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Green Synthesis of Xanthenes: Utilizing Sulfonated Fructose as an Efficient and Eco-friendly Catalyst

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

The synthesis of xanthenes has garnered significant attention due to their extensive biological and therapeutic properties, including antibacterial, antiviral, and anti-inflammatory effects. Xanthenes are indispensable in organic synthesis and are also valued for their spectral properties as dyes in laser industries and fluorescent materials for detecting biological molecules. Despite various methods reported for xanthene synthesis, challenges such as low efficiency, lengthy reaction times, high catalyst requirements, and the use of hazardous organic solvents necessitate the development of more sustainable and efficient alternatives.

This study introduces sulfonated fructose as a novel, green catalyst for the condensation reactions of benzaldehyde, 2-naphthol, and dimedone to synthesize tetrahydrobenzo[a]xanthene-11-ones, and aldehyde and 2-naphthol to synthesize 14H-dibenzo[a,j]xanthenes. The sulfonation of fructose enhances its catalytic activity by increasing its acidity, stability, and selectivity, thus providing significant advantages over pure fructose. These include: 1. Higher Catalytic Activity: Enhanced

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acidity of sulfonated fructose reduces reaction times and increases yields. 2. Greater Stability: Increased stability of the catalyst leads to less degradation and a longer lifespan. 3. Compatibility with Green Chemistry: The use of less toxic and hazardous catalysts aligns with green chemistry principles, reducing environmental pollution. 4. Reduced Need for Toxic Solvents: Reactions can proceed under milder conditions using environmentally friendly solvents like water and ethanol. 5. Improved Selectivity: Sulfonic groups enhance the selectivity of reactions, resulting in fewer by-products and higher purity.

This innovative approach not only improves the efficiency and sustainability of xanthene synthesis but also demonstrates the economic and environmental benefits of using sulfonated fructose. The method offers straightforward operation, reduced costs, shorter reaction times, and easier purification, making it a valuable contribution to the field of green and sustainable chemistry.

Keywords: Agar catalyst; eco-friendly; organic synthesis; fructose sulfonated catalyst; xanthene synthesis; environmentally benign synthesis; biologically active compounds; pharmaceutical compounds.

1. INTRODUCTION

Xanthenes are crystalline organic compounds in which two benzene rings are connected to a central pyran ring, and they represent some of the most important heterocyclic compounds containing oxygen atoms found in nature. Some occur naturally in soil and plants, such as Indigofera angustifolia, while others can be synthesized in the laboratory. This compound serves as a fundamental structure for many drugs and acts as a useful intermediate in the preparation of organic compounds.

Xanthenes were first synthesized by von Bayer in 1871. Von Bayer prepared fluorescein from the condensation reaction of two moles of resorcinol and one mole of phthalic anhydride in the presence of copper chloride. The preparation of xanthenes, especially benzoxanthenes, has received much attention in recent years because these compounds have diverse biological and medicinal properties such as antiviral [1], antibacterial, and anti-inflammatory effects [2]. These compounds can also be used in pH-sensitive fluorescent dye materials, enabling the identification of biomolecules [3], and in laser technology [4], as well as in solar cells. In addition, compounds based on xanthene have been used as insecticides in agricultural activities due to their interesting spectral properties and have a wide range of applications in the field of coloring [5]. They also serve as potent non-peptidic inhibitors and find extensive use in the preparation of perfumed polyamides, which are known for their high thermal resistance and desirable physical and chemical properties.

Derivatives of xanthene can be classified into three groups: fluorans (aminodibenzoxanthenes), rhodols (aminohydroxydibenzoxanthenes), and fluorones (hydroxydibenzoxanthenes). The basic structures of xanthenes are depicted in Fig. 1 [6].

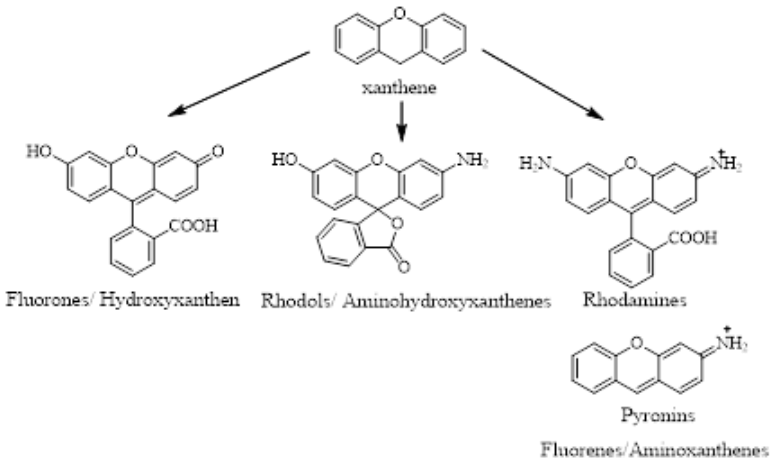


Fig. 1. Basic structure of xanthene

1.1 Applications of Xanthenes

1.1.1 Xanthenes as ligands

Recently, van Leeuwen and colleagues investigated diphosphine ligands with xanthene skeletons. These compounds exhibit an extraordinary effect on catalytic reactions in the presence of metals. The rigid structure of these ligands and their large bite angle aid in catalyst formation and reaction progress [7]. With the expansion of studies in the fields of biochemistry and mineralogy, various types of metalloenzymes have been synthesized. These complexes demonstrate very good catalytic activity in converting organic compounds.

1.1.2 Biological properties of xanthenes

Xanthenes are used as highly effective drugs. Xanthene derivatives possess useful medicinal properties such as relieving muscle pain. They are utilized as chemotherapeutic drugs for cancer treatment and as anti-malarial drugs [8]. Some xanthene 9-thiones and thioxanthenee 9-thiones are employed as antiviral drugs, local anesthetics, bronchodilators, and anticonvulsants [9]. They have also been reported to inhibit the growth of cancer cells [10]. To combat malaria, a wide range of drugs with diverse structures has been developed, many of which have a xanthene tricyclic structure like Chloroquine (CQ) [2].

1.1.3 Xanthenes as dyes

Xanthenes are used as dyes due to their double-bonded linkages and thermodynamic spectral properties. Xanthene luminescent colors include fluorones, pyronines, rosamines, succinines, saccharines, rhodamines, and rhodals. Today, various applications have been proposed for xanthene dyes [11].

1.1.4 Xanthenes in observing biological molecules

Labeling is one of the most important methods used to observe amino acids, peptides, proteins, DNA, and other biological molecules. In this method, radioactive materials or compounds with absorption or fluorescence properties in the UV to near-infrared region are used. Some xanthene compounds with fluorescence properties, including fluorescein, Rhodamine B, Rhodamine 6G, Rhodamine 800, and Rhodamine 123, are widely used for this purpose.

1.2 History of the Three-Component Reaction for Dibenzoxanthene Synthesis

Here, various synthesis methods for xanthenes in recent years are introduced. The synthesis of 1,8-dioxo-hydroxanthenes in the presence of various catalysts, such as indium(III) chloride [12], para-toluenesulfonate-aniline on silica chloride [13], iodine molecule [14], and sodium hydrogen sulfate on a silica gel ($NaHSO_4.SiO_2$) [15], and has been conducted. The preparation of 8,1-dioxo-octahydrindanthrenes from the condensation reaction between dimedone and aromatic aldehydes in the presence of various acidic catalysts, such as para-dodecylbenzene sulfonic acid and diammonium hydrogen phosphate [16], sulfonated succinimide [17], sulfuric silica acid [18], and ionic liquid tetramethylguanidium trifluoroacetate [19], has been carried out.

The most common method that has received attention in recent years for synthesizing benzoxanthenes including microwave irradiation, in the presence of different catalysts such as sulfuric acid [16], oxalic acid [20], para-toluenesulfonic acid [13], sulfamic acid, silica sulfuric acid, $HClO_4$-SiO_2 [21], $NH_4H_2PO_4$ [15], I_2 [14], BF_3SiO_2 [22], lithium bromide [23], alum $KAl(SO_4)_2.12H_2O$ [24], has been conducted.

2. EXPERIMENTAL

This chapter presents the experimental methods conducted in the laboratory. These experiments focused on the quantities and ratios of the compounds used, as well as the selection of solvents, to achieve optimal conditions, aiming to obtain products with the highest efficiency and in the shortest possible time.

