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Pyrano[3,2-c]chromenes Characterization and Evaluation of the Antioxidant and Antimicrobial Activities †

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Abstract: Several studies have shown that the pyrano[3,2-c]chronenes moiety is a source of several molecules possessing interesting and considerable biological activities on the medicinal level, notably antimicrobial, anti-inflammatory, analgesic and anti-anxiolytic, anticancer activity. The main objective of this work is to evaluate the antioxidant and antimicrobial activities of pyrano[3,2-c]chronenes by using classical methods and more developed techniques. Two series of pyrano[3,2-c]chromene derivatives have been prepared by synthetic and catalyst means, with an excellent yield which ranges between (90–96)% and then characterized via infrared and NMR analysis techniques. The antioxidant activity was assessed using the DPPH method and by the power of iron reduction. The determination of antimicrobial activity was carried out against the reference bacteria.

Keywords: pyrano[3,2-c]chromenes; NMR; infrared; antioxidant; antimicrobial activity

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1. Introduction

The use of ecological reagents and solvents as well as efficient and perfectly reusable catalysts represents one of the most efficient ecological chemical techniques. Nanocatalysts have been the subject of several studies in inorganic chemistry materials because of their significant physical properties thant can be used in organic chemistry reaction. since it can be recovered after each use and its potencial degradation to intervene in other reactions[1,2].

Over the past few years, Pyrano[3,2-c]chromene heterocyclic system has proven to be one of the most active synthetic products in a wide range of biological activities, including [4], anti-microbial [5], antifungal [6], anti-coagulant, anti-inflammatoire, antiviral. In addition, they have been used as cognitive enhancers, for the treatment of neurodegenerative diseases,antitumors and antimicrobial among the investigated heterocycles [7]. The result of this work deviates in two parts: the synthesis of pyranochromene derivatives via a condensation reaction using a method that meets one of the criteria of green chemistry, after the compounds will be evaluated by the antioxidant activity and antimicrobial activity used a recent technique that has proven effective. All the compound were screened against three Gram-positive bacteria (*Bacillus cereus* ATCC 10876, *Listeria monocytogenes* ATCC 15313, *Enterococcus faecalis* ATCC 49452) four Gram-negative bacteria

(*Salmonella typhimurium* ATCC 13311, *Proteus mirabilis* ATCC 35659, *Klebsiella pneumoniae* ATCC 700603, *Pseudomonas aeruginosa* ATCC 27853) Upond antimicrobial screening, its was observed that the majority of compound were found to be active against *Salmonella typhimurium* ATCC 13311 as compared to standard Gentamicin.

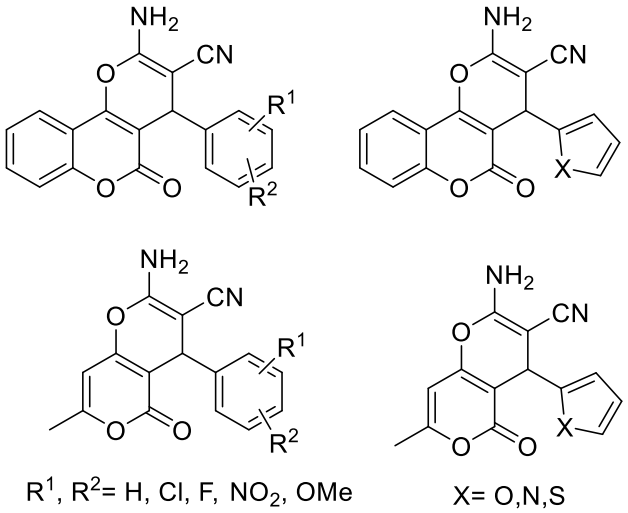

Figure 1. Structure of pyrano[3,2-c]chromenes.

2. Results and Discussion

(a) Synthesis part :

The synthesis process was carried out in a multi-component one pot reaction with heterogeneous materials. Different protocols were also tested by modify the reaction time, temperature and the solvents of reaction in order to optimize the experimental condition.

In order to develop suitable conditions respecting the criteria of green chemistry, we have established a new protocol for the synthesis of [pyrano3,2-c] chromene based on a nanoparticulate catalyst which MgO supports on SBA 15 in the presence of water and ethanol (1/1) as solvent [8]. The reaction mixture is brought to room temperature for a duration which varies between 20–40 min.

Table 1. The synthesis of a few compounds 1–3.

Compound	R^1	Time (min)	Yield (%)
1	H	30	90
2	Cl	20	95
3	F	25	93

(b) Biological part :

The results of antioxidant activity showed that both families of pyrano[3,2-c]chromenes showed a reduction in DPPH radical and iron. While these families have a good antibacterial effect with inhibtion areas ranging from 8 to 12 mm against *Salmonella typhimurium* ATCC 13311.

3. Experimental Procedure

(c) Synthesis part :

Compounds **1,2,3** synthesized in table above using**:** aromatic aldehyd (0.01 mol), maloninitrile (0.01 mol), 4-hydroxycoumarin (0.01 mol), and MgO/ SBA15 (0.01 mol) in H_2O (1 mL) and EtOH (1 mL) in appropriate solution. The mixture reaction was string under heating condition within a time varying between 20–40 min, after completion of the reaction which was monitored by TLC. The reaction system was cooled to room temperature.

The formed solid after cooling was collected by filtration, washed with water and aqueous ethanol and purified by appropriate solvent.

After completing the model reaction, the crude product was isolated by filtration. The calatyst was recovered by evaporating the solvent and washing with ether, in the model reaction the catalyst was recycled five time and reused

(d) Biological part:

DPPH scavenging assay

The free radical scavenging activity of the compounds, was measured by DPPH. (2,2-diphenyl-1-picrylhydrazyl) using the method described by Blois [9].

Reducing power assay

The reducing power was realized to measure the capacity of compounds to reduce (Fe^{3+}) present in the complex $K_3Fe(CN)_6$ to Fe^{2+}. The reducing power was determined by absorbance measurement at 700 nm (Oyaizu) [10].

Antibacterial activity

This study was performed with the following bacteria strains: *Bacillus cereus* ATCC 10876, *Listeria monocytogenes* ATCC 15313, *Enterococcus faecalis* ATCC 49452, *Salmonella typhimurium* ATCC 13311, *Proteus mirabilis* ATCC 35659, *Klebsiella pneumoniae* ATCC 700603, *Pseudomonas aeruginosa* ATCC 27853. The antibacterial activity of different compounds was determined with Agar diffusion method (NCCLS) [11].

The diameters of the inhibition zones was measuring after incubation 24 h to 37°C. The test was analyzed in three replications.

4. Conclusions

In conclusion, we have developed a simple, fast, Efficient green method for the catalytic synthesis of [pyrano3,2-c] chromene derivatives, the reaction conditions used are very mild because the reaction yields obtained are excellent. The method used does not involve the use of volatile organic solvents, therefore it is an environmentally friendly process.

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