Synthesis, antibacterial evaluation of dihydropyridine by using water extract of dragon Fruit Peel as a highly efficient catalyst

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Abstract

Natural compounds are increasingly being used in organic synthesis due to their environmental safety. That is why we identified a natural material that enhanced the organic reaction, and it could be sustainable and obtained from plant sources, and it stimulates the synthesis of dihydropyridine and its derivatives under solvent-free circumstances through this natural substance. We used this process to synthesise highly functional dihydropyridine derivatives since it is cost-effective and free of minerals and solvents. It is encouraged by dragon fruit water extract (WED) at a temperature of (80 ^{0}C). These (WED) promoted reactions have been discovered to provide a high yield for the target compounds, and this method is Protocol an option to the present procedures.

Keywords: Dihydropyridine derivatives; Greener synthesis; Nature derived catalyst; Water extract of dragon (WED).

1. Introduction

In recent years, the upgrading of resources and processes associated with the environment in terms of sustainable chemistry has been a focal focus of the chemical research process. As a result, the creation and implementation of chemical processes, as well as the replacement or modification of old processes with new methodologies, creates a new path towards "green chemistry" through the utilisation of natural resources related to the environment or natural raw materials [1-3].In recent years, nitrogen synthesis containing dihydropyridine isotopes has emerged as the most important MCRS. The significance of these compounds stems from the fact that they contain the basic unit of many natural products, including nucleic acids, alkalis, purines, histidine, and histamine, as well as pharmacological properties such as calcium channel modifiers like ephedrine, antifungal, anti-tumor, and anti-HIV [4-7]. The classical hypothesis of the aforementioned derivatives, human immunity, was tested under difficult conditions,

with the reaction accelerated in the presence of formaldehyde in ammonia or Bronsted / Lewis' acids [8-10]. Following that, numerous dihydropyridine synthesis methods were published, which were either developed by certain solvents [11-25]. Environmentally hazardous synthetic techniques for multicomponent reactions have garnered a lot of attention.

In this protocol " water extract of dragon fruit(WED) " is select as an acid catalyst without using dangerous organic reaction medium , transition metal catalyst , toxic solvents / reagents, to the best of our knowledge, there are no earlier reports of WED used as an acid promoter for nitrogen containing Heterocyclic adducts. the extract of dragon fruit (scientific name : cacti ; family : cactaceae ; gen : selenicereus ; Binomial name: common name : dragon) is prepared by first took the peel of dragon fruit and dry it and then crushed by using mixer then took 10 g of dragon fruit in 100 ml of water and then heat it at (80^0C) and filter it and got water extract of dragon fruit (WED) acid 4.8 pH as in the **Fig. 1**.