2.1 Materials and Equipment

The general structures of all synthesized products were identified through IR spectroscopy and determination of melting point. The melting points of the products were measured with a KRUSS apparatus. The IR spectra of the compounds were obtained using a TENSOR 27 spectrophotometer, and KBr pellets were used for preparation. The ^1H NMR spectra were obtained using Bruker DRX-400 and 500 Advance instruments with $CDCl_3$ and acetone as solvents Reactants, solvents, and chemicals were obtained from Merck, Aldrich, and Fluka,

and used without further purification. The progress of reactions was examined using thin-layer chromatography (TLC) with silica gel Poly-Gram SILG/UV 254 plates.

2.2 Carbohydrates

Carbohydrates are a type of biological molecule known chemically as polyhydroxy aldehydes or polyhydroxy ketones. They consist of small sugar molecules linked together, and their chemical properties depend on the number of sugar units. Carbohydrates can exist as monosaccharides (such as glucose, galactose, fructose, and ribose) or as dimers, trimers, or polymers of these subunits, respectively referred to as disaccharides (e.g., sucrose, maltose, and lactose), oligosaccharides, and polysaccharides (such as starch, pectin, cellulose, and glycogen).

Fructose Catalyst and Its Properties Fructose, or fruit sugar, is one of the simple monosaccharides found in almost every plant. Pure and dry fructose is a solid white substance, extremely sweet, odorless, and crystalline, with greater solubility compared to other monosaccharides. Fructose can be obtained from various sources, including honey, tree and ground fruits, various berries, flowers, and root vegetables. In plants, fructose may exist as a monosaccharide or in combination with glucose (as a disaccharide called sucrose).

2.3 Preparation Method of Sulfonated Fructose as a Catalyst

Initially, Placed a 50-mL flask in an ice bath to maintain a temperature of zero degrees Celsius. Added 1 gram of fructose and 5 mL of chloroform to the flask. Stirred the mixture vigorously using a magnetic stirrer to ensure the fructose was well-dispersed in the chloroform. Used a dropping funnel to add 0.30 grams of chlorosulfonic acid to the flask dropwise over a period of 2 hours. After the complete addition of chlorosulfonic acid, continued stirring the reaction mixture vigorously for another 2 hours. This step was crucial for the removal of the white vapor of HCl gas from the reaction vessel. Proper ventilation or a fume hood was recommended to safely disperse the HCl gas. Filtered the reaction mixture to separate the precipitate from the liquid. Used filter paper suitable for fine precipitates. Washed the precipitate thoroughly with 10 mL of methanol to remove any remaining impurities and solvent. Dried the washed precipitate at room temperature. Ensured the drying process was complete to obtain the sulfonated fructose in its dry form. Maintained a constant temperature of zero degrees Celsius during the addition of chlorosulfonic acid to control the reaction rate and prevent any side reactions. The use of a fume hood was recommended to safely handle and disperse HCl gas generated during the reaction. Ensured that the drying process was done in a clean and dust-free environment to prevent contamination of the catalyst.

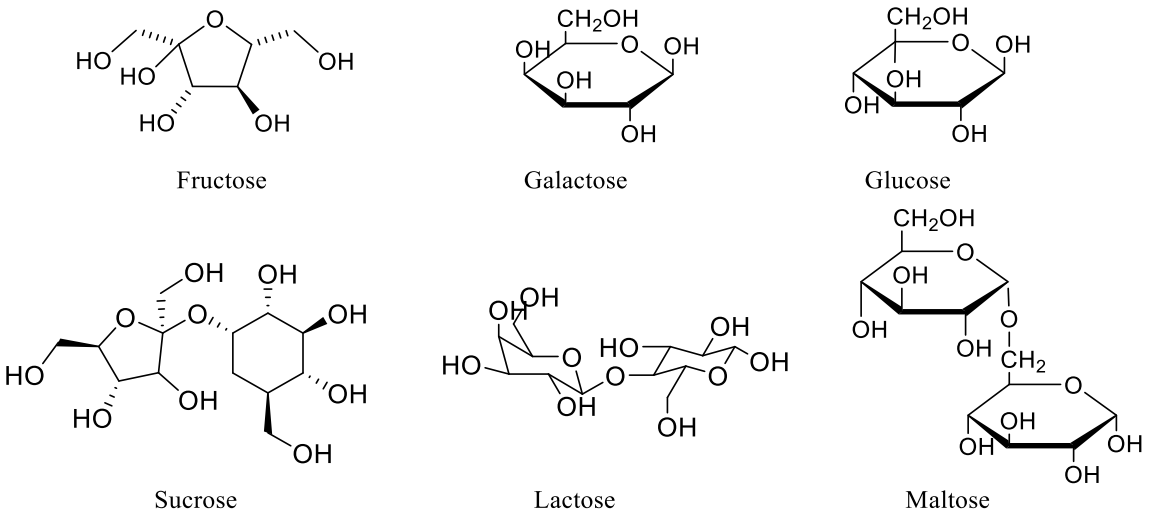


Fig. 2. Structure of polysaccharides

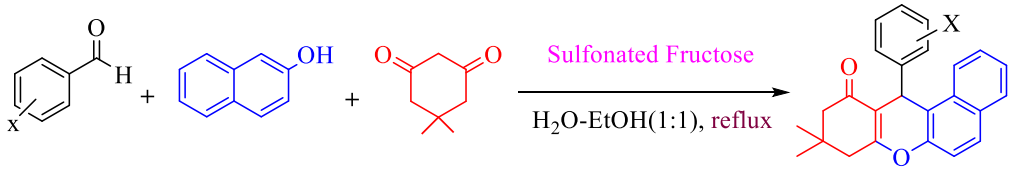
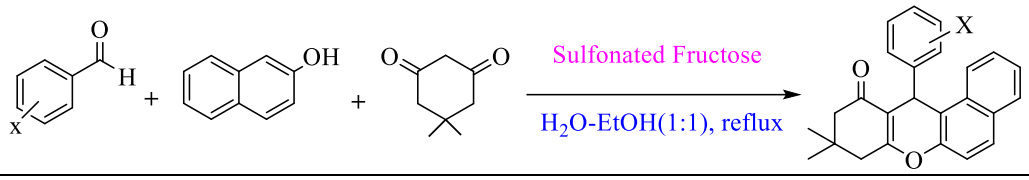


Fig. 3. illustrates the one-pot and three-component synthesis of tetrahydrobenzo[a]xanthen-11-ones in the presence of fructose

Table 1. Preparation of 9,9-Dimethyl-10,9-dihydro-8H-benzo[a]xanthene-11(12H)-one derivatives in the presence of sulfonated fructose catalyst and water-ethanol (1:1) solvent under reflux conditions



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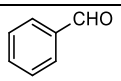
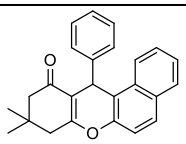
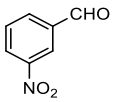
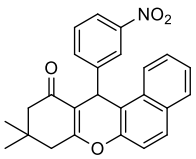
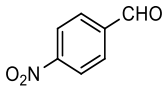
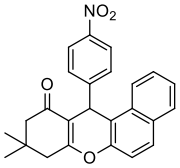
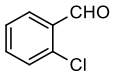
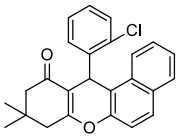
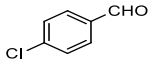
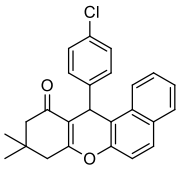
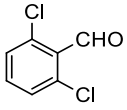
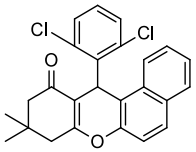
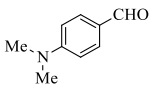
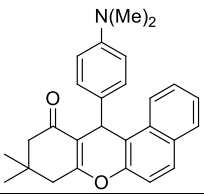
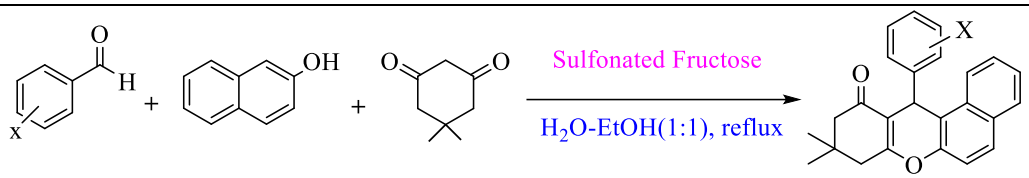
1			35	89	148-150
2			40	86	170- 172
3			30	93	175-177
4			35	91	180-183
5			30	91	178-179
6			25	83	185-187
7			65	81	175-178



