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ENVIRONMENTAL FRIENDLY SYNTHESIS AND CHARACTERIZATION OF BENZOPYRANS USING HEXAFERRITE AS GREEN CATALYST: A SIGNIFICANT STEP TOWARDS SUSTAINABLE CHEMISTRY

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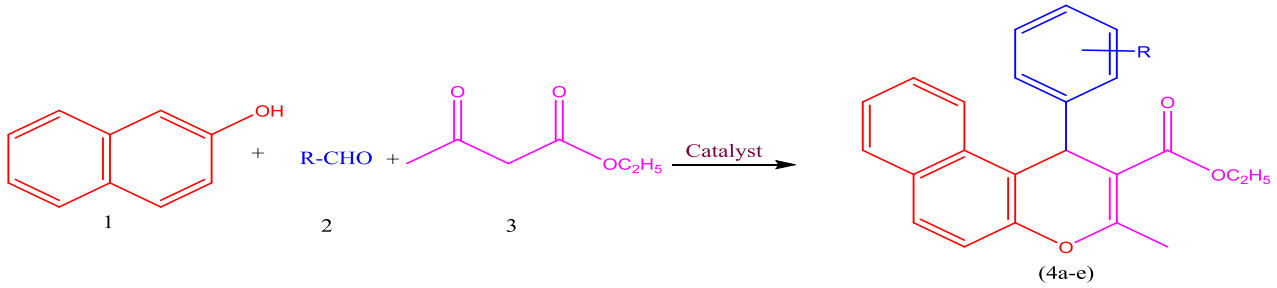
ABSTRACT

This research work aims to explore the synthesis, structural characterization, and biological evaluation of benzopyran derivatives utilizing ethyl acetoacetate, β-naphthol, and aromatic aldehydes with ferrite as catalyst-assisted methodologies. Benzopyrans are of particular interest due to their properties useful in pharmacological and biological activities, as well as their synthetic versatility. The study focuses on enhancing sustainability through efficient synthetic routes. Various nanocatalysts, including organic and inorganic, were investigated to facilitate the formation of benzopyran derivatives. The heterogeneous hexaferrite catalyst is an attractive option for multicomponent reactions due to its ease of preparation, cost-effectiveness, and insolubility in most organic solvents. The protocol offers several advantages, including control over reaction conditions, high yields, easy workup, reproducibility of catalytic activity, compatibility with substrates, and enhanced overall efficiency of the reaction. Additionally, it helps minimize waste generation, reduce energy consumption, and utilize environmentally benign catalysts efficiently. The synthesized compounds were confirmed using FT-IR, ^{1}H NMR spectroscopic data, and melting points, which were compared with reported values. During the work-up procedure, the catalyst can be easily recovered and recycled, retaining its activity for up to four cycles.

KEYWORDS: Benzopyrans, multicomponent reaction, heterogeneous hexaferrite catalyst.

GRAPHICAL ABSTRACT



INTRODUCTION

One of the most important and convergent reactions with remarkable biological and pharmacological activities and industrial significance is the synthesis of benzopyrans among multicomponent reactions (MCRs).[1] Multicomponent reactions adhere to the principles of green chemistry and confer several advantages, including experimentally simple execution, reduced reaction times, high atom efficiency, and synthetic efficiency akin to an ideal organic synthesis. Moreover, they facilitate simpler purification techniques, further enhancing their appeal in organic synthesis.[2-3] there is significant interest in exploring multi component reactions for synthesizing biologically sustainable molecules. Benzopyran is a highly privileged pharmacophore, exhibits remarkable biological potential, including anti-inflammatory,[4-5] anticancer,[6-8] antioxidant,[9] bactericides[10-12] and fungicides.[13] The synthesis of benzopyrans is carried out by multicomponent condensation of aromatic aldehydes, β-naphthol and ethyl acetoacetate, in the presence of various catalysts such as heterogeneous acidic organocatalyst,[14] Palladium[15] and Rhodium.[16] However, some of these methods, are not environmentally friendly and involve longer reaction times, lower yields, multistep reactions, and challenges in the recovery and reusability of the catalysts. Hence,

there has been ongoing attention towards the development of eco-friendly processes and easily recyclable green catalysts at the end of reactions. To fulfill the demand of simple and ecofriendly procedure with heterogeneous catalyst for the preparation of benzopyrans derivatives.[17] In recent years, the multicomponent synthesis of heterocyclic compounds has become not only a vital part of pharmaceutical groups but also a significant tool in the discovery of new drugs.[18] Developing organic reactions carried out in aqueous media shows inimitable reactivity and selectivity in biological activities, making it another attractive area of green chemistry distinct from reactions in organic solvents.[19-20] Magnetoplumbite ferrites, composed primarily of iron (III) oxides serve as catalysts in several multi-component reactions conducted within one-pot synthesis. These ferrites, being mixed metal oxides, exhibit improved catalytic activity facilitating easy separation and recycling of the catalyst compared to conventional methods.[21]

