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Ultrasound-assisted green synthesis of functionalised xanthene derivatives: Advancing sustainable sonochemical strategies

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ABSTRACT

Xanthenes are an important class of heterocycles in medicinal chemistry due to their diverse pharmacological properties. These tricyclic aromatic compounds, characterised by a dibenzo[*b,e*]pyran core with an oxygen atom at their central position, have gained significant attention for their extensive applications. Beyond pharmaceuticals, xanthenes are widely used in textiles, food industries, electro-optical devices, dyes, and bioimaging agents. Xanthene derivatives, particularly 9-substituted xanthenes, exhibit a wide range of biological activities, including antiparasitic, antibacterial, antileishmanial, cytotoxic, neuroprotective, and photophysical effects, making them valuable in drug discovery. The xanthene scaffold is present in various bioactive natural compounds such as mulgravanols A and B, hermannol, (+)-myrtucommulone D, homapanicones A and B, blumeaxanthene II, and acrotrione. Clinically relevant xanthene-based drugs include propantheline bromide (antimuscarinic), methantheline (antispasmodic), and phloxine B (photosensitiser in antimicrobial therapy). Thus, various synthetic approaches have been developed for the construction of xanthenes, with ultrasound-assisted green methodologies gaining prominence. Ultrasound technique offers advantages over conventional methods, including higher yields, faster reaction rates, and improved selectivity under milder conditions. This review comprehensively explores the ultrasound-assisted synthesis of functionalised xanthene derivatives as an eco-friendly alternative. To the best of our knowledge, this is the first in-depth review focusing on the green methodology under ultrasound irradiation.

1. Introduction

Xanthenes are a significant class of heterocyclic aromatic compounds characterised by a dibenzo[*b,e*]pyran core structure [1]. These tricyclic systems feature an oxygen atom at their central position (Fig. 1) and share structural similarities with xanthones [2]. Xanthenes are widely present in synthetic bioactive molecules, natural products, and fluorescent dyes, and they hold considerable importance in drug discovery and development [3]. The majority of known xanthenes have been synthesised through artificial means, primarily employing cyclisation protocols involving appropriate precursor molecules, reflecting their significance as a prominent class of heterocyclic compounds in medicinal and synthetic organic chemistry [4]. Among the various synthetic approaches, the condensation of diverse aldehydes with 1,3-cyclohexanedione or 5,5-dimethyl-1,3-cyclohexanedione stands out as one of the most widely utilised methods for the preparation of xanthene derivatives [1–3]. Numerous methodologies and catalytic systems have been developed for the synthesis of xanthene derivatives over the past two decades [5]. A diverse range of catalysts has been documented, including tetra-*n*-butylammonium fluoride [6], $SmCl_3$ [7], $CeCl_3{\cdot}7H_2O$ [8], $Co(HSO_4)_2$ [9], TMSCl [10], ionic liquids [11], $NaHSO_4.SiO_2$ [12], β-CD-BSA [13], L-proline [14], CsF [15], $BiCl_3$ [16], 2,4,6-trichloro-1,3,5-triazine [17], $Zn(OAc)_2$ [18], Hal-Py-SO_3H [19], and various nanoparticles [20], among others. These catalysts have facilitated significant advancements in xanthenes synthesis.

Xanthene and its derivatives serve as valuable structural frameworks in natural products, industrial chemicals, bioactive compounds, and analytical reagents [21–24]. Several xanthenes have been isolated from natural sources, including the rare oxidised xanthenes, mulgravanols A and B, which were derived from the leaves of *Waterhousia mulgraveana*. Notably, mulgravanol A represents the first reported example of a complex xanthene structure featuring a methine-bridged phloroglucinol

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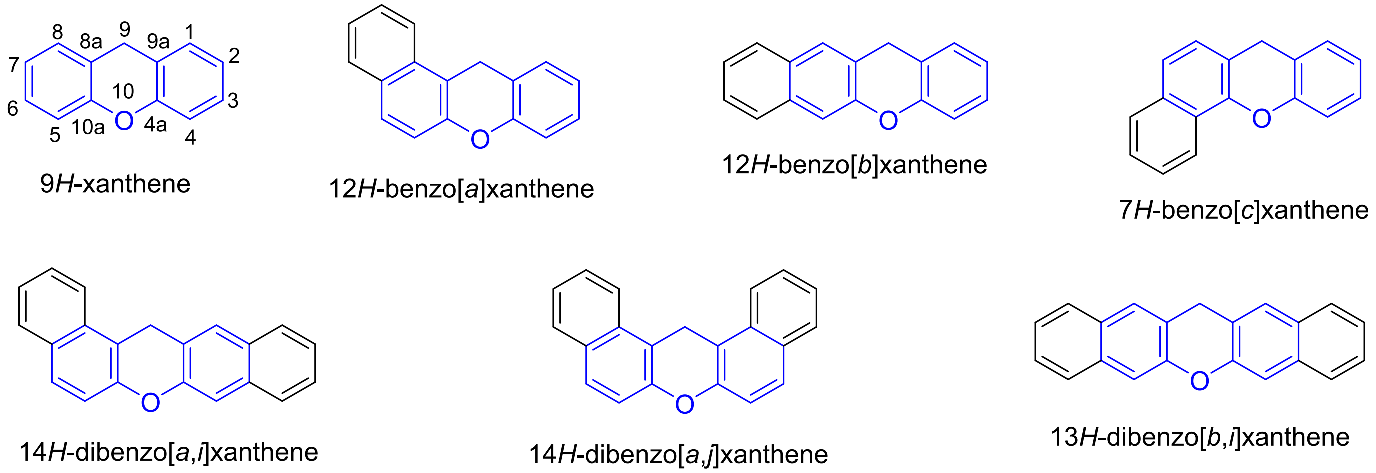
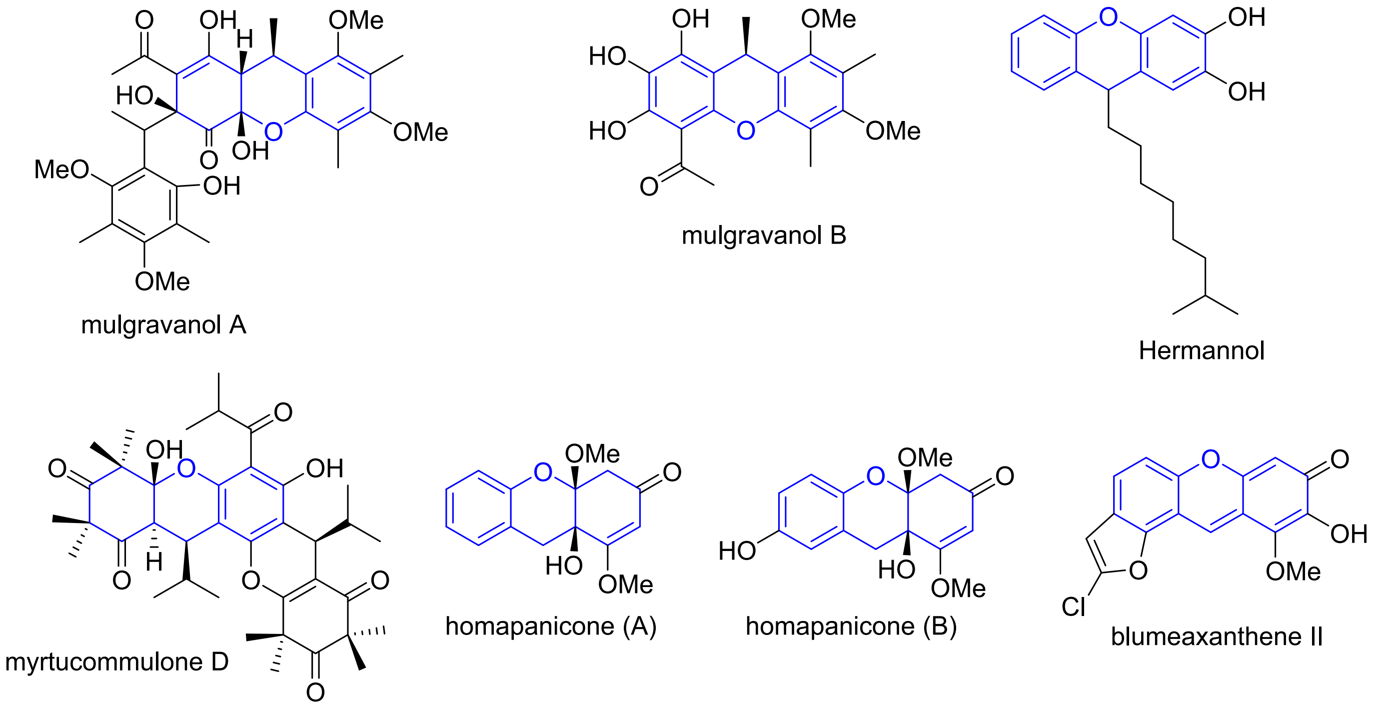


9*H*-xanthene 12*H*-benzo[*a*]xanthene 12*H*-benzo[*b*]xanthene 7*H*-benzo[*c*]xanthene 14*H*-dibenzo[*a*,*i*]xanthene 14*H*-dibenzo[*a*,*j*]xanthene 13*H*-dibenzo[*b*,*i*]xanthene

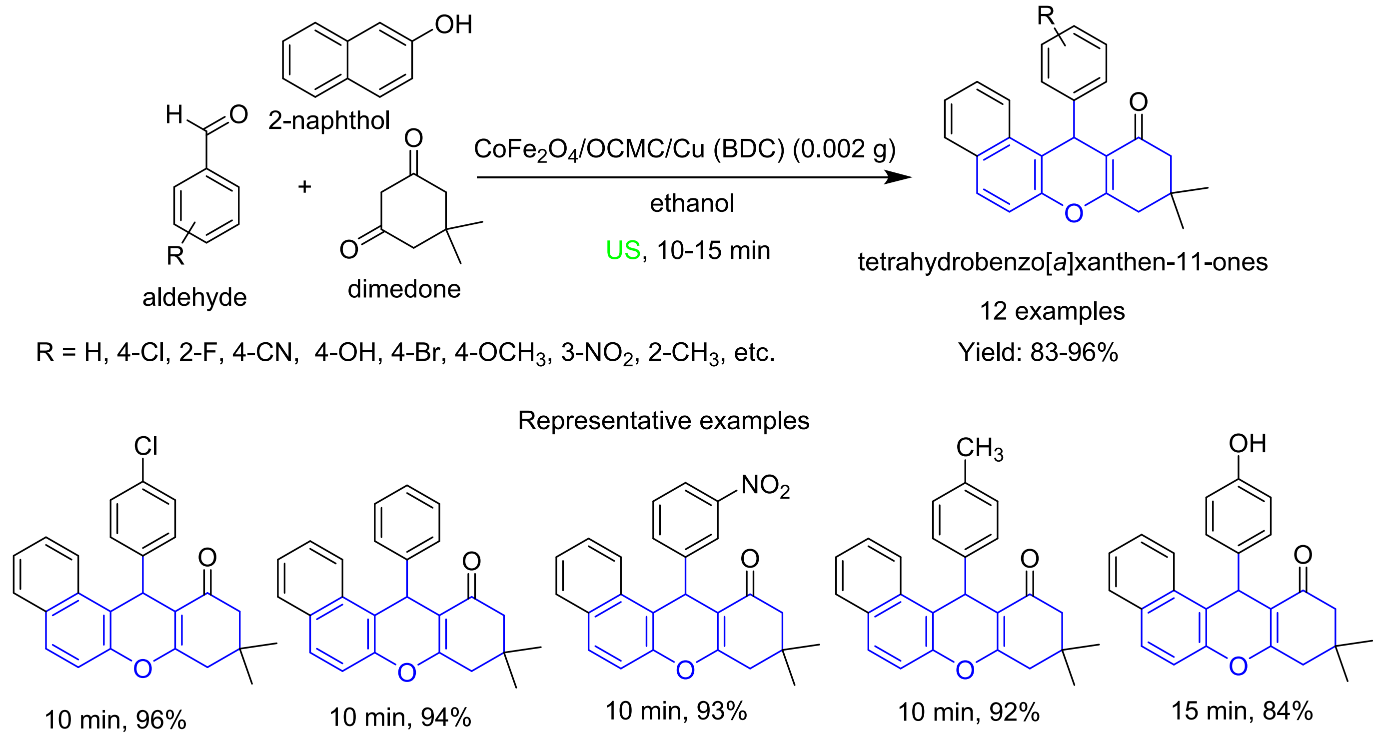
Fig. 1. Chemical structures of 9*H*-xanthene, 12*H*-benzo[*a*]xanthene, 12*H*-benzo[*b*]xanthene, 7*H*-benzo[*c*]xanthene, 14*H*-dibenzo[*a*,*i*]xanthene, 14*H*-dibenzo[*a*,*j*]xanthene and 13*H*-dibenzo[*b*,*i*]xanthene.



mulgravanol A mulgravanol B Hermannol myrtucommulone D homapanicone (A) homapanicone (B) blumeaxanthene II

Fig. 2. Xanthene scaffold: a core structure in bioactive natural products.

unit (Fig. 2) [25]. These naturally occurring xanthenes demonstrated notable anti-inflammatory properties, including the inhibition of nitric oxide production and TNF-α release in RAW 264.7 macrophages, with IC_{50} values ranging from 42 to 55 μM [25]. Additionally, a novel xanthene derivative, hermannol, was isolated from the roots of *Hermannia geniculate*, a flowering plant from the Malnaceae family. The roots of this plant are traditionally used in the treatment of various diseases [26]. This naturally occurring xanthene derivative, (9-(7-methyloctyl)-9*H*-xanthene-2,3-diol), demonstrated strong antioxidant activity against DPPH radicals, with an IC_{50} value of 0.29 ± 0.011 mg/mL. Furthermore, it exhibited superior inhibition of the 5-lipoxygenase enzyme, with an IC_{50} value of 0.67 ± 0.042 mg/mL, outperforming indomethacin, a standard nonsteroidal anti-inflammatory drug [26]. An uncommon angular benzopyrano[2,3-*a*]xanthene, (+)-myrtucommulone D, demonstrated promising antimicrobial activity against *Staphylococcus aureus* and MRSA, with a minimum inhibitory concentration (MIC) of 2 μg/mL [27]. It was isolated from *Myrtus communis* [27]. Additionally, two novel xanthene derivatives, homapanicones A and B, were extracted from the stems of *Homalium paniculiflorum* and are characterised by an oxidised aromatic B unit [28]. These two naturally occurring xanthene derivatives exhibited cytotoxic effects against several human cancer cell lines, with IC_{50} values ranging from 4.08 to 24.14 μM, comparable to those of cisplatin, a standard chemotherapy drug used as a positive control [28]. Additionally, the halogenated xanthene derivative, blumeaxanthene II, was isolated from the medicinal plant *Blumea riparia* and demonstrated cytotoxic activity against Bel-7404 cells *in vitro* [29]. In addition to their diverse biological activities, xanthenes exhibit antiviral [30], anti-psychotic [31], anti-analgesic [32], antiparasitic [33], antifungal [34], and anti-convulsant [35] properties. Xanthenes also occupy a significant role in the dye industry due to their exceptional photochemical and photophysical properties. Widely used commercial xanthene-based dyes include rhodamine B [36], fluorescein [37],



Scheme 1. Ultrasound-assisted synthesis of tetrahydrobenzo[*a*]xanthen-11-ones using a $CoFe_2O_4$/OCMC/Cu (BDC) catalyst.

erythrosine B [38], eosin Y [39], rose bengal [40], and uranine [41]. Xanthenes are utilised as sensitisers in photodynamic therapy [42], and xanthylium salts serve as catalysts in organic photoredox transformations [43,44]. 9-Substituted xanthene derivatives, particularly 9-arylxanthenes, represent an important class of heterocyclic compounds, exhibiting a wide range of biological activities, including antiparasitic, antibacterial, antileishmanial, cytotoxic, and neuroprotective effects [1,45,46], as well as notable photophysical properties [47]. Moreover, attractive xanthenes are significantly useful for bioimaging, which are substituted at various positions [48–50].

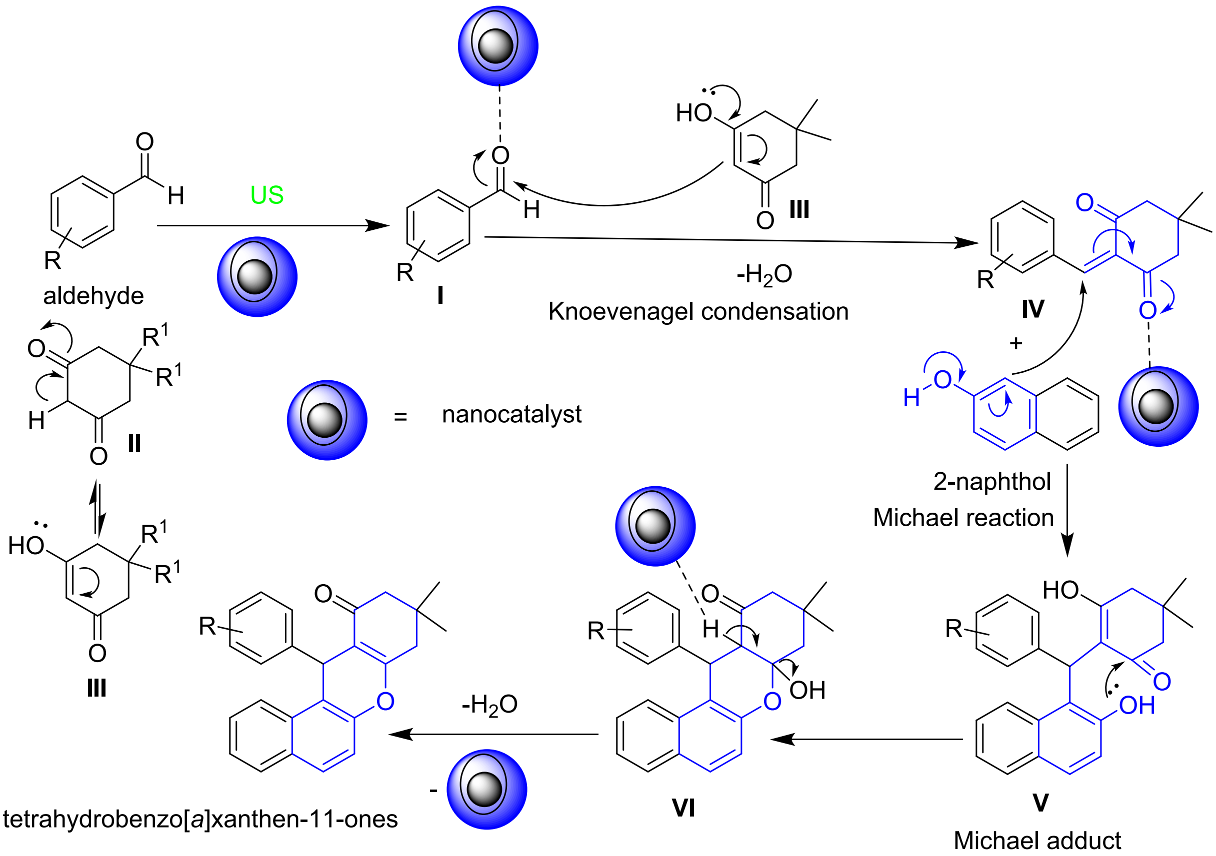
Ultrasound has become a prominent, environmentally friendly tool in green chemistry, and it has a significant role in constructing xanthenes [51]. Besides, photochemistry, electrochemistry, mechanochemistry, microwave-assisted methods, etc. have received attention in the synthesis of xanthene derivatives [52–54]. However, ultrasound-assisted sustainable synthesis offers numerous advantages, such as enhanced yields, higher selectivities, accelerated reaction rates, the production of purer products, and simpler experimental procedures, in contrast to conventional thermal methods and other methods [55]. Ultrasound can be employed as a green technology in different fields, including medicine, food processes, etc. [56–61]. Integrating sonochemistry with catalytic systems represents one of the most effective strategies for accelerating chemical reactions in the synthesis of bioactive compounds [62–68]. This synergistic approach offers significant advantages, including reduced reaction times, enhanced reaction rates, improved selectivities, higher yields, and higher purity of the desired products [69]. The combination of sonochemistry and catalysis provides numerous benefits across various fields, including pharmaceuticals, materials sciences, organic synthesis, and environmental chemistry [70–78]. We aim to provide a thorough overview of recent advancements in the sustainable synthesis of functionalised xanthene derivatives, which are pharmacologically significant *O*-heterocyclic compounds, under ultrasound irradiation with promising catalysts mainly. This approach is being presented for the first time, to the best of our knowledge. This review highlights the role of sonochemistry in the synthesis of various xanthene derivatives, including benzo[*a*]xanthenes, benzo[*b*]xanthenes, benzo[*c*]xanthenes, dibenzo[*a,i*]xanthenes, dibenzo[*b,i*]xanthenes, and octahydroxanthenes, under environmentally friendly conditions. These conditions comprise the use of nanocatalysts, environmentally benign catalysts, catalyst-free reactions, green solvents, solvent-free methods, and room-temperature processes. The review comprehensively covers relevant literature from 2008 to 2024.

