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Research Article

SYNTHESIS AND EVALUATION OF 4-(1- BENZOFURAN-2-YL)-1,3-OXAZOLE-2-AMINE AND ITS DERIVATIVES

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ABSTRACT

Salicylaldehyde upon treatment with chloroacetone in presence of anhydrous potassium carbonate give 2-acetylbenzofuran.This 2-acetylbenzzofuran after chlorination gives chloroacetylbenzofuran. This chloroacetylbenzofuran on treatment with urea in ethanol gives 4 (1-benzofuran-2-yl) 1, 3-oxazole-2-amine.The corresponding compound on treatment with various aldehydes to give different derivative. The characterization of synthesized compounds was identified on the basis of IR, NMR, MASS and elementary analysis. The compound has been evaluated for anti-bacterial activity. The present study is focused on the development of new potent bioactive molecule with less toxic, safer and easy available. Modern therapeutic is based on scientific observation supported by systematic assessment of activity of drug is simulated and clinical condition.

Keywords: chloroacetone, 2-acetylbenzofuran, chlorination, Salicylaldehyde.

INTRODUCTION

Benzofuran nucleus may be combined with nitrogen heterocycle in different ways. Several benzofuran compounds are reported to posses, antibacterial, antifungal, Anti-inflammatory, antidepressant, analgesic and hypoglycemic activities. It has already been pointed out that benzofuran nucleus is very rarely associated with a nitrogen heterocycle. Several isoxazole derivatives are found to possess antitubercular, antimicrobial and anti-inflammatory activities.

The benzofuran nucleus and derivatives occupy apposition of considerable significance for widespread occurrence in plants and their potential as important pharmaceuticals. This fact created interest in synthetic products containing benzofuran nucleus. Kreamer and Spilker discovered benzofuran in coal tar. It was synthesized by Perkin in 1870. Thus the chemistry of benzofuran has developed in a spectacular fashion during the last several years.

MATERIAL AND METHODS

The entire chemical used was purchase from Qualingens, Himedia and Loba-chemicals. Purity of starting materials used for reaction was confirmed by checking their melting point or boiling point and by thin layer chromatography. Purity of compounds was checked on precoated plates, eluent was the mixture of different polar and non-polar solvents in varying proportions and detection was done either by observing in UV (ultra-violet) light or exposure to iodine

vapours as required.The products of all the reactions were purified initially by different workup process to remove unreacted starting materials if any and then by recrystallization using suitable solvent. The absence of any impurity of starting materials or possible by product was ensured by performing qualitative organic analytical tests for various functional groups.

Synthesis of 2-Acetyl Benzofuran (I) [1-3]

In completely dried round bottom flask 12.2 ml of Salicylaldehyde was taken then it is charged with chloroacetone (8.3 ml) with addition of 150 ml anhydrous acetone to this reaction mixture 35 gm of anhydrous acetone was added. Round bottom flask was attach to condenser and reflux for 10 hr. in water bath by maintaing temperature for reflux and stirred it continuously. After 10 hr reaction mixture cooled to room temperature and filtered by funnel to get clear solution then 10-15 ml acetone was used to wash potassium carbonate filtrate was taken in dry flask and acetone was removed by vaccum pump crystallization was achieved by petroleum ether on hot plate.

Melting point of 2-acetylbenzofuran = 79^0C

Synthesis of bromoacetylbenzofuran (II) [4-6]

A solution of bromine (12 gm 0.075 mole)in acetic acid (100ml) was added drop wise with stirring to a solution of 2-acetylbenzofuran (12gm, 0.075 mole) in acetic acid (100ml). After complete addition of bromine, the mixture was stirred for 45 min and allowed to stand for 30 min. then the mixture was decanted in crushed ice, the solid separated was collected and crystallized from ethanol as light green crystals MP =94^0 C.

Synthesis of 4-(1-Benzofuran-2-Yl)-1,3-oxazole-2-Amine (III) [7-10]

A Solution of 2-brmoacetylbenzofuran (11.95gm, 0.05 mole) and urea(3.5gm, 0.05mole) was refluxed in ethanol (250 ml) for 2hrs. the reaction mixture was then cooled, poured in to cold water and neutralized with 5% aqueous sodium acetate. The solid thus obtained was collected and recrystalized from ethanol as colorless tiny crystals.