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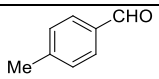
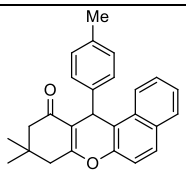
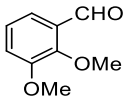
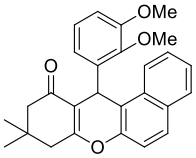
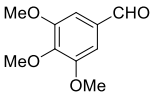
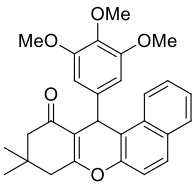
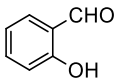
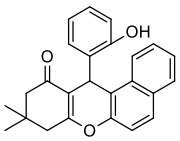
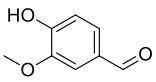
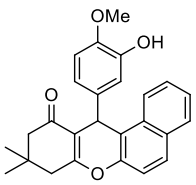
8			50	84	170- 179
9			75	81	203- 205
10			90	78	210-213
11			55	82	223-226
12			33	78	225-227

∗ The mentioned yield corresponds to the product obtained after purification steps

2.4 Synthesis of Tetrahydrobenzo[a] xanthene-11-one Derivatives in the Presence of Sulfonated Fructose as a Catalyst under Reflux Conditions in Water/ethanol

2.4.1 General procedure for the preparation of 12-aryl-8,9,10,12-tetrahydrobenzo[a] xanthene derivatives from the reaction between aldehyde, 2-naphthol, and dimedone in the presence of sulfonated fructose catalyst and water-ethanol solvent under reflux conditions

Prepared a 4 mL water-ethanol solvent mixture in a 1:1 ratio. In a 50-mL round-bottom flask, added 0.25 mmol of benzaldehyde, 0.25 mmol of 2-naphthol, and 0.25 mmol of dimedone and 0.08 g of sulfonated fructose catalyst to the flask. Poured the 4 mL of water-ethanol solvent mixture into the flask. Set up the reflux apparatus and placed the flask on a magnetic stirrer. Refluxed the reaction mixture and stirred it vigorously. Ensured the reaction was uniformly heated and well-mixed. Monitored the progress of the reaction using thin-layer chromatography (TLC) at regular intervals. Once the reaction was complete (as indicated by TLC), stopped the reflux and allowed the mixture to cool to room temperature. Diluted the reaction mixture by adding a sufficient amount of distilled water to the flask. After filtration, the precipitate was washed several times with hot distilled water to remove any soluble impurities and residual catalyst. The crude product was dissolved in a minimal amount of hot ethanol to achieve a clear solution. The solution was allowed to cool slowly to room temperature and then placed in an ice bath to complete the crystallization process. The

purified product was collected by filtration and dried under vacuum or at room temperature. The obtained results are presented in Table 1.

2.4.2 Spectral data related to tetrahydrobenzo[a]xanthene-11-one derivatives

Compound 9,9-dimethyl-12-phenyl-dihydro-8H-benzo[a]xanthen-11(12H)-one

White Solid, **M.P**. 148-150 ^{o}C; **M.F**. $C_{25}H_{22}O_2$; **M.W**. Extract: 354.444; **IR** (KBr) umax (cm^{-1}): 3029 (aromatic C–H), 2922 (aliphatic C-H), 1650 (C=C), 1235 (CO), 693-814 One strong band (1,4-Disubstituted Ring). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.89 (s, 3H), 1.03 (s, 3H), 2.18 (d, *J*= 16.2 Hz, 1H), 2.24 (d, *J*= 16.2 Hz, 1H), 2.48 (s, 2H), 5.71 (s, 1H), 6.99-7.02 (m, 1H), 7.13-7.18 (m, 2H), 7.27-7.37 (m, 5H), 7.67-7.70 (m, 2H), 7.98 (d, *J* = 8.4 Hz, 1H)

Compound 9,9-dimethyl-12-(3-nitrophenyl)-dihydro-8H-benzo[a]xanthen-11(12H)-one

White Solid, **M.P**. Found (^{o}C): 170-172; **M.F**. $C_{26}H_{24}NO_4$; **M.W**. Extract: 414.477; **IR** (KBr) umax (cm^{-1}): 3383 (aromatic C–H), 2960 (aliphatic C-H), 1597 (C=C), 1347 (CO), 730 One strong band (1,4-Disubstituted Ring). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.95 (s, 3H), 1.13 (s, 3H), 2.24 (d, *J* = 16.2 Hz, 1H), 2.32 (d, *J* = 16.2 Hz, 1H), 2.60 (s, 2H), 5.81 (s, 1H), 7.34-7.45 (m, 4H), 7.78-7.81 (m, 3H), 7.86 (d, *J* = 7.2 Hz, 1H), 7.91-7.93 (m, 1H), 8.11-8.12 (m, 1H)

Compound 9,9-dimethyl-12-(4-nitrophenyl)-dihydro-8H-benzo[a]xanthen-11(12H)-one

Pale yellow Solid, **M.P**. Found (^{o}C): 175-177; **M.F**. $C_{27}H_{17}NO_3$; **M.W**. Extract (amu): 403.441; **IR** (KBr) umax (cm^{-1}): 3383 (aromatic C–H), 2960 (aliphatic C-H), 1597 (C=C), 1378 (CO), 763-893 One strong band (1,4-Disubstituted Ring). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.94 (s, 3H), 1.13 (s, 3H), 2.25 (d, *J* = 16.2 Hz, 1H), 2.33 (d, *J* = 16.2 Hz, 1H), 2.60 (s, 2H), 5.81 (s, 1H), 7.35-7.45 (m, 3H), 7.51-7.52 (m, 2H), 7.80-7.84 (m, 3H), 8.03 (d, *J* = 6.6 Hz, 2H)

Compound 12-(2-chlorophenyl)-9,9-dimethyl-dihydro-8H-benzo[a]xanthen-11(12H)-one

White solid, **M.P**. Found (^{o}C): 180-183; **M.F**. $C_{25}H_{21}ClO_2$; **M.W**. Extract (amu): 388.899; **IR** (KBr) umax (cm^{-1}): 3392 (aromatic C–H), 2957 (aliphatic C-H), 1610 (C=C), 1383 (CO), 771 One strong band (1,4-Disubstituted Ring). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.98 (s, 3H), 1.12 (s, 3H), 2.22 (d, *J* = 16.2 Hz, 1H), 2.30 (d, *J* = 16.2 Hz, 1H), 2.55-2.62 (m, 2H), 5.99 (s, 1H), 6.96-7.05 (m, 2H), 7.25-7.48 (m, 5H), 7.72-7.75 (m, 2H), 8.22 (d, *J* = 7.8 Hz, 1H)

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

Pale yellow solid, **M.P**. Found (^{o}C): 178-179; **M.F**. $C_{25}H_{21}ClO_2$; **M.W**. Extract (amu): 388.899; **IR** (KBr) umax (cm^{-1}): 3406 (aromatic C–H), 2958 (aliphatic C-H), 1589 (C=C), 1384 (CO), 771 One strong band (1,4-Disubstituted Ring). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.87 (s, 1H), 7.00-7.03 (m, 2H), 7.08- 7.17 (m, 6H), 7.31-7.46 (m, 9H), 7.83 (d, *J* = 9.0 Hz, 2H), 7.89 (d, *J* = 8.4 Hz, 1H)

Compound 12-(2,6-dichlorophenyl)-9,9-dimethyl-dihydro-8H-benzo[a]xanthen-11(12H)-one

M.P. Found (^{o}C): 185-187; **M.F**. $C_{25}H_{20}Cl_2O_2$; **M.W**. Extract (amu): 422.333; **IR** (KBr) umax (cm^{-1}): 3384 (aromatic C–H), 2958 (aliphatic C-H), 1677(C=C), 1385 (CO), 773 One strong band (1,4-Disubstituted Ring).