2. Ultrasound-assisted green synthesis of functionalised xanthene derivatives: Applications and advancements

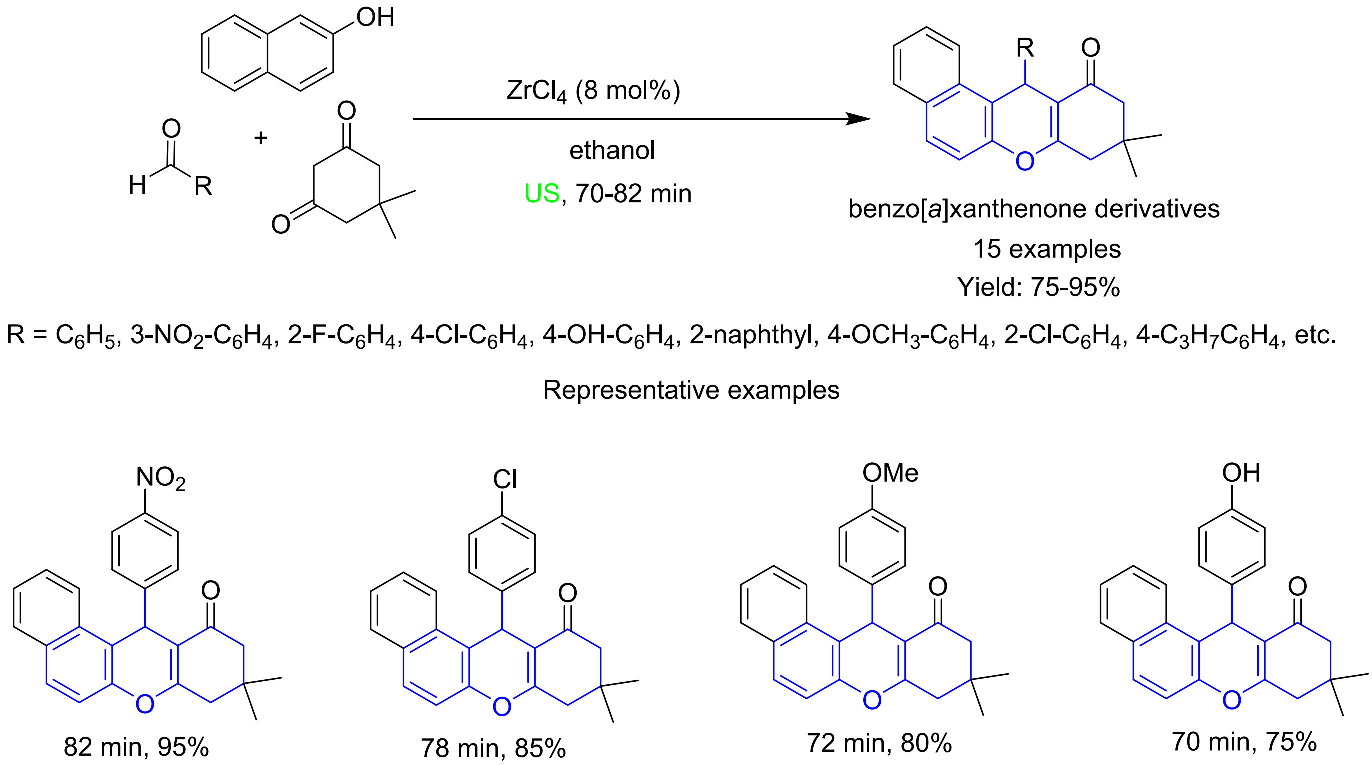
2.1. *Ultrasound-assisted synthesis of benzo[a]xanthenes*

2.1.1. *$CoFe_2O_4$/OCMC/Cu (BDC) nanocomposites as a catalyst*

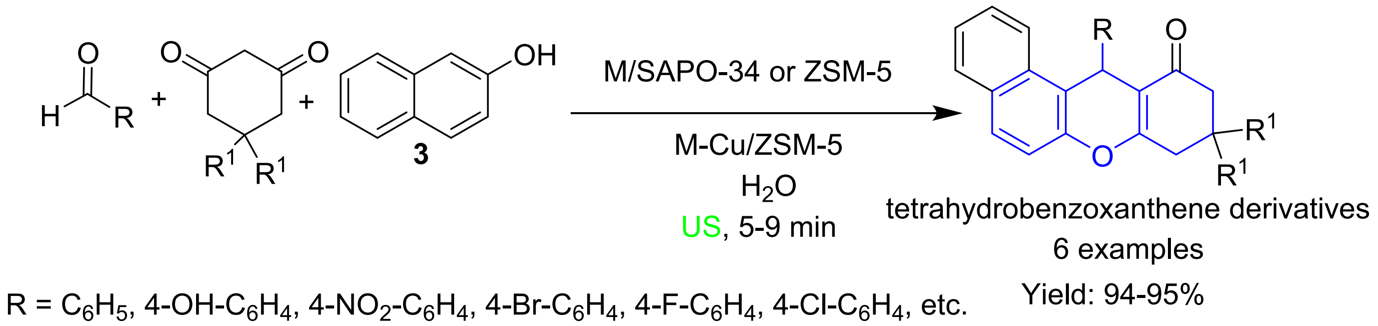
One of the key types of magnetic nanoparticles (MNPs) is metal ferrite nanoparticles, including bimetal oxide magnetic nanoparticles, which have diverse applications in catalysts, biomedicine, pollutant sensing, data storage, and microfluidics [79–81]. Among these, cobalt ferrite ($CoFe_2O_4$) MNPs have garnered significant research attention due to their exceptional properties, including chemical stability, high magnetisation, and mechanical hardness [82]. Ghasemzadeh et al. developed an environmentally friendly method for synthesising tetrahydrobenzo[*a*]xanthen-11-ones in high yields (83–96 %) through a one-pot multicomponent reaction. This reaction involved various aldehydes (1 mmol), dimedone (1 mmol), and 2-naphthol (1 mmol) in a solvent mixture of ethanol (2.5 mL) and water (2.5 mL), using $CoFe_2O_4$/OCMC/Cu (BDC) nanocomposites (0.002 g) as an effective catalyst. The reaction was carried out under sonication at a 30 kHz frequency and room temperature (RT) for 10–15 min (Scheme 1) [83]. The nanocatalyst was characterised using various spectroscopy methods, including FT-IR (Fourier-transform infrared spectroscopy), XRD (X-ray diffraction), BET (N_2 adsorption–desorption isotherm), SEM (scanning electron microscopy), and EDX (energy-dispersive X-ray). Additionally, the synthesised xanthene derivatives were characterised using ^1H NMR and ^{13}C NMR spectroscopy. The nanocatalyst demonstrated good reusability, retaining its catalytic activity for up to six cycles without



Scheme 2. Proposed mechanism for the synthesis of tetrahydrobenzo[*a*]xanthen-11-ones using $CoFe_2O_4$/OCMC/Cu (BDC) catalyst.



Scheme 3. Ultrasound-assisted synthesis of benzo[*a*]xanthenone derivatives using $ZrCl_4$ catalyst.



Scheme 4. Ultrasound-assisted synthesis of xanthenes using Fe-Cu/ZSM-5 catalyst.

significant loss in performance. It could be easily separated from the reaction mixture using an external magnet [83].

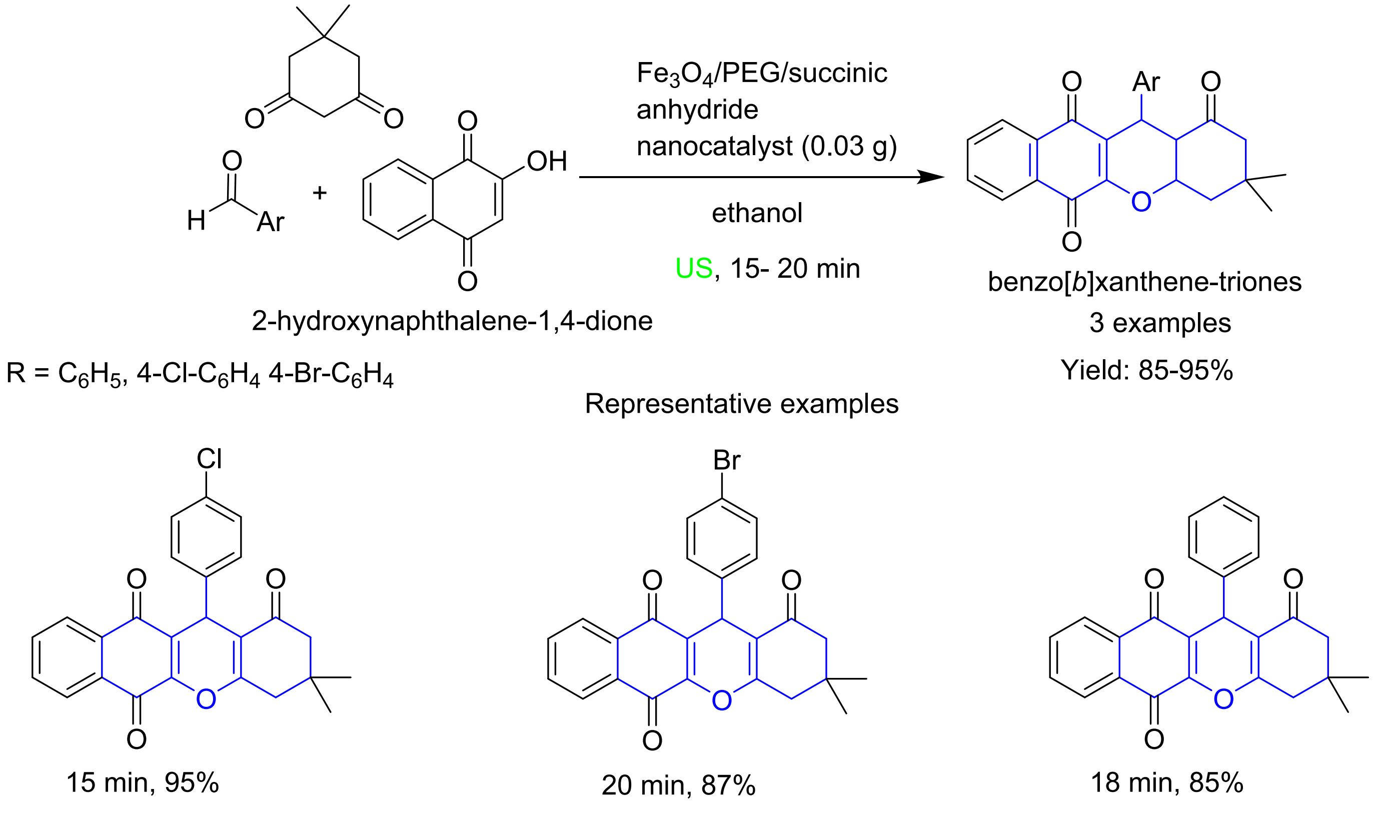
A proposed mechanism for the synthesis of tetrahydrobenzo[*a*]xanthen-11-ones in the presence of $CoFe_2O_4$/OCMC/Cu (BDC) nanocatalyst is outlined in Scheme 2. It is hypothesised that the BDC nanocatalyst enhances the electrophilicity of the carbonyl groups in the aldehydes through strong coordination bonds. In this initial step, the nanocatalyst acts as a Lewis acid, facilitating the reaction [83]. The reaction mechanism involves the nucleophilic addition of dimedone (**III**) to the carbonyl group (**I**), followed by dehydration to form an α,β-unsaturated ketone (**IV**) via a Knoevenagel condensation. Then, 2-naphthol, acting as a Michael donor, attacks the Michael acceptor (**IV**), resulting in the formation of a Michael adduct (**V**) through the formation of a carbon–carbon bond. Finally, the desired xanthenes derivatives are obtained through the intramolecular cyclisation of intermediate (**V**), followed by dehydration of intermediate (**VI**) [83].

2.1.2. Zirconium (IV) chloride as a catalyst

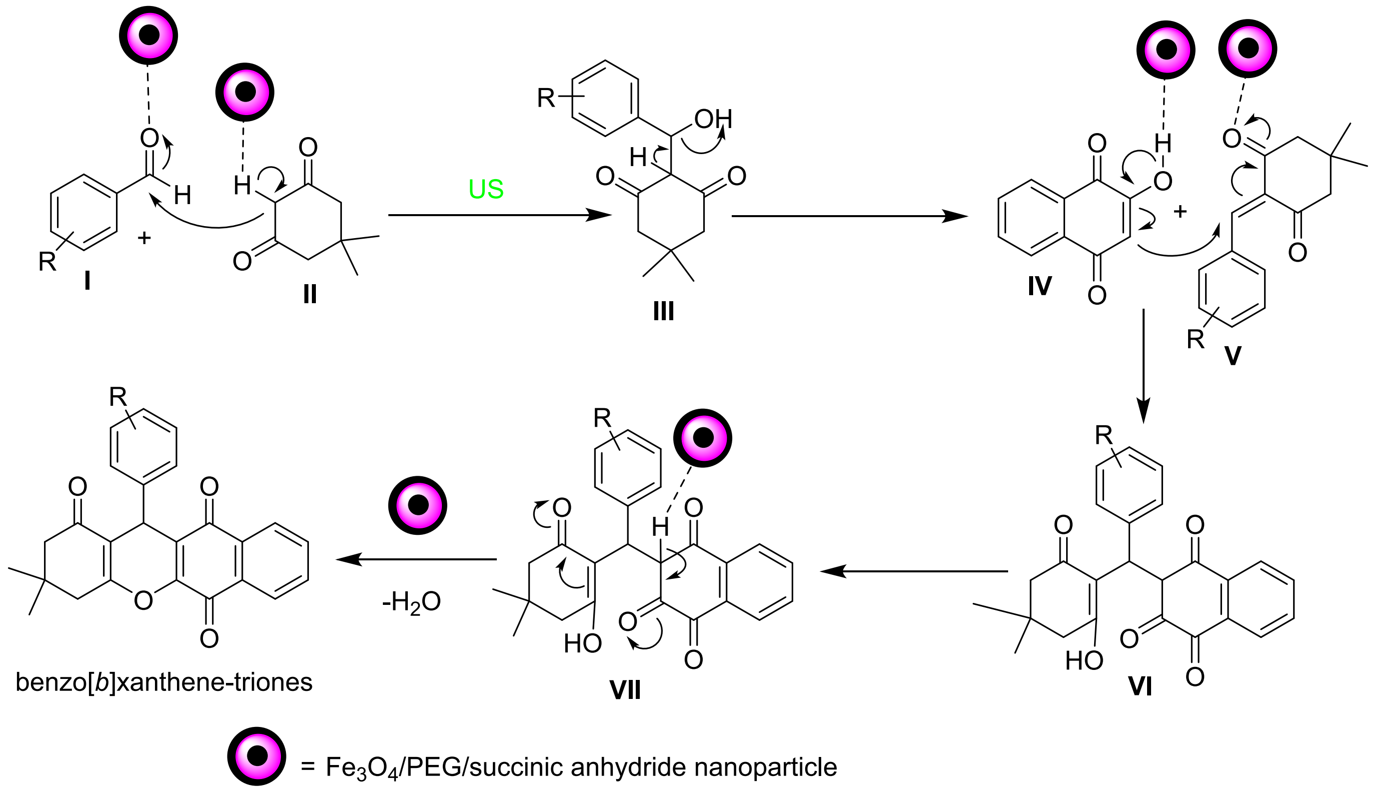
Zirconium (IV) chloride ($ZrCl_4$) is commonly recognised as an inexpensive, environmentally friendly, widely accessible, and low-toxicity catalyst (LD_{50}: 1688 mg/kg) [84]. Amrollahi et al. introduced an efficient method for synthesising functionalised xanthene derivatives with high yields (75–95 %) via a three-component reaction involving 2-naphthol, dimedone, and aldehydes. This process employed $ZrCl_4$ as an eco-friendly catalyst and utilised ultrasonic irradiation as a sustainable technique, with reaction times ranging from 70 to 82 min (Scheme 3) [85]. Various solvents, including H_2O, MeCN, CH_2Cl_2, and CH_3COOEt, as well as solvent-free conditions, were explored in this study. Among these, C_2H_5OH proved to be the most effective solvent for this transformation under ultrasonic irradiation [85].

