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Development of a Green Method for the Synthesis of Xanthene-1,8-dione Derivatives from Dimedone and Aldehydes

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INTRODUCTION & AIM

Xanthene-1,8-dione derivatives are privileged oxygen-containing heterocycles with broad pharmacological and materials relevance. They display diverse biological activities, including antibacterial,[1] antiviral,[2] and antioxidant effects, [3] in addition to applications in dyes, lasers, and photodynamic therapy. [3-5] Conventional syntheses often rely on harsh acids, toxic solvents, or prolonged heating, which limit efficiency and sustainability.[6,7]

In response, green chemistry has promoted the use of biodegradable and operationally simple catalysts. LABSA (linear alkylbenzene sulfonic acid), an industrially available surfactant, combines Brønsted acidity with micellar catalysis in water, enabling cleaner transformations. Its application here introduces a novel, sustainable, and efficient route to xanthene-1,8-diones, representing a valuable addition to greener heterocyclic synthesis.

METHOD

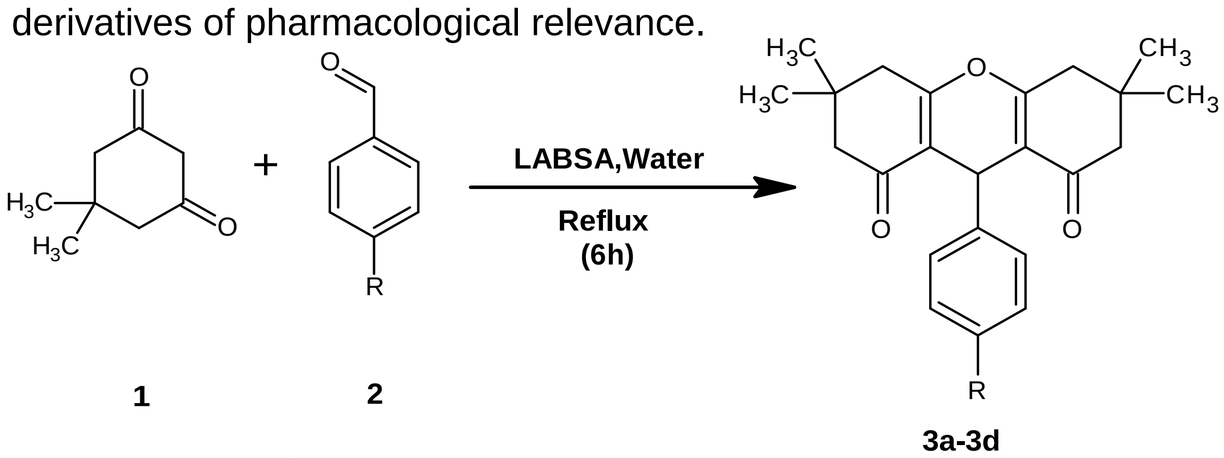
Aromatic aldehydes (1.0 mmol) and 1,3-cyclohexanedione (2.0 mmol) were stirred in distilled water (40 mL) with LABSA (10 mol%). The reaction mixture was refluxed for 6 h under continuous stirring and monitored by TLC on silica gel plates using suitable eluents. After completion, the mixture was cooled, and the crude solid was collected by vacuum filtration. The product was washed with cold distilled water and purified by recrystallization from hot ethanol. Structures and purity were confirmed by FT-IR, ^{1}H and ^{13}C NMR analyses.

RESULTS & DISCUSSION

The reaction of dimedone with a variety of aromatic aldehydes in the presence of LABSA proceeded smoothly to afford the corresponding 1,8-dioxo-octahydroxanthene derivatives in high yields (80–92%).

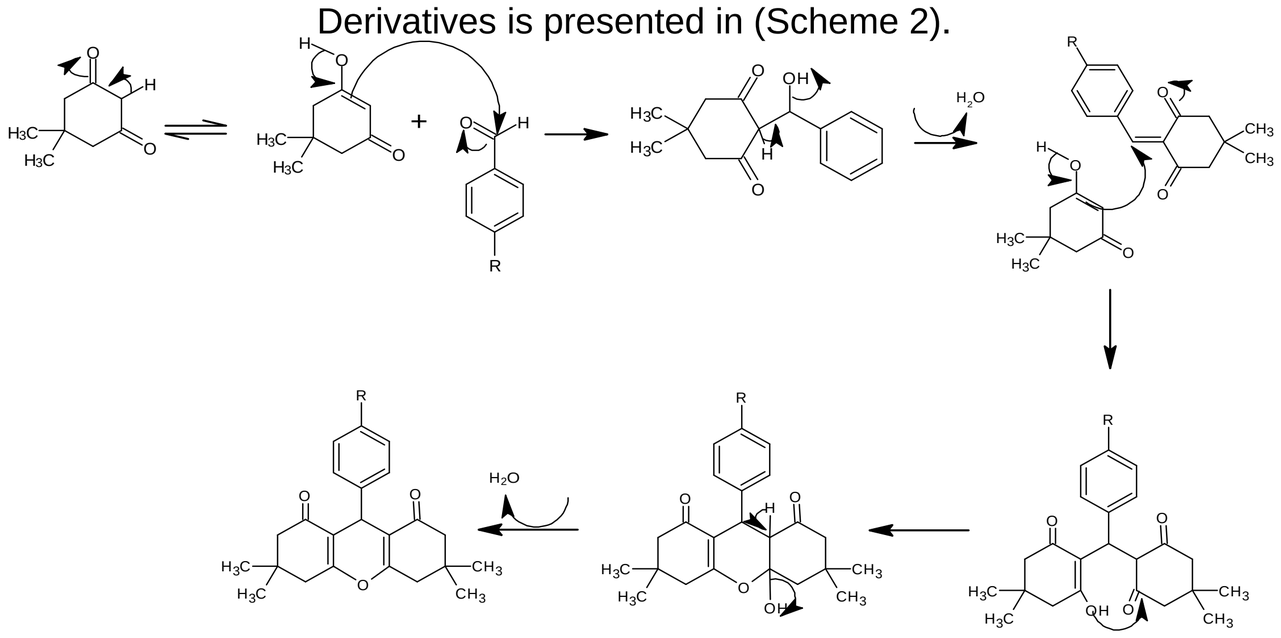
The procedure was general and efficient, accommodating a wide variety of substituents and consistently affording products of excellent purity after simple recrystallization. Conducted under aqueous reflux, the transformation proceeded smoothly and with high selectivity. Figure X presents the overall reaction pathway together with representative examples of the synthesized derivatives.

