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Synthesis and Characterization of Chalcones and Pyrazolines derived from Substituted Aryl ether

Shashiprabha*, B Shivarama Holla†, Vishwanatha P‡ and Nefisath P§

Abstract

Few novel chalcones were synthesised by treating 4-fluoro-3-phenoxy benzaldehyde with different substituted ketones and characterised using ^1H NMR and mass spectrometry. The chalcones synthesised were further treated with hydrazine hydrate to get corresponding pyrazolines. The newly synthesised pyrazolines were characterised by ^1H NMR and mass spectrometry.

Keywords: 4-Fluoro-3-phenoxy benzaldehyde, Chalcones, Pyrazoline, Spectral Data

1. Introduction

Heterocyclic compounds are widely distributed in nature. They find application in pharmaceuticals, agrochemicals and related fields. There are many compounds which are derived from natural products and used in the betterment of mankind. In many cases, an

* PG Department of Chemistry, Sri Dharmasthala Manjunatheshwara College, Ujire, (SDM College, Ujire), Dakshina Kannada, India; shashi-sudha@sdmcejire.in

† (SDM College, Ujire), hollabs@yahoo.com

‡ (SDM College, Ujire), drvishwanathap@rediffmail.com

§ (SDM College, Ujire), nefisathp@gmail.com

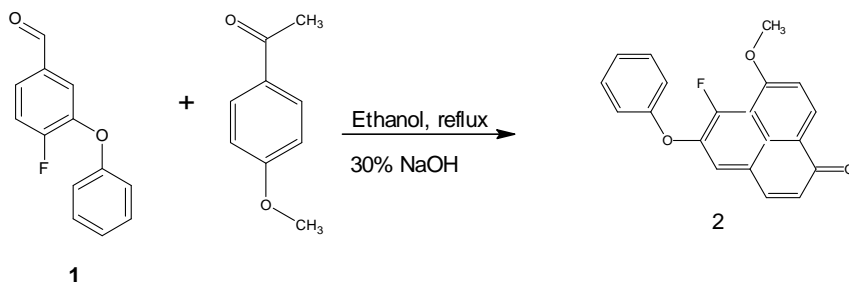
observation of the natural products provides information regarding the biological properties. They are improved further by modifying the structure of natural products. Aryl ethers are an important class of compounds which influence the biological property of the products derived from them [1-2].