2.1.3. Fe-Cu/ZSM-5 as a catalyst

Zeolites have attracted significant attention in the synthesis of specialty and fine chemicals due to their exceptional thermal stability, structural diversity, adjustable acidity, and precise pore dimensions [86,87]. Multicomponent reactions utilising green catalysts in aqueous solutions represent a promising approach for advancing sustainable organic synthesis, offering advantages such as reduced reaction steps, minimised waste generation, and lower energy requirements [88,89]. Safa et al. demonstrated the synthesis of various xanthenes using zeolite-

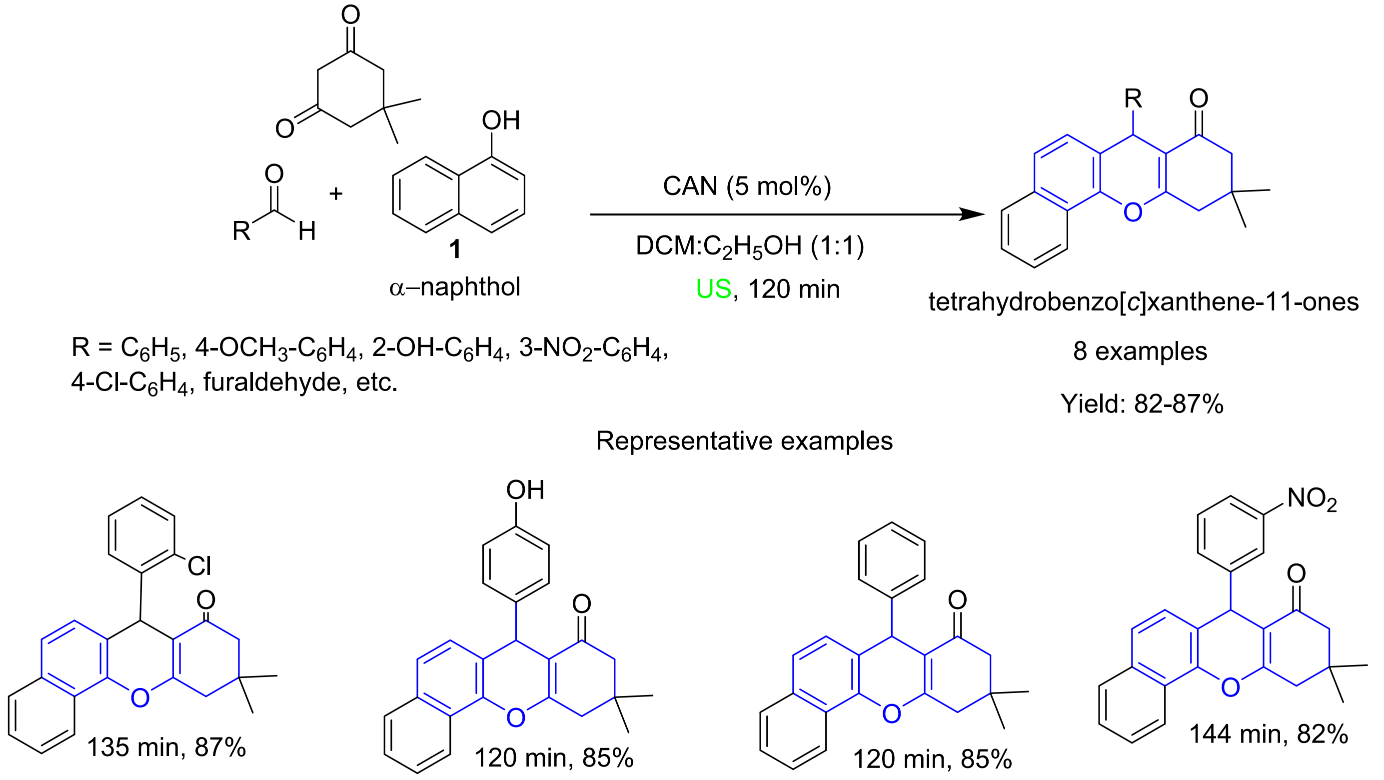


Scheme 5. Ultrasound-assisted synthesis of benzo[*b*]xanthenes using Fe_3O_4/PEG/succinic anhydride nanocatalyst.

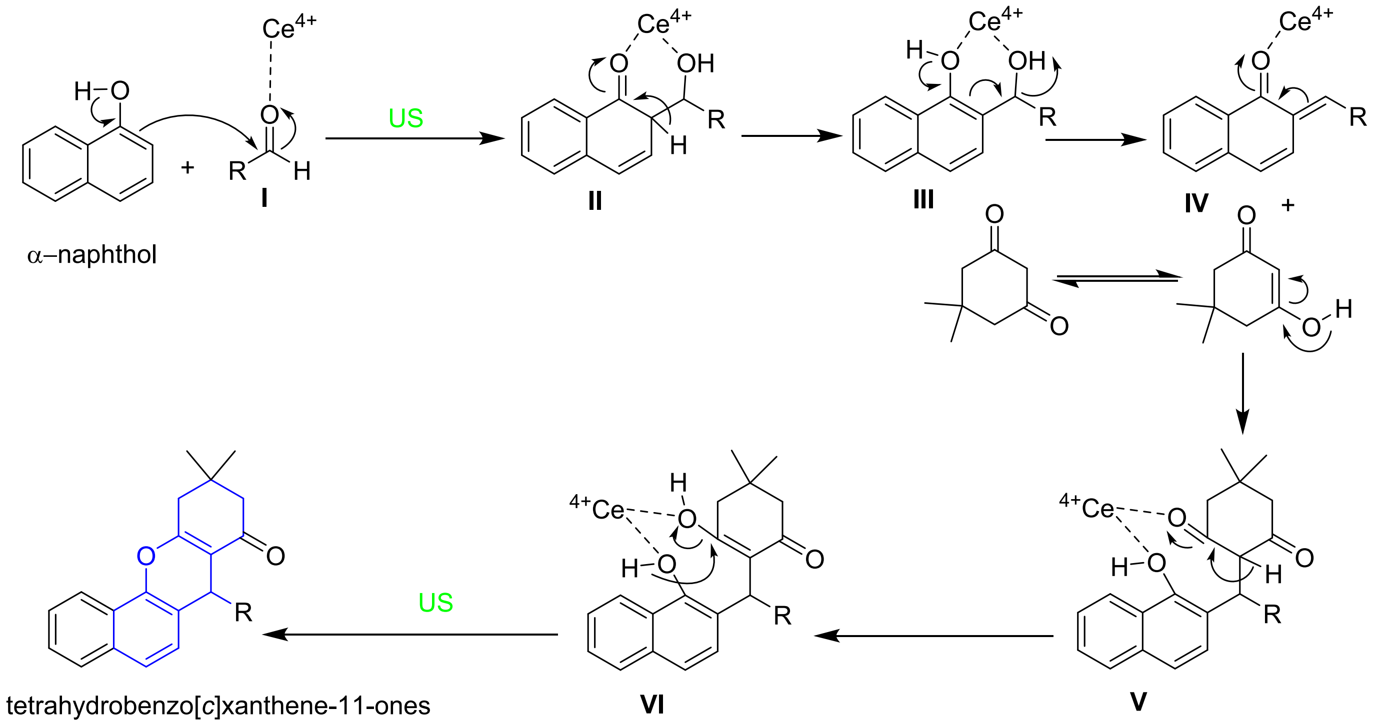


Scheme 6. Proposed mechanism for the synthesis of benzo[*b*]xanthene-triones using Fe_3O_4/PEG/succinic anhydride nanoparticles.

supported transition metal catalysts under ultrasound irradiation, employing ultrasound as an environmentally friendly energy source at 40 % processor power (Scheme 4) [90]. In this one-pot synthesis, Fe-Cu/ZSM-5 demonstrated the highest catalytic activity as a heterogeneous catalyst (3 wt% bimetallic composition) in an aqueous medium. The reported approach offers a simple and environmentally friendly method for reacting diverse aldehydes, cyclic 1,3-diketones, and 2-naphthol under ambient temperature conditions [90].



Scheme 7. Ultrasound-assisted synthesis of benzo[*c*]xanthenes using CAN catalyst.



Scheme 8. Proposed mechanism for the synthesis of benzo[*c*]xanthenes using CAN.

2.2. *Ultrasound-assisted synthesis of benzo[b]xanthenes*

2.2.1. *Fe_3O_4/PEG/succinic anhydride as a catalyst*

Magnetic nanoparticles play a key role in catalysis and synthesis [91,92], as their surfaces can be readily functionalised through appropriate surface modifications [93]. This adaptability enables the incorporation of a wide range of beneficial functional groups [94]. Safaei-Ghomi developed an efficient and eco-friendly method for synthesising benzo[*b*]xanthene-triones with high yields (85–95 %) via a multicomponent reaction involving benzaldehydes (1 mmol), 2-hydroxynaphthalene-1,4-dione (1 mmol), and dimedone (1 mmol). The reaction employed Fe_3O_4/PEG/succinic anhydride nanocatalyst (0.03 g) as a green catalyst in ethanol (10 mL) under sonication at 60 W power for 15–20 min (Scheme 5) [95]. The Fe_3O_4/PEG/succinic anhydride nanocatalyst was initially synthesised and subsequently characterised using various techniques, including SEM (scanning electronic microscopy), XRD (X-ray diffraction), VSM (vibrating sample magnetometer), DLS (dynamic laser scattering), TGA (thermal gravimetric analysis), and FT-IR spectroscopy [95].

A proposed mechanism for the formation of benzo[*b*]xanthene-triones using the Fe_3O_4/PEG/succinic anhydride nanoparticle catalyst is shown in Scheme 6 [95]. This mechanism involves the activation of the carbonyl group by the nanocatalyst, followed by Knoevenagel condensation, Michael addition, and cyclisation process, aligning with the steps outlined in Scheme 2 [83].

2.3. *Ultrasound-assisted synthesis of benzo[c]xanthenes*

2.3.1. *Ceric ammonium nitrate as a catalyst*

The synthesis of tetrahydrobenzo xanthene-11-ones has been achieved starting from β-naphthol. However, a literature review indicates that these xanthene-11-ones have not been synthesised from α-naphthol, as the electron density at the β-position of α-naphthol is insufficient for the formation of the corresponding *ortho*-Quinone Methides (a highly reactive chemical motif), under similar conditions (Scheme 8) [96,97]. Pasha et al. successfully synthesised tetrahydrobenzo[*c*]xanthenes-11-ones from α-naphthol (Scheme 7) [98]. The multicomponent reaction involved aromatic aldehydes (2 mmol), α-naphthol (2 mmol), and dimedone (2 mmol) in the presence of ceric ammonium nitrate (CAN) (5 mol%) as a catalyst, using a DCM:C_2H_5OH (1:1, 2 mL) solvent mixture. The reaction was carried out in an ultrasonic bath at 26 °C, resulting in the desired tetrahydrobenzo[*c*]xanthene-11-ones in good yields (82–87 %) [98].

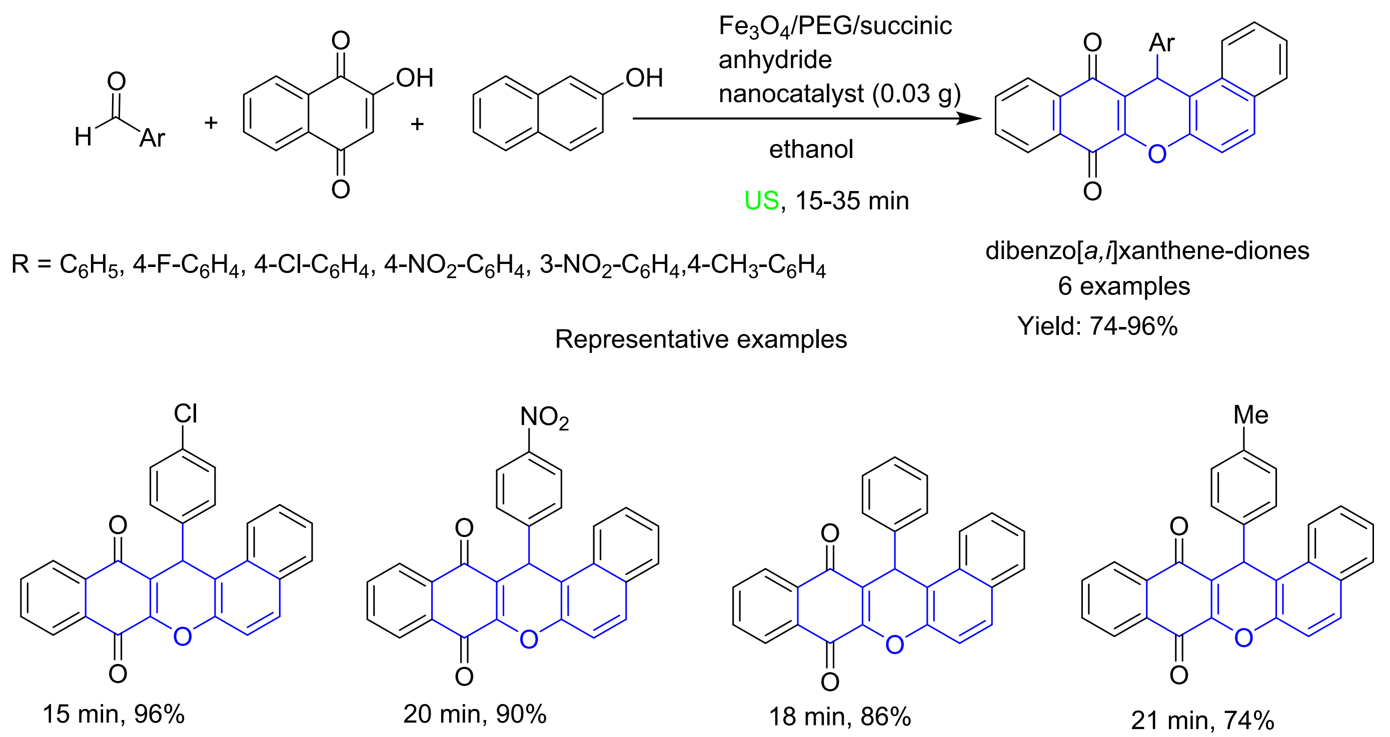
Scheme 8 presents a plausible mechanism for the synthesis of benzo[*c*]xanthenes using CAN catalyst under sonication [98]. Ultrasonic cavitation generates the shear forces and jet streams near the surface of the vessel, which, combined with the catalyst, may activate the relatively inert α-naphthol by facilitating the sonolysis of the O–H bond. The CAN catalyst activates the carbonyl group of the aromatic aldehyde, enabling it to react with the activated α-naphthol to form the corresponding *o*-QM intermediate. Subsequently, the active methylene group of dimedone reacts with the *o*-QM intermediate, leading to the formation of tetrahydrobenzo[*c*]xanthene-11-one, with the elimination of a water molecule.

2.4. *Ultrasound-assisted synthesis of dibenzo[a,i]xanthenes*

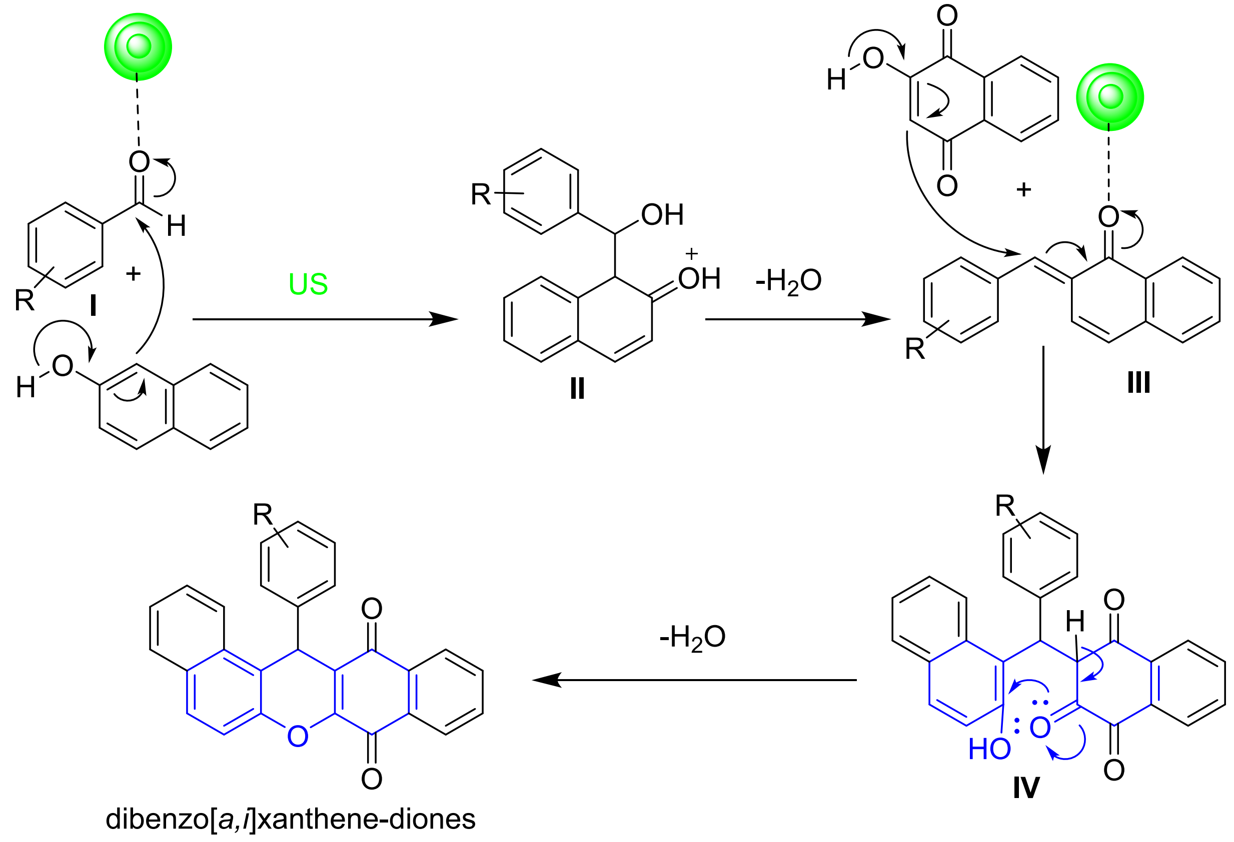
2.4.1. *Fe_3O_4/PEG/succinic anhydride as a magnetic nanocatalyst*

Heterocyclic compounds have a significant impact across various fields of science and technology [99,100]. The synthesis of xanthene derivatives, particularly dibenzo xanthenes, is a crucial area in organic chemistry due to their notable biological activities, especially their antiviral potential [101]. As a result, the development of straightforward methods for the synthesis of dibenzo xanthenes is currently of considerable interest. To address the limitations of traditional methods, the exploration of an effective approach utilising ultrasound and nanocatalyst for the synthesis of dibenzo[*a,i*]xanthene-diones is increasingly preferred. This technique offers advantages such as cost and energy savings, as well as higher yields and faster reaction rates compared to conventional methods [102,103].