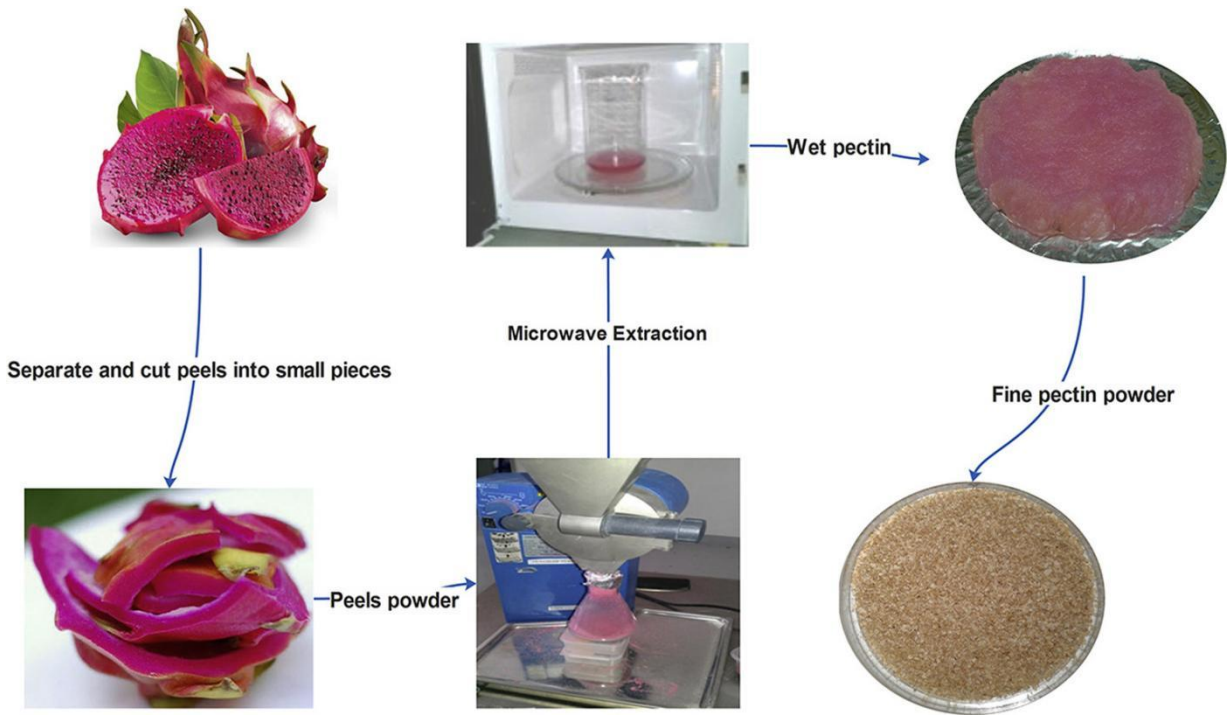


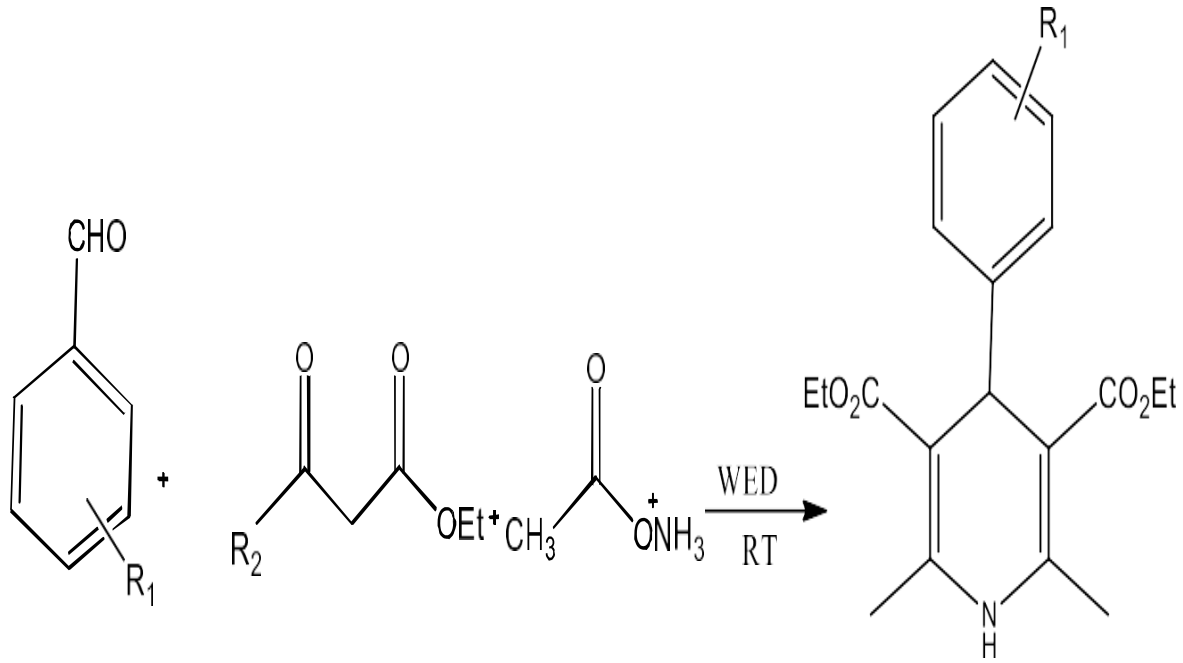
Fig. 1. This fruit (dragon fruit) is low in calories. It contains different minerals and vitamins. One of them, equivalent to 227 g contains 136 calories. 29 g of carbohydrates and 7 g of dietary fibre.