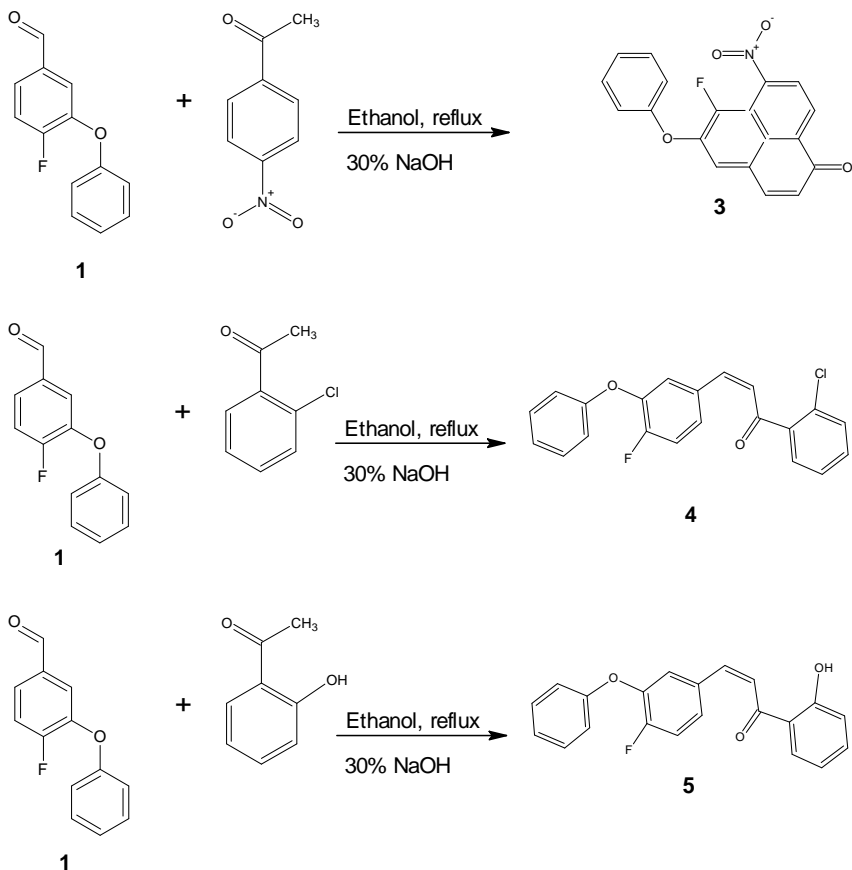
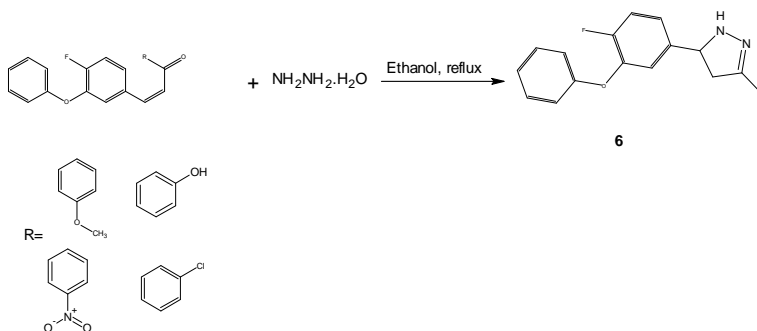
A wide variety of heterocycles have been explored for their biological activities. Isoxazolines[2-4] have been found to play an important role in medicinal and agrochemical industry. Pyrazolines are known to possess anti-bacterial [5-6], anti-fungal [7], anti-inflammatory [8-9], analgesic [10], anti-depressant [11], anti-pyretic and hypoglycaemic properties. A number of isoxazoline derivatives are also associated with insecticidal and acaricidal activities. Incorporation of different structural moieties to pyrazoline and isoxazoline framework with a view to enhance the biological activity has been reported by a number of research groups [12-16].

2. Present Study

Prompted by these findings we propose to synthesise the following aryl ether derivatives and characterise the newly synthesised compounds. In the present investigation, the study takes up systems of proven biological activity to prepare and characterise the synthesised compounds. In order to achieve such objectives, the following compounds were synthesised as per the following scheme.

3. Experimental Methods



**Scheme 1:** Synthesis of Different Chalcones from 4-Fluoro-3-phenoxy Benzaldehyde**Scheme 2:** Synthesis of Pyrazolines from Chalcones Synthesised in Scheme-1

The melting points of the compounds were recorded by the open capillary method and are uncorrected and recorded on BUCHI melting point instrument B-540. ^1H NMR spectra were recorded (in $\text{DMSO-d}_6/\text{CDCl}_3$) on a 500MHz Bruker NMR spectrometer using TMS as an internal standard. The mass spectra were recorded on BUCHI B-540 spectrometer operating at 70ev. Progress of the reactions and the purity of the products were monitored by thin layer chromatography (TLC). Appropriate solvent systems were used as eluents.

4. Results and Discussion

4-Fluoro-3-phenoxy benzaldehyde (**1**) was reacted with substituted acetophenones by refluxing in ethanol using 30% sodium hydroxide as a base to get chalcones (**2-5**). These chalcones were reacted with hydrazine hydrate using ethanol as a solvent to get corresponding pyrazolines (**6a-6d**). The newly synthesised compounds were characterised using NMR and mass spectral data. 4-Fluoro-3-phenoxy benzaldehyde (**1**) and substituted acetophenones required for the work were procured from S.D.Fine chemicals (LR grade).