Safaei-Ghomi et al. developed an eco-friendly method for synthesising dibenzo[*a,i*]xanthene-dione derivatives with good yields (74–96 %) using the Fe_3O_4/PEG/succinic anhydride nanocatalyst under ultrasound irradiation, which serves as a non-polluting energy source



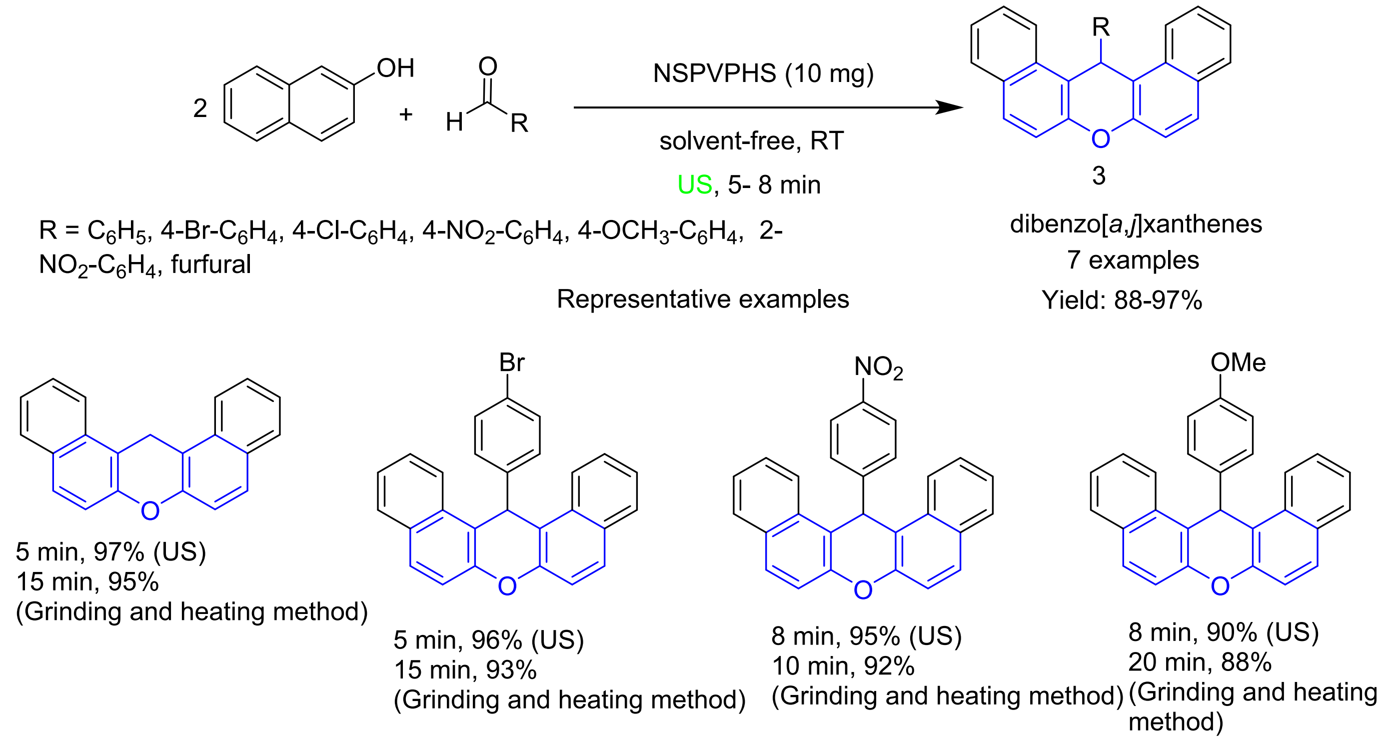
Scheme 9. Ultrasound-assisted synthesis of dibenzo[*a,i*]xanthene derivatives using Fe_3O_4/PEG/succinic anhydride nanocatalyst.



Scheme 10. Proposed mechanism for the synthesis of dibenzo[*a,i*]xanthene-diones using nanocatalyst.

(Scheme 9) [95]. This protocol involves a multicomponent reaction between various benzaldehydes (1 mmol), 2-hydroxynaphthalene-1,4-dione (1 mmol), and 2-naphthol (1 mmol) in ethanol (10 mL), utilising the magnetic Fe_3O_4/PEG/succinic anhydride nanocatalyst (0.03 g) under sonication at 60 W power for 15–35 min [95].

A plausible mechanism for the synthesis of dibenzo[*a,i*]xanthene-



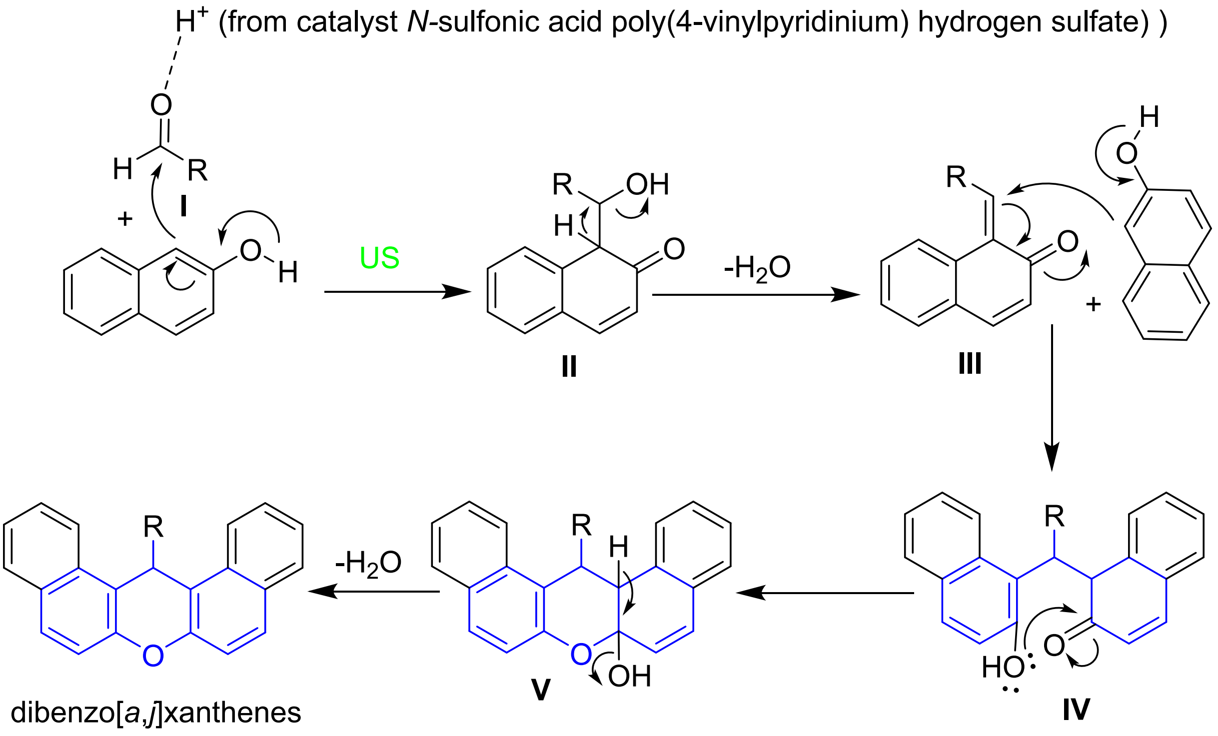
Scheme 11. Ultrasound-assisted synthesis of xanthene derivatives using NSPVPHS catalyst.

diones is depicted in Scheme 10.

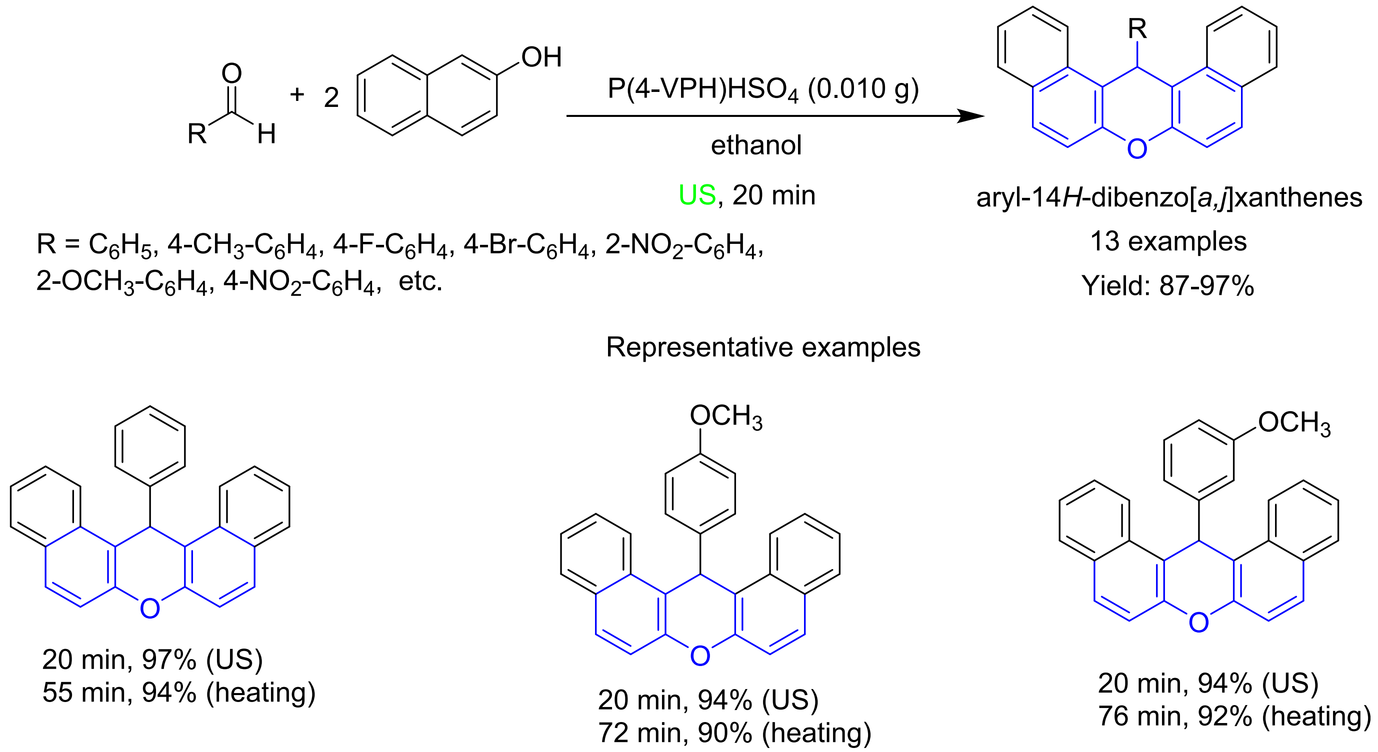
2.5. *Ultrasound-assisted synthesis of dibenzo[a,j]xanthenes*

2.5.1. *N-sulfonic acid poly(4-vinylpyridinium) hydrogen sulfate as a catalyst*

Heterogeneous catalysts play a key role in industrial chemical manufacturing [104,105]. Their utilisation in dry media not only improves the yields of target products but also facilitates the conversion or removal of undesirable byproducts, eliminating the need for tedious separation processes [106]. In organic chemistry, supported reagents have received significant attention due to their reusability and ease of recovery from the reaction mixtures [107]. Among these, poly(4-vinylpyridine) cross-link with divinylbenzene P(4-VP) has emerged as

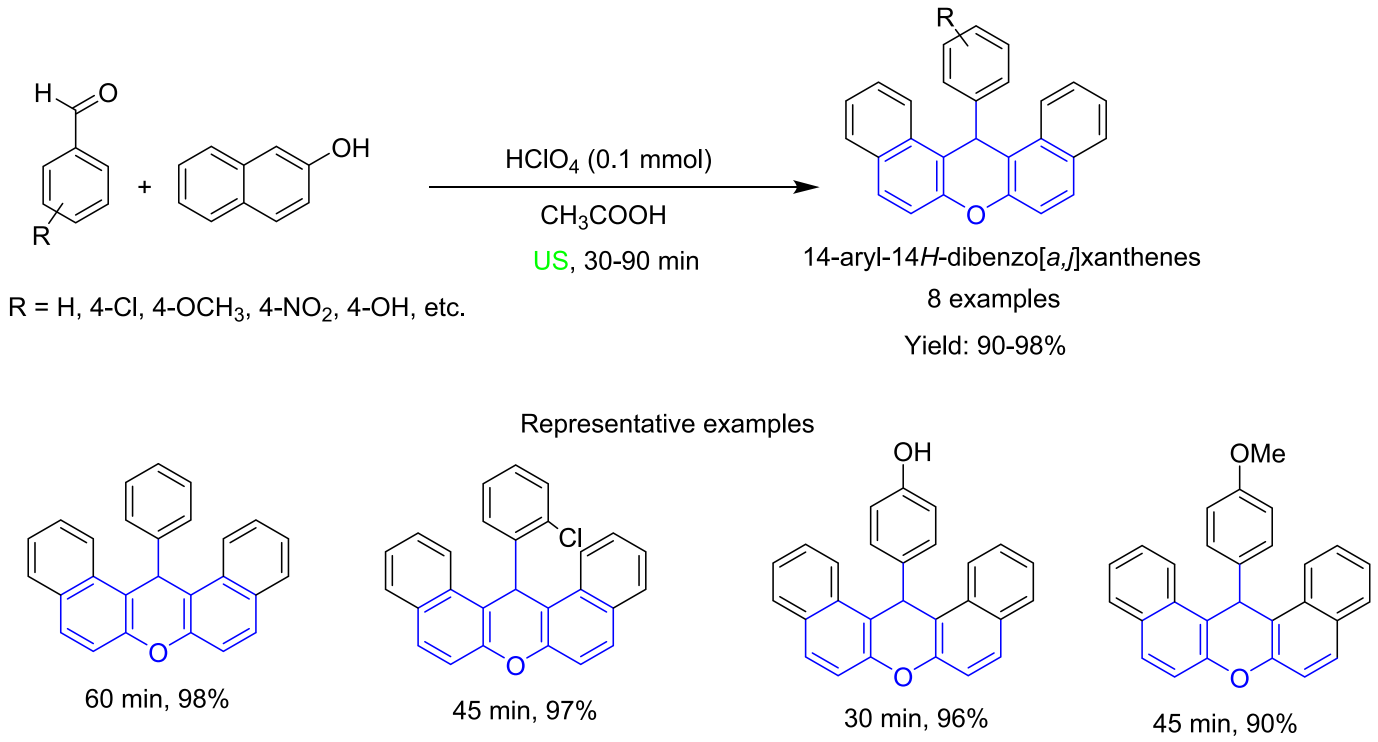


Scheme 12. Proposed mechanism for the ultrasound-assisted synthesis of dibenzo[*a,i*]xanthene-diones using NSPVPHS.

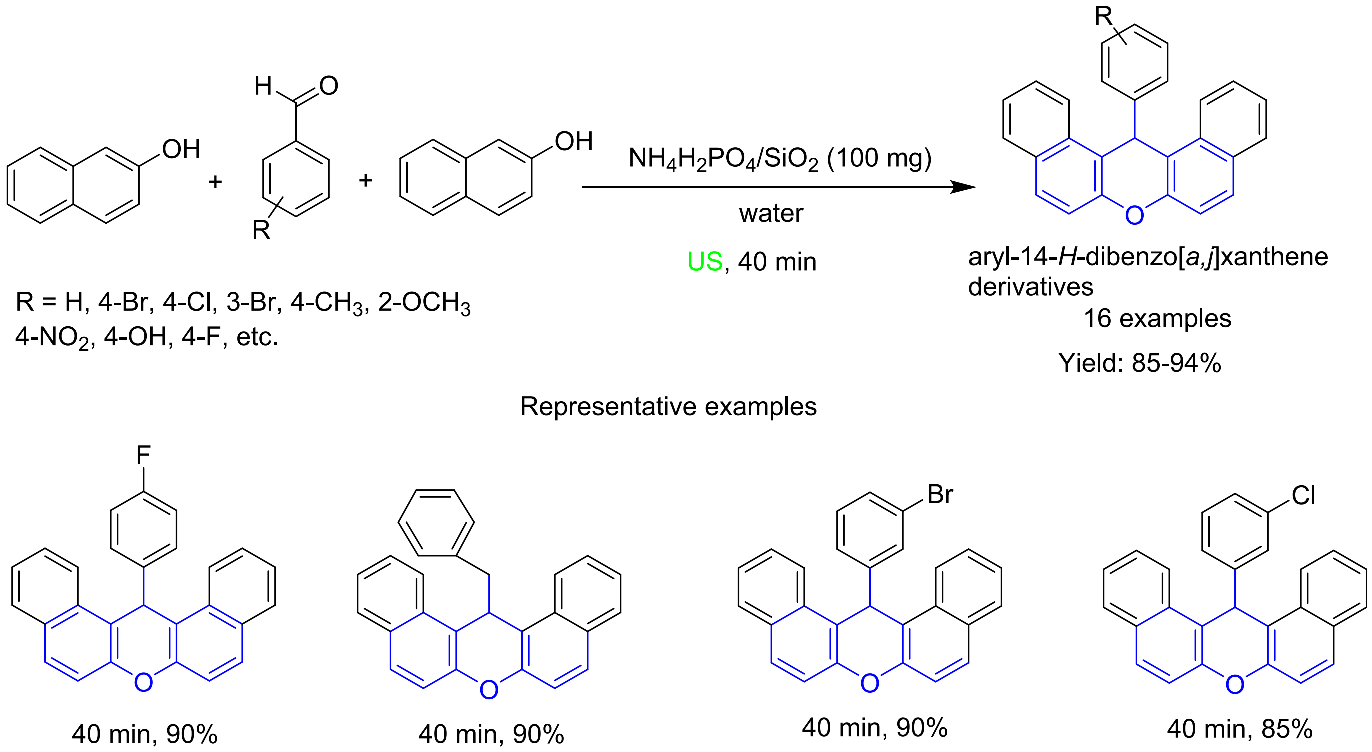


Scheme 13. Ultrasound-assisted synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes using P(4-VPH)HSO_4 catalyst.

a widely favored heterogeneous polymeric support in organic synthesis [108]. Khaligh et al. reported a study aimed at enhancing the synthesis of various xanthene derivatives by reacting aldehyde (1 mmol) with 2-naphthol (2 mmol) in the presence of NSPVPHS (*N*-sulfonic acid poly (4-vinylpyridinium) hydrogen sulfate) as a heterogeneous solid acid catalyst (10 mg). The reaction was conducted at room temperature under solvent-free conditions, utilising ultrasound irradiation as a green energy source (Scheme 11) [109]. The reaction between 4-chloro-benzaldehyde (1 mmol) and 2-naphthol (2 mmol) was used as a model to evaluate the optimised reaction conditions with various solvents. The superior catalytic performance of *N*-sulfonic acid poly(4-vinylpyridinium) hydrogen sulfate under solvent-free (neat) conditions compared to solvents such as MeCN, PhMe, THF, EtOH, DCM, Et_2O, and H_2O cany be attributed to the enhanced electrostatic interactions of



Scheme 14. Ultrasound-assisted synthesis of dibenzo[*a,j*]xanthenes using $HClO_4$ catalyst.