2. Results and Discussion

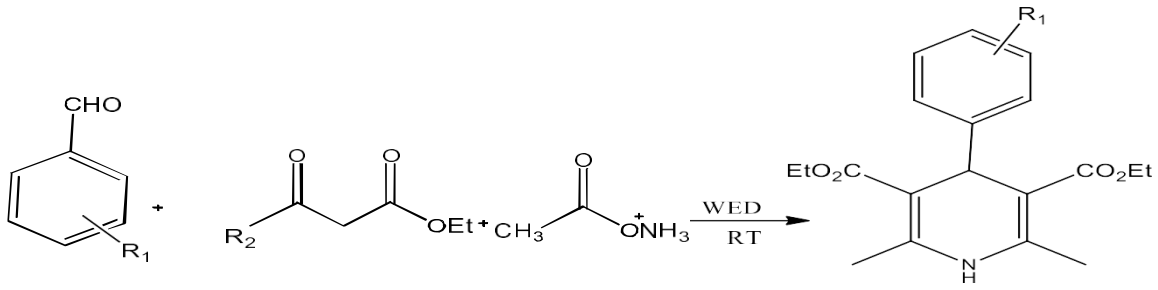
Our main goal is to create a more environmentally friendly and effective synthetic pathway for the easy conversion of dihydropyridine at room temperature. The ability of the catalytic condition was evaluated in order to analyse the optimal reaction conditions for our suggested processes. To complete this synthetic pathway and investigate the impact of the amount of (WED), In this protocol " water extract of dragon fruit(WED) " is select as an acid catalyst without using dangerous organic reaction medium , transition metal catalyst , toxic solvents / reagents , To the best of our knowledge, there are no earlier reports of (WED) used as an acid promoter for nitrogen containing Heterocyclic adducts. the extract of dragon fruit (scientific name: cacti ; family : cactaceae ; gen : selenicereus ; Binomial name: common name : dragon) is prepared by first took the peel of dragon fruit and dry it and then crushed by using mixer then took 10 g of dragon fruit in 100 ml of water and then heat it at (80^0C) and filter it and got water extract of dragon fruit (WED) acid 4.8 pH We have done the best method for preparing dihydropyridine by using dragon fruit as a catalyst, and another example of preparing its derivatives is shown in T**able. 1.** We investigated the substrate scope by condensing several substituted aldehydes 1.ethyl acetoacetate 2 and ammonium acetate 3 to obtain desirable dihydropyridine derivatives T**able. 1.** Initially, commercially viable substituted aldehydes were permitted to react with ethyl acetoacetate and ammonium acetate in a 1:2:1 ratio under the aforementioned conditions **Table.** 1. Even when the reaction was done on numerous substrates featuring electron-withdrawing or electron-donating groups on the aromatic ring of the aldehyde, a significant yield of the desired products was produced. It is worth noting that aldehydes with halogens as functional groups on the aromatic ring converted smoothly to dihydropyridine derivatives T**able. 1. (4aa - 4ag).** However, when heterocyclic aldehydes were employed in the identical reaction conditions, the same amount of dihydropyridine conversion was found. Furthermore, when acetyl acetone was replaced by ethyl acetoacetate and allowed to react with ammonium acetate, the expected dihydropyridine products were formed, and the promoter was found to be extremely active, yielding up to 92% of isolated yield. We reasoned that there should be more room for further innovation towards softer reaction conditions employing different cactus fruit sources as a promoter in order to produce more favourable reaction conditions. Meanwhile, we discovered that practically all cactus fruit extracts provided excellent conversion for both processes. As a result, we completed these MCRs separately utilising these fruit extracts in the same reaction setting **Table. 2.** Following that, in order to determine various catalytic conditions, we repeated our typical reactions T**able. 1.** with different fruit cactus sources (WED-1 and WED-2). Remarkably, using the same amount of these promoters in the improved reaction environment resulted in identical product conversion. The stability and tolerance of the numerous functional groups, such as hydroxyl, methoxy, nitro, halides, and heterocycles, is a remarkable aspect of this proposed synthetic method. We are highly intrigued by this; equally substantial results were achieved

when other water extracts of fruit promoters (WED-1 and WED-2) were utilised in the experiments instead of WED.

T**able. 1.** Preparation of dihydropyridine derivatives.