All synthesised compounds were characterised by ^1H NMR and mass spectral data. The 500 MHz ^1H NMR spectrum of compound (**2**) showed a singlet at δ 3.87ppm corresponding to three protons of OCH_3 . The four protons of phenyl ring bearing methoxy group appeared as doublets at 6.956-6.973ppm ($J=8.5\text{Hz}$) and 7.007-7.022ppm ($J=7.5\text{Hz}$). The two protons attached to carbons bearing double bonds resonated as a multiplet at 7.119-7.201ppm and 7.218-7.258ppm. The five protons of phenoxy ring appeared as multiplet in the range 7.328-7.407ppm. The doublet at 7.653-7.684ppm corresponds to one proton ortho to phenoxy ring. The doublet appeared in the range 7.989-8.007ppm corresponds to the two protons of the phenyl ring bearing fluorine. The mass spectrum of (**2**), showed molecular ion peak $(m+1)^+$ at 349 corresponding to the molecular formula $\text{C}_{22}\text{H}_{17}\text{FO}_3$.

The 500 MHz ^1H NMR spectrum of Compound (**4**) showed doublet integrating for two protons which appeared at 6.992-7.008ppm and corresponds to the protons of the phenyl ring bearing chlorine. A

triplet centred at 7.136ppm corresponds to one proton of phenyl ring which is meta to the chlorine atom. The multiplet at 7.267-7.287ppm and 7.332-7.358ppm corresponds to two protons attached to carbons bearing double bond. The four protons of the phenoxy ring resonated as multiplet and appeared at 7.363-7.478ppm. One proton of the phenyl ring bearing chlorine and one proton of phenoxy ring appeared in the range 7.556-7.587ppm. The three protons of the phenyl ring bearing fluorine appeared in the range 7.694-8.037ppm. The mass spectrum of (2), showed molecular ion peak $(m+1)^+$ at 353 corresponding to the molecular formula $C_{21}H_{14}ClFO_2$.

1H NMR spectrum of compound (6a) showed a doublet centred at 3.56ppm and corresponds to two protons of CH_2 group in the pyrazoline ring. The one proton of the pyrazoline ring appeared as triplet centred at 4.86ppm. The N-H proton of the pyrazoline ring appeared as a broad singlet at 5.98ppm. The four protons of phenyl ring bearing methoxy group appeared as doublets at 6.987-6.996ppm and 7.018-7.033ppm. The five protons of phenoxy ring appeared as multiplet in the range 7.334-7.401ppm. The doublet at 7.663-7.695ppm corresponds to one proton ortho to phenoxy ring. The doublet appeared in the range 7.978-8.000ppm and corresponds to the two protons of the phenyl ring bearing fluorine. The mass spectrum of (2), showed molecular ion peak $(m+1)^+$ at 363 corresponding to the molecular formula $C_{22}H_{19}FN_2O_2$.

5. Experimental Study

5.1 Procedure for the Synthesis of Chalcones:

To a solution of substituted acetophenone (0.0025mol) in 20ml ethanol, added 4-fluoro-3-phenoxy benzaldehyde (0.0025mol) in 20ml ethanol. To this solution, 0.5ml 30% aqueous sodium hydroxide was added and stirred well. The mixture was stirred at room temperature for (30 min.) until the formation of pale yellow crystals of chalcone was formed and then the solution was kept under stirring overnight at room temperature. The solid crystals were separated by suction filtration, washed with ethanol and water to neutralize, dried and purified.

5.2 Procedure for the Synthesis of Substituted Pyrazolines

A mixture of chalcone derivative (0.25mmoles), hydrazine hydrate (1.25mmoles) and sodium hydroxide (2.5ml, 0.4%) in ethanol (10ml) was refluxed with stirring for 4hrs and reaction was monitored by TLC. The precipitate was isolated by filtration, washed with ethanol and water to neutralise, dried and purified.

6. Conclusion

Few novel chalcones were synthesised by treating 4-fluoro-3-phenoxy benzaldehyde with different substituted ketones. The chalcones synthesised were further treated with hydrazine hydrate to get corresponding pyrazolines. The newly synthesised chalcones and pyrazolines were characterised by ^1H NMR and mass spectrometry. The biological activities of these synthesised compounds, however, need to be taken forward in future work.

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