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Short communication

Synthesis and antibacterial activity of some new 2,3-dimethoxy-3-hydroxy-2-(1-phenyl-3-aryl-4-pyrazolyl)chromanones

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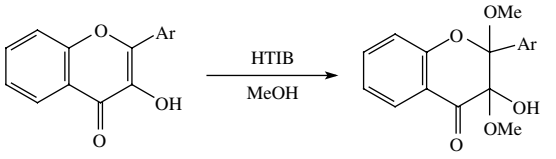
Abstract

Seven new 2,3-dimethoxy-3-hydroxy-2-(1-phenyl-3-aryl-4-pyrazolyl)chromanones (**5**) have been synthesized by the oxidation of 3-hydroxy-2-(1-phenyl-3-aryl-4-pyrazolyl)chromones (**4**) with iodobenzene diacetate in methanol. The structures of compounds **5** were established by the combined use of ^{1}H NMR, IR and mass spectra. All the seven compounds (**5**) were tested *in vitro* for their antibacterial activity against Gram-positive bacteria namely, *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Bacillus pumilus* and two Gram-negative bacteria namely, *Salmonella typhi* and *Pseudomonas aeruginosa*. Three compounds, **5d**, **5f** and **5g**, have displayed antibacterial activity comparable to the commercial antibiotics, Linezolid, Cefaclor and Cefuroxime axetial.

Keywords: Hypervalent iodine; Iodobenzene diacetate; 2,3-Dimethoxy-3-hydroxy-2-(1-phenyl-3-aryl-4-pyrazolyl)chromanones; 3-Hydroxy-2-(1-phenyl-3-aryl-4-pyrazolyl)chromones; Antibacterial activity

1. Introduction

Flavonoids are a group of natural products present in a wide variety of plants. They are found in seeds, citrus fruits, olive oil, tea and red wine and are commonly consumed with the human diet [1,2]. Flavonoids exhibit a broad range of biological activities, including antiviral, antiinflammatory, antioxidant, antiallergic, hepatoprotective, antithrombotic and antitumoral actions [3–5]. Furthermore, these compounds are used in bacteriology, pharmacology and medicine due to their bactericidal activities [6]. On the other hand, substituted pyrazoles also exhibit a broad spectrum of biological activities such as antidiabetic [7], antibacterial [8–10], antimicrobial [11–14] and herbicidal [15,16]. The use of hypervalent iodine reagents such as iodobenzene diacetate (IBD) [17–19], [hydroxy(tosyloxy)-iodo]benzene (HTIB; Koser's reagent) [20,21], etc. find interesting applications in heterocyclic compounds especially flavonoids. Among the various such applications, one noteworthy example is the oxidation of flavonols with [hydroxy(tosyloxy)iodo]benzene (HTIB) offering an efficient and convenient synthesis of 2,3-dimethoxy-3-hydroxyflavanones (Eq. (1)) [22].



(1)

A literature survey revealed that the title compounds 2,3-dimethoxy-3-hydroxy-2-(1-phenyl-3-aryl-4-pyrazolyl)chromanones (**5**) remain unknown. These observations, coupled with the diverse biological properties associated with pyrazole and flavanone derivatives, prompted us to study the scope of the synthetic route outlined in Eq. (1) on the oxidation of 2-pyrazolyl analogues of flavonol (**4**). There has been a particular interest in the synthesis of flavonoids with a pyrazole ring at position C-2 to find new and more potent biological activities

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[23]. We report herein synthesis of **5a–5g** by the oxidation of **4a–4g** using iodobenzene diacetate (IBD) in methanol with an expectation to find new and more potent antibacterial agents.

