7     | 4-CH₃     | 30         | 73      | 172-174                      |

Characterization of Benzoxanthones.

3.1. 12-(4-chlorophenyl)-9,9-dimethyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one

![Figure 2. Structure of compound 3.1](image)

M.P. = 180-182 ⁰C
IR (KBr, cm⁻¹): 1629.9(C=O), 1182.4(C-O Str.)
¹H NMR (400 MHz,CDCl₃): δ ppm: 7.88 (d. J=8Hz,1H, Ar-H), 7.77-7.75 (m, 2H,Ar-H), 7.27-7.10 (m, 7H,Ar-H), 5.67(s, 1H,CH), 2.56(s, 2H, CH₂), 2.32(dd,2H, CH₂), 1.1 (s, 3H,CH₃), 0.95 (s, 3H,CH₃)
¹³C-NMR (400 MHz, CDCl₃): δ ppm: 196.9, 164.15, 147.8, 143.4, 132.0, 131.6, 131.3, 129.9, 129.2, 128.6, 128.5, 127.2, 125.1, 123.5, 117.2, 113.8, 50.9, 41.4, 34.3, 32.3, 29.4, 27.1.
MS (ESI): m/z=389.12 [M+H]⁺

3.2. 12-(4-Bromophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-one.

![Figure 3. Structure of compound 3.2](image)

M.P. = 185-186 ⁰C
IR (cm⁻¹) (KBr): 1649.19 (C=O), 1170.83 (C-O Str.)
¹H- NMR (400 MHz, CDCl₃): δ ppm: 7.90 (d, J=8 Hz, 1H, Ar-H), 7.79-7.75 (m, 2H, Ar-H), 7.43-7.20 (m, 7H, Ar-H), 5.66 (s, 1H, CH), 2.55 (s, 2H, CH₂), 2.32 (dd, 2H, CH₂), 1.11 (s, 3H, CH₃), 0.95 (s, 3H, CH₃)
¹³C-NMR (400 MHz, CDCl₃): δ ppm: 197.0, 164.19, 147.79, 143.85, 131.58, 131.43, 131.27, 130.30, 129.22, 128.59, 127.24, 125.13, 123.54, 120.20, 117.14, 117.05, 113.80, 50.94, 41.47, 34.35, 32.36, 29.41, 27.24.
MS (ESI): m/z= 433.09 [M+H]⁺

3.3. 12-(4-Fluorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-one.

![Figure 4. Structure of compound 3.3](image)

M.P. = 176-178 ⁰C
IR (KBr) cm⁻¹: 1653.05 (C=O), 1162.15 (C-O Str.)
¹H NMR (400 MHz, CDCl₃): δ ppm: 7.94 (d, J= 8 Hz, 1H, Ar-H), 7.77 (t, J= 8.0 Hz, 2H, Ar-H), 7.43-7.29 (m, 5H, Ar-H), 6.85 (t, J= 8 Hz, 2H, Ar-H), 5.70 (s, 1H,CH), 2.55(s, 2H, CH₂), 2.33 (dd, 2H, CH₂), 1.11 (s, 3H, CH₃), 0.95 (s, 3H, CH₃)
¹³C NMR (400 MHz, CDCl₃): δ ppm: 197.06, 164.05, 162.49, 160.06, 147.81, 140.67, 140.65, 131.60, 131.33, 129.12, 128.58, 127.17, 125.09, 123.62, 117.46, 117.17, 115.26, 115.04, 114.17, 50.95, 41.48, 34.09, 32.35, 29.43, 27.16
MS (ESI): m/z= 369.20 [M+H]⁺

3.4. 12-(2-nitrophenyl)-9, 9-Dimethyl-8, 9, 10, 12-tetrahydrobenzo[a]xanthene-11-one.

![Figure 5. Structure of compound 3.4](image)

M.P. =216-218⁰C.
IR (KBr, cm⁻¹): 1656.91(C=O), 1173.72 (C-O Str.)
¹H NMR (400 MHz, CDCl₃): δ ppm: 8.56 (d, J=8.4,1H, Ar-H), 7.84-7.80 (m, 3H, Ar-H), 7.39–7.17 (m, 5H, Ar-H), 7.07-7.03(m, 1H, Ar), 6.57 (s, 1H, CH), 2.54 (dd, 2H, CH₂), 2.23(dd, 2H, CH₂), 1.08 (s, 3H, CH₃), 0.86(s, 3H, CH₃)
¹³C-NMR (400 MHz, CDCl₃): δ ppm: 196.97, 163.86, 149.32, 148.31, 139.24, 132.87, 131.89, 131.63, 131.18, 129.82, 128.33, 127.71, 127.17, 125.37, 124.78, 124.57, 117.03, 116.28, 113.48, 50.55, 41.52, 32.27, 30.36, 29.23, 27.15
MS (ESI): m/z= 400 [M+H]⁺

3.5. 12-(3-nitrophenyl)-9, 9-Dimethyl-8, 9, 10, 12-tetrahydrobenzo[a]xanthene-11-one.

