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AN EFFICIENT SYNTHESIS OF HETEROCYCLIC COMPOUNDS AND ITS ANTI-MICROBIAL ACTIVITY

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Abstract:*The present work is to devise a simple and convenient route to synthesis 2- amino -4-phenyl-4H-pyrano[3,2-h]quinoline-3-carboxylic acid ethyl esters by treatment of 8-hydroxyquinoline with aromatic aldehyde and ethyl cyano acetate using InCl3 as a catalyst. The synthesized heterocyclic compounds exhibited promising biological activities. Therefore, considerable effects have been directed towards the preparation and synthetic manipulation of this molecules .As a result ,a number of compounds have been obtained with diverse biological activities are synthesised*

Key words: biological activities, quinoline derivatives

1. Introduction

The importance of quinoline and its annulated derivatives is well recognized by synthetic and biological chemists. Compounds possessing this ring system have a wide range of applications as drugs and pharmaceuticals.Pyranoquinolines that constitute the basic frameworks of a number of alkaloids with biological significance. The development of environmentally benign and economical methods for the synthesis of biologically interesting compounds remains a significant challenge in synthetic chemistry [1, 2].

2. Materials and methods

Materials required

- 8-hydroxy Quinoline
- Ethyl cyanoacetate
- Aromatic aldeydes
- Catalyst
- Triethyl amine
- Dimethyl amino pyridine
- L-proline
- Indium triflate or chloride
- Ethanol

The present work incorporates the synthesis of 2- amino-4-aryl-4H-pyrano [3,2-h]quinoline-3-carboxylic acid ethyl esters from the reaction of 8-hydroxyquinoline(1mmol), with ethyl cyanoacetate (1mmol) and aromatic aldehydes(benzaldehyde) (1mmol) in 20 ml of ethanol at reflux temperature.

3. Results and discussion

3.1 Screening of various catalysis on the one-pot reaction

Entry 1

The above reaction was carried out without using catalyst refluxing for 5 hours and the yield obtained was in trace amount.

Entry 2

The reaction was carried out by using triethyl amine (20 mol %) as a catalyst refluxing for 5 hours and the yield was 29%

Entry 3

The reaction was carried out by using dimethyl amino pyridine (20mol %) as a catalyst yield was17% by refluxing it for 5 hours

Entry 4

The effectiveness was tested by using L-Proline (20mol %) as a catalyst the yield increased to about 34 %

Entry 5

In the same reaction conditions Indium chloride (20mol %) was used as a catalyst which yielded about 48% which is the maximum yield compare to the above catalyst

Table: 1 screening of various catalysts on the one-pot reaction

Entry	Catalyst (20mol %)	Time (h)[b]	Yield (%)[c]
1	-	5	*d*
2	Et_3N	5	29
3	DMAP	5	17
4	L-Proline	5	34
5	$InCl_3$	5	**48**

Reaction conditions: [b]Time duration of reaction in hours

[c]Isolated pure product

[d]Trace amounts

3.2 Eco-Friendly synthetic pathway using micro wave vessel

In order to optimize the reaction Indium chloride catalysed reaction was evaluated by using microwave irradiation by different concentration of the catalyst.

Entry 1

The reaction was carried out by using 5 mol% of Indium chloride for 7 mins and the yield was noted

Entry 2

The reaction was processed by using 10 mol% of Indium chloride for 7 mins and the yield was noted

Entry 3

The reaction was processed by using 15 mol% of Indium chloride for 7 mins and the yield was noted

Entry 4

The reaction was processed by using 20 mol% of Indium chloride for 7 mins and the yield was noted

Entry 5

The reaction was processed by using 25 mol% of Indium chloride for 7 mins and the yield was noted

Table: 2 Evaluation of most appropriate loading of Indium (III) chloride

Entry	Catalyst $Incl_3$ (mol %)	Time (min)[b]	Yield (%)[c]
1	5	7	18
2	10	7	39
3	15	7	63
4	20	7	81
5	25	7	**87**

Reaction conditions: [b]Time duration of reaction in mins

[c]Isolated pure product

No increase in yield after 7 mins

By thin layer chromatography it was revealed to be single spot of the desired product

IR Specturm analysis

- The IR spectrum of the compound showed absorption peaks at 3389, 3285 and 1676 cm^{-1} which is attributed to the presence of amino and ester groups respectively.

H^1 NMR analysis

- The H^1 NMR Spectrum of the compound in DMSO-d^6 showed the following peaks

A three proton triplet at □1.07 (J=7.0 Hz) due to CH_2CH_3

A two proton quartet at □3.098 due to CH_2CH_3

A one proton Singlet at □5.08 due to C_4-H

A three proton triplet at □7.10 (J=7.0 Hz) due to $C_{4'}$-H

A two proton doublet at □7.21 (J=8.5 Hz) due to C, $2C_{6'}$-H

A one proton doublet of doublet at □7.58 (J=4.5 Hz) due to C_8–H

C^{13}NMR analysis

- C^{13} NMR showed peaks at

□168.78,161.78,150.58,148.19,143.45,138.04,136.44,128.73,

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127.94,127.83,127.80,126.59,125.41,123.92,122.36,76.50,59.14,40.76and 14.71 due to 21 carbons.

- The elemental analysis was in good agreement with the proposed molecular structure C_{21} H_{18} N_2 O_3
- All the spectral and analytical details were attested the compound as 2- amino -4-phenyl-4H-pyrano[3,2-h]quinoline-3-carboxylic acid ethyl esters

4. Antibacterial Activity

The synthesized product is tested with different bacteria for antibacterial activity. The bacteria selected for this study are E. coli responsible for food poisoning and infections [3], S. aureus caused serious life-threatening complications such as infection of the blood bones or lungs [4], P. aeruginosa is considered a human pathogen more often responsible for nosocomial infections [5] and V. parahaemolyticus represent a serious and global threat to human health [6]. The antibacterial activity was determined by using the agar disk diffusion assay. A bacterial culture of 24 hours was spread on the surface of the Muller-Hinton agar plate. A disc of sterile 6 mm whatmann paper was saturated with 10 µl of solution of the quinoline compounds under investigation in dimethylsulfoxide (DMSO). After 1 h of diffusion, the Petri dishes were incubated at 37 °C for 24 hours and the zones of inhibition of the development were measured and compared with those of the reference discs of penicillin G.

Table:3 The synthesized compounds compared with standard antibiotic penicillin G against Gram positive and Gram negative bacteria at 10^{-3} g/ml

Compound	Inhibition Zone diameter (mm)			
	Gram positive bacteria	Gram negative bacteria		
	s.aureus	*v.parahaemolyticus*	*E.Coli*	*p.aerugino*
	38	32	28	15
Pencillium G (standard)	11	5	12	9

4. Conclusion

An effectiveness of the catalyst InCl3 is was reported .And the generality of the reaction was tested against other aromatic aldehyde derivatives. And a plausible mechanism for the formation of the product has been proposed. From the screening results, we conclude that the antibacterial activity of the synthesized compounds. In this study, the synthesis of pyran derivatives based on 8-hydroxyquinoline was carried out by condensation of ethyl cyano acetate with benzaldehyde .And substituted benzaldehyde and 8- hydroxyquinoline are future scope of research These products were identified by elemental analysis data, IR, 1H and 13C NMR spectroscopy, the data spectral obtained show good coherence with the assigned structures. All these compounds have been evaluated and screened “in vitro” by the disk diffusion technique against Gram- negative bacterial strains (E. coli), and Gram-positive bacterial strains (S. aureus, V. parahaemolyticus and P. aeruginosa) and its efficiency against human pathogens is promising.

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