Here, in view of the significance associated with this class of reaction, we report the synthesis of benzopyrans derivatives. The synthesis involves the condensation of aromatic aldehydes, ethyl acetoacetate and β-naphthol in the presence of reusable lanthanum ferrite as a catalyst. The reaction mixture was stirred at 70°C temperature for the desired time in ethanol.

EXPERIMENTAL WORK

MATERIALS AND METHODS

Analytical grade chemicals were utilized, and when necessary, they were distilled prior to use. Solvents procured from commercial sources were dried using standard methods as required. All metal salts, obtained from SD Fine Chemicals, were used without further purification. Melting points were determined using a quality digital melting point apparatus. IR spectra were recorded using a Bruker FT-IR spectrometer. NMR spectra were recorded on a Bruker Avance spectrometer (300 and 400 MHz), with $CDCl_3$ and DMSO-d_6 as solvents. Reaction monitoring was conducted via thin-layer chromatography using Merck silica gel 60F254 aluminum sheets.

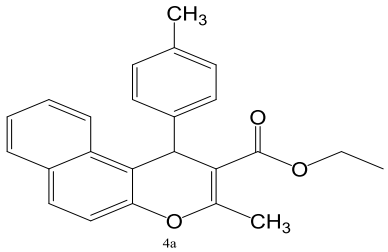
Preparation of $LaFe_{12}O_{19}$ ferrite

Lanthanum ferrite ($LaFe_{12}O_{19}$) was synthesized following a modified literature method.[22] Initially, $Fe(NO_3)_3.9H_2O$ and $La(NO_3)_2$ were dissolved in deionized water to yield an aqueous solution with a concentration of 0.1 M. Simultaneously, an aqueous solution of citric acid was prepared and mixed with the metal nitrates solution. The molar ratio of the solutes in the solution was maintained at La^{+2}: Fe^{+3}: $C_3H_4(OH)(COOH)_3$ = 1:12:19. The pH of the solution was adjusted to neutral solution by using NH_4OH. Subsequently, the solution was refluxed at 90°C for 2 hours to ensure complete chelation of the metallic ions by the carboxyl groups of citric acid. Following this, the solution was subjected to microwave heating for 30 minutes to obtain a solid precursor. Finally, the precursor was calcinated in a muffle furnace at 500°C for 4 hours, resulting in the formation of hexaferrite powder.

General procedure for the synthesis of benzopyrans

A 100 mL round bottom flask was charged with a mixture of ethyl acetoacetate, β-naphthol, and aromatic aldehydes along with 10 wt% of $LaFe_{12}O_{19}$ catalyst. The reaction mixture was stirred in 5 mL of ethanol at 70 °C for the desired duration. Progress of the reaction was monitored via thin layer chromatography. Upon completion, the mixture was filtered to separate the catalyst, which was subsequently recovered for reuse without any loss in activity. Product characterization was conducted based on their spectroscopic properties, comparing them with authentic samples. Purity assessment included FT-IR, ^{1}H NMR spectroscopy, melting point determination, and TLC analysis.

Spectral data of synthesized compound: Ethyl 3-methyl-1-(p-tolyl)-1*H*-benzo[f]chromene-2-carboxylate (4a).