Compound 12-(4-(dimethylamino)phenyl)-9,9-dimethyl-dihydro-8H-benzo[a]xanthen-11(12H)-one

White **solid, M.P**. Found (^{o}C): 175-178; **M.F**. $C_{27}H_{27}NO_2$; **M.W**. Extract (amu): 397-511; **IR** (KBr) umax (cm^{-1}): 3382 (aromatic C–H), 2958 (aliphatic C-H), 1662 (C=C), 1371 (CO), -853-773 One strong band (1,4-Disubstituted Ring). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.00 (s, 3H), 1.11 (s, 3H), 2.23 – 2.32 (q, J = 16.5 Hz, 8.5 Hz, 2H), 2.82 (s, 6H), 2.56 (s, 2H), 5.61 (s, 1H), 6.54 – 6.55 (d, J = 8.5 Hz, 2H), 7.19 – 7.17 (d, J = 8.5 Hz, 2H), 7.29 – 7.31 (d, J = 9.0 Hz, 1H), 7.34 – 7.37 (t, J = 7.0 Hz, 14.5 Hz, 1H), 7.41 – 7.44 (t, J = 7.5 Hz, 15.5 Hz, 1H), 7.72 – 7.77 (dd, J = 8.0 Hz, 9.0 Hz, 2H), 8.03 – 8.04 (d, J = 8.5 Hz, 1H)

Compound 9,9-dimethyl-12-(p-tolyl)-dihydro-8H-benzo[a]xanthen-11(12H)-one

White solid, **M.P**. Found (^{o}C): 170-179; **M.F**. $C_{26}H_{24}O_2$; **M.W**. Extract (amu): 368-477; **IR** (KBr) umax (cm^{-1}): 3412 (aromatic C–H), 3337 (aliphatic C-H), 1611 (C=C), 1194 (CO), -755-784 One strong band (1,4-Disubstituted Ring). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.97 (s, 3H), 1.11 (s, 3H), 2.19 (s, 3H), 2.24 (d, *J* = 16.8 Hz, 1H), 2.29 (d, *J* = 16.2 Hz, 1H), 2.56 (s, 2H), 5.66 (s, 1H), 6.96 (d, *J* = 7.8 Hz, 2H), 7.21-7.43 (m, 5H), 7.72-7.76 (m, 2H), 8.00 (d, *J* = 8.4 Hz, 1H)

Compound 9,9-dimethyl-12-(3,4,5-trimethoxyphenyl)-dihydro-8H-benzo[a]xanthen-11(12H)-one

M.P. Found (°C): 203-205; **M.F**. $C_{28}H_{28}O_5$; **M.W**. Extract (amu): 444-522; **IR** (KBr) umax (cm^{-1}): 3386 (aromatic C–H), 2956 (aliphatic C-H), 1591(C=C), 1274 (CO), 774-879 One strong band (1,4-Disubstituted Ring).

Compound 12-(2-hydroxyphenyl)-9,9-dimethyl-dihydro-8H-benzo[a]xanthen-11(12H)-one

White Solid, **M.P**. Found (°C): 210-213; **M.F**. $C_{25}H_{22}O_3$; **M.W**. Extract (amu): 459-555; **IR** (KBr) umax (cm^{-1}): 3357 (aromatic C–H), 2957 (aliphatic C-H), 1557(C=C), 1236 (CO), -794-878 One strong band (1,4-Disubstituted Ring). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.99 (s, 3H), 1.15 (s, 3H), 2.36 (d, *J* = 16.2 Hz, 1H), 2.41 (d, *J* = 16.2 Hz, 1H), 2.61 (s, 2H), 5.77 (s, 1H), 6.59-6.63 (m, 2H), 6.98-7.02 (m, 2H), 7.32-7.41 (m, 3H), 7.67 (d, *J* = 9.6 Hz, 1H), 7.76-7.79 (m, 2H), 9.26 (s, 1H)

Compound 12-(3-hydroxy-4-methoxyphenyl)-9,9-dimethyl-9,10-dihydro-8H-benzo[a]xanthen-11-one

M.P. Found (°C): 223-226; **M.F**. $C_{29}H_{31}O_5$; **M.W**. Extract (amu): 459-555; **IR** (KBr) umax (cm^{-1}): 3382 (aromatic C–H), 2956 (aliphatic C-H), 1662(C=C), 1371 (CO), 548-773 One strong band (1,4-Disubstituted Ring).

2.5 Synthesis of 14H-Dibenzo[a,j]xanthenes in the Presence of Sulfonated Fructose as a Catalyst

2.5.1 General procedure for the preparation of 14-aryl-14h-dibenzo[a,j]xanthenes from the reaction between aldehydes and 2-naphthol in the presence of sulfonated fructose and water-ethanol solvent under reflux conditions

Prepared a 4 mL water-ethanol solvent mixture in a 2:1 ratio. In a 50-mL round-bottom flask, added 1 mmol of the aryl aldehyde and 2 mmol of 2-naphthol and 1.25 g of sulfonated fructose catalyst to the flask. Poured the 4 mL of water-ethanol solvent mixture into the flask. Set up the reflux apparatus and placed the flask on a magnetic stirrer. Refluxed the reaction mixture and stirred it vigorously. Ensured the reaction was uniformly heated and well-mixed. Monitored the progress of the reaction using thin-layer chromatography (TLC) at regular intervals. Once the reaction was complete (as indicated by TLC), stopped the reflux and allowed the mixture to cool to room temperature. Diluted the reaction mixture by adding a sufficient amount of distilled water to the flask. After filtration, the precipitate was washed several times with hot distilled water to remove any soluble impurities and residual catalyst. The crude product was dissolved in a minimal amount of hot ethanol to achieve a clear solution. The solution was allowed to cool slowly to room temperature and then placed in an ice bath to complete the crystallization process. The purified product was collected by filtration and dried under vacuum or at room temperature. The obtained results are presented in Table 2.

2.5.2 Spectral data related to 14-Phenyl-14H-dibenzo[a,j]xanthene derivatives

Compound 14-Phenyl-14H-dibenzo[a,j]xanthene

M.P. Found (°C): 183-185; **M.P**. Reported (°C) [Lit]: 181-183; Pale yellow solid**, M.F.** : $C_{27}H_{18}O$; **M.W**. Extract: 358.444; **IR** (KBr) u_{max} (cm^{-1}): 3071 (aromatic C–H), 2923 (aliphatic C-H), 1624 (C=C), 1249 (C-O). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.50 (s, 1H, CH), 6.98–7.01 (t, 1H, *J* = 7.6, Ar), 7.13–7.17 (t, 2H, *J* = 7.6, Ar), 7.40–7.43 (t, 2H, *J* = 7.6, Ar), 7.48–7.54 (m, 4H, Ar), 7.56–7.60 (t, 2H, *J* = 7.2, Ar), 7.81–7.92 (d, 2H, *J* = 8.8, Ar), 7.82–7.84 (d, 2H, *J* = 8.0, Ar), 8.39–8.41 (d, 2H, *J* = 8.8, Ar)

Compound 14-(3-Nitrophenyl)-14H-dibenzo[a,j]xanthene

M.P. Found (°C): 208-210; **M.P**. Reported (°C) [Lit]: 211-212; yellow solid, **M.F**. $C_{27}H_{17}NO_3$; **M.W**. Extract: 403.441; **IR** (KBr) u_{max} (cm^{-1}): 3074 (aromatic C–H), 2923 (aliphatic C-H), 1625 (C=C), 1559 (NO_2), 1346 (NO_2), 1249 (C–O), 690-900 three bond (1,3-disubstituted ring). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.62 (s, 1H, CH), 7.28–7.32 (t, 1H, *J* = 7.6, Ar), 7.43–7.47 (t, 2H, *J* = 7.6, Ar), 7.51–7.53 (d, 2H, *J* = 8.8, Ar), 7.60–7.64 (t, 2H, *J* = 7.2, Ar), 7.81–7.87 (m, 6H, Ar), 8.30–8.32 (d, 2H, *J* = 8.4, Ar), 8.42 (s, 1H, Ar)

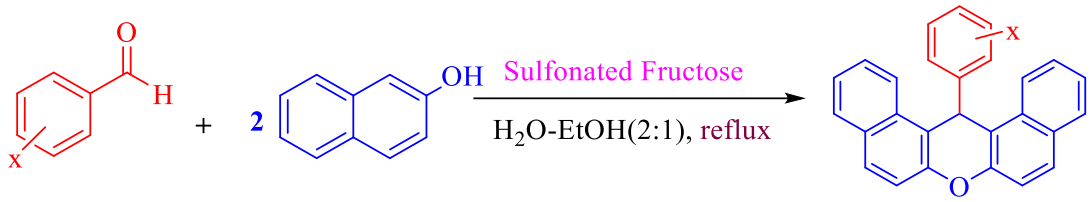
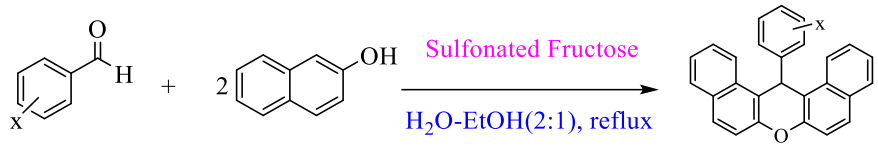
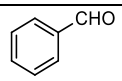
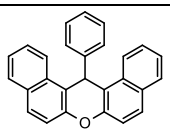
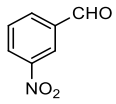
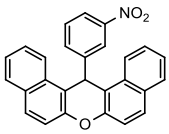
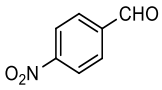
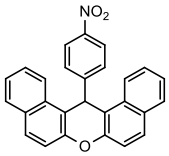
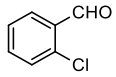
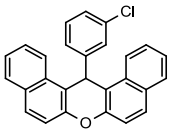
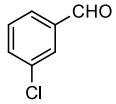
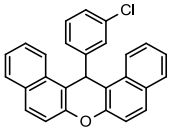
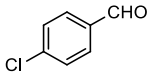
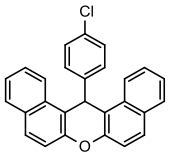
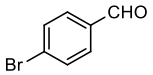
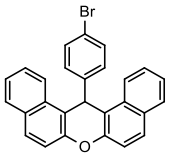
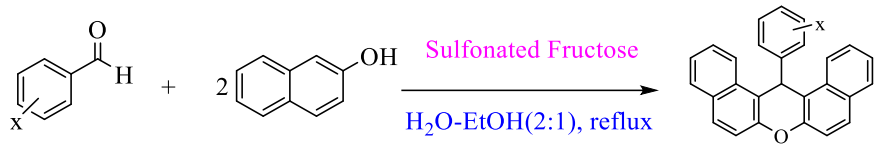


