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Research Article

NOVEL SYNTHESIS OF BIOACTIVE PYRAZOLINE DERIVATIVES THROUGH REACTIVE CHALCONES

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ABSTRACT

A mixture of furan-2-carbaldehyde (I) and substituted acetophenone (IIa-d) stirring in methanol with the help of magnetic stirrer. Add 10 ml NaOH solution to this mixture. Stir this reaction mixture for 10 minutes. Cool in an ice-water bath until crystal formation of (E)-3-(furan-2-yl)-1-phenylprop-2-en-1-one and its derivatives (IIIa-d). A mixture of IIIa-d and hydrazine on reflux with methanol for 3 hours. Cool the reaction mixture in ice-water bath until crystal formation is complete. Add ice-cold water to the flask and the product was filtered, washed with water and then dried. The product recrystallized from ethyl alcohol. This gives 5-(furan-2-yl)-4,5-dihydro-3-phenyl-1H-pyrazole and its derivatives (IVa-d). All these newly synthesized compounds were screened for antibacterial activity and characterized by elemental analysis and spectral data.

Keywords: Furan-2-carbaldehyde, substituted acetophenone, NaOH, methanol, hydrazine

INTRODUCTION

The chemistry of chalcones has generated intensive scientific studies throughout the world. Especially interest has been focused on the synthesis and biodynamic activities of chalcones. The name “Chalcones” was given by Kostanecki and Tambor[1]. These compounds are also known as benzylidene acetophenone. In chalcones, two aromatic rings are linked by an aliphatic three carbon chain. Chalcone bears a very good synthon so that variety of novel heterocycles with good pharmaceutical profile can be designed. Chalcones are α, β-unsaturated ketone containing the reactive ketoethylenic group –CO-CH=CH-. These are coloured compounds because of the presence of the chromophore -CO-CH=CH-, which depends in the presence of other auxochromes. Different methods are available for the preparation of chalcones[2-4].The most convenient method is the Claisen-Schimdt condensation of equimolar quantities of aryl methyl ketone with aryl aldehyde in the presence of alcoholic alkali[5]. Chalcones are used to synthesize several derivatives like cyanopyridines, pyrazolines isoxazoles and pyrimidines having different heterocyclic ring systems[6-9].

Chalcones (*trans*-1,3-diaryl-2-propen-1-ones) are natural products belong to flavonoid, are considered as intermediate in the flavonoids biosynthesis, and are widespread in plants. The existence of the α, β-unsaturated ketone moiety in chalcones is a common part found in a large number of biological active compounds. Therefore, chalcone derivatives from nature or synthetic origin exhibit diverse pharmacological activities, such as antimicrobial[10], antitumor[11], anticancer[12,13], radical scavenger[14], and inhibitor of topoisomerase-I[15]. However, isolation of chalcone derivatives from nature requires a long and usually complicated procedure which does not comparable to the yield obtained. Due to time consuming and intensive process in the isolation procedure, and to their diverse pharmacological activities, the development of an efficient synthetic protocol of chalcone derivatives attracts many researchers. A good synthetic method gives us advantages to obtain chalcone derivatives attaching various substituents in excellent yield which possibly do not exist in nature. Furthermore, chalcones

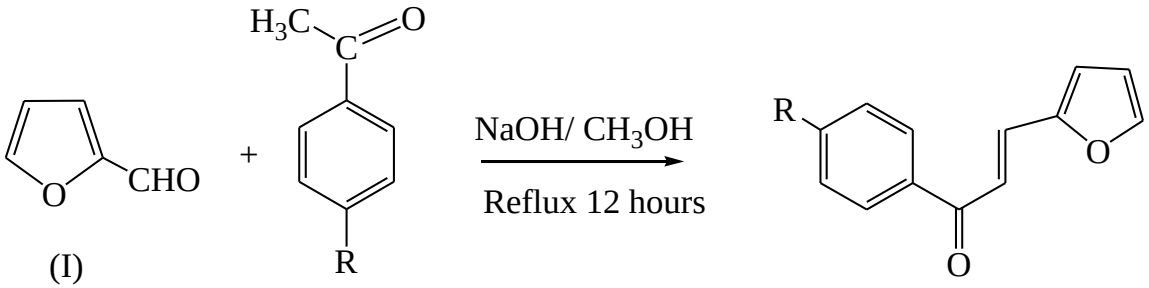
are known as the key intermediate in the synthesis of various biologically important heterocyclic compounds. In this article, the preparation methods of chalcones, structure diversity, role of chalcone as synthon for the synthesis of diverse heterocyclic compounds, and their biological activity are reviewed.