Page | 4313
M.P. =167-168°C.
IR (KBr, cm⁻¹): 1649.19 (C=O), 1171.79 (C-O Str.)
¹H NMR (400 MHz, CDCl₃): δ ppm: 8.11 (d, J=8.1H, Ar-H), 7.81-7.78 (m, 5H, Ar-H), 7.44-7.33 (m, 4H, Ar-H), 5.80 (s, 1H, CH), 2.59 (s, 2H, CH₂), 2.33(dd, 2H, CH₂), 1.12 (s, 3H, CH₃), 0.94(s,3H,CH₃)
¹³C-NMR (400 MHz, CDCl₃): δ ppm: 196.89, 164.74, 151.97, 147.84, 146.39, 131.64, 131.09, 129.73, 129.46, 129.15, 128.76, 127.49, 125.34, 123.74, 123.2, 117.2, 113.05, 50.85, 41.49, 34.95, 32.37, 29.41, 27.17
MS (ESI): m/z= m/z=400 [M+H]+

3.7. 9,9-Dimethyl-12-p-tolyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one.

M.P. =172-174°C.
IR (KBr, cm⁻¹): 1648.23 (C=O), 1184.33 (C-O Str.)
¹H NMR (400 MHz, CDCl₃): δ ppm: 8.01 (d, J=8.1H, Ar-H), 7.77-7.73 (m, 2H, Ar-H), 7.44-7.21 (m, 5H, Ar-H), 6.97(d, 2H, Ar), 5.66 (s, 1H, CH), 2.56 (s, 2H, CH₂), 2.34(dd, 2H, CH₂), 2.15(s, 3H,CH₃) 1.11 (s, 3H, CH₃), 0.96(s,3H,CH₃)
¹³C-NMR (400 MHz, CDCl₃): δ ppm: 197.09, 163.89, 148.00, 141.94, 135.75, 131.56, 129.02, 128.79, 128.46, 128.36, 127.06, 124.94, 123.77, 117.13, 114.45, 51.00, 41.49, 34.36, 32.4, 29.36, 27.38, 21.09
MS (ESI): m/z= 369.15 [M+H]+

4. CONCLUSIONS
It was first of its kind study where a completely new ecofriendly methodology was developed for the synthesis of benzoxanthones by making aromatic aldehydes react with dimidone and beta naphthol. All the reactions were carried out in water medium and biodegradable oxalic acid was used as green ecofriendly catalyst for synthesis of this class of compound for the very first time ever. All the reactions were completed within 25-44 minutes time duration under microwave irradiation. Various aromatic aldehydes with various electronic natures have given a considerably good percentage of yield. It was 4-nitro derivatives which have made the reaction to be most feasible. Thus an easy, economic, ecofriendly, simple, new methodology is developed for the very first time ever for synthesis of benzoxanthones in water medium employing biodegradable acid as catalyst. It has opened a new door of opportunity for the chemist to employ oxalic or such biodegradable strong acid as green catalyst instead of using toxic catalyst for synthesis of pharmaceutically potent heterocyclic compounds in water medium.

5. REFERENCES
1. Hideo, T.; Teruomi, J. Benzopyrano[2,3-b]xanthen derivatives. Jpn. Patent 1981, 56, 480.
2. Lambert, R.W.; Martin, J.A.; Merrett, J.H.; Parkes, K.E.B.; Thomas, G.J. Preparation of pyridine nucleosides as thymidine kinase inhibitors and virucides PCT Int. Appl. WO 1997, 9,706,178.
3. Poupelin, J.P.; Saint-Ruf, G.; Foussard-Blanpin, O.; Narcisse, G.; Uchida-Ernfou; G.; Lacroix, R. Synthesis and anti-inflammatory properties of bis[2-hydroxy-1-naphthyl]-methane derivatives, I: Monosubstituted derivatives. Eur. J. Med. Chem. 1978, 13, 67.
Microwave assisted green synthesis of pharmaceutically potent benzoxanthone analogues employing biodegradable oxalic acid as ecofriendly catalyst

4. Ignatouchenko, M.V.; Winter, R.W.; Riscoe, M. Xanthones As Antimalarial Agents: Stage Specificity. Am. J. Trop. Med. Hyg. 2000, 62, 77. https://doi.org/10.4269/ajtmh.2000.62.77.