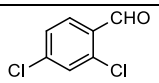
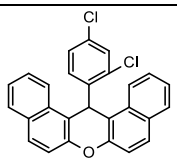
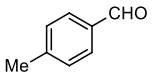
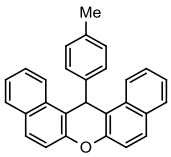
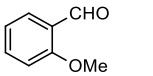
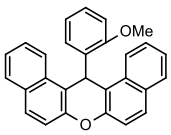
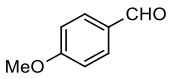
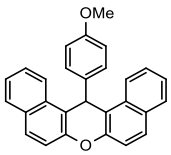
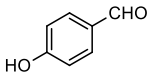
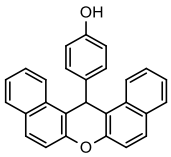
Fig. 4. Synthesis of mono- and tri-substituted 14-phenyl-14h-dibenzo[a,j]xanthenes in the presence of fructose

Table 2. Preparation of 14-Aryl-14H-dibenzo[a,j]xanthenes in the presence of sulfonated fructose and water-ethanol (2:1) solvent under reflux conditions



Row	Aldehyde	Product	Time (min)	Yield (%)	Reference / Melting Point (°C) [30-33]
1			30	91	185-186/183
2			45	90	217-219/213
3			25	95	>300/312
4			40	93	211-214/213-215
5			40	92	169-171/174
6			40	90	282-283/286-288
7			35	91	240/237-238



Row	Aldehyde	Product	Time (min)	Yield (%)	Reference / Melting Point (°C) [30-33]
8			35	88	229-230/227
9			65	89	225-227/228
10			80	90	256-259/258-259
11			75	88	205-206/202
12			75	84	144/140

∗ *The mentioned yield corresponds to the product obtained after purification steps*

Compound 14-(4-Nitrophenyl)-14H-dibenzo[a,j]xanthene

M.P. Found (°C): 310-312; **M.P**. Reported (°C) [Lit]: 310-312; Yellow solid, **M.F.** $C_{27}H_{17}NO_3$; **M.W**. Extract: 403.441; **IR** (KBr) υ_{max} (cm^{-1}): 3074 (aromatic C–H), 2923 (aliphatic C-H), 1625 (C=C), 1559 (NO_2), 1346 (NO_2), 1249 (C–O), 690-900 three bond (1,3-disubstituted ring). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.62 (s, 1H, C-H), 7.44 (ddd, 2H, *J*1 = 8.1, *J*2 = 6.8 and *J*3 = 1.0 Hz),

7.53 (d, 2H, *J* = 8.8 Hz), 7.62 (ddd, 2H, *J*1 = 8.3, *J*2 = 6.8 and *J*3 = 1.4 Hz), 7.68 (d, 2H, *J* = 8.8 Hz), 7.83–7.90 (m, 4H), 8.0 (d, 2H, *J* = 8.8 Hz), 8.29 (d, 2H, *J* = 8.3 Hz)

Compound 14-(2-Chlorophenyl)-14H-dibenzo[a,j]xanthene

M.P. Found (°C): 213-215; **M.P**. Reported (°C) [Lit]: 214-215; white solid, **M.F**. $C_{27}H_{17}ClO$; **M.W**. Extract: 392.889; **IR** (KBr) υ_{max} (cm^{-1}): 3056 (aromatic C–H), 2924 2992 (aliphatic C-H), 1247 (C-O), near 750 One strong band (1,2-disubstituted rings), 711. ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 6.81 (s, 1H, CH), 6.92 (m, 2H, Ar), 7.40–7.44 (m, 3H, Ar), 7.48–7.51 (d, 2H, *J* = 8.8, Ar), 7.61–7.64 (m, 5H, Ar), 8.74–8.76 (d, 2H, *J* = 8.4, Ar)

Compound 14-(4-Chlorophenyl)-14H-dibenzo[a,j]xanthene

M.P. Found (°C): 287; **M.P**. Reported (°C) [Lit]: 287-289; Brown solid, **M.F**. $C_{27}H_{17}ClO$; **M.W**. Extract: 392.889; **IR** (KBr) υ_{max} (cm^{-1}): 3050 (aromatic C–H), 2922 (aliphatic C-H), 1625 (C-C), 1244 (C-O), 800-850 One strong band (1,4-disubstituted ring), 742. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.48 (s, 1H, CH), 7.10–7.12 (d, 2H, *J* = 8.4, Ar), 7. 41–7.47 (m, 4H, Ar), 7.48–7.50 (d, 2H, *J* = 8.8, Ar), 7.57–7.61 (t, 2H, *J* = 7.6, Ar), 7.80–7.82 (d, 2H, *J*

= 8.8, Ar), 7.84–7.86 (d, 2H, *J* = 8.0, Ar), 8.32–8.34 (d, 2H, *J* = 8.4, Ar)

Compound 14-(2,4-Dichlorophenyl)-14H-dibenzo[a,j]xanthene

M.P. Found (°C): 252-253; **M.P**. Reported (°C) [Lit]: 254-255; pale yellow solid, **M.F**. $C_{27}H_{16}Cl_2O$; **M.W**. Extract: 427.32; **IR** (KBr) υ_{max} (cm^{-1}): 3061 (aromatic C–H), 2923 (aliphatic C-H), 1624 (C-C), 1247 (C-O), 808, 742, 711. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 6 (s, 1H, CH), 6.79 (d, 1H, 6.77 (s, 1H, CH), 6.90–6.92 (d, 1H, Ar), 7.28–7.32 (m, 2H, Ar), 7.43–7.50 (m, 4H, Ar), 7.61–7.65 (t, 2H, *J* = 7.6, Ar), 7.81–7.85 (t, 4H, *J* = 9.0, Ar), 8.65–8.67 (d, 2H, *J* = 8.0, Ar)

Compound 14-(Para-tolyl)-14H-dibenzo [a,j] xanthene

M.P. Found (°C): 226; **M.P**. Reported (°C) [Lit]: 228-230); pale yellow solid, **M.F**. $C_{28}H_{20}O$; **M.W**. Extract: 372 **IR** (KBr) υ_{max} (cm^{-1}): 3061 (aromatic C–H), 2923 (aliphatic C-H), 1624 (C-C), 1247 (C-O), 800-850 One strong band (1,4-Disubstituted Ring). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 6.46 (s, 1H, CH), 6.95–6.97 (d, 2H, *J* = 8.0, Ar), 7.39–7.43 (m, 4H, Ar), 7.47–7.50 (d, 2H, *J* = 9.2, Ar), 7.56–7.60 (t, 2H, *J* = 9.2, Ar), 7.78–7.80 (d, 2H, *J* = 8.8, Ar), 7.82–8.84 (d, 2H, *J* = 8.0, Ar), 8.39–8.41 (d, 2H, *J* = 8.8, Ar)

Compound 14-(4-Methoxyphenyl)-14H-dibenzo [a,j]xanthene

M.P. Found (°C): 263-265; **M.P**. Reported (°C) [Lit]: 264; **M.F**. $C_{28}H_{20}O_2$; **M.W**. Extract: 388.470; **IR** (KBr) υ_{max} (cm^{-1}): 3051 (aromatic C–H), 2921 (aliphatic C-H), 1622 (C-C), 1247 (C-O), near 750 One strong band (1,2-disubstituted rings). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.66 (s, 3 H), 6.49 (s, 1 H),

6.71 (d, *J*= 8.8 Hz, 2 H), 7.43 7.47 (m, 4 H), 7.52 (d, *J*= 8.9 Hz, 2 H), 7.63 (t, *J*= 8.1 Hz, 2 H), 7.82 (d, *J*= 8.9 Hz, 2 H), 7.87 (d, *J*= 8.0 Hz, 2 H), 8.43 (d, *J*= 8.5 Hz, 2 H)