Scheme 15. Ultrasound-assisted synthesis of 14-*H*-dibenzo[*a,j*]xanthene derivatives using $NH_4H_2PO_4/SiO_2$ catalyst.

ionic aggregates in the solid state, which facilitate substrate activation. This protocol was also implemented using the grinding and heating method, achieving yields of 78–95 % within 10–25 min. However, ultrasound irradiation demonstrated superior efficiency, providing higher yields (88–97 %) in a significantly shorter time (5–8 min). This approach highlights the critical role of the hydrogen sulfate anion in driving the one-pot multi-component reactions. Furthermore, the catalyst was easily recovered through simple filtration and reused for up to five cycles without any significant decline in catalytic activity [109].

A plausible mechanism for the ultrasound-assisted synthesis of dibenzo[*a,j*]xanthenes catalysed by NSPVPHS is illustrated in Scheme 12. Notably, the acid sites of the catalyst, combined with the energy supplied by ultrasonic waves, provide the necessary activation energy for the reactants to overcome the transition state barrier at RT [109].

2.5.2. Poly(4-vinylpyridinium)hydrogen sulfate as a solid acid catalyst

Solid acids offer several advantages over liquid acids, including the absence of effluent disposal issues, reduced corrosion risks, and a lower environmental impact [110]. Additionally, solid acids can be easily separated from liquid products and reused, enhancing their practicality and sustainability [111]. Consequently, the replacement of conventional homogeneous catalysts with solid acids has attracted increasing attention in both industry and chemistry [112]. In this context, Khaligh synthesised various 14-aryl-14*H*-dibenzo[*a,j*]xanthenes using solid acid catalyst $P(4\text{-}VPH)HSO_4$ under traditional heating at 100 ^{0}C and ultrasound irradiation, as illustrated in Scheme 13 [113]. The described method provides an environmentally friendly approach for the condensation of various aryl aldehydes with 2-naphthol in the presence of $P(4\text{-}VPH)HSO_4$ (0.010 g) as an inexpensive catalyst. The reaction, conducted in ethanol (10 mL) under ultrasound irradiation, efficiently produces the desired dibenzo[*a,j*]xanthene derivatives with good yields (87–97 %) in a short reaction time of 20 min [113].

2.5.3. Perchloric acid as a catalyst

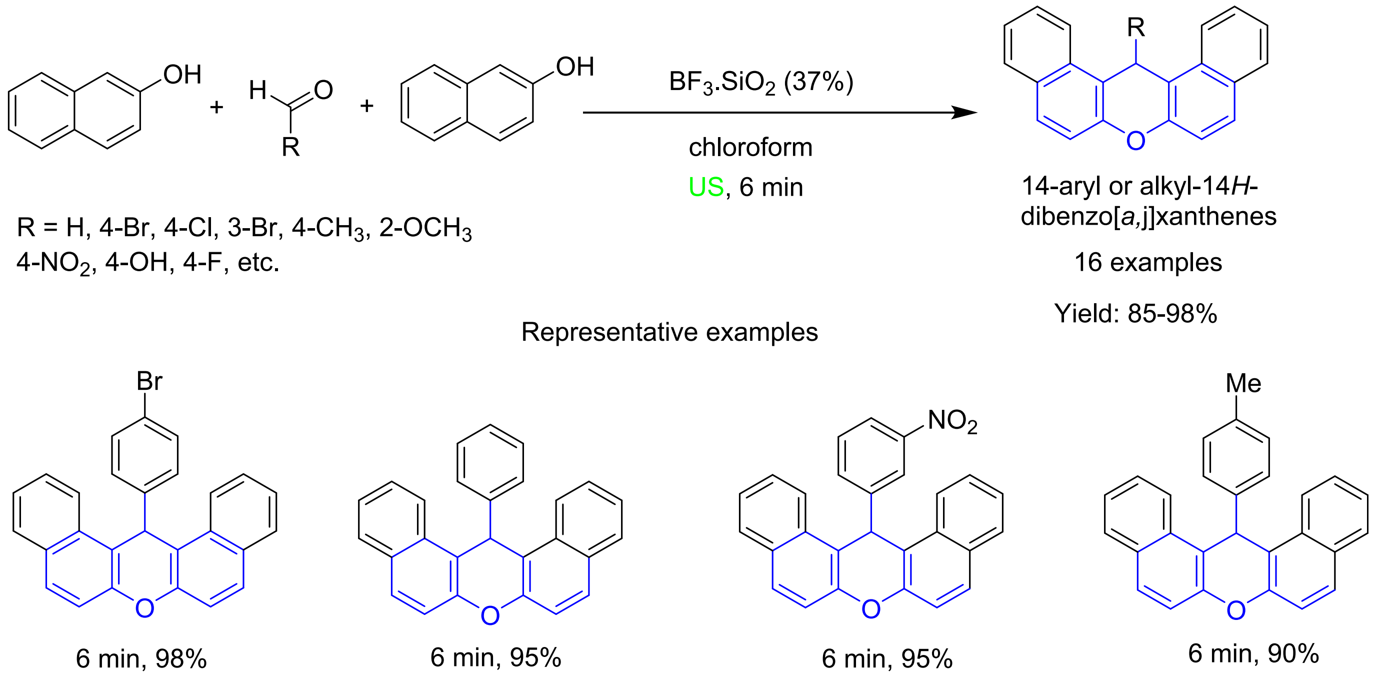
Aryl-14*H*-dibenzo[*a,j*]xanthenes have received increasing attention due to their broad spectrum of biological activities [114,115]. Perchloric acid ($HClO_4$) has been utilised as a key catalyst in the synthesis of xanthenes, highlighting its importance in these reactions [116]. Nazeruddin et al. reported a green synthesis of 14-aryl-14*H*-dibenzo[*a,j*] xanthenes using a catalytic amount of $HClO_4$ (0.1 mmol) under mild reaction conditions (Scheme 14) [117]. The ultrasound-assisted condensation reaction involved aryl aldehydes and β-naphthol in glacial acetic acid, yielding the desired xanthene derivatives in good to excellent yields (90–98 %) within 30–90 min [117].

2.5.4. Silica-supported ammonium dihydrogen phosphate as a catalyst

In organic synthesis, $NH_4H_2PO_4/SiO_2$ has become an important catalyst due to its low cost, low toxicity, superior catalytic activity, and ease of handling compared to traditional catalysts [118]. Mahdavinia et al. developed an eco-friendly synthetic method for the preparation of aryl-14-*H*-dibenzo[*a,j*]xanthene derivatives, utilising $NH_4H_2PO_4/SiO_2$ (100 mg) as an efficient catalyst (Scheme 15) [119]. The ultrasound-assisted condensation of various aldehydes (1 mmol) with β-naphthol (2 mmol) in water (10 mL) as an environmentally friendly solvent was carried out. This eco-sustainable approach resulted in good yields (85–94 %) and significantly reduced reaction times (40 min). Aromatic aldehydes with both electron-donating and electron-withdrawing groups produced good yields of the desired products under milder conditions. The solid catalyst was easily separated by simple filtration and could be reused for up to five cycles without a significant loss of activity [119].

2.5.5. Silica-supported boron trifluoride as a catalyst

Various homogeneous acidic catalysts, such as HCl, H_2SO_4, and BF_3, are commonly used in organic transformations. However, these catalysts present several drawbacks, including toxicity, volatility, corrosiveness, and the generation of large amounts of waste [120]. In contrast, silica-supported boron trifluoride, $BF_3.SiO_2$ (a solid superacid) offers improved accessibility of reactants to active sites and is easier to handle, making it an efficient bench-top catalyst [121]. Mirjalili et al. reported the synthesis of 14-aryl or alkyl-14*H*-dibenzo[*a,j*]xanthenes using 37 % $BF_3.SiO_2$ as a reusable catalyst [122]. The condensation reaction



Scheme 16. Ultrasound-assisted synthesis of 14-aryl or alkyl-14*H*-dibenzo[*a,j*]xanthenes using $BF_3.SiO_2$ catalyst.

between various aldehydes (1 mmol) and 2-naphthol (2 mmol) was conducted under sonication (20 kHz), yielding the desired xanthene derivatives in good to excellent yields (85–98 %) within 6 min (Scheme 16) [122].

2.6. Ultrasound-assisted synthesis of dibenzo[b,i]xanthenes

2.6.1. N-sulfonic acid poly(4-vinylpyridinium) hydrogen sulfate (NSPVPHS) as a solid acid catalyst

The three-component condensation reaction is crucial for the synthesis of xanthene derivatives, typically catalysed by Brönsted or Lewis acids [96,123]. However, due to the limitations of traditional methods, such as environmental impact and convenience, there remains a need for more environmentally friendly and efficient protocols for xanthene synthesis [124]. In green chemistry, ultrasound plays a significant role compared to conventional thermal methods, offering an eco-friendly energy source [125]. Khaligh et al. developed a method for synthesising dibenzo[*b,i*]xanthene derivatives through a three-component reaction involving various aldehydes (1 mmol), 2-hydroxynaphthalene-1,4-dione (2 mmol), catalysed by *N*-sulfonic acid poly(4-vinylpyridinium) hydrogen sulfate under ultrasound irradiation as a sustainable technique (Scheme 17) [109]. This protocol achieved high yields (90–95 %) of the desired dibenzo[*b,i*]xanthene-tetraones in a short reaction time (5–10 min) [109].

A plausible mechanism for the synthesis of dibenzo[*b,i*]xanthene-tetraones is illustrated in Scheme 18 [109].

2.7. Ultrasound-assisted synthesis of octahydroxanthenes

2.7.1. Zinc acetate as a catalyst

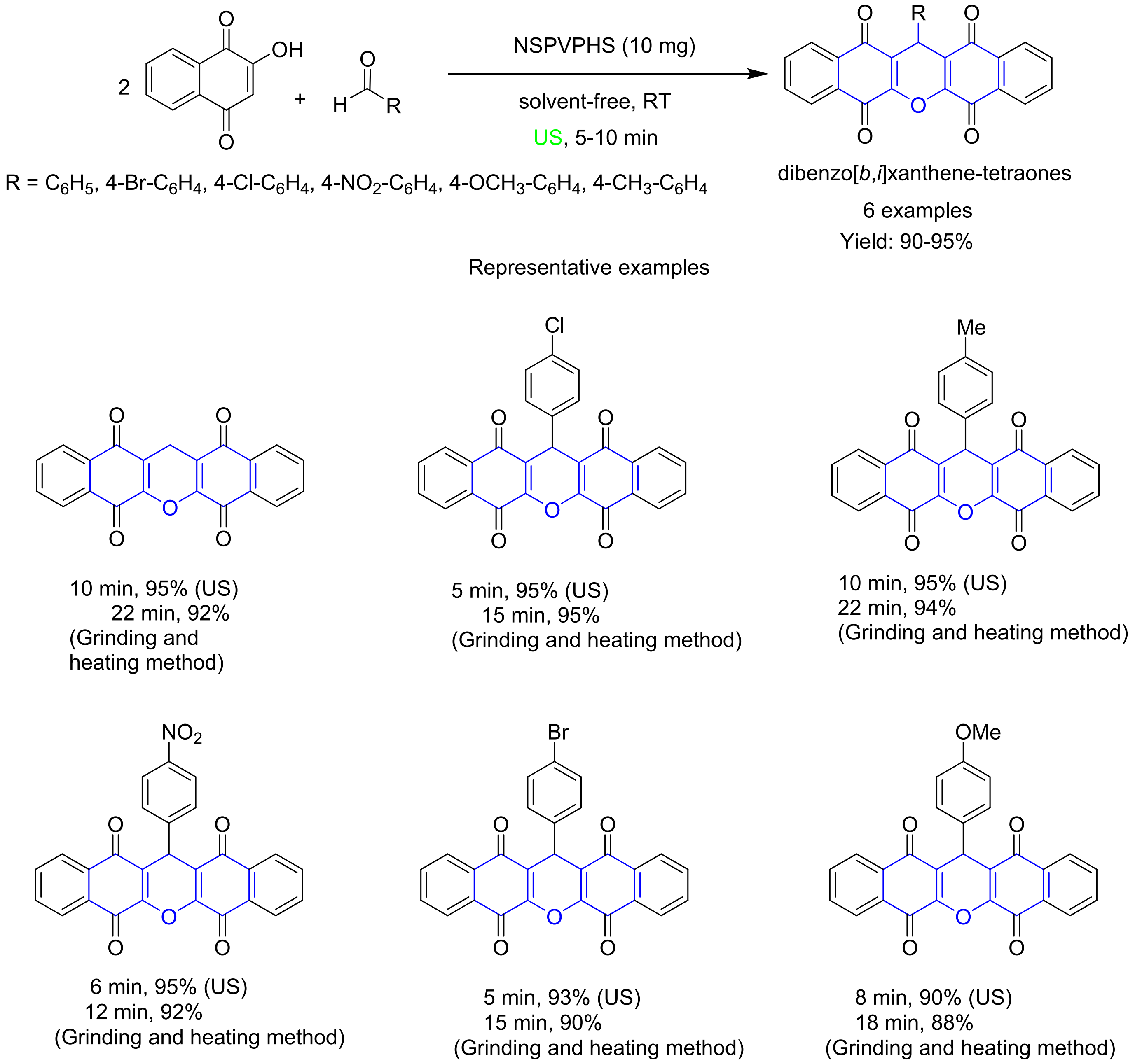
Various traditional approaches are associated with certain drawbacks, including low product yields, expensive catalysts, extended reaction times, the use of hazardous organic solvents, and harsh reaction conditions [126]. In organic synthesis, zinc acetate ($Zn(OAc)_2$) has gained recognition as a valuable Lewis acid catalyst, offering excellent performance compared to traditional Lewis acids. It is inexpensive, readily available, environmentally friendly, recyclable, and exhibits a high degree of compatibility, making it an attractive option for various reactions [126,127]. Bouzina et al. developed a simple and environmentally friendly method for synthesising xanthene derivatives from various aromatic aldehydes (1 mmol) and cyclic diketones such as dimedone (2 mmol) or 1,3-cyclohexanedione (2 mmol) in ethanol (2 mL). The reaction, catalysed by $Zn(OAc)_2$ (10 mol%) under ultrasound irradiation as an alternative energy source, resulted in good to excellent yields (84–95 %) within a short reaction time (15–45 min) (Scheme 19) [18]. Various spectroscopic techniques and X-ray crystallography were employed to confirm the structures of all xanthene derivatives, including two newly synthesised compounds. Additionally, molecular docking studies revealed that the prepared compounds effectively inhibited the VEGFR-2 enzyme [18]. To analyse the electronic and geometric properties, including HOMO and LUMO bandgap energies, molecular electrostatic potential surfaces were also investigated through DFT calculations [18].

Various catalysts have been employed for the synthesis of xanthenes under ultrasound irradiation. Table 1 provides a concise summary of selected studies reported in the literature [18].

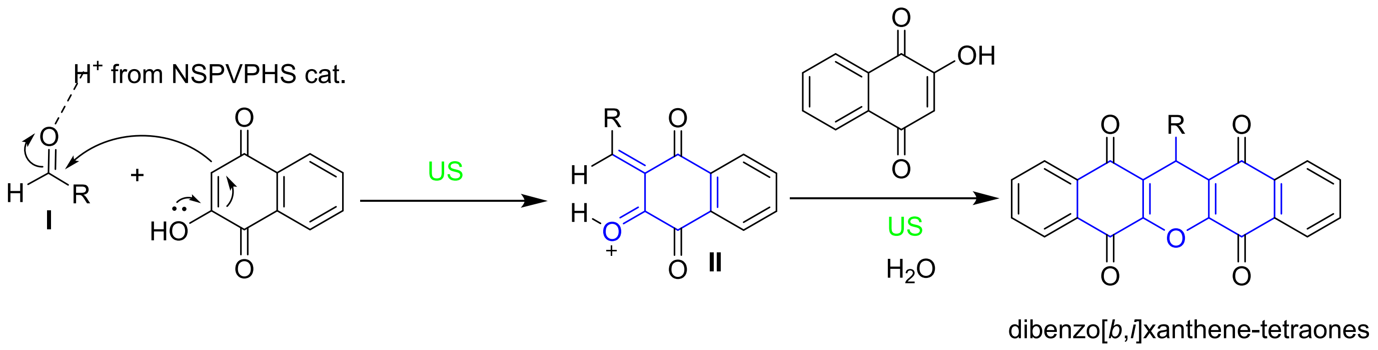
A plausible mechanism for the synthesis of octahydroxanthenes is depicted in Scheme 20 [18].

