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GREEN APPROACH: SYNTHESIS OF SPIRO PERIMIDINE DERIVATIVES

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ABSTRACT

A green and efficient way to make spiro perimidine derivatives is through a one pot reaction of 1,8-diaminonaphthalene with different acetophenone derivatives using tamarind (Tamarindus indica L.) juice. The reactions were carried out in mild conditions, giving us the desired products in good or excellent yields with short reaction times. Tamarind juice was inexpensive, and easily available, and it was a metal-free and eco-friendly catalyst. The protocol is easy to follow, easy to separate products, low amount of catalyst, and does not include hazardous chemicals and chromatographic purification. This green way shows that tamarind juice is a good green catalyst for biologically important perimidine derivatives.

KEYWORDS: Tamarind Juice, Biocatalyst, spiro Perimidine, Heterocyclic chemistry, One-pot Synthesis.

INTRODUCTION

The development of sustainable and environmentally benign synthetic methodologies has gained significant attention in recent years due to increasing concerns about environmental pollution, depletion of natural resources, and the adverse effects of hazardous chemicals. Green chemistry aims to design chemical processes that minimize the generation and use of toxic substances while improving efficiency, safety, and economic viability. One of the fundamental principles of green chemistry is the replacement of hazardous solvents and corrosive catalysts with renewable, biodegradable, and environmentally friendly alternatives.

In this context, naturally occurring biocatalysts and aqueous reaction media have emerged as promising tools for sustainable organic synthesis because of their non-toxic nature, ease of handling, low cost, and minimal environmental impact. Among various green catalytic systems, fruit extracts have attracted considerable attention owing to their abundance, biodegradability, easy availability, and excellent catalytic performance. Fruit juices such as lemon, pineapple, coconut, and tamarind have been successfully employed as eco-friendly catalysts in a variety of organic transformations, including the Biginelli reaction, Knoevenagel–Michael condensation, Schiff base formation, and the synthesis of various heterocyclic compounds. Tamarind (*Tamarindus indica* L.), a member of the Fabaceae family, represents an efficient natural catalytic system because its fruit pulp contains significant amounts of organic acids, predominantly tartaric acid, along with smaller quantities of citric, malic, and ascorbic acids. These naturally occurring acids impart an acidic nature (pH ≈ 3) to the aqueous tamarind extract, enabling it to effectively catalyze acid-mediated organic reactions. In addition to organic acids, tamarind fruit is rich in carbohydrates, flavonoids, polyphenols, vitamins, minerals, and other bioactive constituents that further enhance its value as a sustainable and environmentally benign catalyst for organic synthesis.[1–12]

Nitrogen-containing heterocyclic compounds constitute one of the most important classes of molecules in medicinal and pharmaceutical chemistry because of their broad spectrum of biological activities and diverse industrial applications. Among these, perimidine derivatives have attracted considerable research interest due to their unique structural features and remarkable pharmacological as well as physicochemical properties. Perimidines are commonly synthesized through the condensation of 1,8-diaminonaphthalene with aldehydes or ketones, resulting in the formation of highly functionalized heterocyclic frameworks. Numerous studies have demonstrated that perimidine derivatives exhibit a wide range of biological activities, including antimicrobial, antifungal, antiviral, anticancer, anti-inflammatory, and antioxidant properties. Besides their pharmaceutical significance, these compounds have found applications as fluorescent probes, chemosensors, corrosion inhibitors, dyes, optical materials, and functional materials because of their excellent electronic and photophysical characteristics. Several synthetic methods have been reported for the preparation of perimidine derivatives. However, many of these methods require the use of strong mineral acids, metal-based catalysts, elevated reaction temperatures, prolonged reaction times, and toxic organic solvents. These limitations not only increase production

costs and energy consumption but also generate hazardous waste, thereby reducing the environmental sustainability of the process. Therefore, the development of simple, efficient, cost-effective, and environmentally friendly protocols employing naturally derived catalysts has become highly desirable. In this regard, the use of tamarind juice as a green, biodegradable, and renewable catalyst offers an attractive alternative for the sustainable synthesis of perimidine derivatives under mild reaction conditions, aligning well with the fundamental principles of green chemistry.[13–24]

Here, I report the environmentally friendly synthesis of four different derivatives of spiro perimidine using the natural biocatalyst from the extract of tamarind fruits by condensation of 1,8-diaminonaphthalene with 4-substituted acetophenone compounds.