Compound 14-(4-Methoxyphenyl)-14H-dibenzo[a,j]xanthene

M.P. Found (°C): 203-204; **M.P**. Reported (°C) [Lit]: 202–204; **M.F**. $C_{28}H_{20}O_2$; **M.W**. Extract: 388.470; **IR** (KBr) υ_{max} (cm^{-1}): 3050 (aromatic C–H), 2922 (aliphatic C-H), 1593 (C=C), 1247 (C-O), 800-850 One strong band (1,4-Disubstituted Ring). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 6.45 (s, 1H, CH), 6.67–6.69 (d, 2H, *J* = 8.4, Ar), 7.40–7.44 (m, 4H, Ar), 7.47–7.49 (d, 2H, *J* = 8.8, Ar), 7.56–7.60 (t, 2H, *J* = 7.2, Ar), 7.78–7.80 (d, 2H, *J* = 8.8, Ar), 7.82–8.84 (d, 2H, *J* = 8.0, Ar), 8.38–8.40 (d, 2H, *J* = 8.4, Ar)

3. RESULTS AND DISCUSSION

3.1 Optimization of Reaction Conditions for the Preparation of Tetrahydrobenzo[a]xanthen-11-one in the Presence of Fructose

Optimizing reaction conditions, including the amount of materials, temperature, type, and amount of solvent during chemical reactions, is one of the most important stages of any reaction. This process can significantly affect the efficiency of reaction conditions, the yield of the obtained products, and the reaction time. Optimal conditions should be selected to evaluate the reaction both in terms of time and suitable yield. To this end, the reaction of 4-chlorobenzaldehyde, 2-naphthol, and dimedone in a 1:1:1 molar ratio was chosen as a model reaction, and reaction conditions were investigated in terms of temperature, solvent, different catalysts, and various amounts of the catalyst. The results obtained are presented in Table 3.

As evident, the highest yield and the shortest reaction time were achieved under reflux conditions and using water-ethanol (1:1) as the solvent, with 0.08 gr of sulfonated fructose employed as the catalyst.

3.1.1 Investigation of reaction conditions and optimization of catalyst amount, temperature, and solvent in the synthesis of tetrahydrobenzo[a]xanthen-11-one derivatives

In this study, the compound tetrahydrobenzo[a]xanthen-11-one was synthesized. Various derivatives of xanthens were prepared from the reaction between dimedone, 2-naphthol, and benzaldehyde derivatives through different methods. To determine the optimal temperature, the reaction between 4-chlorobenzaldehyde, 2-naphthol, and dimedone in a 1:1:1 molar ratio was chosen as the reference reaction. Initially, 1 mmol of the starting materials was placed in test tubes, to

which 4 mL of ethanol and 1.0 gr of fructose were added, and the reaction conditions were examined at different temperatures. The results obtained are presented in Table 3. As observed in the Table 3, reflux conditions were selected as the optimal temperature (Table 3, row 3). For selecting the suitable solvent, a comparison between ethanol and water-ethanol was made, where the water-ethanol solvent (Table 3, row 4) showed better results. Further investigations indicated that the ratio of 1:1 of water yielded better results compared to ratios of 1:2 and 2:1 (Table 3, row 4). To determine the more suitable catalyst, the same reaction under reflux conditions with water-ethanol (1:1) solvent in the presence of fructose, maltose, and sulfonated fructose, which had been prepared, was repeated, showing that sulfonated fructose provided better results (Table 3, row 8). To optimize the amount of sulfonated fructose as the catalyst, the same reaction was tested under reflux conditions with different amounts (0.5, 1.0, and 1.5 gr). The product obtained in the presence of 0.8 gr of sulfonated fructose showed the highest yield and the shortest reaction time, and increasing the amount of catalyst had no significant effect on the yield (Table 3, row 12).

3.1.2 Investigation of proposed mechanism for the synthesis of tetrahydrobenzo[a]xanthen-11-one derivatives using aromatic aldehydes, 2-naphthol, and dimedone in the presence of fructose catalyst

While we do not have a specific mechanism for the formation of tetrahydrobenzo [a]xanthen-11-one derivatives in the presence of fructose, a plausible mechanism for this synthesis has been proposed based on our investigations and considering the mechanisms reported in the articles [38] (Fig. 5).

We have demonstrated that fructose forms some kind of micelle-like structures, which can hold molecules and further catalyze reactions, possibly activated by hydrogen bonds. Hydrogen bonding can be formed between protons in OH groups of the agarose polymer in the agar and the substrate, leading to activation during the reaction [34-37].

We speculate that fructose predominantly catalyzes the reactions through hydrogen bonding. Initially, the free OH groups on the surface of fructose activate the carbonyl group.

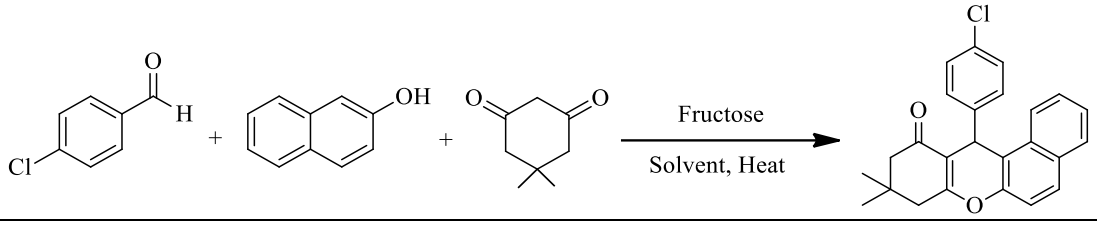
After the activation of the aldehyde by the catalyst and nucleophilic attack of 2-naphthol on it from the alpha position, which has higher electron density, an intermediate (3) (ortho-quinomethide (o-QMs)) is formed by the elimination of a water molecule. Then, with the addition of dimedone, the activated Michael molecule forms an unsaturated carbonyl intermediate (3), creating intermediate (4). In the next step, intermediate (5) is formed by the nucleophilic attack of the enol oxygen on the activated carbonyl group of intermediate (4). Finally, cyclization occurs, creating the hemi-ketal ring, which, upon proton transfer and elimination of water, leads to the formation of the product (7).

3.1.3 Investigation of results obtained from the reaction of aldehydes, 2-naphthol, and dimedone in the presence of sulfonated fructose for the synthesis of tetrahydrobenzo[a]xanthen-11-one derivatives

Xanthens possess extensive biological and pharmacological properties, as well as various applications in different fields. Over the past years, hundreds of articles have been published regarding the methods of preparation, pharmacological properties, and industrial applications of these compounds. Due to their wide-ranging properties, these compounds have attracted much attention from researchers. Therefore, presenting new methods or improving existing ones can be of significant importance. Some methods are harmful to the environment or lack significant yields. Hence, a simple and efficient method for synthesizing these compounds is needed.

To demonstrate the advantage of using sulfonated fructose as a catalyst compared to other catalysts in the synthesis of these compounds, the results obtained from this green catalyst have been compared with those obtained from other catalysts reported in reputable scientific articles.

Table 3. Optimization of reaction conditions for the preparation of tetrahydrobenzo[a]xanthen-11-one in the presence of different amounts of sugar, temperature, and solvent



Row	Catalyst	Catalyst Amount (g)	Temp.(°C)	Solvent	Time (min)	Yield (%)
1	Fructose	0.1	r.t	EtOH	24	Trace
2	Fructose	0.1	50	EtOH	180	38
3	Fructose	0.1	reflux	EtOH	45	86
4	Fructose	0.1	reflux	H_2O-EtOH(1:1)	40	89
5	Fructose	0.1	reflux	H_2O-EtOH(1:2)	40	88
6	Fructose	0.1	reflux	H_2O-EtOH(2:1)	45	85
7	Maltose	0.1	reflux	H_2O-EtOH(1:1)	35	87
8	Sulfonated Fructose	0.1	reflux	H_2O-EtOH(1:1)	30	90
9	Sulfonated Fructose	0.05	reflux	H_2O-EtOH(1:1)	35	85
10	**Sulfonated Fructose**	**0.08**	**reflux**	**H_2O-EtOH(1:1)**	**30**	**91**
11	Sulfonated Fructose	0.15	reflux	H_2O-EtOH(1:1)	30	90
12	Sulfonated Fructose	0.08	90	S.F	70	82

∗ The mentioned yield corresponds to the product obtained after purification steps