5. Chen, S.X.; Wan, M.; Loh, B.N. Active constituents against HIV-1 protease from Garcinia mangostana. Planta Med. 1996, 62, 381. https://doi.org/10.1055/s-2006-957916.

6. Barnes, A.C.; Hair sine, P.W.; Matharu, S.S.; Ram, P.J.; Taylor, J.B. Pharmacologically active sulfoximides: 5-hexyl-7-(S-methylsulfinimidoyl)xanthone-2-carboxylic acid, a potent antiallergic agent J. Med. Chem. 1979, 22, 418. https://doi.org/10.1021/jm00190a012.

7. Madan, B.; Singh, I.; Kumar, A.; Prasad, A.; Raj, H.; Parmar, V.; Ghosh, B. Xanthones as inhibitors of microsomal lipid peroxidation and TNF-α induced ICAM-1 expression on human umbilical vein endothelial cells (HUVECs). Bioorg. Med. Chem. 2002, 10, 3431. https://doi.org/10.1016/S0968-0896(02)00262-6.

8. Rajtar, G.; Zolkowska, D.; Kleinrok, Z.; Marona, H. Antipla telets activity of some xanthone derivatives. Acta Pol. Pharm. 1999, 56, 319.

9. Hong, D.; Yin, F.; Hu, L.H.; Lu, P. Sulfonated xanthones from Hypericum sampsonii. Phytochemistry 2004, 65, 2595. https://doi.org/10.1016/j.phytochem.2004.08.014.

10. Miura, T.; Iwamoto, N.; Kato, M.; Ichiki, H.; Kubo, M.; Komatsu, Y.; Ishida, T.; Okada, M.; Tanigawa, K. The suppressive effect of mangiferin with exercise on blood lipids in type 2 diabetes. Biol. Pharm. Bull. 2001, 24, 1091. https://doi.org/10.1248/bpb.24.1091.

11. Zhang, H.Z.; Kasibhatla, S.; Wang, Y.; Herich, J.; Guastella, J.; Tseng, B.; Drew, J.; Cai, S.X. Discovery, characterization and SAR of gambogic acid as a potent apoptosis inducer by an HTS assay. Bioorg. Med. Chem. 2004, 12, 309. https://doi.org/10.1016/j.biochem.2003.11.013.

12. Ion, R. M.; Planner, A.; Wikt orowicz, K.; Frackowiak, D. The incorporation of various porphyrins into blood cells measured via flow cytometry, absorption, and emission spectroscopy. Acta Biochim. Pol. 1998, 45, 833.

13. Menchen, S.M.; Benson, S.C.; Lam, J.Y.L.; Chen, W.G.; Sun, D.Q.; Rosenblum, B.B.; Khan, S.H.; Taing, M. Sulfonated Diarylhydrides Dyes. U.S. Patent 2003, 6,583.

14. Ahmad, M.; King, T. A.; Ko, D.-K.; Cha, B. H.; Lee, J. Performance and photostability of xanthene and pyrromethene laser dyes in sol-gel phases. J. Phys. D: Appl. Phys. 2002, 35, 1473. https://doi.org/10.1088/0022-3727/35/13/303.

15. Knight, C.G.; Stephens, T. Xanthene-dye labelled phosphatidylethanolamines as probes of interfacial pH. Studies in phospholipid vesicles. Biochem. J. 1989, 258, 683. https://doi.org/10.1042/bj2580683.

16. Saint-Ruf, G.; Hieu, H.T.; Pou pelin, J.P. The effect of dibenzoxanthenes on the paralyzing action of zoaxolamine Naturwissenschaften 1975, 62, 584. https://doi.org/10.1007/BF01166986.

17. Li, J.; Tang, W.; Lu, L.; Su, W. Strontium triflate catalyzed one-pot condensation of β-naphthol, aldehydes, and cyclic 1,3-dicarbonyl compounds. Tetrahedron Lett. 2008, 49, 7117. https://doi.org/10.1016/j.tetlet.2008.09.129.

18. Nandi, G.C.; Samai, S.; Kumar, R.; Singh, M.S. An efficient one-pot synthesis of tetrahydrobenzo[a]xanthene-11-one and diazabenz[a]anthracene 9,11-dione derivatives under solvent-free condition. Tetrahedron 2009, 65, 7129. https://doi.org/10.1016/j.tet.2009.06.024.