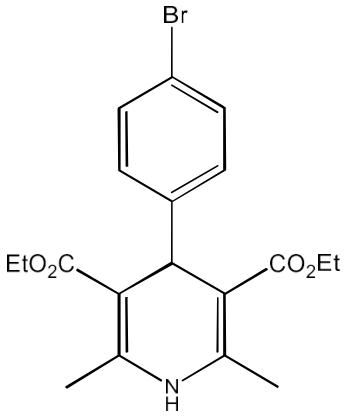


R_2=alkyl, aryl, hetero R_2=H_3C;-OC_2H_5

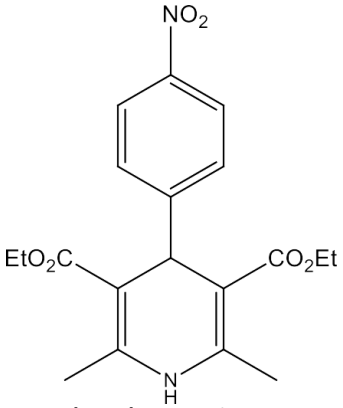


R_2=alkyl, aryl, hetero

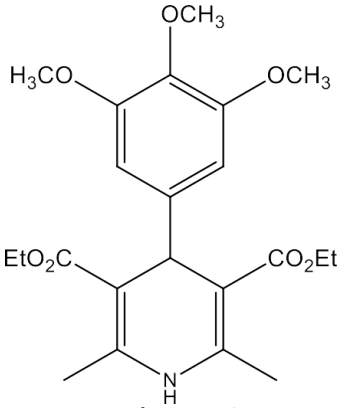
R_2=H_3C,-OC_2H_5



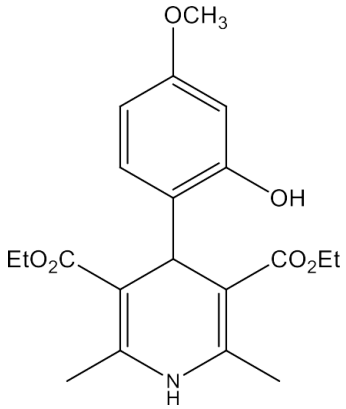
4aa, 11h, 92%



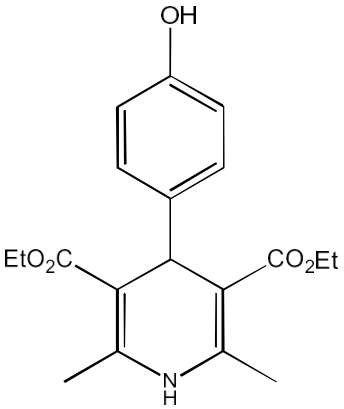
4ab, 9h, 88%



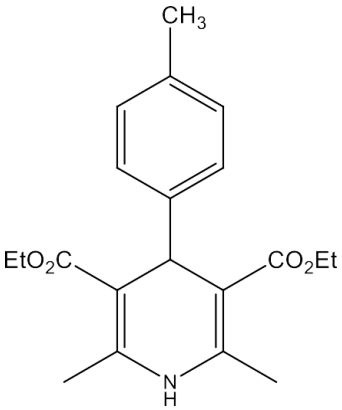
4ac, 8h, 87%



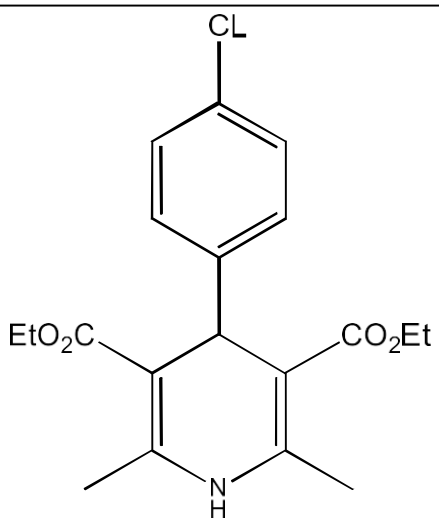
4ad, 12h, 84%



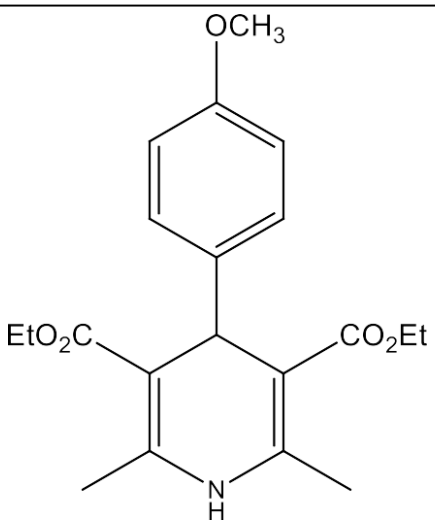
4ae, 10h, 77%



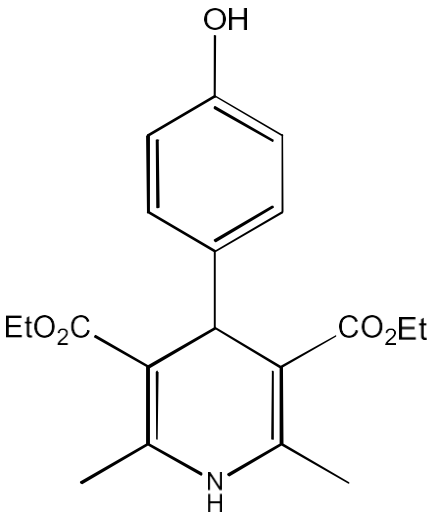
4af, 10h, 78%



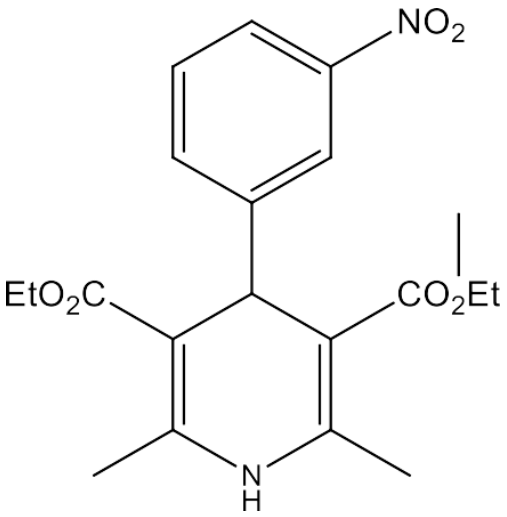
4ag, 12h, 91%



4ah, 12h, 72%



4ai, 11h, 68%



4aj, 11h, 60%

WED catalyzed cycle-condensation for synthesis of dihydropyridine derivatives[a] Reaction conditions: aldehyde (1mmol), ethyl acetoacetate (2mmol), ammonium acetate(1mmol), promoter(100mg) at room temperature. All yields are isolated after recrystallization from ethanol.

Several dragon fruit sources are used to prepare dihydropyridine and its derivatives in order to produce more reaction conditions using various cactus fruit sources as a catalyst. At the same time, we notice that

all of the dragon fruit fruit extracts generated a stunning transformation for each of the reactions. As a result, we conducted MCRs utilising separate fruit extracts in the same reaction environment, as well as knowledge of alternative catalytic circumstances. We also tested reactions with different types of cactus fruit (WED-1 EWD-2). Surprisingly, a similar product was converted utilising the same amount of reaction. Similar substantial findings were obtained when another water extract of fruit promoter (WED-1 and WED-2) was employed in the reaction instead of WED. As illustrated below.

Different dragon fruits source used in the preparation of dihydropyridine and derivatives.

Entry	promoter code	fruit source	species scientific name
1	WED	dragon fruit	Hylocereus undatus
2	WED-1	dragon fruit	Hylocereus costaricensis
3	WED-2	dragon fruit	Hylocereus megalanthus

Table. 2. by using different dragon fruits source, it gives as same the results and discussion as scheme 1.