General Procedure for Preparation of 4-(1-Benzofuran-2-yl)-1,3-oxazole-2-Amine Derivatives (IIIa-b)

In two necked round bottom flask take 20mlabsolute ethanol. to this add 1gm of . 4-(1-benzofuran-2-yl)-1, 3-oxazole-2-amine to this solution add equimolar amount of different aromatic aldehydes reflux for 7-8 hr. The resultant reaction mixture was cooled, poured into the ice-cold water. The solid separated was filtered and dried. The solid was recrystalized into ethanol.

Anti-bacterial activity[14]

Preparation of Test Solution

10 mg of the compound was dissolved in 10 ml of DMSO. From this 2 ml of solution was taken and diluted up to 10 ml with DMSO. Now the concentration of the test solution was 200 µg/ml.

Preparation of Standard Solution

Amoxicillin was used as standard antibiotic for comparison and solutions were prepared by using sterile water, as they were water soluble. The solutions are diluted by using sterile water so that the concentration of the solutions was 200 µg/ml.

Preparation of Discs

Discs of 6-7 mm in diameter were punched from NO: 1 Whattmann filter paper with sterile cork borer of same size. These discs were sterilized by keeping in oven at 1400c for 60 minutes. Then standard and test solutions were added to each disc and discs were air-dried.

Method of Testing

The sterilized media was cooled to 45^0 C with gentle shaking to bring about uniform cooling and then inoculated with 18-24 hrs old culture under aseptic conditions, mixed well by gentle shaking. This was poured in to sterile Petri dishes (properly labeled) and allowed the medium to set. After solidification all the Petri dishes were transferred to laminar flow unit. Then the discs which were previously prepared were carefully kept on the solidified media by using sterilized forceps. These Petri dishes were kept as it is for one-hour diffusion at room temperature and then for incubation at 37^0C for 24 hours in an incubator. The extent diameter of inhibition after 24 hours was measured as the zone of inhibition in millimeters.

RESULT AND DISCUSSION

All the reactions were monitored by TLC, structures and purity of the anticipated compounds were characterize by physical constant and FTIR spectral studies initially

followed by 1H-NMR and Mass spectroscopy Absence of TLC spots for starting materials and appearance of new TLC spot at different Rf value were ensured to declare completion of reaction. The TLC plates were visualized either by Iodine vapours or by viewing in UV-Visible chamber. Most of the steps were optimized in order to achieve quantitative yields i.e. more than 70% yields.

The FT-IR in KBr (cm-1) spectra of compound 3, indicated decrease in band strength of C=O (1664) due to intermolecular hydrogen bonding and specific band of C=C at 1588, C-O-C at 1080 thus confirming the formation of 2-Acetyl benzofuran. The FT-IR in KBr (cm^{-1}) spectra of compound 4 showing bands at 1583.23 (Ar-CH), 1088 (C-O-C), 828.42 (C-Br), 1345. The FT-IR in KBr (cm^{-1}) spectra of compound 5 showing a characteristic band at 3315.90 (–NH2) which confirms the attachment of urea and formation of 2-amino-4-(benzofuran-2-yl) oxazole Final derivatives showed the expected bands for the characteristic groups which are present in the compounds such as- C-N and –C-O-C bands. Formation of new peaks at around 3000, 600-800 confirms the formation of derivatives.