19. Das, B.; Laxminarayana, K.; Krishnaiah, M.; Srinivas, Y.A. Simple and Green Approach for the Synthesis of Tetrahydrobenzo[a]xanthene-11-one Derivatives Using Tetrabutyl Ammonium Fluoride in Water. Synlett, 2007, 3107. https://doi.org/10.1055/s-2007-990922.

20. Nazeruddin N. Gulam Mohammed, Mahesh S. Microwave Promoted, Perchloric Acid catalyzed One Pot Synthesis of Xanthene Derivatives under solvent –free conditions. Pandharipatte Der Pharma Chemica 2011, 3, 65-71.

21. Li, J.; Li, J.; Fang, J.; Su, W. Efficient One-Pot Condensation of β-Naphthol, Aldehydes, and Cyclic 1,3-Dicarbonyl Compounds Catalyzed by p-TSA Under Solvent-Free and Saponification Conditions. Synth Commun 2010, 40, 1029. https://doi.org/10.1080/00397910903029966.

22. Oskooie, H.A.; Heravi, M.M.; Karimi, N.; Kohansal, G.Cu/SiO2 Catalyzed One-Pot synthesis of 12-Aryl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-ones Under Solvent-Free Conditions. Synth Commun. 2011, 41, 2763-2768. https://doi.org/10.1080/003979111.2010.515355.

23. Karimi, N.; Oskooie, H.A.; Heravi, M.M.; Taherhamsi, L.Caroso’s Acid–Silica Gel–Catalyzed One-Pot Synthesis of 12-Aryl-8,9,10,12-tetrahydrobenzo[a] xanthene-11-ones. Synth Commun. 2010, 41, 307-312. https://doi.org/10.1080/00397910903537372.

24. Zhang, Z.H.; Zhang, P.; Yang, S.H.; Wang, H.J.; Deng, J. Multicomponent, solvent-free synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a]-xanthen-11-one derivatives catalyzed by cyanuric chloride J. Chem Sci 2010, 122, 427.

25. Pravin, V.S.; Bapurao, B.S.; Murlidhar, S.S. An Organocatalyzed Expedient Synthetic Route to Tetrahydrobenzo[a]xanthene-11-ones via Grinding Technique. Lett Org Chem. 2011, 8, 568-572. https://doi.org/10.2174/157017811797249308.

26. Wang, H.J.; Ren, X.Q.; Zhang, Y.Y.; Zhang, Z.H. Synthesis of 12-aryl or12-alkyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one derivatives catalyzed by Dodecatungstophosphoric acid. Braz. Chem. Soc. 2009, 20, 1939. https://doi.org/10.1590/S0103-50532009001000025.

27. Wang, R.-Z.; Zhang, L.F.; Cui, Z.S.Iodine-catalyzed synthesis of 12-aryl-8,9,10,12 tetrahydrobenzo[a]xanthen-11-one derivatives via multicomponent reaction. Synthetic Commun. 2009, 39, 2101. https://doi.org/10.1080/00397910802638511.
ruthenium chloride hydrate as a homogeneous catalyst. *Can J Chem.* 2011, 89, 623-627. [https://doi.org/10.1139/v11-042](https://doi.org/10.1139/v11-042).

29. Lakouraj, M.M.; Tashakkorian, H.; Rouhi, M. One-Pot Synthesis of Xanthones and Dianthrones Using Calix[4]arene Sulfonic Acid Under Solvent Free Condition. *Chem Sci Trans.* 2013, 2, 739-748.

30. Heravi, M.; Alinejhad, H.; Bakhtiari, K.; Oskooie, H. Sulfamic acid catalyzed solvent free synthesis of 10-aryl-7,7-dimethyl-6,7,8,10-tetrahydro-9H-[1,3]-dioxolo[4,5- b]xanthene-9-ones and 12-aryl-9,9-dimethyl-8,9,10,12-tetrahydro-11H-benzo[a]xanthen-11-ones. *Mol Diver* 2011, 15, 239. [https://doi.org/10.1007/s11030-009-9196-y](https://doi.org/10.1007/s11030-009-9196-y).

31. Nazeruddin, G.M.; Abdulkarim, M.A.; Al-Kadasi, Ultrasound Assisted One-Pot Synthesis of 12-Aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one Derivatives Using Chlorosulphonic Acid as a Catalyst under Solvent-free Conditions. *Research Journal Of Pharmaceutical, Biological And Chemical Sciences* 2011, 2, 71-76.