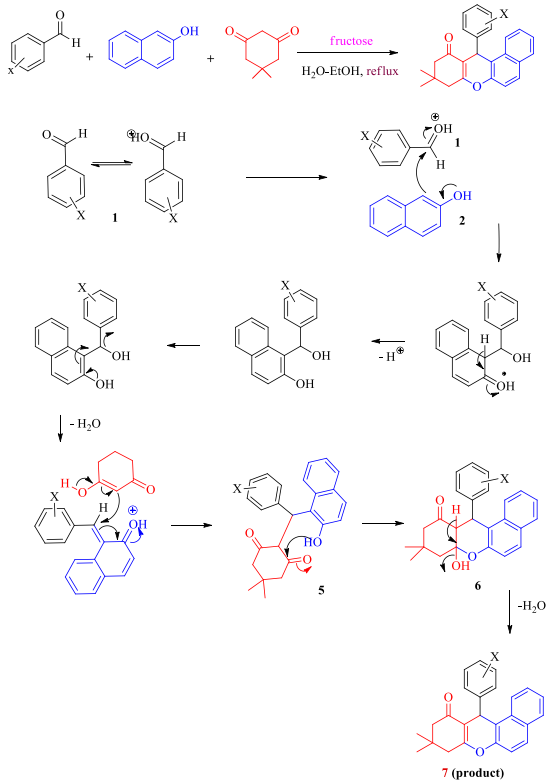


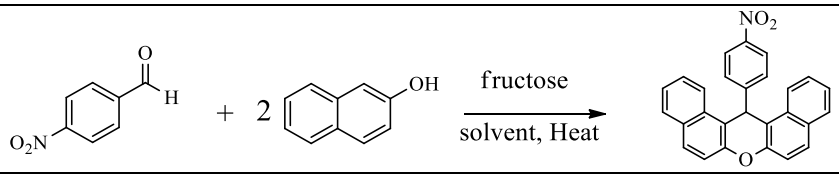
Fig. 5. Investigation of the proposed mechanism for the synthesis of tetrahydrobenzo[a]xanthen-11-one derivatives using aldehyde and 2-naphthol in the presence of sulfonated fructose

Table 4. Comparison of results obtained in the synthesis of 9,9-dimethyl-10,9-dihydro-8h-benzo[a]xanthen-11(12h)-one derivatives in the presence of sulfonated fructose and other catalysts mentioned in scientific articles

Row	Catalyst	Conditions	Time (Min)	Yield	Reference
1	$NaHSO_4.SiO_2$	CH_2Cl_2 and reflux	300	9	[15]
2	$InCl_3$ (30 mol%)	No solvent and 120 °C	30	80	[12]
3	P_2O_5 (20 mol%)	No solvent and 120 °C	40	78	[38]
4	$HClO_4$-SiO_2	No solvent and 80 °C	60	95	[39]
5	TBAF (10mol%)	Water and reflux	180	30	[40]
6	SPA(0.04)	Ethanol and reflux	540	99	[41]
7	Sulfonated Fructose	Water-Ethanol and reflux	50	90	Present study

** The reported yield is for the product obtained after purification steps and is based on benzaldehyde*

Table 5. Optimization of reaction conditions for the preparation of 14-Aryl-14H-dibenzo[a,j]xanthenes in the presence of different amounts of catalyst, temperature, and solvent



Row	Catalyst	Catalyst Amount (g)	Temp. (°C)	Solvent	Time (min)	Yield (%)
1	Fructose	0.1	r.t	EtOH	24	Trace
2	Fructose	0.1	50	EtOH	120	34
3	Fructose	0.1	reflux	EtOH	45	86
4	Fructose	0.1	reflux	EtOH	40	79
5	Fructose	0.1	reflux	H_2O-EtOH(1:1)	40	85
6	Fructose	0.1	reflux	H_2O-EtOH(1:2)	40	84
7	Fructose	0.1	reflux	H_2O-EtOH(3:1)	35	84
8	Maltose	0.1	reflux	H_2O-EtOH(1:1)	35	87
9	Sulfonated Fructose	0.1	reflux	H_2O-EtOH(2:1)	35	89
10	Sulfonated Fructose	0.1	reflux	H_2O-EtOH(2:1)	25	92
11	Sulfonated Fructose	0.05	reflux	H_2O-EtOH(2:1)	40	82
12	**Sulfonated Fructose**	**0.125**	**reflux**	**H_2O-EtOH(2:1)**	**25**	**95**
13	Sulfonated Fructose	0.15	reflux	H_2O-EtOH(2:1)	25	94

** The mentioned yield corresponds to the product obtained after purification steps*

In this research, the synthesis of tetrahydrobenzo[a]xanthen-11-one has been developed by considering the principles of green chemistry and utilizing environmentally benign, cost-effective, and readily available catalysts. In presenting new and practical methods for synthesizing these heterocyclic compounds, we have introduced an environmentally friendly and efficient method through the three-component reaction of 2-naphthol, dimedone, and aromatic aldehydes in the presence of fructose as the catalyst. As Table 4 indicates, compared to other methods such as the use of catalysts like $NaHSO_4.SiO_2$, $InCl_3$, $HClO_4$-SiO_2, TBAF, SPA, and P_2O_5, our method offers easier conditions.

3.2 Optimization of Reaction Conditions for the Preparation of 14-Aryl-14H-Dibenzo[a,j]xanthenes in the Presence of Fructose

To perform the reaction more efficiently, meaning to obtain the desired product in a shorter time

with a higher yield, the following investigations were conducted:

To determine the optimal temperature, we selected the reaction between 4-nitrobenzaldehyde and 2-naphthol in a molar ratio of 1:2 as the reference reaction. This reaction was performed in the presence of 4 mL of ethanol and 1.0 gr of sulfonated fructose at various temperatures. The results obtained are presented in Table 5. The highest yield and shortest reaction time were achieved under reflux conditions using a water-ethanol solvent (2:1) and employing 1.25 gr of sulfonated fructose catalyst.

3.2.1 Investigation of reaction conditions and optimization of catalyst amount, temperature, and solvent in the synthesis of 14h-dibenzo[a,j]xanthene derivatives

As observed in the table, reflux conditions were selected as the optimal temperature (Table 5, row 3). To select the suitable solvent, a comparison between ethanol, water-ethanol, and water-ethanol solvent (Table 5, row 7) indicated better results with a 2:1 ratio of water to ethanol compared to ratios of 1:1, 2:1, 3:1, and 1:2 (Table 5, row 6). To determine the suitable catalyst for the reaction in the presence of fructose, maltose, and sulfonated fructose, it was repeated, and sulfonated fructose was recognized as the better catalyst (Table 5, row 9). In optimizing the amount of sulfonated fructose as the catalyst, the same reaction under reflux conditions with different amounts of catalyst (0.5, 1.0, 1.25, and 1.5 gr) was tested. In the presence of 1.25 gr of catalyst, the product was obtained with the highest yield and in the shortest time, and increasing the amount of catalyst had no significant effect on the yield (Table 5, row 11).

3.2.2 Investigation of proposed mechanism for the synthesis of 14h-dibenzo[a,j]xanthene derivatives using aldehyde and 2 molar equivalents of 2-naphthol in the presence of fructose

Based on the mechanisms reported in the articles by Firouzabadi [42], and Naimi [43], the proposed mechanism is presented in Fig. 6. We speculate that fructose predominantly catalyzes the reactions through hydrogen bonding.

Initially, the OH groups on the surface of fructose activate the carbonyl group, leading to the condensation of the aldehyde and 2-naphthol, forming an intermediate (3) (ortho-quinomethide (o-QMs)) by the elimination of water. Subsequently, with the attack of the second molecule of 2-naphthol on this intermediate and the nucleophilic addition at positions 1 and 4, intermediate (4) is formed. In the next step, intermediate (5) is formed by the nucleophilic attack of the enol oxygen on the activated carbonyl group of intermediate (4). Intramolecular ring formation and proton transfer, followed by the elimination of a water molecule, lead to the formation of the dibenzothiazine product (6).

3.2.3 Examination of results obtained from the reaction of aldehyde and 2-naphthol in the presence of sulfonated fructose for the synthesis of 14h-dibenzo[a,j]xanthene derivatives

To demonstrate the advantage of using sulfonated fructose as a catalyst compared to other catalysts in the synthesis of these compounds, the results obtained from this green catalyst have been compared with other catalysts reported in reputable scientific articles.

In this reaction, as indicated by the data in Table 6, the method we have employed for synthesizing 14H-Dibenzo[a,j]xanthene derivatives through the three-component reaction of 2 molar equivalents of 2-naphthol and aromatic aldehydes in the presence of sulfonated fructose as the catalyst offers easier conditions compared to other methods such as I_2, sulfamic acid, silica sulfuric acid, para-toluenesulfonic acid, H-β zeolite, and $Mg(OTf)_2$, and it provides a suitable reaction time and yield.