Substituted pyrazolines are useful in pharmaceutical and agrochemical research. Pyrazoline derivatives with a phenyl group at the 5-position possess good film-forming properties, exhibit excellent characteristics of blue photoluminescence and electroluminescence[16]. Pyrazolines are also used as optical brighteners and whiteners. Pyrazolines display various biological activities such as antimicrobial[17], antifungal[18], antidepressant[19], immunosuppressive[20], anticonvulsant[21], anti-tumor[22], antiamoebic[23], antibacterial[24] and antiinflammatory[25] activities. Syntheses of pyrazolines by reaction of α,β-unsaturated carbonyl compounds with diazoalkanes[26] or with hydrazine hydrate[27,28] were reported in literature.

Experimental Section

All melting points were determined in open capillary tube and were uncorrected. IR spectra were recorded with potassium bromide pellets technique, ^{1}H NMR spectra were recorded on AVANCE 300 MHz Spectrometer in DMSO using TMS as internal standard. Mass spectra were recorded on a FT VG-7070 H Mass Spectrometer using EI technique at 70 eV. All the reactions were monitored by Thin layer chromatography.

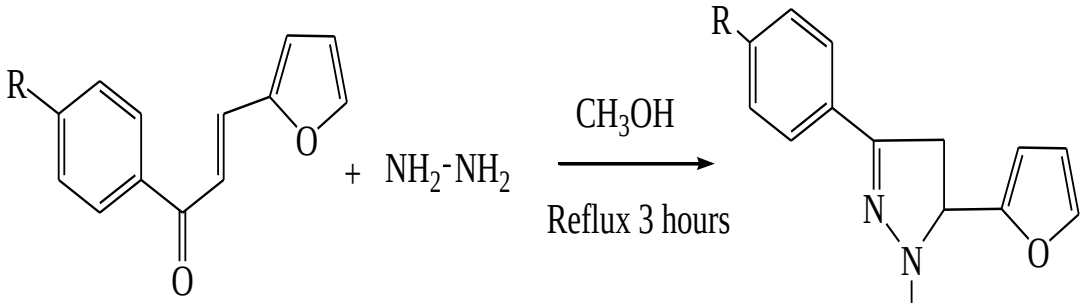
MATERIALS AND METHOD



(I) (II a-d) (III a-d)

R = H, Cl, OCH_3, NO_2

(Scheme : 1)



(III a-d) (IV a-d)

R = H, Cl, OCH_3, NO_2

(Scheme : 2)

Experimental

Synthesis of Reactive Chalcones (Scheme-1)

1) Synthesis of (E)-3-(furan-2-yl)-1-phenylprop-2-en-1-one (IIIa)

Dissolve 0.01 mol of the furan-2-carbaldehyde (I) and 0.01 mol of the acetophenone (IIa) in 10 ml methanol in a flask with a magnetic stirring. Add 3.5 ml of 6M NaOH solution. Stir the reaction mixture for 10 minutes. Cool in an ice-water bath until crystal formation is complete. Add 2 ml of ice-cold water to the flask. Wash the crystals with 5 ml of water followed by 3-5 ml of ice-cold methanol. This gives (E)-3-(furan-2-yl)-1-phenylprop-2-en-1-one (IIIa). The product was filtered, washed with water and then dried. The product recrystallized from ethyl alcohol.

2) Synthesis of (E)-1-(4-chlorophenyl)-3-(furan-2-yl) prop-2-en-1-one (IIIb)

Dissolve 0.01 mol of the furan-2-carbaldehyde (I) and 0.01 mol of the 1-(4-chlorophenyl) ethanone (IIb) in 10 ml methanol in a flask with a magnetic stirring. Add 3.5 ml of 6M NaOH solution. Stir the reaction mixture for 10 minutes. Cool in an ice-water bath until crystal formation is complete. Add 2 ml of ice-cold water to the flask. Wash the crystals with 5 ml of water followed by 3-5 ml of ice-cold methanol. This gives (E)-1-(4-chlorophenyl)-3-(furan-2-yl) prop-2-en-1-one (IIIb). The product was filtered, washed with water and then dried. The product recrystallized from ethyl alcohol.