32. Nazeruddin, G.M.; Pandharpatte, M.S.; Mulani, K.B. Ultrasound Assisted One-Pot Synthesis of 12-Aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one Derivatives Using Chlorosulphonic Acid as a Catalyst under Solvent-free Conditions *Indian Journal of Chemistry* 2011, 50, 1532-1537.

33. Gao, S.; Tsai, C. H.; Yao, C.F. A Simple and Green Approach for the Synthesis of Tetrahydrobenzo[a]-xanthen-11-one Derivatives Using Tetrabutyl Ammonium Fluoride in Water. *Synlett* 2009, 6, 949. [https://doi.org/10.1055/s-0028-1088214](https://doi.org/10.1055/s-0028-1088214).

34. Li, J.; Lu, L.; Su, W.A new strategy for the synthesis of benzoanthrones catalyzed by proline trflate in water. *Tetrahedron Lett* 2010, 51, 2434. [https://doi.org/10.1016/j.tetlet.2010.02.149](https://doi.org/10.1016/j.tetlet.2010.02.149).

35. Foroughifar, N.; Mobinikhahledi, A.; Moghanian, H.Catalytic and Green Procedure for Synthesis of 12-Aryl- or 12-Alky1-8,9,10,12-Tetrahydrobenzo[a]xanthen-11-one Derivatives under Solvent-Free Conditions. *Int. J. Green Nanotech. Phy. Chem.* 2009, 1, 57. [https://doi.org/10.1080/19430870903119887](https://doi.org/10.1080/19430870903119887).

36. Safaei-Ghomi, J.; Ghasemzadeh, M.A.A Simple and Efficient Synthesis of 12-Aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones by ZnO Nanoparticles Catalyzed Three Component Coupling Reaction of Aldehydes, 2-Naphthol and Dimedone. *Afr. J. Chem.* 2014, 67, 27-32.

37. Hassankhani, A.; Mosaddegh, E.; Ebrahimimour, S.Y.H; SiW 12-O40 Catalyzed One-Pot Synthesis of 12-Aryl-8,9,10,12-tetrahydrobenzo[a] Xanthan-11-ones Under Solvent-Free Conditions. *E-Journal of Chemistry* 2012, 9, 786-790. [http://dx.doi.org/10.1155/2012/930251](http://dx.doi.org/10.1155/2012/930251).

38. Zhang, Z.H.; Wang, H.J.; Ren, X.Q.; Zhang, Y.Y. A facile and efficient method for synthesis of xanthone derivatives catalyzed by HBF4/SiO2 under solvent-free conditions. *Monatsh Chem* 2009, 140,1481. [https://doi.org/10.1007/s00706-009-0204-9](https://doi.org/10.1007/s00706-009-0204-9).

39. Khurana, J.M.; Magoo, D.PTSACatalyzed one-pot synthesis of 12-aryl-8,9,10,12 tetrahydrobenzo[a]xanthen-11-ones in ionic liquid and neat conditions. *Tetrahedron Lett* 2009, 50, 4777. [https://doi.org/10.1016/j.tetlet.2009.06.029](https://doi.org/10.1016/j.tetlet.2009.06.029).

40. Kumar, A.; Sharma, S.; Maurya, R.A.; Sarkar, J. Diversity Oriented Synthesis of Benzoanthene and Benzochromene Libraries via One-Pot, Three-Component Reactions and Their Anti proliferative Activity. *J. Comb. Chem.* 2010, 12, 20. [https://doi.org/10.1021/cc900143b](https://doi.org/10.1021/cc900143b).

41. Shitole, N.V.; Sapkal, S.B; Shingate, B.B.; Shingare, M.S.A Simple and Green Synthesis of Tetrahydrobenzo[a]-xanthen-11-one Using PEG-400 as Efficient and Recyclable Reaction Media. *Bull. Korean Chem. Soc.* 2011, 32, 35. [https://doi.org/10.5012/bkcs.2011.32.1.35](https://doi.org/10.5012/bkcs.2011.32.1.35).

42. Gao, S.; Tsai, C.H.; Yao, C.F.A Simple and Green Approach for the Synthesis of Tetrahydrobenzo[a]-xanthen-11-one Derivatives Using Tetrabutyl Ammonium Fluoride in Water. *Synlett* 2009, 949. [https://doi.org/10.1055/s-0028-1088214](https://doi.org/10.1055/s-0028-1088214).

© 2019 by the authors. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).