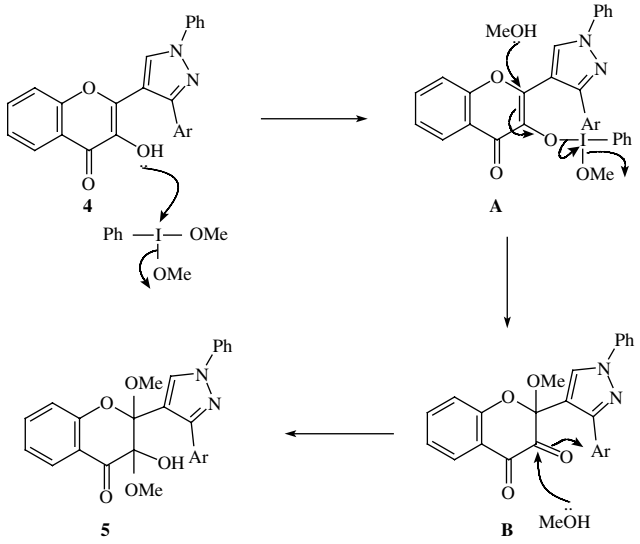
2. Results and discussion

2.1. Chemistry

The starting material 2-pyrazolyl analogues of flavonol **4** needed for the synthesis of **5** were prepared by the cyclization of pyrazolyl analogues of *o*-hydroxychalcone **3** with hydrogen peroxide (H_2O_2) in KOH–MeOH from our previous work involving Algar Flynn Oymanda (AFO) reaction [23]. The reaction of **4a** was carried out by treatment with 1.1 equiv of IBD in methanol by stirring at room temperature for 15–20 min. Usual work-up of the reaction afforded the pure crystalline product **5a** in 78% yield. Encouraged by the feasibility of our strategy for **5a**, we studied oxidation of a wide range of substituted **4b–4g** under similar conditions. This IBD mediated oxidative approach worked nicely to give the desired products **5b–5g** in all cases (Scheme 1).

The structures of all new compounds **5a–5g** were confirmed by their spectral (IR, ^{1}H NMR and mass) and elemental analytical data. The IR spectra of compounds **5a–5g** exhibited characteristic absorption band at 1690–1700 cm^{-1} and 3410–3420 cm^{-1} due to carbonyl and hydroxyl functional groups, respectively. The ^{1}H NMR spectra of all the products **5a–5g** showed two characteristic singlets due to C(2) and C(3) methoxy group protons at δ 3.00 and δ 3.15 present. The C(3)–OH proton appeared as broad singlet at δ 4.6–4.8 ppm and C(5)–H in pyrazole ring appeared as singlet at δ 8.30. Other protons appeared in the aromatic regions.

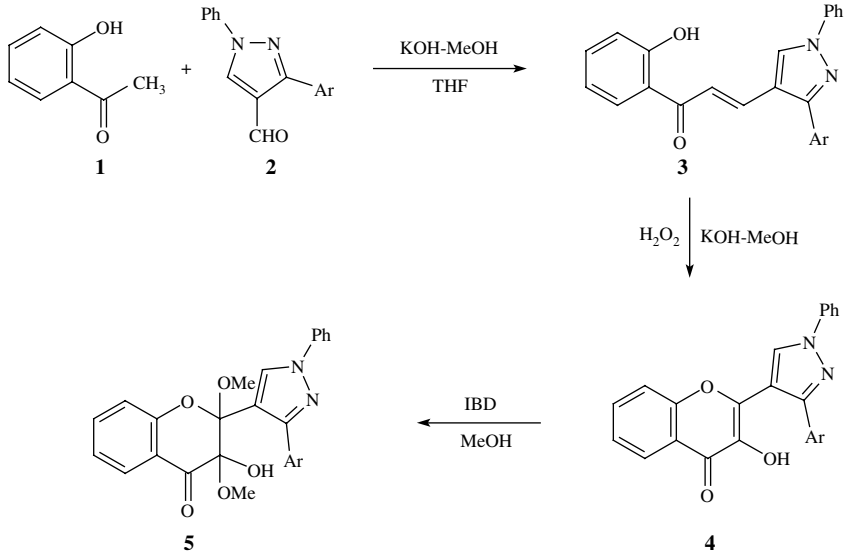
The conversion of **4** → **5** probably proceeds accordingly to Scheme 2 which is analogous to earlier reports [24].



Scheme 2.

2.2. Antibacterial activity

All the seven compounds (**5a–5g**) were tested *in vitro* for their antibacterial activity against three Gram-positive bacteria namely, *Staphylococcus aureus* (MTCC 3160), *Staphylococcus epidermidis* (MTCC 2639), and *Bacillus pumilus* (MTCC 1456), and two Gram-negative bacteria namely, *Salmonella typhi* (MTCC 733) and *Pseudomonas aeruginosa* (MTCC 3541) (Tables 1 and 2). Three of these compounds (**5d**, **5f** and **5g**) exhibited good antibacterial activity against both Gram-positive and Gram-negative bacteria. All of the seven compounds showed activity against Gram-positive bacteria namely *S. aureus* (MTCC 3160). Compound **5g** showed maximum antibacterial activity against *S. aureus* (MIC 2 μg/ml) and *S. epidermidis* (MIC 8 μg/ml). It also displayed inhibitory activity against *B.*



Ar = **a**, C_6H_5; **b**, 4-$CH_3C_6H_4$; **c**, 4-$OCH_3C_6H_4$, **d**, 4-ClC_6H_4; **e**, 4-BrC_6H_4; **f**, 4-FC_6H_4; **g**, 4-$NO_2C_6H_4$

Scheme 1.