2.7.2. Choline-chloride:tartaric acid as a catalyst

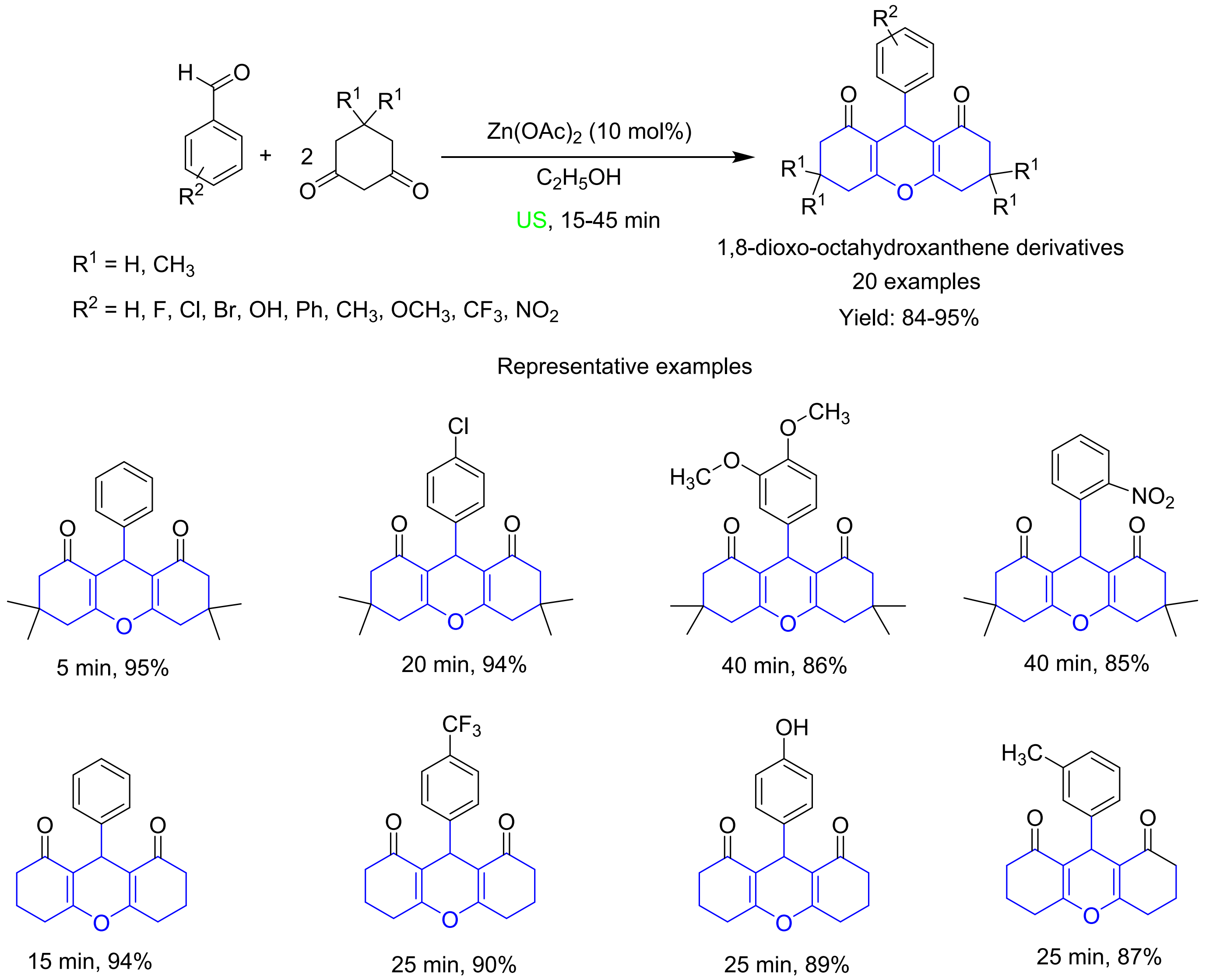
Diabetes mellitus (DM) is one of the most critical global health emergencies of the 21st century. This chronic condition arises either from insufficient insulin production by the pancreas, a hormone essential for regulating blood glucose levels or from the body's inability to effectively utilise the insulin it produces [134–136]. Patel et al. reported the efficient synthesis of 1,2,3-triazole-based xanthene derivatives with high yields (82–92 %) using substituted aldehydes (1 mmol) and 1,3-dicarbonyl compound (2 mmol). The reaction was conducted in the presence of a Choline-chloride-based DES (deep eutectic solvent) (3 mL) under sonication (130 W, 28 kHz) as an eco-friendly energy source. This method represents a recent effort to develop novel α-glucosidase and α-amylase inhibitors for the treatment of T2DM (type 2 diabetes mellitus) (Scheme 21) [137]. Substituted aldehyde derivatives were first synthesised using propargyl bromide and 4-hydroxy-benzaldehyde derivatives as starting materials. Notably, the DES exhibited dual functionality, serving both as a reaction medium and a reusable catalyst. The results of the *in vitro* antidiabetic activity indicated that several compounds exhibited potent inhibitory activity, with IC_{50} values ranging



Scheme 17. Ultrasound-assisted synthesis of dibenzo[*b,i*]xanthene derivatives using NSPVPHS catalyst.



Scheme 18. Proposed mechanism for the ultrasound generation of dibenzo[*b,i*]xanthenes using NSPVPHS.



Scheme 19. Ultrasound-assisted synthesis of 1,8-dioxooctahydroxanthene derivatives using $Zn(OAc)_2$ catalyst.

from 3.24 ± 0.07 to 5.03 ± 0.05 μM against α-glucosidase and α-amylase enzymes. Furthermore, the synthesised compounds were subjected to kinetic studies and *in vitro* cytotoxicity assessments. Kinetic analysis of the most potent compounds revealed a mixed-type inhibition mechanism for both α-amylase and α-glucosidase, providing insights into their mode of action. Additionally, DFT calculations were performed on the synthesised compounds to correlate their biological efficacy with theoretical quantum descriptors. Molecular electrostatic potential (MESP) 3D plots were also generated to provide further insights into their electronic and reactive properties. The structure–activity relationship analysis revealed that incorporating a –COOH group at the *para* position, a $–NO_2$ group at the *ortho* position, and a CH_3 group at the *meta* position significantly enhanced α-amylase and α-glucosidase inhibition. Substituting a H atom with an $–OCH_3$ group further improved inhibition, whereas replacing the –COOH group with a halogen reduced inhibitory activity against these enzymes [137].

2.7.3. Lime juice as a catalyst

Retnosari et al. synthesised 9-(4-hydroxyphenyl)-3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione using lime juice as an eco-friendly catalyst under ultrasound irradiation [138]. The application of ultrasonic waves effectively reduced the reaction time and resulted in a high yield of the desired product in 89 %. The compound was subsequently evaluated for antibacterial activity, revealing weak activity against *Escherichia coli* and no activity against *Staphylococcus aureus* [138].

2.7.4. Boric acid as a catalyst

In organic synthesis, the development of an accessible methodology for constructing simple heterocycles with diverse functional groups has recently garnered increased attention [139,140]. Many natural products contain the xanthenedione moiety, which serves as a valuable synthon due to the inherent reactivity of its pyran ring [141,142]. The synthesis of xanthenedione derivatives has attracted significant interest from synthetic organic and medicinal chemists due to their wide-ranging applications in pharmaceutics and medicine [143,144]. Begum et al. achieved an ultrasound-assisted synthesis of various xanthenediones with excellent yields (81–98 %) by condensing aromatic aldehydes and dimedone in the presence of boric acid (H_3BO_3) as a catalyst, using an ethanol–water mixture as an eco-friendly solvent system (Scheme 22) [145]. Notably, they were the first to employ H_3BO_3 as a catalyst for the synthesis of xanthendione derivatives. Various spectroscopic techniques, including ^1H, ^{13}C NMR, and ESI-MS, were used to characterise the synthesised compounds. Additionally, two of the xanthendiones derivatives formed good-quality crystals upon recrystallisation, and their molecular structures were confirmed through single crystal X-ray diffraction analysis [145]. The stability of the molecular structure was

Table 1
Literature review on ultrasound-assisted catalytic systems for the synthesis of octahydroxanthenes [18].

Entry	Catalyst	Conditions	Time (min)	Yield (%)	Reference
1	*N*-Methyl-2-pyrrolidinium hydrogen sulfate $[H\text{-}NMP]^+[HSO_4]^-$ (20 mol%)	US (20 kHz), 60 ^{0}C, water (20 mL)	50	86	[128]
2	MCM-41-SO_3H (5 mol %)	US (25 kHz), 60 ^{0}C, water (5 mL)	60	95	[129]
3	Melamine trisulfonic acid (MSTA) (7.5 mol %)	US (34–37 kHz), 60 ^{0}C, ethyl acetate (3 mL)	110	86	[130]
4	Ceric(IV) ammonium nitrate (CAN) (5 mol %)	US (40 kHz), 50 ^{0}C, isopropanol (2 mL)	35	98	[131]
5	1-Carboxymethyl-3-methylimidazolium tetrafluoroborate $[cmmim][BF_4]$ (200 mg)	US (50 kHz), 30 ^{0}C methanol (1 mL)	50	87	[132]
6	TiO_2 (5 mol%)	US (50 kHz), RT, ACN (2 mL)	6	90	[133]
7	Zinc acetate (Zn $(OAc)_2$) (10 mol%)	US (40 kHz), 60 °C, EtOH (2 mL)	15	95	[18]

primarily attributed to weak intermolecular N–H …O and C–H …O hydrogen bonds. The Hirshfeld surface analysis revealed that the H-H interactions (54.7 % and 53.7 %) made the largest contribution to the overall intermolecular interactions. Furthermore, the HOMO-LUMO energy gaps (3.9261 eV and 4.6436 eV) indicated that the xanthendiones exhibited good stability [145].

2.7.5. *Brønsted acidic ionic liquid as a catalyst*

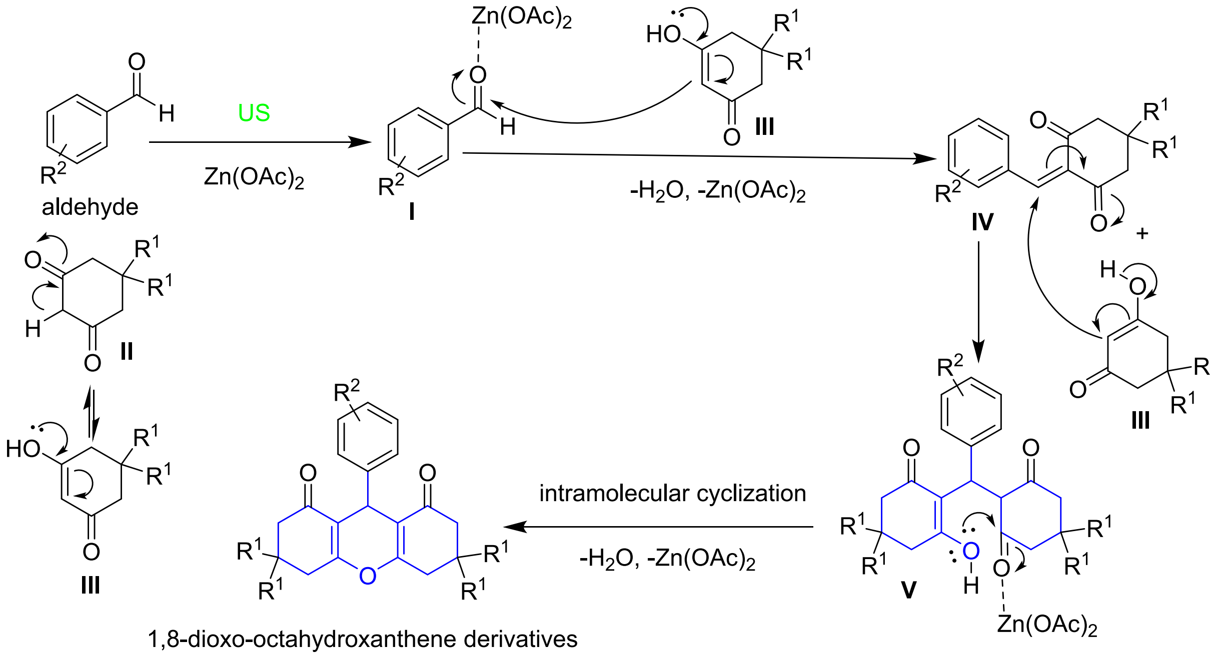
Xanthenes and benzoxanthenes are among the most widely studied active oxygen heterocycles, serving as key intermediates in drug synthesis [146,147]. Several methodologies exist for the preparation of 1,8-dioxo-octahydroxanthene scaffolds [148,149]. However, some of these methods present limitations, such as low yields, excessive use of reagents and catalysts, and extended reaction times. Therefore, a more environmentally friendly synthetic approach is required for the preparation of 1,8-dioxooctahydroxanthenes. Naeimi developed a sustainable methodology for synthesising 1,8-dioxooctahydroxanthene derivatives with good yields (70–94 %) under ultrasonic irradiation (40 W) as a clean energy source, requiring only 40–75 min of reaction time (Scheme 23) [128]. The ultrasound-assisted reaction involved various aromatic aldehydes (1 mmol) reacting with dimedone (2 mmol) in water (20 mL) as an eco-friendly solvent. Brønsted acidic ionic liquid ($[H\text{-}NMP]^+[HSO_4]^-$) was used as a cost-effective and recyclable catalyst (20 mol%) for the reaction. The ionic liquids were successfully recycled five times without significant loss of catalytic activity or purity, with yields ranging from 86-94 % [128]. The synthesised products were identified and confirmed using various physical and spectroscopic techniques, including IR, ^{1}H NMR, and ^{13}C NMR [128].

2.7.6. *Melamine trisulfonic acid as a catalyst*

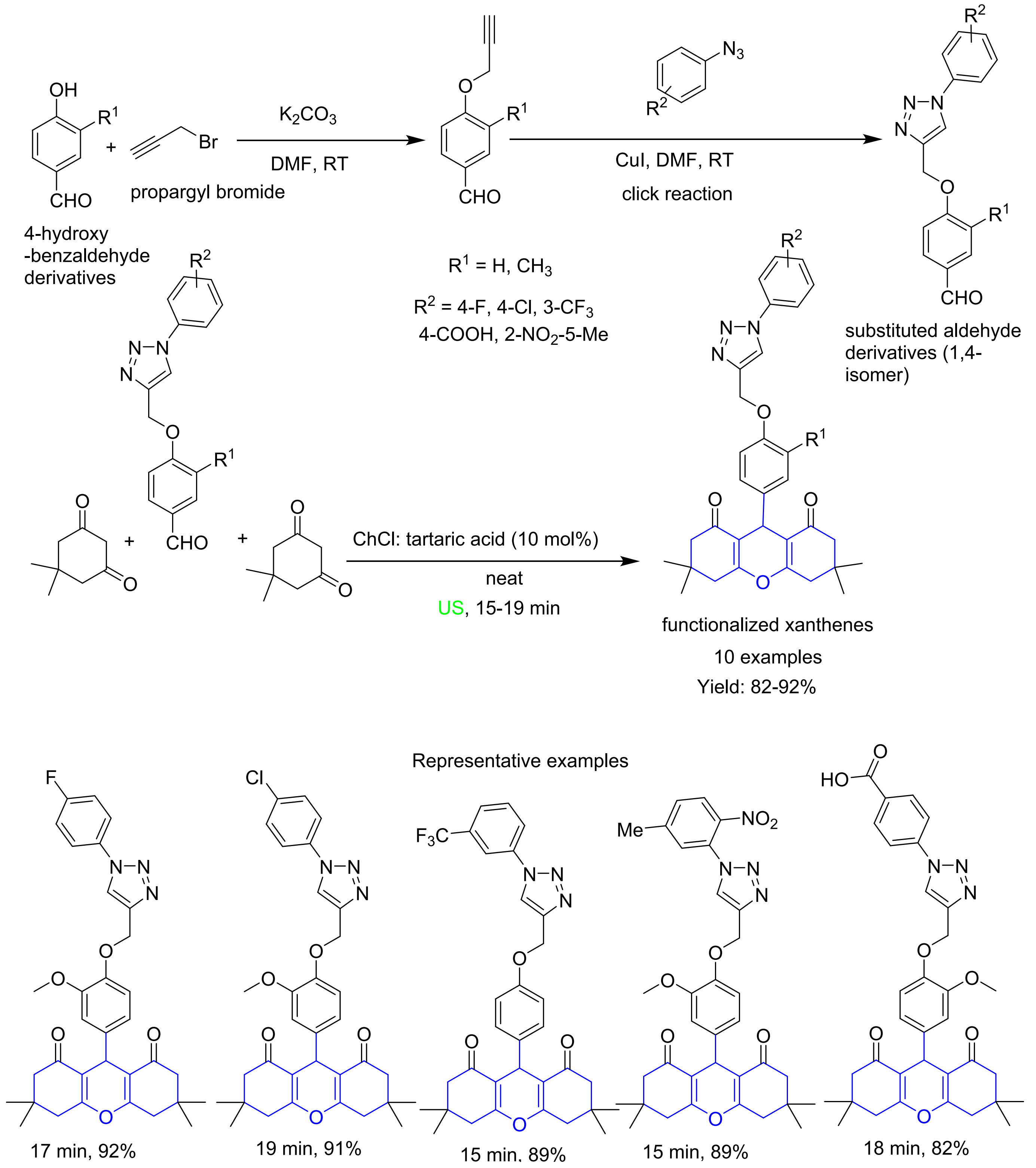
In organic synthesis, the use of SO_3H-bearing catalysts has gained significant attention due to their low cost, high reactivity, easy accessibility, and non-toxic nature [150]. Among these, melamine trisulfonic acid (MTSA) is a particularly attractive SO_3H-containing catalyst, widely employed in various organic transformations [151,152]. Scheme 24 illustrates the preparation of MTSA from chlorosulfonic acid and melamine [130]. Moosavi-Zare et al. reported a method for synthesising 9-aryl-1,8-dioxo-octahydroxanthenes with good yields (80–96 %) using MTSA as an efficient catalyst (7.5 mol%) [130]. This method involves the condensation of various aryl aldehydes with 1,3-cyclohexanediones in ethyl acetate under ultrasound irradiation (34–37 kHz/350 W/60 ^{0}C) for 75–220 min [130].

2.7.7. *Titanium dioxide as a catalyst*

Titanium dioxide (TiO_2) has become an increasingly popular catalyst due to its low cost, high efficiency, and environmental compatibility [153]. Pathak et al. introduced a simple method for synthesising 9-aryl-1,8-dioxooctahydroxanthenes with high yields (87–95 %) using TiO_2 as



Scheme 20. Proposed mechanism for the ultrasound generation of octahydroxanthenes using $Zn(OAc)_2$.

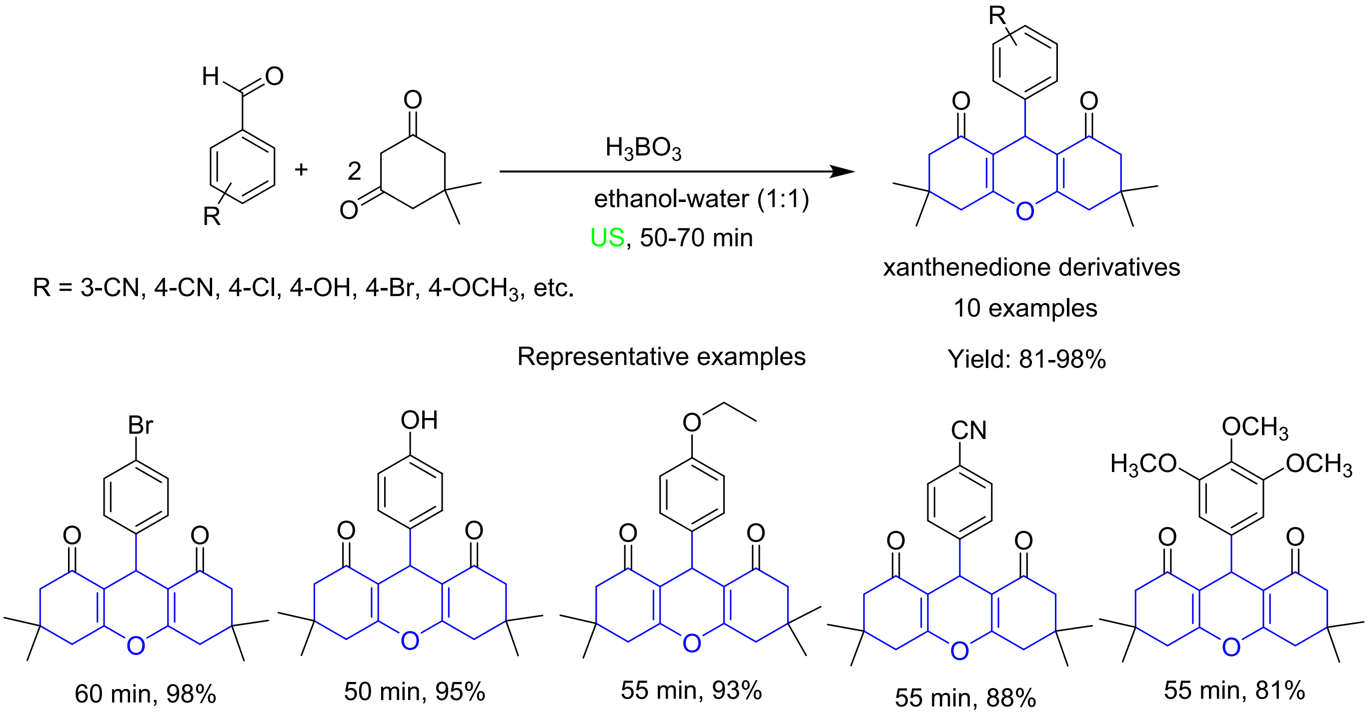


Scheme 21. Ultrasound-assisted synthesis of triazole-based xanthene derivatives using ChCl:tartaric acid catalyst.