EXPERIMENTAL

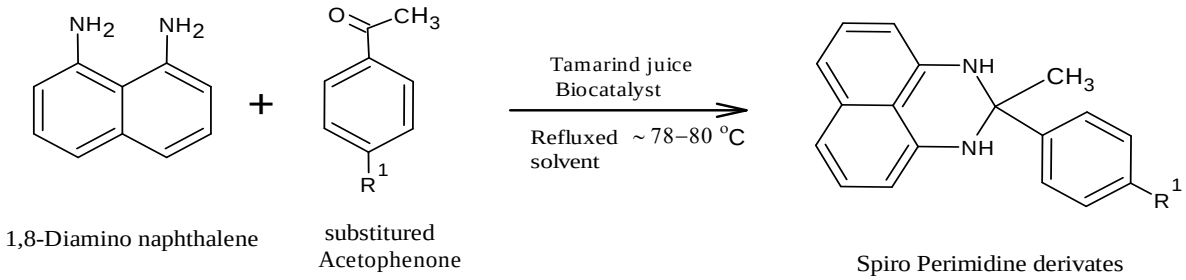


Figure 1: Reaction scheme of synthesis of Spiro Perimidine derivatives.

MATERIALS AND METHODS

All the necessary chemicals came from Sigma-Aldrich, E. Merck (India), SDFC Ltd., and Loba Chemie. They were used with no extra purification. Melting points for the new compounds were determined in open glass capillary tubes. Thin layer chromatography, run on Merck aluminum plates coated with silica gel, helped check the purity of the prepared compounds and track how each reaction progressed. An iodine chamber made the spots visible. Infrared spectra were recorded on a Shimadzu FTIR model 4800S spectrophotometer, using KBr pellets across the 4000-400 cm-1 range. The 1H NMR spectrum came from a Bruker AV-300 (300 MHz) machine, with DMSO-d6 as the solvent and TMS as the internal standard.

Preparation of Tamarind Fruit Extract (Biocatalyst)

Fresh tamarind fruits, known scientifically as Tamarindus indica, were bought from a local market. Their hard shells and seeds were removed by hand, and 10 grams of the pulp were collected. The pulp sat in 50 mL of distilled water for 5 hours, which helped pull out the

water-soluble parts. Then the mixture was heated and stirred for 2 hours to create a uniform extract. After cooling down to room temperature, it was filtered twice to get rid of any solids, then spun in a microcentrifuge. The final clear liquid had a pH around 3.0, thanks to natural organic acids like tartaric, citric, and malic acids. This fresh tamarind extract was stored at 3-5 °C and used as a green biocatalyst to make perimidine derivatives.[25,26]

General Procedure for the Synthesis of 2-methyl-2-phenyl-2, 3-dihydro-1H-perimidine and its derivatives

We took a mix of 4-substituted acetophenone and acetophenone (0.01 mol) with 1,8-diaminonaphthalene (0.01 mol) in a small amount of ethanol. It was stirred with 10 ml of tamarind juice at about ph 3 for a few minutes at room temperature. Then we heated it under reflux for the time shown in table 2. Thin-layer chromatography, or tlc, used to track the reaction as it progressed. Once the reaction was done, the mixture was concentrated under vacuum. After cooling, a solid formed. Collected it by filtration, washing it several times with a little ice-cold water to get the crude product. This crude product was recrystallized from ethanol to give a pure product, which is dried in a vacuum desiccator over anhydrous $cacl_2$. Melting points for all made compounds were noted down and matched with known data.[27,28]

