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Review Article

A CRITICAL REVIEW ON SYNTHETIC PATHWAY OF BENZOFURANS

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ABSTRACT

"Benzofuran" a heterocyclic moiety which act as a lead molecule for several biologically active compounds. Besides, benzofuran derivatives show several activities like anti-tubercular, anti-tumor, anti plasmodial, cytotoxic and herbicidal. So, they found a variety of applications in manufacturing drugs as pharmacological agents and used in other fields of agriculture and organic chemistry. They are present as natural products which were isolated from Machilus glaucescens, Krameria ramosissima and Zanthoxylum ailanthoidol. One of such natural benzofuran derivative namely Napthofurans which have profound biological activities and represent a major class of heterocyclic compounds. The present literature reviews that the synthesis of different benzofuran derivatives and their biological activities in present day life.

KEY WORDS: *Benzofuran, Biological activities, Heterocyclic compound.*

INTRODUCTION

Due to their natural existence and enormous biological activities benzofurans occupy a cardinal position in heterocyclic compounds [1]. Benzofuran is of fused benzene with furan ring which is a colourless liquid and that is a component of coal tar [2]. United States Food and Drug Administration (USFDA) approved more than 30 drugs containing benzofuran nucleus [1].

Benzofuran hybrids consists of a wide variety of biological activities like Herbicidal [3], anti-cancer, dual inhibitors of Alzheimer's disease, protein kinase inhibitors[1], immunosuppressive, antioxidant, antifungal, anti-inflammatory, antimicrobial, analgesia, antihypertensive[4], antitubercular [5], anti-hyperglycaemia [2], antiplasmodial, HIV and hepatitis C virus inhibitory activities [6]. Benzofuran moieties have certain application like fluorescent sensor, brightening agents etc [2]. Some of the natural benzofurans which are biologically active are Cicerfuran, Conocarpan and Ailanthoidol. Of all these Cicerfuran has anti-fungal activity, Conocarpan has anti-fungal and antitypanosomal agent and Ailanthoidol shows anti-cancer, antiviral, immunosuppressive, anti-oxidant etc. Synthetic benzofurans moieties include Amiodarone, Bufuralol etc [4].

In view of these many biological activities numerous methods have been step forwarded to synthesize benzofuran and its derivatives. These methods include Rhenium catalysed intra molecular carboxylation and carboamination of alkynes [7], Lewis or Bronsted acid catalysed, or base promoted cyclisation's. But in all methods costly substrates or metals or harsh conditions are required, in order to avoid these a facile way to synthesize benzofurans are done by taking phenols and ᾱ-halo ketones as starting materials[1] or base controlled cyclization of N- phenoxyamides with 1-[(triisopropylsilyl) ethynyl)]-1,2- benziodoxol- 3(1H)-one [8].

LITERATURE REVIEW

Prashantha Karunakar *et al.,*[9] reported on In Silico Antitubercular Activity Analysis of Benzofuran and Naphthofuran Derivatives. However due to its anti-microtubule activity novel Benzo[b]furans enhancethe expression of apoptotic genes and arrest of leukemia cells occur in G2/M phase. Molecular docking revealsthat benzo[b]furans 1 and 2 with the help of colchicine binding pocket binds to tubulinand the presence of hydrophobic interactions stabilizes the complex. 1,1'-[3-(bromomethyl)-5,6-dimethoxy-1-benzofuran-2,7-diyl] diethanone (1) and methyl 4-bromo-6-(dibromoacetyl)-5-hydroxy-2-methyl-1-benzofuran-3-carboxylate (2).

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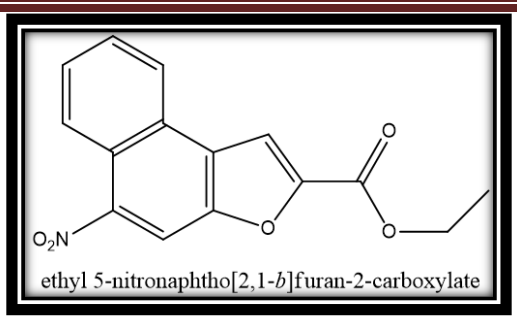
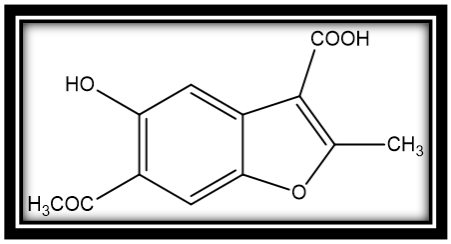


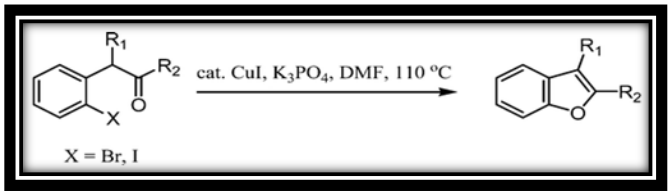
Napiórkowska, Mariola, et al., [10] "Synthesis of New derivaties of Benzofuran as Potential Anticancer Agents.



