SYNTHESIS OF 3-[4-{1-BENZOFURAN-2-YL}-1,3-THIAZOL-2-YL]-2-(4-ARYL)-1,3-THIAZOLIDIN-4-ONE DERIVATIVES AS BIOLOGICAL AGENTS

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A protocol for the synthesis of 3-[4-(1-benzofuran-2-yl)-1,3-thiazol-2-yl]-2-(4-aryl)-1,3-thiazolidin-4-one derivatives (5a-e) has been developed from 1-(1-benzofuran-2-yl)-2-bromoethanone (2), which served as a key intermediate for the synthesis of the title compounds. The reaction of compound 2 with thiourea furnished 4-(1-benzofuran-2-yl)-1,3-thiazol-2-amine 3, which upon further reaction with various aromatic aldehydes, gave Schiff bases 4a-e. These Schiff bases, when treated with thioacetic acid in the presence of catalytic amount of anhydrous ZnCl₂, yielded thiazolidinone derivatives 5a-e. All the newly synthesized compounds have been characterized by analytical and spectral data and screened for their antimicrobial and analgesic activity.

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Keywords Analgesic and antimicrobial activity; anhydrous ZnCl₂; 1-(1-benzofuran-2-yl)-2-bromoethanone; Schiff base; thiazolidinone ring; thioacetic acid.

INTRODUCTION

The structural and therapeutic diversity coupled with commercial viability of small heterocyclic molecules has fascinated organic and medicinal chemists. Benzo[b]furan derivatives are an important class of organic compounds, which are known to be present in many natural products and possess physiological activity. They have found applications in agrochemicals, pharmaceuticals, and cosmetics. Benzo[b]furans are building blocks of optical brighteners. Many natural benzo[b]furans have physiological, pharmacological, and toxic properties, and as a result, there is continuing interest in their chemical synthesis. Cyclization reactions of various types have been used to produce substituted benzo[b]furans. In recent years, 4-thiazolidinones and oxazolidinones are the most...
Synthesis of Some Mannich Bases and Novel Benzo furan Derivatives Containing Imidazo[2,1-b][1,3,4]thiadiazoles as Biological Agents

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taining Imidazo[2,1-b][1,3,4]thiadiazole as Biological Agents

Abstract: An efficient route for the synthesis of 6-(1-benzo furan-2-yl)-2-phenyl imidazo[2,1-b][1,3,4]thiadiazol(4a-e), was achieved by the reaction of 1-(1-benzo furan-2-yl)-2-bromoethanone (2) with 5-aryl-1,3,4-thiadiazol-2-amine(3a-e). The reaction mixture containing compound 4d with secondary amines and formaldehyde with catalytic amount of acetic acid, furnished Mannich bases (5-7). All newly synthesized compounds were screened for analgesic and antimicrobial activity. Among all the compounds tested for antibacterial activity, compound 7 showed significant activity against S. aureus when compared to other compounds. Compound 4a, 4d and 5 exhibited highest activity against B. subtilis. Compound 4b, 4d and 7 exhibited equipotent activity against K. pneumoniae and compound 6 exhibited promising activity against E. coli comparable with the standard drug Tetracycline. Among all the compounds tested for antifungal activity, the compound 4b and 4e exhibited significant activity against A. niger. Compound 4c and 4e showed highest activity against C. albicans, compound 7 exhibited promising activity against P. chrysoszenous and compound 4a and 4b exhibited highest activity against T. virid as compared with standard drug Fluconazole. Compound 4b and 4d proved to be potent analgesic agents, as they exhibited significant analgesic activity comparable to standard drug and the remaining compounds showed moderate activity as compared to standard drug.

Keywords: 2-Acetyl benzofuran, Mannich bases, imidazo[2,1-b][1,3,4]thiadiazole, analgesic and antimicrobial activity.

1. INTRODUCTION

A wide variety of pharmacological properties have been shown to be associated with benzofuran derivatives [1-4]. Benzo[b]furan derivatives are an important class of organic compounds, which were known to be present in many natural products [5]. They find their applications in agrochemicals [6,7], pharmaceuticals [8-13] and cosmetics [14]. Benzo[b]furans are building blocks of optical brighteners [15]. Many of the natural Benzo[b]furans have physiological, pharmacological and toxic properties and as a result, there is continuing interest in their chemical synthesis. Cyclization reactions of various types have been used, to produce substituted benzo[b]furans [16-19]. 1,3,4-thiadiazole derivatives are well known for their wide spectrum of biological, pharmacological and antileukemic activity [20-22].