RESULTS AND DISCUSSION

We selected the reaction between acetophenone and 1,8-diaminonaphthalene to develop a green method for making spiro perimidine derivatives. The reaction was run under reflux for one hour using tamarind juice as a natural biocatalyst (see Scheme 1). Acetophenone served as the initial test ketone to optimize the amount of catalyst. After the reaction was done in ethanol without tamarind juice, only a small amount of product formed, showing that a catalyst is necessary (Entry 1, Table 1). The reaction was tested with different amounts of tamarind juice (2-10 mL) and found that the amount of catalyst had a strong effect on yield. With 2 mL of tamarind juice, the product 2-methyl-2-phenyl-2,3-dihydro-1H-perimidine was obtained in 20% yield (Entry 2, Table 1). Increasing the catalyst to 4 mL raised the yield to 42% (Entry 3, Table 1). Using 6 mL of tamarind juice gave a 63% yield (Entry 4, Table 1). When we used 8 mL, the yield increased to 84% (Entry 5, Table 1). With 10 mL, the yield was 85% (Entry 6, Table 1). These results suggest that the optimal conditions are reached during the reaction. Melting point, FT-IR, and NMR analyses confirmed that the product matched published data[29,30], showing that 2-methyl-2-phenyl-2,3-dihydro-1H-perimidine was successfully synthesized and that tamarind juice worked well as a biocatalyst.

Table 1: Optimization of Tamarind Juice Amount for the Synthesis of Spiro Perimidine Derivatives.

Entry	Catalyst Loading	Volume (mL)	Time (min.)	Yield (%)
1	Tamarind Juice	0	60	Trace
2	Tamarind Juice	2	60	20
3	Tamarind Juice	4	60	42
4	Tamarind Juice	6	60	63
5	Tamarind Juice	8	60	84
6	Tamarind Juice	10	60	85

A possible mechanism for the tamarind-juice-catalyzed synthesis of spiro perimidines is illustrated in Figure 2. Protonation of the carbonyl group of aromatic ketone (1) results in the generation of intermediate (2), in which the carbonyl carbon is activated as an electrophile toward nucleophilic addition. In this regard, the amino group of 1,8-diaminonaphthalene (3) attacks the carbonyl carbon of intermediate (2), resulting in the generation of carbinolamine intermediate (4). Deprotonation of intermediate (4) provides intermediate (5), in which the second amino group engages in intramolecular nucleophilic addition to cyclize and generate intermediate (7). Final generation of the spiro perimidine derivative is achieved upon deprotonation of intermediate (7) to give compound (8).

Overall, the tamarind juice efficiently catalyses the reaction under mild conditions, giving the products in a good yield with satisfactory selectivity, likely by a mechanism involving substrate activation via proton transfer.

