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Green Synthesis of Pyran Derivatives Using Lemon Peel Powder as a Natural Catalyst and their Antimicrobial Activity

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Abstract

A simple and green one pot protocol for the synthesis of bioactive pyran annulated heterocyclic compounds at room temperature in ethanol has been developed using lemon peel powder as a catalyst. This method provides operational simplicity and environmentally benign green approach. All the synthesized compounds were evaluated for antimicrobial activity against *E. coli*, *Welsiella sp.* and *fusarium moniliforme.*

Keywords: Lemon peel; Green synthesis; Pyran; Antimicrobial

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Introduction

Multi component reactions (MCRs), an important subclass of tandem reactions are the one-pot reactions in which three or more easily approachable components react to form a single product [1]. The search for alternative reaction media to replace volatile, flammable and toxic organic solvents is an important objective in the development of green chemical process. Hence organic synthesis in a green solvent is preferred from environmental point of view. Ethanol is a green solvent used in huge amount in academic and industrial research.

Heterocyclic compounds like pyrans add functional diversity to the molecule and provide fruitful area to study their bioactivity. Pyran shows various pharmacological activities like spasmolytic [2] and serves as useful building blocks in the generation of variety of natural products [3]. Pyran derivative scaffold shows various biological activities like antitumour [4], antimicrobial [5], antiviral [6] etc.

Owing to the biological importance, scientists have developed several methodologies for the synthesis of pyrans by using different catalyst such as *S-proline* [7], *L-proline* [8], *trisodium citrate* [9]. However some of these methods have certain limitations; like use of harsh reaction conditions and low yield of the corresponding products. Furthermore some of the nano and other catalysts used for this transformation are expensive and hazardous. Whereas, the lemon peel powder obtained from house hold waste is ecofriendly and can be easily recovered after the completion of reaction.

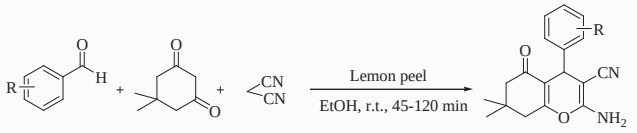
In continuation of our efforts in the development of environmentally benign synthetic approaches towards the design and synthesis of heterocyclic compounds [10-12], herein we wish to report one pot three component synthesis of pyran heterocyclic compounds by the reaction of aromatic aldehyde, malononitrile and dimedone using lemon peel powder as a natural catalyst in ethanol at room temperature in short time.

Experimental

All reagents and chemicals were of analytical grade and used without further purification. Melting points were determined in open capillary tube at one end.

General procedure for the synthesis of substituted pyran derivatives

In a 25mL round bottom flask substituted benzaldehyde (1mmol), malononitrile (1mmol), dimedone (1mmol) and lemon peel powder (10wt%) were taken in 5mL ethanol as a green solvent. The resulting reaction mixture was stirred at room temperature as indicated in Table 1. The progress of reaction was monitored by using TLC (30% ethyl acetate: n-hexane). After completion of reaction;



Scheme 1: Synthesis of pyran derivatives using lemon peel powder as a green catalyst.

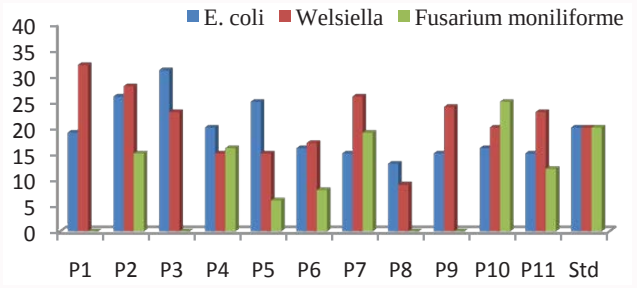


Figure 1: Antimicrobial activity of pyran derivatives (zones of inhibition in mm).

the solid product obtained was filtered off along with the catalyst, washed with water. The mixture containing crude product along with the catalyst was diluted with hot ethanol and filtered off to separate residue as the recovered catalyst and filtrate was concentrated on rotary evaporator and finally recrystallized with hot ethanol to afford the pure product. All the synthesized compounds were confirmed by comparing their melting points with the reported values, IR and ^{1}H NMR data [13-19].

Spectral data of synthesized compound

2-Amino-7, 7-dimethyl-5-oxo- 4-(2-nitrophenyl)-5, 6, 7, 8-tetrahydro-4H-chromene-3-carbonitrile: Brown solid. IR (KBr): cm^{-1} 3464.15 (NH_2), 2194.99 (CN), 1678.07 (C=C), 1517.98 (C=O), 3203.76 (Aro. C-H), ^{1}H NMR: (200 MHz, $CDCl_3$) δ 0.99 (s, 3H), 1.09 (s, 3H), 2.17 (d, 2H), 2.45 (s, 2H), 4.69 (s, 2H), 5.19 (s, 1H,), 7.26 (m, 2H), 7.52 (d, 1H), 7.77-7.82 (dd, 1H).