Nitrogen and sulphur containing heterocyclic compounds are of biological interest and the development of new synthetic approaches for their synthesis is a challenge for organic chemists. The presence of imidazo[2,1-b][1,3,4]thiadiazole ring reflects interesting biological properties [23-25]. Thus, encouraged by their potential clinical application and as part of our research to synthesize new bioactive compounds, in the present investigation, we made an efficient attempt in synthesizing a new series of benzofuran derivatives containing a imidazo[2,1-b][1,3,4]thiadiazole moiety at the 2-position.

2. RESULT AND DISCUSSION

We report herein the synthesis of new series of benzofuran containing imidazo[2,1-b][1,3,4]thiadiazole and mannich bases and the bioactivity of the newly synthesized compounds (Scheme 1). The key intermediate, 1-(1-benzo furan-2-yl)-2-bromoethanone (2) was synthesized by the bromination of 2-acetyl benzofuran (1) in acetic acid media with good yield about 88% [26].

The treatment of compound 2 with 5-aryl-1,3,4-thiadiazol-2-amines (3a-e) [27] in dry ethanol furnished 6-(1-benzo furan-2-yl)-2-arylimidazo[2,1-b][1,3,4]thiadiazole derivatives (4a-e). The structure of compounds 4a-e was confirmed by IR, 1HNMR and Mass spectral data. The IR spectrum of compounds 4a-e showed the absorption band between 1576-1532 and 1478-1450 cm\(^{-1}\) due to C=N and C=C respectively. 1HNMR spectrum of (4a-e) displayed a multiplet between δ 8.40-7.19 due to nine aromatic protons and a singlet at δ 8.03 due to one proton of imidazole ring. The reaction of the compound 4d with secondary cyclic amines like pyrrolidine, piperidine and morpholine in presence of formaldehyde with catalytic amount of acetic acid furnished Mannich bases (5-7) the structure of which is confirmed by elemental analysis and spectral data.

All newly synthesized compounds were screened for antimicrobial and analgesic activities and the results are tabulated in Tables 1-3 respectively.
A FACILE SYNTHESIS OF BROMO-SUBSTITUTED BENZOFURAN CONTAINING THIAZOLIDINONE NUCLEUS BRIDGED WITH QUINOLINE DERIVATIVES: POTENT ANALGESIC AND ANTIMICROBIAL AGENTS

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Treatment of 5-bromo-2-acetyl benzofuran with hydrazine followed by condensation of the resulting hydrazone with different quinoline derivatives gave the corresponding Schiff bases. Reaction of these Schiff bases with thioacetic acid furnished the target thiazolidinone molecule. Some of the newly synthesized compounds show promising analgesic and antimicrobial activity.

Supplemental materials are available for this article. Go to the publisher’s online edition of Phosphorus, Sulfur, and Silicon and the Related Elements to view the free supplemental file.

Keywords: Antimicrobial agent; 5-bromo-salicylaldehyde; cyclic voltammetry; quinoline derivatives; Schiff base; thioacetic acid

INTRODUCTION

Benzofurans are of great synthetic interest because of their wide distribution in nature and useful biological activities. The benzo[b]furan ring is often incorporated in pharmaceutical agents as a core structural motif, and as a result it continues to attract extensive synthetic efforts. Many reported synthetic approaches are based on the construction of furan rings from various arene derivatives. Benzofuran and its derivatives exhibit various biological activities. Such derivatives were investigated as antibacterial or anti-fungal agents. Moreover, many researchers have synthesized fused or coupled nitrogen-containing heterocycles, which have shown very good biological activities. Quinoline is the important nitrogen-containing heterocyclic compound having biological activity. The presence of a halogen atom also shows good antimicrobial properties. Quinoline and its derivatives are known for their antimarial and therapeutic effects. A number of quinoline
Synthesis and biological evaluation of some innovative coumarin derivatives containing thiazolidin-4-one ring

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The reaction of ethyl 2-oxo-2H-chromene-3-carboxylate with hydrazine followed by condensation of the resulting hydrazone with different aromatic aldehydes give the corresponding Schiff bases 5a-e. Reaction of these Schiff bases with mercaptoacetic acid furnishes the target thiazolidinone molecules 6a-e. The newly synthesized compounds have been screened for antibacterial and analgesic activities.