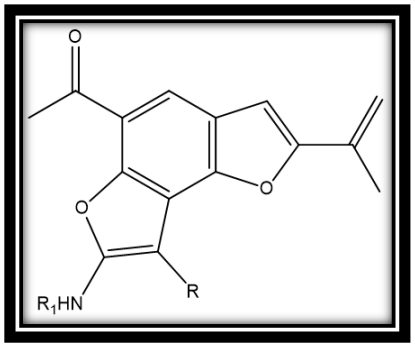
6-acetyl-5-hydroxy-2-methylbenzofuran-3-carboxylic acid

Primarily, 2'-hydroxy-5'-nitro acetophenone (1) was reacted with substituted phenacylbromide (2) in presence of K2CO3 in DMF to obtain aryl-3- methyl-5-nitro-1-benzofuran-2-ylmethanone (3) and was reduced to aryl-5-amino-3-methyl- 1-benzofuran-2-ylmethanone (4). Compound 4 was reacted with 5-chloronicotinoyl chloride to give N-(2-aroyl)-3-methyl-1-benzofuran-5-yl)-6-chloronicotinamide (5). Compound 5 was further treated with various substituted amines in pyridine to get benzofuran derivatives 6(a-r), respectively.

S. S. Rindheet et al., [11] reported on benzofuran derivatives as an antioxidant agent of benzofurans formed by ring closure reaction of 2-haloaromatic ketones through CuI catalyst with 72-99%yield.



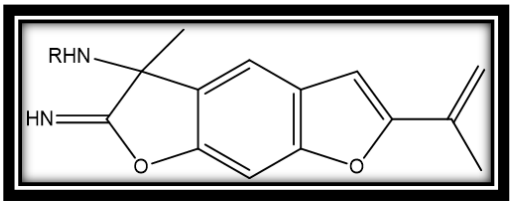
Elham Ezzatzadeh & Zinatossadat Hossaini et al., [12] reported on Green synthesis and antioxidant activity of novel series of benzofurans from euparin extracted of *Petasites hybridus*



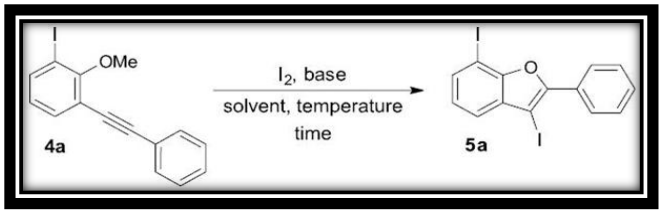
Under solvent free conditions, isocyanide-based MCR, euparin and aldehydes were collectively reacted under catalyst ZnO-nanorods at room temperature to give a new series of benzofuran derivaties. The synthesised compounds such as 4a, 4b, 10a and 10b were evaluated for anti oxidant activities by DPPH radical scavenging and ferric reduction activity potential (FRAP) assays. Compound 10b showed moderate anti oxidant activity against standard (BHT and TBHQ).

Elham Ezzatzadeh et al., [13] reported on A novel one-pot three-component synthesis of benzofuran derivatives *via* Strecker reaction: Study of antioxidant activity

1-(6-hydroxy-2-isopropenyl-1-benzofuran-yl)-1-ethanone(euparin), primary amines and trimethylsilyl cyanide (TMSCN) were reacted collectively with ZnO-nanorods (ZnO-NR) and piperidine in acetonitrile at room temperature to give benzofuran derivatives and these are called as three component strecker type reactions.

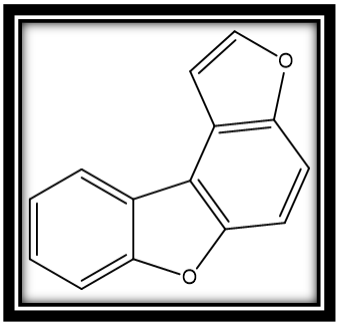


Mehta et al., [14] reported on S. Benzofuran Synthesis through Iodocyclization Reactions: Recent Advances.



Alkynylated 2-iodoanysole **4a** reacted with 2 equiv. of iodine in dichloromethane to givediiodo-functionalized benzo[*b*]furan **5a.** Based on the duration of time and temperature the percentage yield varies. 5 % yield was obtained when the reaction was exposed to room temperature for 3 hrs, in order to increase the percentage yield the same reaction was carried for 12hrs which results in 34% of yield. Further improvisation of yield (44%) was obtained when the reaction temperature was raised to 40°C.

Thirumal Yempala et al., [15] reported on Design, synthesis and antitubercular evaluation of novel 2-substituted-3*H*-benzofuro benzofurans via palladium–copper catalysed Sonagashira coupling reaction



Using molecular hybridization technique a number of new compounds like 2-substiuted-3*H*- benzofurobenzofurans were synthesized with high proportions. 2-dibenzofuranol was iodinised by iodine monochloride followed by palladium–copper catalyzed Sonagashira-coupling of 1-iododibenzofuran-2-ol with various alkyl and aryl acetylenes to give benzofurans derivatives. When screened for in vitro anti-mycobacterial activity against *Mycobacterium tuberculosis* H37Rv,Out of all synthesized compounds, Compound 2-(4-methoxy-2-methyl phenyl)-3*H*-benzofuro[3,2-*e*]benzofuran (**7c**) was found to have more MIC 3.12 µg/mL and have a good range of therapeutic activity with less cytotoxicity.

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