3. Anti bacterial activity

The antibacterial activity of synthesized compounds was evaluated against six bacteria by using the good diffusion method. Gentamycin was employed as a standard drug to compare the results. Strains of Bacillus subtilis MTCC 441, Bacillus cereus ATCC 9372, Staphylococcus aureus ATCC 96, E. coli ATCC 8739, Klebsiella pneumoniae MTCC 109, Salmonella typhi ATCC 4420. The bacterial cultures were developed by selective nutrient broth at 37 C and stored at 4 C for further use. The nutrient broth was used for the preparation of inoculums of the bacteria and their results were tabulated in **Table. 3.**

Table. 3. Antibacterial activity of compounds 4 (aa - aj)

Compound	Conc.	Zone of inhibition in mm					
		E. coli	S. typhi	K. pneumoniae	S. aureus	B. subtilis	B.cereus
4aa	10	6	8	6	5	5	6
	20	7	9	6	6	7	8
4ab	10	8	10	10	9	8	9
	20	10	12	11	11	9	12
4ac	10	12	13	13	12	11	13
	20	16	14	15	13	12	14
4ad	10	8	9	8	7	7	8
	20	10	10	9	8	8	9
4ae	10	12	12	11	10	10	11
	20	13	14	13	12	12	13
4af	10	6	5	5	4	5	4
	20	8	7	6	6	6	7
4ag	10	11	10	12	11	10	11
	20	15	11	14	12	11	13
4ah	10	13	11	12	11	10	13
	20	17	12	13	12	11	14
4ai	10	10	9	8	7	6	7
	20	11	10	9	9	9	8
4aj	10	8	8	6	7	6	8
	20	9	9	7	7	8	9
Standard	10	18	15	15	14	15	16
	20	19	16	17	15	17	19

4. Conclusion

Finally, we devised a unique approach of dragon fruit extract encouraged an efficient, affordable, and environmentally friendly one pot multi component reactions for the manufacture of highly physiologically active dihydropyridine derivatives. This method is metal and solvent free, with no additional additions, co-catalysts, or severe conditions to produce high yielding products. Further investigations at room temperature were carried out effectively by experimenting with different substituents using our greener synthesis protocol. Using this type of natural feedstock in organic transformations would be more decisive and extremely beneficial to academic and industry research.

5. Conflict of interest

The authors declare no conflict of interest

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