Antimicrobial activity

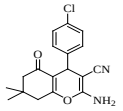
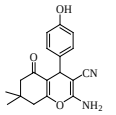
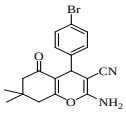
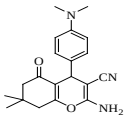
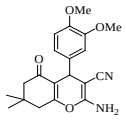
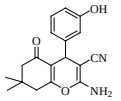
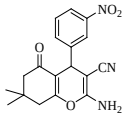
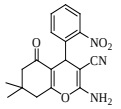
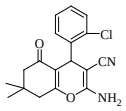
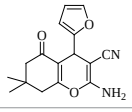
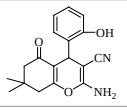
The authentic cultures of microbial species used were collected from the department of Microbiology, Deogiri College, Station road, Aurangabad, Maharashtra and the synthesized compounds were screened for antibacterial and antifungal activity.

Well diffusion method

Well diffusion method [16,17] was used for antibacterial screening of the synthesized pyran derivatives. About 100 µL sterile Mac Conkey broths were added onto each well along with 2µL serial diluted plant pathogenic bacteria suspension in each well. Different concentrations of each pyran derivative, viz. 2, 4, 6 µL were loaded in each well and results are summarized in Table 2 for 4µL concentration. Control was prepared by Mac Conkey broth and bacterial suspension without adding solution of compound. The prepared well plate was sealed with parafilm and incubated at 37°C for 24 hours in incubator.

a) Antibacterial activity: Pyran derivatives at different concentrations were tested against plant pathogenic bacteria *E. coli* and *Welsiella sp.* using same method. Compounds P2, P3 and P5 showed excellent activity against bacteria *E. coli* whereas other compounds showed moderate to less activity as compared to standard streptomycin.

Table 1: Synthesis of substituted pyran derivatives.

Sr. No.	Aldehyde	Product	Time (min)	Yield (%)	M.P. (^{0}C) Found	M.P.[Ref.]
P1			60	96	210-212	208-210 [13]
P2			120	90	222-224	207-209 [14]
P3			120	94	198-200	200-203 [14]
P4			90	88	108-110	199-201 [16]
P5			90	86	156-158	157-159 [13]
P6			120	92	230-231	229-231 [18]
P7			45	94	209-211	210-212 [17]
P8			60	92	222-223	227-230 [17]
P9			60	96	209-211	210-212 [13]
P10			45	94	214 -216	215-217 [15]
P11			120	92	-	-

Similarly, compounds P1, P2, P3, P7, P9 and P11 showed excellent activity against bacteria *Welsiella sp.* whereas other compounds showed moderate to less activity as compared to standard streptomycin.

b) Antifungal activity: Antifungal activity of the synthesized compounds was screened against fungal species *Fusarium moniliforme* using agar well disc diffusion method. Observations were recorded after 72 hrs and the zone of inhibition was measured in millimeter.

All the synthesized compounds showed antifungal activity against *Fusarium moniliforme.* Compounds P7 and P10 showed excellent

Table 2: Antimicrobial activity of the synthesized pyran derivatives.

Compound No.	Antimicrobial activity (Zone of inhibition in mm)*		
	Antibacterial		Antifungal
	E. coli	*Welsiella sp.*	*Fusarium moniliforme*
P1	19	32	-
P2	26	28	15
P3	31	23	-
P4	20	15	16
P5	25	15	06
P6	16	17	08
P7	15	26	19
P8	13	09	-
P9	15	24	-
P10	16	20	25
P11	15	23	12
Streptomycin	20	20	10

*Zones of inhibition for 4 µl concentration.

Table 3: Effect of different solvents on synthesis of pyran derivatives.

Entry	Solvent	Time (min)	Yield (%)
1	H_2O	180	85
2	EtOH	45	96
3	DMSO	300	90

Table 4: Effect of catalyst concentration on the synthesis of pyran derivatives.

Entry	Amount of catalyst (wt %)	Yield (%)
1	5	40
2	10	96
3	20	95
4	30	94

activity against *Fusarium moniliforme* whereas other compounds showed moderate activity as compared to standard streptomycin (Figure 1).

Results and Discussion

To optimize the reaction conditions we have carried out the model reaction of 4-Cl-benzaldehyde, malononitrile, dimedone and lemon peel powder as a catalyst by using water, ethanol and DMSO as solvents at room temperature. The results obtained are presented in (Table 3). High yield of products were obtained with 96% yield in 45 minutes at room temperature by using ethanol as a solvent.

In order to understand amount of catalyst to obtain maximum yield we have carried out model reaction with different amount of catalyst (Table 4) and found that 10wt% of catalyst is sufficient. Further increase in the amount of catalyst does not affect the yield.

Conclusion

In conclusion, we have achieved synthesis of pyran derivatives by one pot multicomponent reaction using a green synthetic protocol at room temperature. The advantages of this method are short reaction time, easy work up procedure, use of green catalyst and solvent and high atom economy. All the synthesized derivatives of pyran showed good antibacterial and antifungal activity at low concentration.

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