Keywords: Salicylaldehyde, biological agent, Schiff base, mercaptoacetic acid, thiazolidinone

The synthesis of coumarins and their derivatives has attracted considerable attention from organic and medicinal chemists for many years as large number of natural products contain this heterocyclic nucleus. They are widely used as additives in food, perfumes, cosmetics, pharmaceuticals, optical brighteners, dispersed fluorescent and laser dyes. A considerable number of natural and synthetic coumarin derivatives display pharmacological properties with a wide range of activity and others are useful for optical applications. Thus the synthesis of this heterocyclic nucleus is of much interest. 4-Thiazolidinones have been reported to show a broad spectrum of biological activities and a wide range of pharmacological activities such as hypnotic-sedative, analgesic activity, anticonvulsant, antifungal, antibacterial and antitumurcal activity against M. tuberculosis H37Rv. β-Lactamase is generally considered to be responsible for microbial resistance against a broad spectrum of β-lactam antibiotics. In view of the pharmacological properties of 4-thiazolidinones, we were interested in synthesizing several new compounds bearing coumarin nucleus, attached to 4-thiazolidinone moieties.

Results and Discussion

As part of our aim to search for biologically active heterocycles containing sulfur and nitrogen, we report in this paper synthesis of a series of 2-oxo-N-(4-oxo-2-substituted phenyl-1,3-thiazolidin-3-yl)-2H-chromene-3-carboxamide 6a-e and on estimation of their biological properties. For this purpose, ethyl 2-oxo-2H-chromene-3-carboxylate 3 was a key intermediate which was originally prepared by the reaction of salicylaldehyde with diethyl malonate in the presence of catalytic amount of piperidine. Applying hydrazinolysis on ethyl 2-oxo-2H-chromene-3-carboxylate 3, with hydrazine hydrate in methanol at room temperature, 2-oxo-2H-chromene-3-carboxyhydrazide 4 was obtained in good yield. The carboxyhydrazide 4 was then condensed with different aromatic aldehydes in methanol to furnish the corresponding Schiff's bases, 5a-e. The structures of the products 5a-e were confirmed from their analytical and spectral data.

The reaction of Schiff bases 5a-e with mercaptoacetic acid in the presence of catalytic amount of anhydrous zinc chloride in DMF for about 8 hr furnished the compounds 6a-e (Scheme 1) whose structures were assigned on the basis of spectral data and elemental analysis.

Biological studies

Antibacterial activity

The newly synthesized compounds were screened for their antibacterial activity by the cup plate method. The in vitro antibacterial activity was carried out against 24 hr old culture for four bacteria and four fungal organisms. The bacteria used were Staphylococcus aureus, Bacillus subtilis, Klebsiella pneumoniae and Escherichia coli. The compounds were tested at a concentration of 0.001 mol/mL in DMF against all the organisms. Ciprofloxacin (0.001 mol/mL) was used as standard for the comparison of antibacterial activity. The zone of inhibition was compared with the standard drug after 24 hr of incubation at 37°C.

Among the compounds tested for antibacterial activity (Table 1), compound 6a showed high activity against S. aureus, B. subtilis and moderate activity against K. pneumoniae and E. coli. Compounds 6b and 6c have exhibited moderate activity against S. aureus, B. subtilis and weak activity against K. pneumoniae and E. coli.
A novel method for the synthesis of 6-bromo-2-(3,4-dichlorophenyl)imidazo[1,2-a]pyridine using microwave irradiation

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Abstract: A simple and novel route to the synthesis of imidazopyridines was developed. The present work involves the synthesis of 6-bromo-2-(3,4-dichlorophenyl)imidazo[1,2-a]pyridine (3) by using microwave irradiation. The synthesized compound (3) was well characterized by NMR, IR, LCMS and elemental analysis.

Keywords: 5-bromo-2-aminopyridine, DMF, Microwave, MTBE.