Compared with conventional acid-catalyzed syntheses, the LABSA-mediated protocol offers significant advantages, including shorter work-up, cleaner transformations, and the elimination of toxic organic solvents. The use of LABSA, a biodegradable and industrially available surfactant-acid, is unprecedented in this context and establishes a novel, sustainable, and scalable route for the preparation of xanthene derivatives of pharmacological relevance.



Scheme 1. Synthesis of Xanthene Derivatives.

The possible reaction mechanism for the synthesis of Xanthene-1,8-dione Derivatives is presented in (Scheme 2).



Scheme 1. Mechanistic proposal for the synthesis of Xanthene-1,8-dione Derivatives

The supplemental materials contain characterization of the new synthesized products with 1HNMR, 13CNMR, and Infrared spectra.

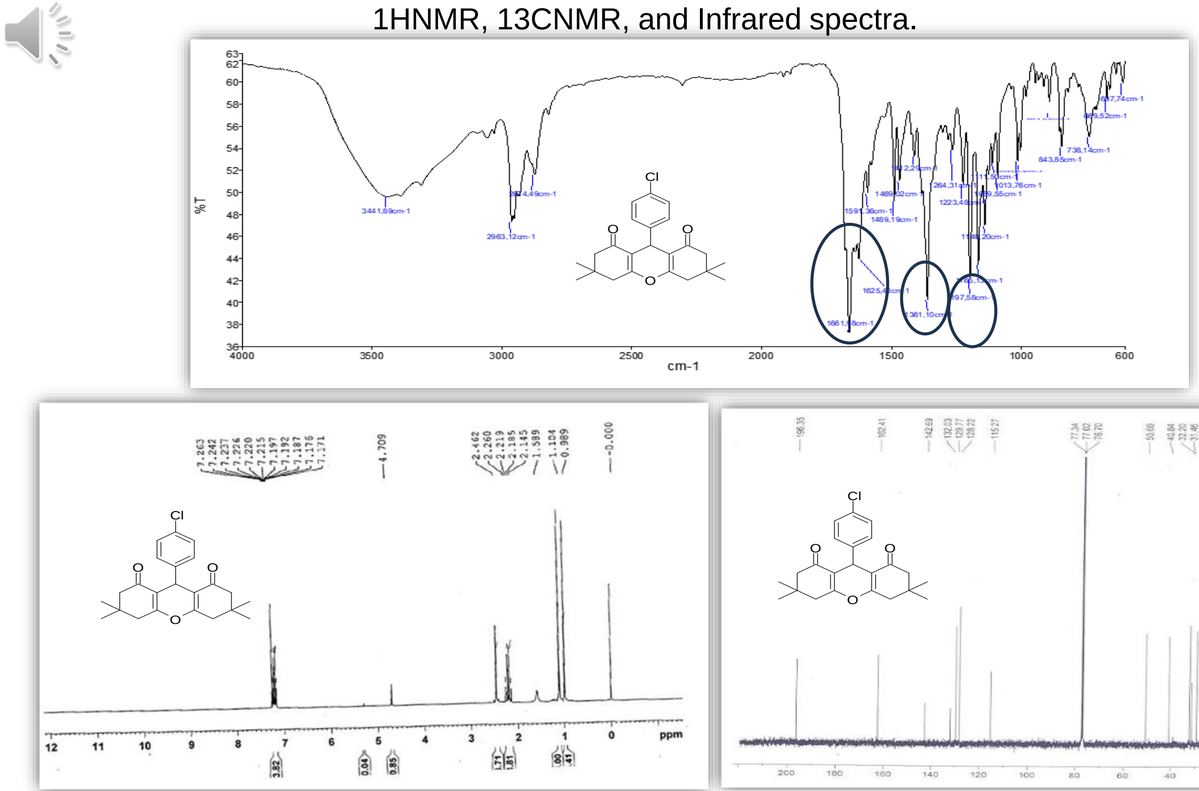


Figure. Spectrum 1HRMN, 13CRMN and IR of 9-(4-chlorophenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9 -hexahydro-1H-xanthene-1,8(2H)-dione

CONCLUSION

The LABSA-mediated synthesis of xanthene-1,8-dione derivatives represents a novel and sustainable approach to heterocyclic chemistry. The method is simple, reproducible, and efficient, consistently affording high yields in aqueous medium under mild conditions. By eliminating toxic solvents and employing a biodegradable surfactant-acid, this protocol aligns with the principles of green chemistry while offering scalability and operational simplicity. Overall, the study establishes LABSA as a valuable catalyst for the eco-friendly preparation of pharmacologically important xanthene derivatives.

FUTURE WORK / REFERENCES

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