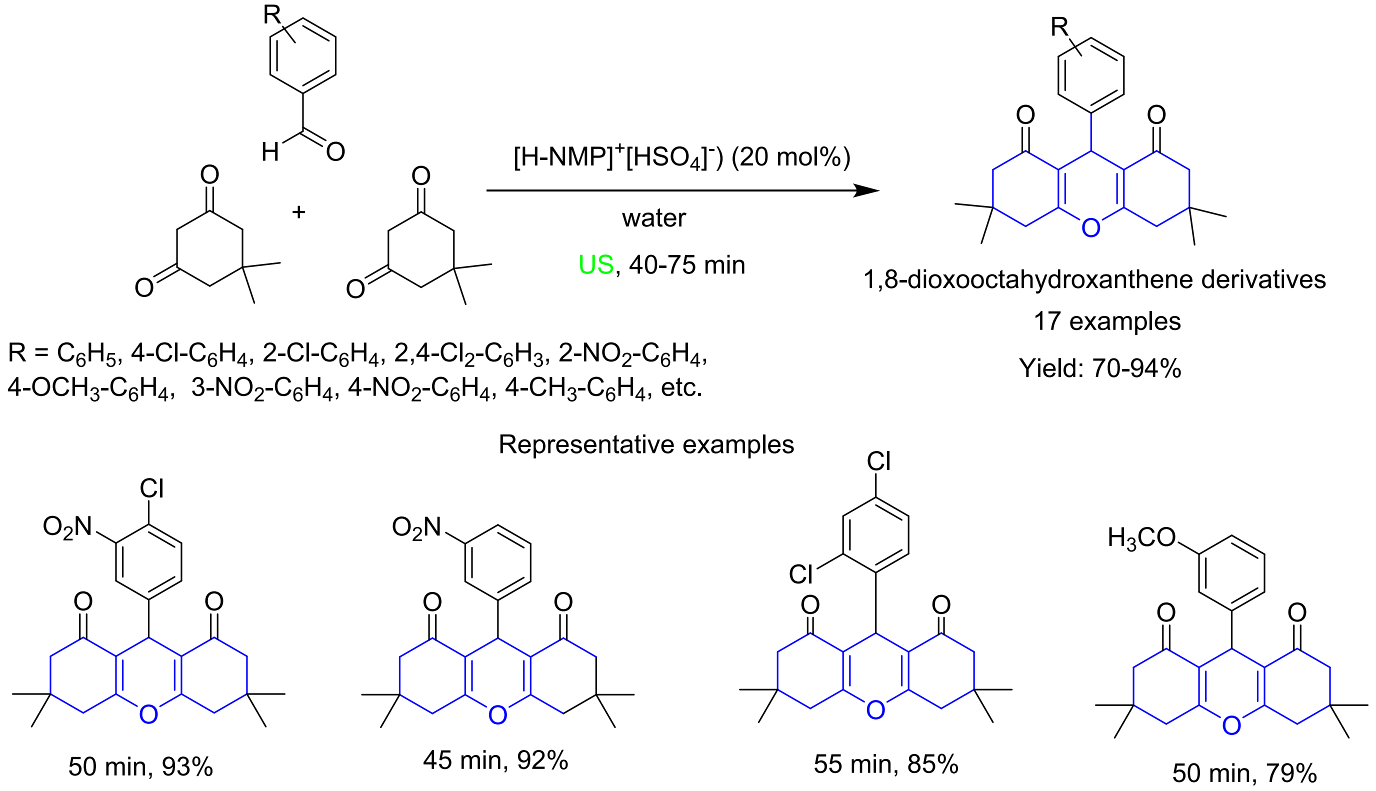
an efficient and recyclable catalyst (5 mol %) [133]. This green approach involves the reaction of aldehydes (1 mmol) with dimedone (2 mmol) in acetonitrile (2 mL) under ultrasound irradiation at RT for 5 to 15 min as an alternative energy source [133].

2.7.8. *Ceric(IV) ammonium nitrate as a catalyst*

Ceric ammonium nitrate (CAN) [$(NH_4)_2Ce(NO_3)_6$] has been recognised as an effective catalyst for the formation of various carbon-heteroatom and carbon–carbon bonds. Its advantages include high solubility in water, simple work-up procedures, and an environmentally friendly profile [154–157]. Additionally, CAN has been used to catalyse several organic reactions, leveraging its electron transfer capability and its role as a Brønsted acid [158,159]. Pal et al. developed an environmentally friendly methodology for synthesising 1,8-dioxo-

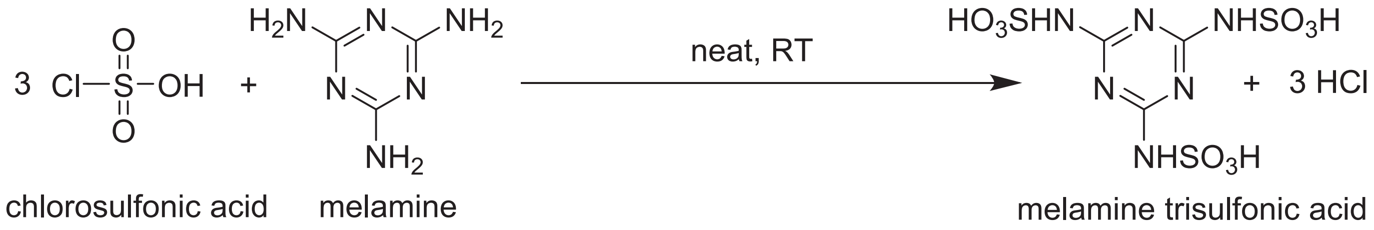


Scheme 22. Ultrasound-assisted synthesis of xanthenedione derivatives using H_3BO_3 catalyst.

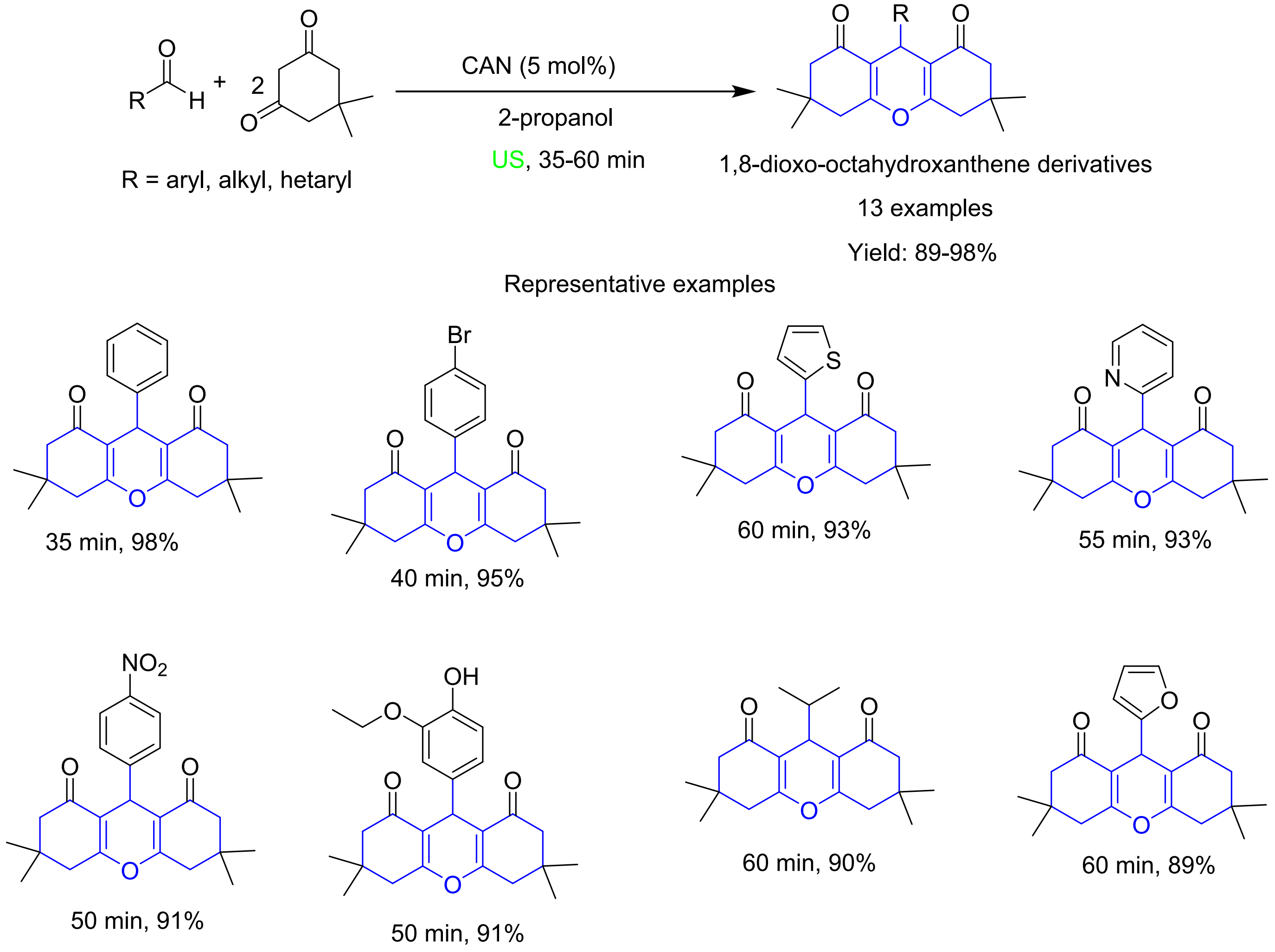


Scheme 23. Ultrasound-assisted synthesis of octahydroxanthene derivatives using ($[H\text{-}NMP]^+[HSO_4]^-$) catalyst.

octahydroxanthene derivatives with good to excellent yields (89–98 %) through a one-pot, three-component reaction. This reaction involves various aldehydes and 5,5-dimethyl-1,3-cyclohexanedione using CAN as an efficient catalyst in 2-propanol under ultrasound irradiation for 35–60 min (Scheme 25) [131]. Various compounds, including 9-alkyl/aryl/heteroaryl substituted 3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-diones, were synthesised without the use of harmful chlorinated solvents [131].



Scheme 24. Synthesis of melamine trisulfonic acid.



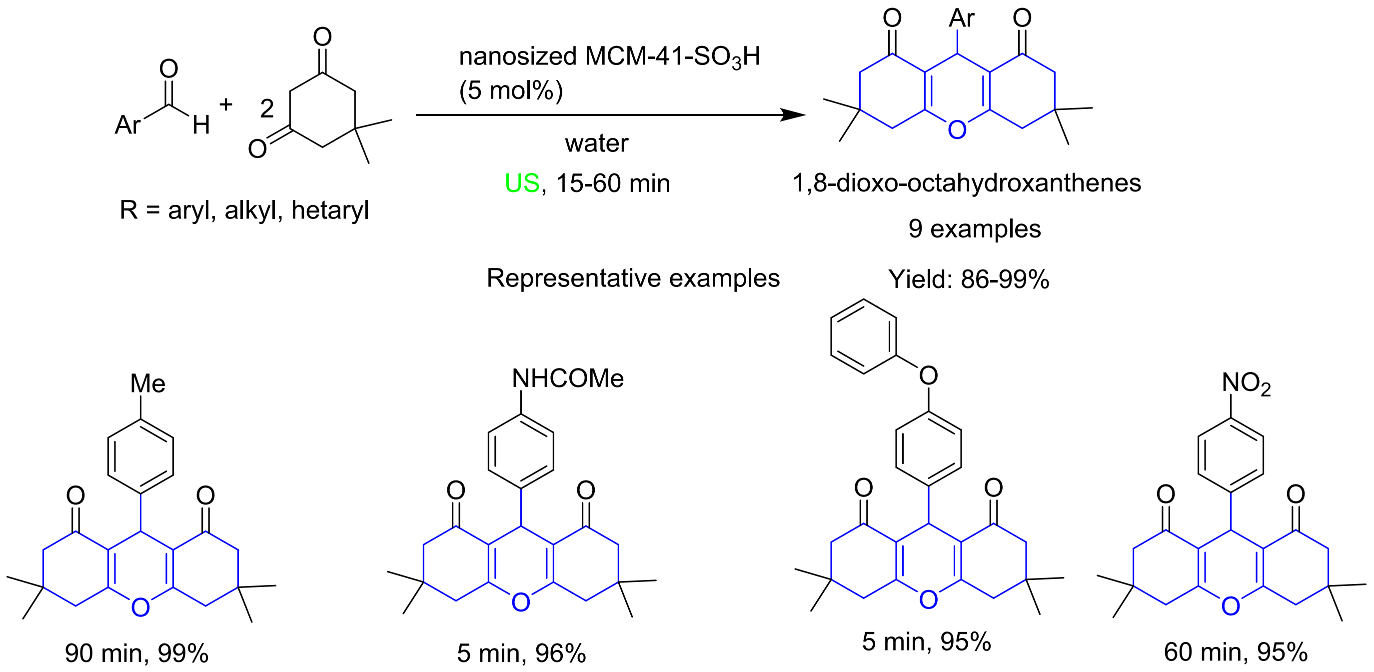
Scheme 25. Ultrasound-assisted synthesis of 9-substituted xanthene derivatives using CAN catalyst.

2.7.9. Carboxy functionalized ionic liquid 1-carboxymethyl-3-methylimidazolium tetrafluoroborate as a catalyst

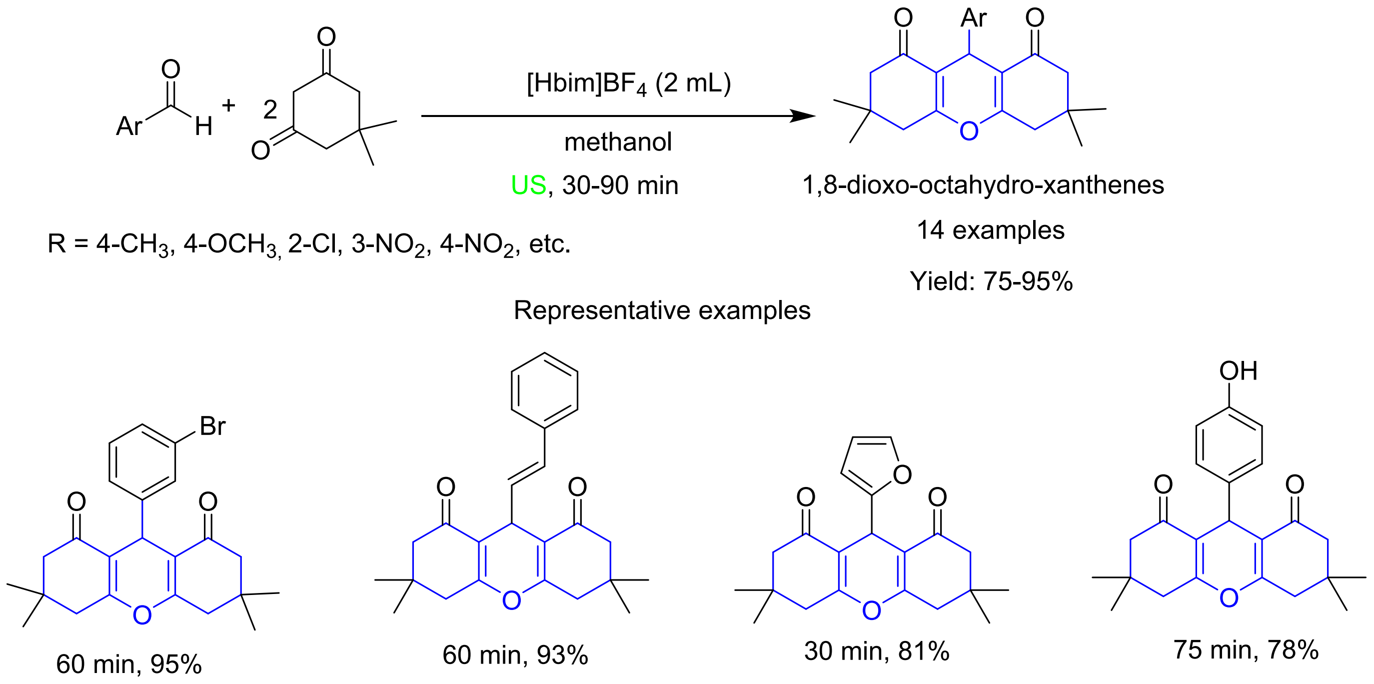
The growing demand for environmentally friendly and cost-effective methods for synthesising xanthene derivatives highlights the need for improvement in this area [160]. Non-aqueous room-temperature ionic liquids have emerged as an eco-friendly alternative to volatile organic solvents [161]. Raval et al. achieved the sonochemical synthesis of functionalised xanthenes by using [cmmim][BF_4] (1-carboxymethyl-3-methylimidazolium tetrafluoroborate), a carboxy functionalised ionic liquid, at room temperature without the need for any additional catalyst [132]. Various aldehydes were condensed with dimedone (5,5-dimethyl-1,3-cyclohexanedione) to provide 1,8-dioxo-octahydroxanthenes in good yields (78–92 %) within 30–85 min. The ionic liquid was recycled and successfully reused at least six times without a significant decrease in its catalytic activity [132].