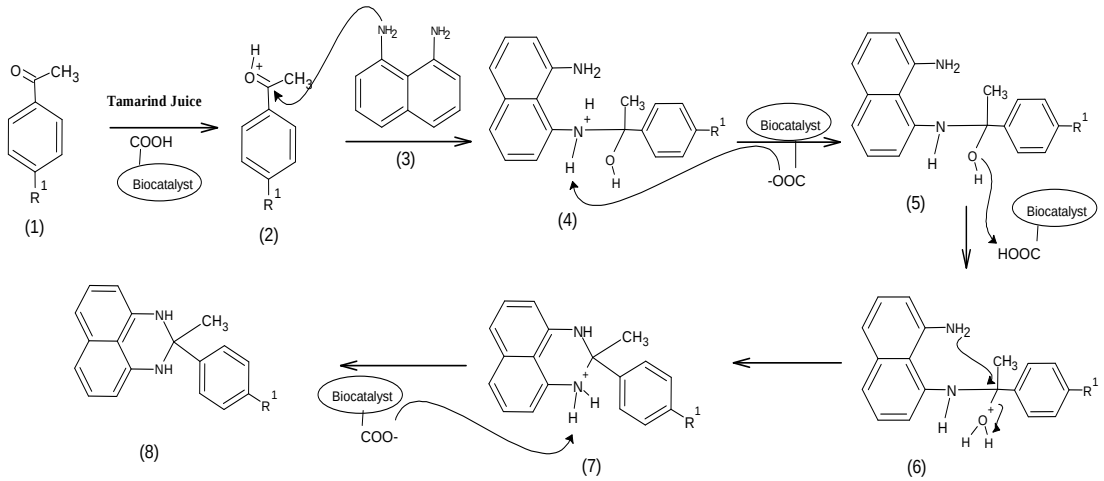
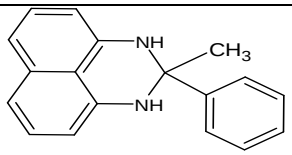
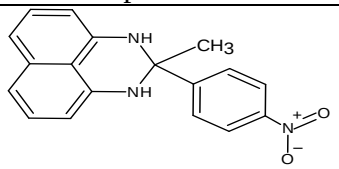
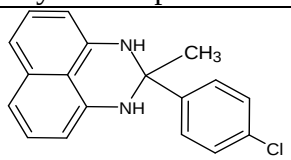
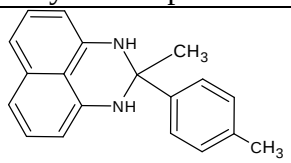


Figure 2: Proposed catalytic mechanism for the Synthesis of Spiro Perimidine derivatives using Tamarind juice.

The optimization experiment revealed that 10 mL of tamarind extract was sufficient to efficiently catalyze the reaction within a very brief timeframe. Increasing the catalyst amount did not lead to a significant enhancement in yield. Consequently, 10 mL was selected as the optimal catalyst loading for subsequent reactions. Under these optimized conditions, various aromatic ketones, whether bearing electron-donating or electron-withdrawing substituents, readily underwent reaction with 1,8-diaminonaphthalene to afford the corresponding spiro perimidine derivatives in good to excellent yields.

Table 2: Optimization study of Substrate for the Synthesis of Spiro Perimidine Derivatives.

Sr. No.	Aldehyde	Product/Name	Time (min.)	Yield (%)	Melting point (^{0}C)	
					Observed	Lit. value
1	R^1=H,	 2-methyl-2-phenyl-2, 3-dihydro-1H-perimidine	60	84	136-138	136-138[29]
2	$R^1 = NO_2$	 2-methyl-2-(4-nitrophenyl)-2, 3-dihydro-1H-perimidine	50	89	190-192	193-194[29]
3	R^1 = Cl	 2-(4-chlorophenyl)-2-methyl-2, 3-dihydro-1H-perimidine	75	82	130-132	129-130[30]
4	$R^1 = CH_3$	 2-methyl-2-(p-tolyl)-2, 3-dihydro-1H-perimidine	95	78	116-118	117-119[29]

2-methyl-2-phenyl-2, 3-dihydro-1H-perimidine

IR: 3372, 3290 ν(N-H), 3056, 2905 ν(C-H), 1598 ν(C=C), 1410, 1256, 816, 755, 705.

^{1}H-NMR (DMSO-d_6): 1.765 (s, 3H, CH_3), 7.56–6.46 (13H, 11C_{Ar}-H, 2N-H).

CONCLUSION

This paper describes how spiro perimidine-based derivatives can be synthesized using tamarind juice as a natural biocatalyst. Tamarind juice helps the reactions proceed efficiently, leading to effective formation of spiro perimidine derivatives. It is easy to obtain and environmentally friendly, which shortens reaction times and makes product separation simpler. This method shows that tamarind juice is a practical and green option for making perimidine derivatives.

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