Various substituted aldehydes carrying electron-withdrawing or electron-donating groups participated in this reaction, producing 14H-dibenzo[a,j]xanthene derivatives with good yields. As shown in Table 2, aldehyde derivatives containing electron-withdrawing groups reacted faster and also yielded higher compared to derivatives with electron-donating substituents. This is because the LUMO of the alkene bond is at a lower level in the presence of electron-withdrawing groups compared to its counterpart in the presence of electron-donating groups, resulting in the desired compounds being obtained with good and high yields.

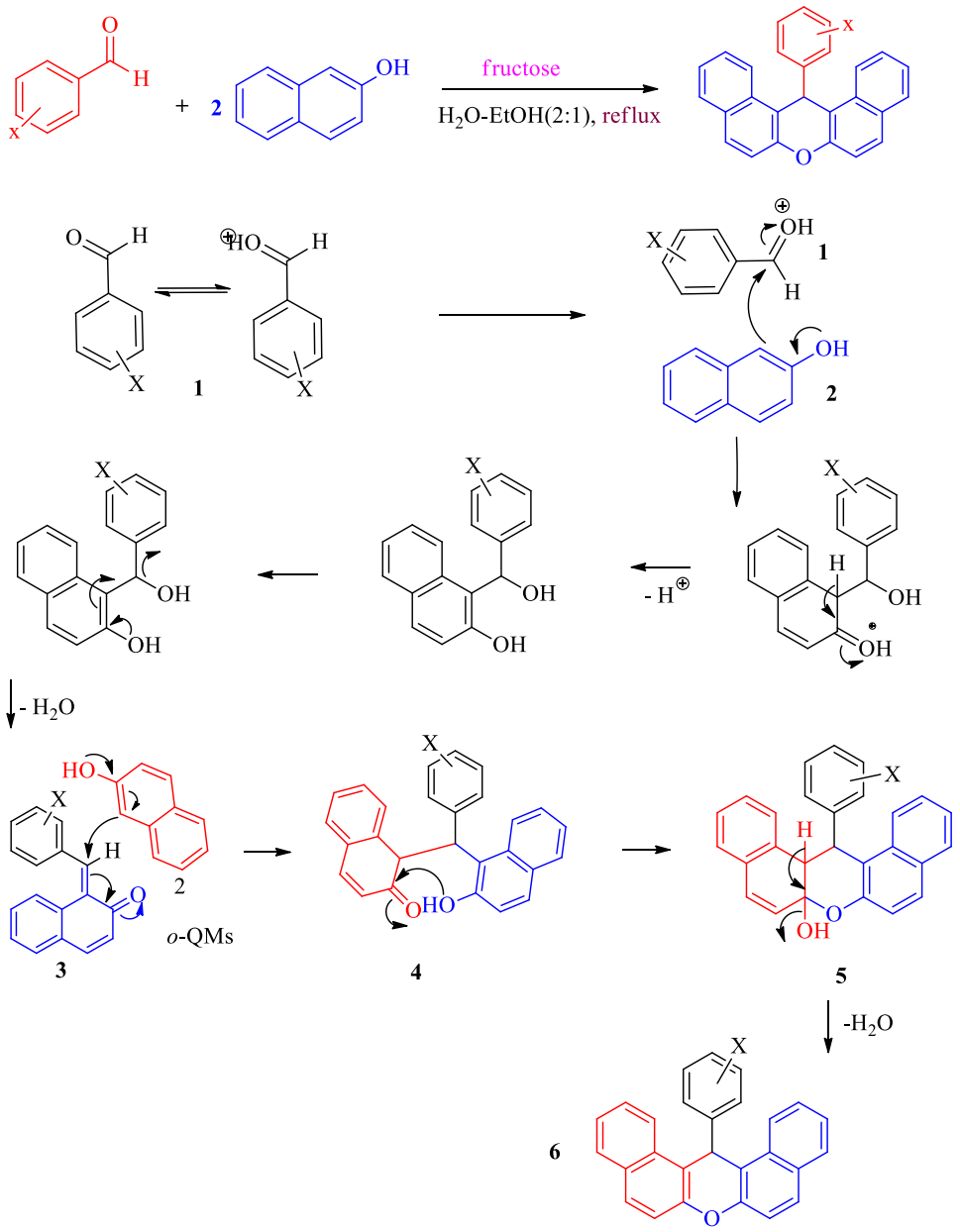


Fig. 6. Investigation of the proposed mechanism for the synthesis of 14h-dibenzo[a,j]xanthene derivatives using aldehyde and 2-naphthol in the presence of sulfonated fructose

Table 6. Comparison of results obtained in the synthesis of 14-phenyl-14h-dibenzo[a,j]xanthene derivatives in the presence of sulfonated fructose and other catalysts mentioned in scientific articles

Row	Catalyst	Conditions	Time (min)	*Yield	Reference
1	I_2	Ethanol and 80 C	120	90	[34]
2	H-*β* zeolite	Water	300	95	[35]
3	$Mg(OTf)_2$	80°C, without solvent	38	95	[33]
4	Sulfonated fructose	Water-ethanol and reflux	30	92	Present study

**The reported yield refers to the product obtained after purification steps and is based on benzaldehyde*

4. CONCLUSIONS

Due to the increasing demand for green chemistry and environmentally friendly technologies, catalysts have been extensively studied. Recently, there has been significant attention to the use of natural catalysts and compounds in organic reactions. In this regard, this study aims to improve reaction conditions and obtain an ideal catalyst that is non-toxic to the environment. Biological catalysts, such as fructose, have been utilized to prepare heterocyclic compounds with important biological and pharmacological properties.

The synthesis of xanthenes has proven to be a vital area of research due to their extensive biological and therapeutic properties, including antibacterial, antiviral, and anti-inflammatory effects. These properties make xanthenes indispensable in the field of organic synthesis. Furthermore, the application of xanthenes as spectral dyes in laser industries and fluorescent materials for detecting biological molecules highlights their versatile utility. Despite the availability of various synthetic methods, challenges such as low efficiency, lengthy reaction times, high catalyst requirements, and the use of hazardous organic solvents have underscored the need for more sustainable and efficient alternatives.

This study has demonstrated that fructosylated sulfonated catalysts offer a promising solution to these challenges.

One might wonder why we sulfonated fructose for catalytic use in this research?

Sulfonated fructose as a catalyst has several advantages over pure fructose:

1. Higher Catalytic Activity: The sulfonation of fructose increases its acidity, which can enhance its catalytic activity. This leads to reduced reaction times and higher production yields.

2. Greater Stability: Sulfonated fructose typically has greater stability compared to pure fructose. This increased stability can result in less catalyst degradation and a longer useful lifespan.

3. Compatibility with Green Chemistry Principles: Using less toxic and hazardous acidic catalysts like sulfonated fructose aligns better with green chemistry principles. This helps in reducing environmental pollution.

4. Reduced Need for Toxic Solvents: Sulfonated fructose may allow reactions to proceed under milder conditions and with the use of less toxic solvents, such as water and ethanol.

5. Improved Selectivity: The presence of sulfonic groups in the fructose structure can enhance the selectivity of catalytic reactions, leading to fewer by-products and higher purity of the final product.

Given these advantages, sulfonated fructose is a more efficient and effective catalyst compared to pure fructose, making it an optimal choice for green and sustainable chemistry practices.

This method, considering the variety of reactants and catalysts, ease of operation, and green aspects while avoiding the use of corrosive or expensive catalysts, presents significant advancements. Based on the experimental results, these catalysts could provide acceptable yields within an appropriate reaction time. Fructose offers economic benefits in catalyst and solvent consumption, reduces environmental pollutants, and is more environmentally friendly and compatible with green chemistry. The use of inexpensive and readily available materials, non-toxic solvents, shorter reaction times, more selection options, easier separation, straightforward purification, and good product yield are among the advantages of using these catalysts and this technique.

FUTURE DIRECTIONS AND POTENTIAL APPLICATIONS

Apply sulfonated fructose to other organic reactions to assess its versatility and effectiveness. Conduct scale-up experiments to evaluate practicality and economic benefits in industrial-scale synthesis. Investigate the biological activities of synthesized xanthene derivatives for potential pharmaceutical applications. Perform life cycle assessments to quantify environmental benefits and explore recyclability and reusability of the catalyst. Synthesize novel xanthene derivatives and study their structure-activity relationships for potential industrial and pharmaceutical applications.

These directions highlight the potential for further research and applications, enhancing the impact and sustainability of using sulfonated fructose as a green catalyst.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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