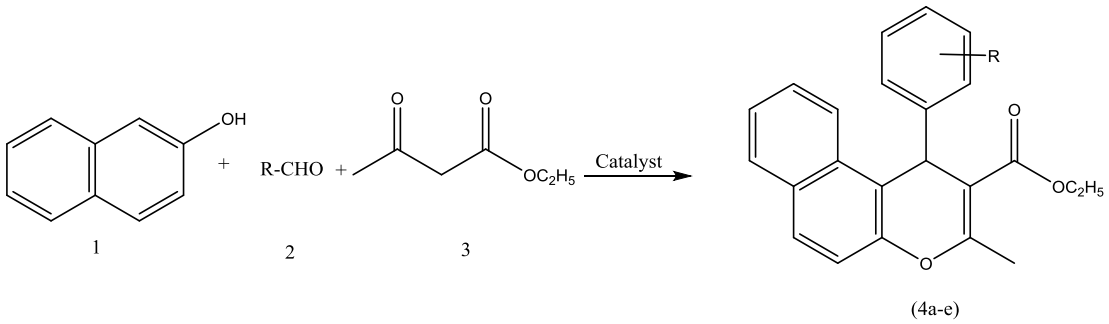
4a

ethyl 3-methyl-1-(*p*-tolyl)-1*H*-benzo[*f*]chromene-2-carboxylate

FT-IR (KBr) ν_{max} (cm^{-1}): 780, 812, 1070, 1150, 1238, 1590; ^{1}H-NMR (400 MHz, DMSO-*d*6,δ, ppm): 1.3 (t,3H) , 2.0 (t, 3H) , 2.1 (t, 3H), 2.5 (d, 2H), 3.3 (s, 1H); MS: m/z 358 (M); m.p 198-199 ^{o}C (lit. 197-198). Anal. Calcd. $C_{24}H_{22}O_3$ (358.1) C, 80.42; H, 6.19; O, 13.39.

RESULTS AND DISCUSSIONS

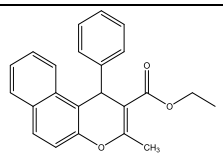
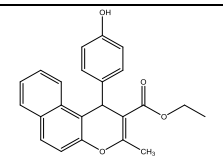
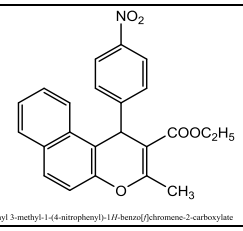
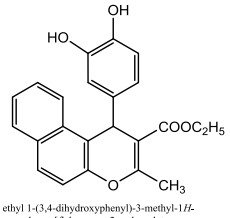
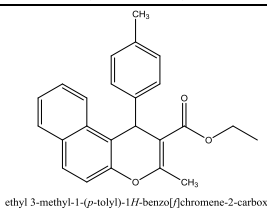
To examine the role of catalyst for synthesis of benzopyrans as model reaction using ethyl aceto acetate, β-naphthol and aromatic aldehydes employing hexaferrite as catalyst and reaction mixture was stirred for desired time in ethanol (10 mL) at desired temperature (Scheme 1). The reaction was completed in 80 minutes to give compound 4a was selected as a model reaction to optimize the reaction conditions.



Scheme 1. Benzopyrans synthesis using ethyl aceto acetate, β-naphthol and aromatic aldehydes employing hexaferrite as catalyst.

The investigation of Lanthanum ferrite's catalytic efficiency in a solvent-free model reaction offers several advantages, including eco-friendliness, simplified workups, cleaner product profiles, and enhanced selectivity, reduced by-products, and accelerated reaction rates. This study aimed to identify optimal reaction conditions through the systematic investigation of various parameters for the synthesis of compound 4a. The results are summarized in Table 1.

Table 1: Synthesis of benzopyrans derivatives in presence of Lanthanum ferrite as a catalyst.

Sr. No.	Substrate R	Naphtol	Product	Reaction Time (min.)	Yield (%)	Melting Point °C	
						Found	Reported
1	C_6H_5CHO (4b)	β-naphthol	 ethyl 3-methyl-1-phenyl-1*H*-benzo[*f*]chromene-2-carboxylate	85	91	195-196	196-198
2	$C_6H_4OH(CHO)$ (4c)	β-naphthol	 ethyl 1-(4-hydroxyphenyl)-3-methyl-1*H*-benzo[*f*]chromene-2-carboxylate	83	90	246-247	247-249
3	$4\text{-}(NO_2)C_6H_4CHO$ (4d)	β-naphthol	 ethyl 3-methyl-1-(4-nitrophenyl)-1*H*-benzo[*f*]chromene-2-carboxylate	90	85	169-170	167-169
4	$(HO)_2C_6H_3CHO$ (4e)	β-naphthol	 ethyl 1-(3,4-dihydroxyphenyl)-3-methyl-1*H*-benzo[*f*]chromene-2-carboxylate	92	89	246-248	248-249
5	$CH_3C_6H_4CHO$ (4a)	β-naphthol	 ethyl 3-methyl-1-(*p*-tolyl)-1*H*-benzo[*f*]chromene-2-carboxylate	80	93	198-199	197-198