3) Synthesis of (E)-3-(furan-2-yl)-1-(4-methoxyphenyl) prop-2-en-1-one (IIIc)

Dissolve 0.01 mol of the furan-2-carbaldehyde (I) and 0.01 mol of the 1-(4-methoxyphenyl) ethanone (IIc) in 10 ml methanol in a flask with a magnetic stirring. Add 3.5 ml of 6M NaOH solution. Stir the reaction mixture for 10 minutes. Cool in an ice-water bath until crystal formation is complete. Add 2 ml of ice-cold water to the flask. Wash the crystals with 5 ml of water followed by 3-5 ml of ice-cold methanol. This gives (E)-3-(furan-2-yl)-1-(4-methoxyphenyl)prop-2-en-1-one (IIIc). The product was filtered, washed with water and then dried. The product recrystallized from ethyl alcohol.

4) Synthesis of (E)-3-(furan-2-yl)-1-(4-nitrophenyl) prop-2-en-1-one (IIId)

Dissolve 0.01 mol of the furan-2-carbaldehyde (I) and 0.01 mol of the 1-(4-nitrophenyl) ethanone (IId) in 10 ml methanol in a flask with a magnetic stirring. Add 3.5 ml of 6M NaOH solution. Stir the reaction mixture for 10 minutes. Cool in an ice-water bath until crystal formation is complete. Add 2 ml of ice-cold water to the flask. Wash the crystals with 5 ml of water followed by 3-5 ml of ice-cold methanol. This gives (E) -3- (furan-2-yl) -1- (4-nitrophenyl) prop-2-en-1-one (IIId). The product was filtered, washed with water and then dried. The product recrystallized from ethyl alcohol.

Synthesis of substituted pyrazoline (Scheme-2)

5) Synthesis of 5-(furan-2-yl)-4,5-dihydro-3-phenyl-1H-pyrazole (IVa)

A mixture of (E)-3-(furan-2-yl)-1-phenylprop-2-en-1-one (IIIa) and hydrazine on reflux with methanol for 3 hours. Cool the reaction mixture in ice-water bath until crystal formation is complete. Add ice-cold water to the flask and the product was filtered, washed with water and then dried. The product recrystallized from ethyl alcohol. This gives 5-(furan-2-yl)-4,5-dihydro-3-phenyl-1H-pyrazole (IVa).

6) Synthesis of 3-(4-chlorophenyl)-5-(furan-2-yl)-4,5-dihydro-1H-pyrazole (IVb)

A mixture of (E)-1-(4-chlorophenyl)-3-(furan-2-yl) prop-2-en-1-one (IIIb) and hydrazine on reflux with methanol for 3 hours. Cool the reaction mixture in ice-water bath until crystal formation is complete. Add ice-cold water to the flask and the product was filtered, washed with water and then dried. The product recrystallized from ethyl alcohol. This gives 3-(4-chlorophenyl)-5-(furan-2-yl)-4,5-dihydro-1H-pyrazole (IVb).

7) Synthesis of 5-(furan-2-yl)-4,5-dihydro-3-(4-methoxyphenyl)-1H-pyrazole (IVc)

A mixture of (E)-3-(furan-2-yl)-1-(4-methoxyphenyl) prop-2-en-1-one (IIIc) and hydrazine on reflux with methanol for 3 hours. Cool the reaction mixture in ice-water bath until crystal formation is complete. Add ice-cold water to the flask and the product was filtered, washed with water and then dried. The product recrystallized from ethyl alcohol. This gives 5-(furan-2-yl)-4,5-dihydro-3-(4-methoxyphenyl)-1H-pyrazole (IVc).

8) Synthesis of 5-(furan-2-yl)-4,5-dihydro-3-(4-nitrophenyl)-1H-pyrazole (IVd)

A mixture of (E)-3-(furan-2-yl)-1-(4-nitrophenyl) prop-2-en-1-one (IIId) and hydrazine on reflux with methanol for 3 hours. Cool the reaction mixture in ice-water bath until crystal formation is complete. Add ice-cold water to the flask and the product was filtered, washed with

water and then dried. The product recrystallized from ethyl alcohol. This gives 5-(furan-2-yl)-4,5-dihydro-3-(4-nitrophenyl)-1H-pyrazole (IVd).

RESULT AND DISCUSSION

The objectives of the present work are to synthesize substituted pyrazoline derivatives and study their biological properties. Thus an attempt has been made in this direction. As expected substituted pyrazoline exhibited antibacterial, anticancer, anti inflammatory, antitumor activities. In the view of this study, further research can be carried out on the development of new effective anticancer agents by the modification of compound.

CONCLUSION

Pyrazolines are well known and important nitrogen containing 5-membered heterocyclic compounds and various methods have been worked out for their synthesis. Numerous pyrazoline derivatives have been found to possess considerable biological activities, which stimulated the research activity in this field. The manuscript is a brief about different pyrazoline derivatives synthesized through reactive chalcones.

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