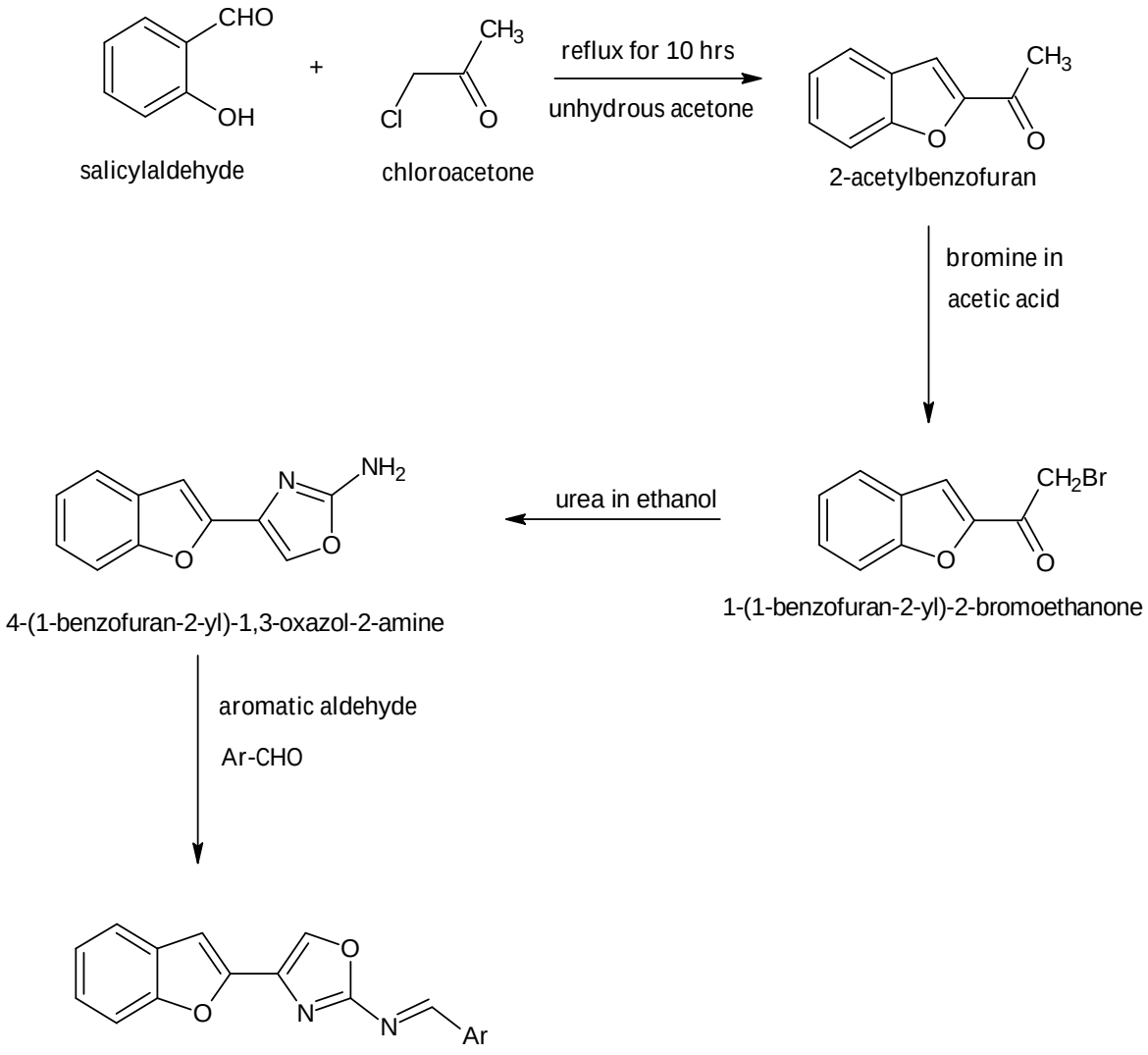


Fig. 1: Scheme for synthesis of 4-(1-Benzofuran-2-yl)-1,3-oxazole-2-Amine

Table 1: 4-(1-Benzofuran-2-yl)-1, 3-oxazole-2-Amine Derivatives

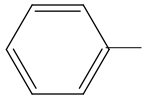
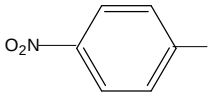
Compound	Aryl group	Molecular formula	Molecular weight	% yield	Melting point uncorrected
III a		$C_{18}H_{12}N_20_2$	288	60%	238°C
III b		$C_{18}H_{11}N_30_4$	333	65%	250°C

Table 2: Antibacterial Study of 4-(1-Benzofuran-2-yl)-1, 3-oxazole-2-Amine Derivatives

S. no.	compounds	Zone of Inhibition in mm	
		E-coli	*S. aureus*
1	III a	20	17
2	III b	18	15
3	Amoxicillin	30	27
4	DMSO*	00	00

*DMSO:-Dimethyl sulfoxide

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