Building upon the promising outcomes of the previously optimized reaction conditions, this study aimed to demonstrate the versatility and applicability of the developed protocol for a series of benzopyrans derivatives were synthesized using Lanthanum ferrite as a catalyst under optimized conditions. The results,

showcasing high product yields and efficient reaction kinetics, are summarized in (Table 1). It is therefore suggested that such reactions for production of the benzopyrans derivatives may be more useful and economical. Further this reaction was tested for synthesis of ethyl 3-methyl-1-(p-tolyl)-1H-benzo[f]chromene-2-carboxylate (4a) as a model reaction (Table 1). The hexaferrite catalyst was prepared by literature method with slight modification[22] and recovered in ethanol and reused for four more cycles (Table 2).

Table 2: Reusability of catalyst.

Entry	Catalyst recovery [a] (%)	Yield [b] (%)
1	--	93
2	88	90
3	86	88
4	83	82

[a]catalyst recovered by filtration and washing with ethanol, [b] isolated yield

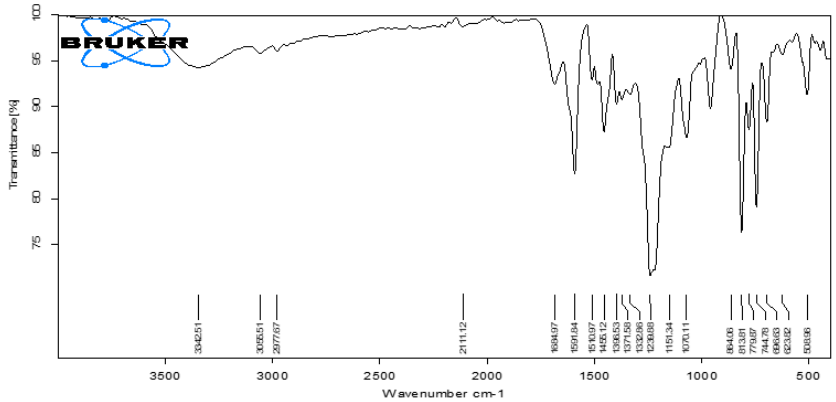


Fig. 1: FTIR of ethyl 3-methyl-1-(p-tolyl)-1H-benzo[f]chromene-2-carboxylate.

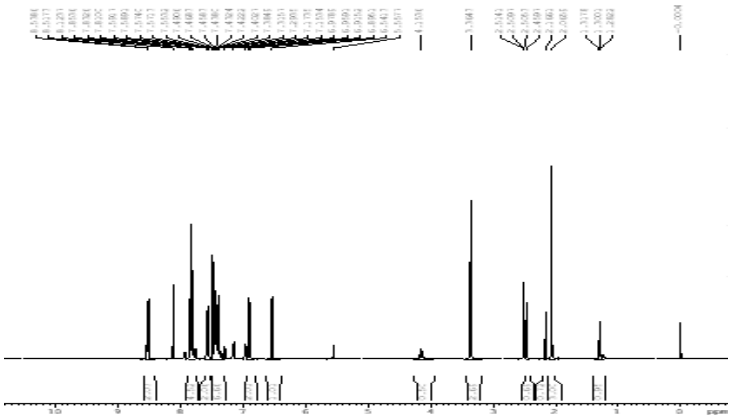


Fig. 2: ^{1}H-NMR of ethyl 3-methyl-1-(p-tolyl)-1H-benzo[f]chromene-2-carboxylate.

CONCLUSION

The benzopyrans derivatives ethyl 3-methyl-1-(p-tolyl)-1H-benzo[f]chromene-2-carboxylate was synthesized by a reaction of ethyl aceto acetate, β-naphthol and aromatic aldehydes employing hexaferrite as catalyst. This catalyst is easily separable and reused without any significant loss of catalytic activity after four runs. The crude product obtained was filtered and recrystallized using chloroform. Purity of the product is checked by melting point and TLC. The structure of synthesized compound is confirmed by FT-IR, ^{1}H- NMR and mass spectral data. Small amount of catalyst is sufficient to complete the reaction without any side product. Multicomponent reactions have garnered significant interest due to their environmentally friendly characteristics, including high atom economy, green conditions, rapid reaction times, excellent product yields, and coupled with simplified straightforward experimental procedures.

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