Imidazopyridines were previously synthesized e.g. by the reaction between 5-bromo-2-aminopyridine (1) and 2-bromo-1-(3,4-dichlorophenyl)ethanone (2) using different methods [1-4]. In the usual methods, bases like sodium bicarbonate or potassium carbonate were employed in polar solvents such as methanol or ethanol under reflux for 4-6 hours. The present work deals with the synthesis of 6-bromo-2-(3,4-dichlorophenyl)imidazo[1,2-a]pyridine (3) using microwave irradiation. It is a simple method to prepare imidazo-pyridines.
SYNTHESIS AND BIOLOGICAL EVALUATION OF 3-ARYL-1-(2-BENZOFURYL)-2-PROPEN-1-OANE ANALOGUES

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Claisen-Schmidt condensation of 2-acetyl benzofuran 1 with aromatic aldehydes in presence of strong alkali gave 3-aryl-1-(2-benzofuryl)-2-propen-1-ones 2a-c. Reaction of 2a-c with guanidine nitrate in ethanol in presence of sodium hydroxide yielded 2-amino-6-aryl-4-(benzofuran-2-yl) pyrimidines 3a-c. The reactions of 3a-c with different reagents furnished compounds 4,5,6 and 7. Newly synthesized compounds were evaluated for their antimicrobial and antiinflammatory activities.

In view of the significant biological activities of aminopyrimidines and in continuation of our work on the synthesis of biologically active heterocycles containing benzofuran nucleus coupled with nitrogen rings we report herein the synthesis of some new biheterocycles bearing benzofuran nucleus. Synthetic route to the title compounds is shown in Scheme-1. The readily accessible 2-acetyl benzofuran 1 served as the key intermediate for the synthesis of desired 3-aryl-1-(2-benzofuryl)-2-propen-1-ones 2a-c. 2-Acetyl benzofuran 1 was subjected to Claisen-Schmidt condensation with benzaldehyde in the presence of strong aq sodium hydroxide to give 3-phenyl-1-(2-benzofuryl)-2-propen-1-one 2a in good yield. The identity of 2a was established by its IR and 1H NMR spectral data. The IR spectrum of 2a showed an abs band at 1680 cm⁻¹ due to aᵦ-unsaturated carbonyl group. The 1H NMR spectrum of 2a exhibited a multiplet merged with doublet of doublet at δ 7.22-8.1 attributable to aromatic and -CO-CH=CH- protons. Compounds 2b-c (Table-1) were prepared similarly from 2-acetyl benzofuran by condensation with various aromatic aldehydes.

The reaction of 3-phenyl-1-(2-benzofuryl)-2-propen-1-one 2a with guanidine nitrate in ethanol in presence of aq sodium hydroxide resulted in the formation of a pale yellow crystalline compound which was identified as 2-amino-6-phenyl-4-(benzofuran-2-yl) pyrimidine 3a. The formation of 3a was confirmed by the presence of IR abs band in the region 3330-3440 due to symmetric and asymmetric stretching frequencies of primary amine and another band at 1596 due to C=N. The absence of abs band at 1680 due to C=O confirmed the involvement of -CO-CH=CH- functionality of 2a in pyrimidine ring formation. The 1H NMR spectrum of 3a exhibited a broad singlet at 5.8 ppm due to two protons of amino group, a sharp singlet at 8.1 ppm due to methine proton of pyrimidine ring and a multiplet in the region 7.0-8.0 was due to nine aromatic protons. Mass spectrum of 3a exhibited the molecular ion peak M⁺ at m/z 287 equivalent to the molecular weight of 3a. The same procedure was followed for compounds 3b-c.

Acetylation of 3a using acetic anhydride gave 2-acetylamino compound 4a. The IR spectrum of 4a showed an abs band at 3250 due to NH and two distinct bands at 1674 and 1600 due to acetyl carbonyl and C=N functionality respectively. Compounds 4b-c (Table-1) were similarly prepared from 3b-c.

The reaction of 3a with benzaldehyde in dioxan gave 2-benzylideneamino-6-phenyl-4-(benzofuran-2-yl) pyrimidine 5a which was characterized by its IR and 1H NMR spectral data. The IR spectrum of 5a showed the disappearance of NH₃ band at 3330-3440 and appearance of a peak at 1620 due to C=N. The 1H NMR spectrum of 5a displayed a multiplet in the region 6.8-8.1 due to nine aromatic protons and one methine proton which merged with aromatic protons. Compounds 5b-f (Table-1) were prepared similarly from 3b-c by condensation with various aromatic aldehydes.