2.7.10. MCM-41 as a catalyst

Recently, ordered silica materials have garnered significant attention due to their unique properties [162–164]. Among these, sulfonic acid-functionalised Mobil Composition of Matter No. 41 (MCM-41) stands out as a prominent example. This mesoporous material features a highly organised structure, a narrow pore size range of 1.5 and 10 nm, and a remarkably high surface area of up to 1500 m^2g^{-1}, attributed to the role of surfactant cations in its synthesis [165,166]. Rostamizadeh et al. reported a straightforward method for synthesising various 1,8-dioxo-octahydroxanthenes using aldehydes (1 mmol) and dimedone (2 mmol) in the presence of nanosized MCM-41-SO_3H (approximately 5 mol%) as a nanocatalyst. The reaction was carried out in water (5 mL) as an eco-friendly solvent under ultrasound irradiation (25 kHz), demonstrating a green and efficient approach (Scheme 26) [129]. Aromatic aldehydes with both electron-donating and electron-withdrawing



Scheme 26. Ultrasound-assisted synthesis of functionalised xanthene derivatives using MCM-41-SO$_3$H catalyst.

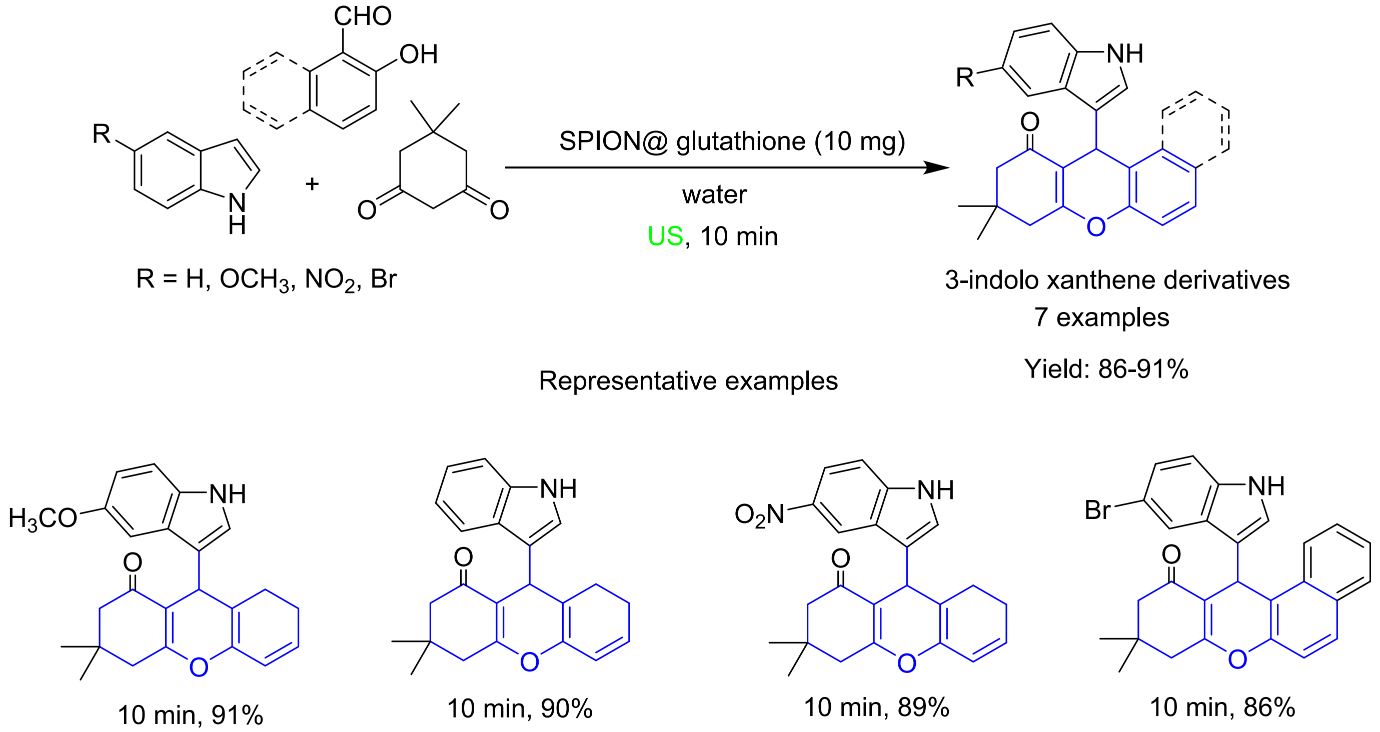


Scheme 27. Ultrasound-assisted synthesis of octahydro-xanthene derivatives using [Hbim]BF$_4$ catalyst.

substituents efficiently participated in the condensation reaction, yielding the corresponding 1,8-dioxo-octahydroxanthenes in high yields (86–99 %) within short reaction times (15–60 min) [129].

2.7.11. *[Hbim]BF$_4$ ionic liquid as a catalyst*

In organic synthesis, non-aqueous room temperature ionic liquids (ILs) have attracted considerable attention as green solvents due to their excellent solvating properties, negligible vapour pressure, and ease of recyclability [167–169]. Srinivasan et al. introduced a protocol for synthesising 1,8-dioxo-octahydro-xanthene derivatives using the ionic liquid [Hbim]BF$_4$ as the reaction medium, supplemented with methanol as a co-solvent (0.5 mL) (Scheme 27) [148]. The non-volatile ionic liquid [Hbim]BF$_4$ (IL) (2 mL) effectively catalysed the condensation of various aldehydes (2.0 mmol) with diketone (4.0 mmol) at ambient temperature under ultrasonic irradiation, producing the desired xanthenes in good to high yields (75–95 %) within 30–90 min. Notably, this methodology does not require an added catalyst. A comparable protocol was also conducted under thermal conditions using *p*-TSA as a catalyst. The products were isolated using a straightforward work-up process involving water dilution and filtration of the precipitated target compounds [148].

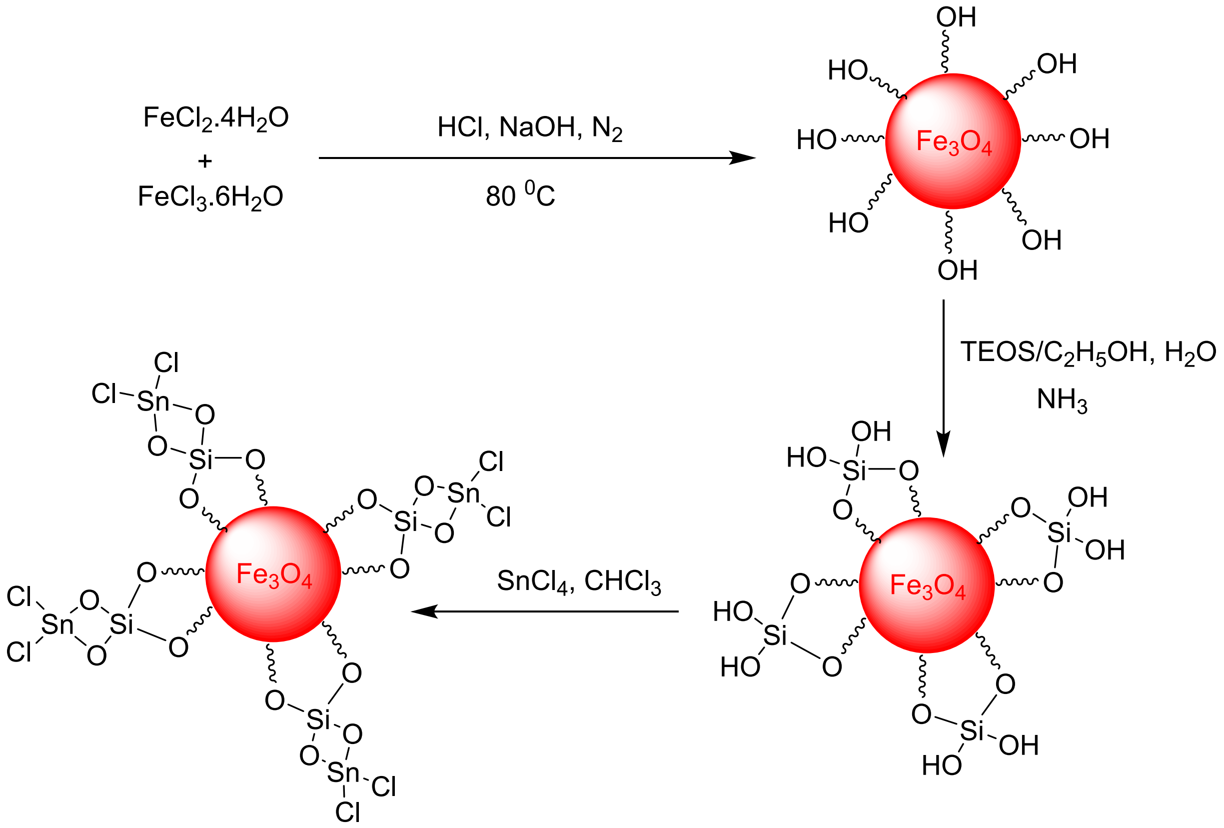


Scheme 28. Ultrasound-assisted synthesis of indolo xanthene derivatives using SPION@glutathione catalyst.

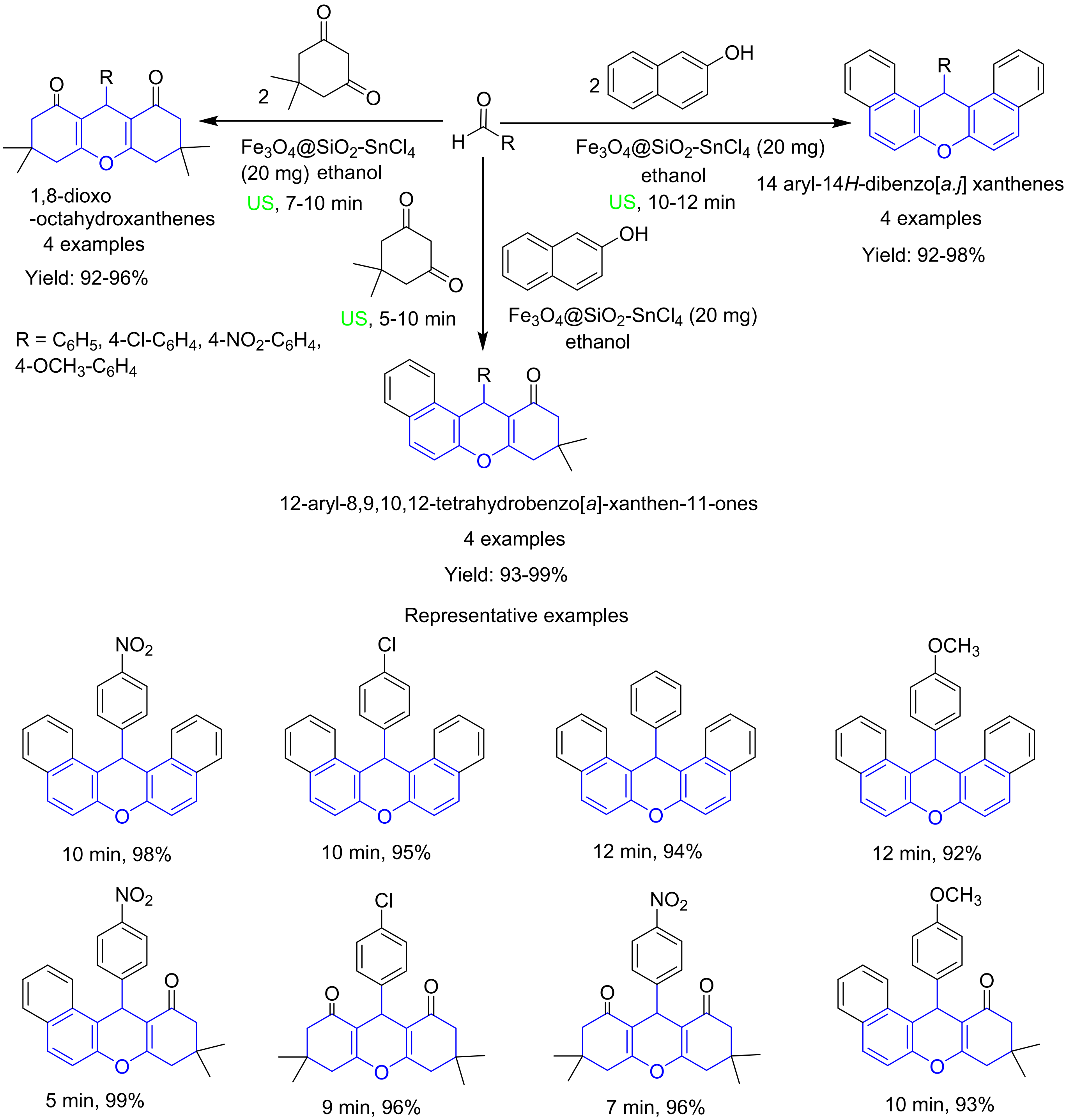
2.8. *Miscellaneous*

2.8.1. *SPION@glutathione as a nano-organocatalyst*

The use of small organic molecules as catalysts (organocatalysts) has gained increasing attention for the synthesis of enantiomerically enriched compounds. This interest arises from their lower toxicity, cost-effectiveness, environmental friendliness (as they avoid the use of metals), ease of preparation, and ability to facilitate reactions under



Scheme 29. Schematic representation of $Fe_3O_4@SiO_2$-$SnCl_4$ nanoparticle synthesis.



Scheme 30. Ultrasound-assisted synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]-xanthen-11-ones using Fe$_3$O$_4$@SiO$_2$-SnCl$_4$ catalyst.

mild conditions compared to metal-based catalysts or enzymes [170–173]. This represents a major advancement in green chemistry [172]. Organocatalysis is now recognised as the third fundamental pillar of asymmetric catalysis, alongside organometallic catalysis and enzymatic catalysis [174]. The significance of this breakthrough was highlighted when the 2021 Nobel Prize in Chemistry was awarded jointly to Benjamin List and David MacMillan for their pioneering work in the "*development of asymmetric organocatalysis*" [175]. Building on these advancements, Nongthombam et al. developed an environmentally friendly methodology for synthesising indolo xanthene derivatives. The reaction involved dimedone (1 mmol), indole (1 mmol), and salicylaldehyde or 2-hydroxy-1-naphthaldehyde (1 mmol) in the presence of SPION@glutathione (10 mg) as a nano-organocatalyst. The process was carried out in water (10 mL) as a green solvent under ultrasonication (60/240 W) for just 10 min, yielding the target compounds in excellent yields (86–91 %) (Scheme 28) [176]. Glutathione, a water-soluble tripeptide composed of glutamic acid, glycine, and cysteine, has recently demonstrated both antioxidant and catalytic activity, particularly in carbon–oxygen ring cyclisation reactions [177,178]. To improve its catalytic performance and enhance its magnetic recyclability, glutathione molecules were immobilised onto superparamagnetic iron-oxide nanoparticles. Quantum chemical studies were performed to examine the influence of the nano-organocatalyst on the carbon–oxygen ring cyclisation process. These studies were conducted using the Gaussian program with the B3LYP [176].

2.8.2. Fe_3O_4@SiO_2-$SnCl_4$ as a nano-organocatalyst

Numerous methods have been developed for synthesising xanthene derivatives, utilising both heterogenous and homogenous catalysts [179–183], driven by their diverse biological and therapeutic applications [184]. However, conventional approaches often suffer from notable drawbacks, including extended reaction durations, low product yields, labor-intensive purification processes, and reliance on toxic and expensive catalysts. As a result, the development of efficient and sustainable methodologies remains a priority. In this context, Bamoniria et al. synthesised Fe_3O_4@SiO_2-$SnCl_4$ nanoparticles (Scheme 29) [185] and introduced a direct approach for the high-yield synthesis of xanthene derivatives (92–99 %). This method involves the condensation of dimedone (2 mmol or 1 mmol), a mixture of *β*-naphthol (2 mmol or 1 mmol) and dimedone (2 mmol or 1 mmol), or *β*-naphthol (2 mmol or 1 mmol) with various aromatic aldehydes (1 mmol). The reaction employs Fe_3O_4@SiO_2-$SnCl_4$ as an innovative solid acid catalyst (20 mg) in ethanol under sonication at 50 W for 5–12 min (Scheme 30) [185]. To evaluate the catalytic performance of this magnetic catalyst, functionalised xanthenes were synthesised via the condensation of aldehydes with *β*-naphthol. Additionally, 1,8-dioxo-octahydroxanthenes were prepared through the condensation of aldehydes with dimedone, while 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]-xanthen-11-ones were generated by reacting aldehydes with a mixture of dimedone and *β*-naphthol under ultrasound irradiation. Additionally, the reusability of the catalyst was assessed, showing a gradual decrease in product yields with successive reuse (run 1, 98 %; run 2, 97 %; run 3, 94 %; run 4, 90 %; run 5, 88 %) [185].

3. Conclusions

Xanthenes find extensive applications across diverse fields, including laser dyes, the textile industry, electro-optical devices, the food industry, and biomedical devices. Their significant therapeutic and biological activities have drawn considerable interest in the synthesis of xanthene derivatives. It plays a key role in drug discovery and development. Consequently, various methods have been employed to synthesise xanthene derivatives using different catalysts. However, many of the reported methodologies rely on toxic reagents, hazardous solvents, and strong protonic acids as catalysts. Hence, there is a pressing need to develop a well-designed, green synthetic strategy to address these challenges. To promote eco-friendly synthetic methods, ultrasound-assisted green approaches have garnered significant attention for the synthesis of xanthene derivatives, offering advantages over conventional methods in terms of higher yields, faster reaction rates, and improved selectivity. Ultrasound has been regarded as a significant intensification technology in mass transfer processes. Besides, ultrasound in medicine has a crucial role in both therapeutic uses and imaging. Functionalised xanthene derivatives, especially 9-substituted xanthene derivatives, represent a prominent class of heterocycles with remarkable biological activities and medicinal applications. Thus, this review focuses on the use of ultrasound as an environmentally friendly energy source for the synthesis of these functionalised xanthene derivatives. Therefore, this review is expected to have a significant impact by encouraging the next generation to explore ultrasound as a tool for the sustainable synthesis of various xanthene derivatives. It also aims to promote the application of green technology in the development of novel medicines for the benefit of society. This review presents various synthetic schemes, highlighting mechanistic details clearly and straightforwardly. The use of sonochemistry in the synthesis of functionalised xanthene derivatives exemplifies the continuous progress of sustainable chemistry. It reflects the shared goal of achieving sustainable industrial practices while maintaining the pursuit of scientific innovation and advancement.

CRediT authorship contribution statement

Sasadhar Majhi: Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Sivakumar Manickam:** Conceptualization, Funding acquisition, Investigation, Writing – original draft, Writing – review & editing, Resources, Software. **Giancarlo Cravotto:** Funding acquisition, Investigation, Project administration, Software, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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