The condensation of 3a-b with chloroacetyl chloride in dry benzene gave 2-chloroacetamido-6-aryl-4-(benzofuran-2-yl) pyrimidines 6a-b. The IR spectrum of 6b exhibited abs band in the region 3150-3300 due to
A facile synthesis of bromo-substituted benzofuran containing quinoline derivatives: potent antimicrobial agent

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Abstract

The present paper deals with the treatment of Bromo substituted 2-acetyl benzofuran with hydrazine hydrate followed by condensation of the resulting hydrazide with different quinoline derivatives. The newly synthesized heterocycles were characterized by spectral data like IR, $^1$HNMR and Mass spectral data. The established derivatives were screened for antimicrobial activity.
Synthesis and Electrochemical Studies of Bromo-Substituted Benzofuran Containing Schiff base Nucleus Bridged with Quinoline Derivatives

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Abstract

The treatment of 5-bromo-2-acetyl benzofuran with hydrazine followed by condensation of the resulting hydrazone with different substituted 2-chloro-3-formyl-quinoline derivatives gave the corresponding Schiff bases (5a-e). Further, the electrochemical behavior of Schiff bases were studied by cyclic voltammetry.

Keywords: 5-Bromo-salicyaldehyde, cyclic voltameter, Quinoline derivatives and thioacetic acid

1. Introduction

Since the generalization of high throughput screening in drug discovery, there has been significant interest in the design of chemical libraries with the goal of identifying new lead compounds for further development. The benzo[α]furans are of great synthetic interest because of their wide distribution in nature and useful biological activities. The benzo[α]furan ring is often incorporated in pharmaceutical agents as a core structural motif, and as a result continues to attract extensive synthetic efforts.

2. Results and Discussion

In continuation of study in developing condensed quinoline derivatives due to their significant biological activities, the compound 2 was reacted with hydrazine hydrate under acidic condition in ethanol at reflux temperature to obtain 1-(5-bromo-1-benzofuran-2-yl)ethanone hydrazone 3 in good yield. The structure of 3 was confirmed by IR and H-NMR.
Synthesis Of Some Mannich Bases And Novel Benzofuran Derivatives Of Imidazo[2,1-\(B\)][1,3,4]Thiadiazoles And Thiazolidin Derivatives

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A protocol for the synthesis of 6-(1-benzofuran-2-yl)-2-phenyl-5,7a-dihydroimidazo[2,1-\(b\)][1,3,4] thiadiazole and 3-[4-(1-benzofuran-2-yl)-1,3-thiazol-2-yl]-2-phenyl-1,3-thiazolidin-4-one derivatives has been developed and all the compounds were characterized by analytical and spectral data. The title compounds were obtained by the reaction of 1-(1-benzofuran-2-yl)-2-bromoethanone and with various 5-phenyl-1,3,4-thiadiazol-2-amine, and with thiourea and urea to afford 6-(1-benzofuran-2-yl)-2-(4-chlorophenyl)imidazo[2,1-\(b\)][1,3,4]thiadiazole 4-(1-benzofuran-2-yl)-1,3-thiazol-2-amine derivatives respectively. Further, the reaction with various aromatic aldehydes gave different Schiff bases. These Schiff bases are further treated with thioacetic acid which furnished the thiazolidinone derivatives.
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ONE POT SYNTHESIS OF SOME BENZOFURAN DERIVATIVES CONTAINING PYRIDINE NUCLEUS
BY CHICHIBABINE REACTION AS BIOLOGICALLY ACTIVE COMPOSITE

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In the present investigation, the synthesis of some benzo[1]furane derivative was carried out by one pot multi component reaction (MCR) reaction of some 4-substituted aromatic aldehyde (2a-f) with 1-(benzofuran-2-y1)ethanone (1) in presence of NH$_4$OAc and acetic acid as solvent. The reaction follows three steps, first formation of imine followed by aldol condensation and then, Michael addition reaction. All new synthesized compounds were characterized and screened for biological activity.
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Certificate

This certificate is awarded to Dr./Mr./Ms. Venkatesh K.B. for his/her participation as a delegate/resource person/volunteer in the National School on New Dimension to NMR: From Molecules to Human Behavior, organized by NMR Research Centre, Indian Institute of Science, Bangalore.

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