Review Article

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SYNTHESIS AND BIOLOGICAL ACTIVITY OF FURAN DERIVATIVES

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ABSTRACT
Furan derivative are an important class of heterocyclic compound that possess important biological properties.
From last few decades a considerable amount of attention has been focussed on synthesis of Furan derivatives and screening them for different pharmacological activities.
The furan ring system is the basic skeleton of numerous compounds possessing cardiovascular activities. An iodinated lipophilic furan derivative is widely used in the treatment of ventricular and atrial fibrillation. These moieties are widely employed as antibacterial, antiviral, anti-inflammatory, antifungal, antitumor, Antihyperglycemic, Analgesic, Anticonvulsant etc. Slight change in substitution pattern in furan nucleus causes distinguishable difference in their biological activities. In this review we are discussing about synthesis and various biological activities of newly synthesized furan derivatives.
Keyword: Furan, Antihyperglycemic, Analgesic, Anticonvulsant activity.

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INTRODUCTION

Furan Fig.1, The name furan comes from the Latin *furfur*, which means bran. The first furan derivative to be described was 2-furoic acid, by Carl Wilhelm Scheele in 1780[1]

Furan is a class of organic compounds of the heterocyclic aromatic series characterized by a ring structure composed of one oxygen atom and four carbon atoms. The simplest member of the furan family is furan itself, a colourless, volatile, and somewhat toxic liquid that boils at 31.36° C (88.45° F). Several other members of the furan family are produced on a large scale for use as solvents and chemical raw materials. The first furan compound discovered was pyromucic acid (2-furoic acid), prepared in 1780[2]

Furanand related compound have been reported to possess various biological activities such as Antihyperglycemic[3], Analgesic[3], Antiinflammatory[3], Antibacterial[3], Antifungal[3], Antitumor activities[3].

SYNTHESIS OF SUBSTITUTED FURAN DERIVATIVES

Scheme1

The oxime-olefin was synthesized by cycloaddition reaction with substituted olefins in the presence of chloramine-T[17] to produce isoxazolines[4]. Fig.2

Scheme2

The (5-mercapto-indol-1-yl)-acetic acid core was prepared by alkylating commercially available 5 benzyloxyindole in dimethylformamide with methylbromoacetate using sodium hydride as base. The resulting compound was then de-benzylated using hydrogen and palladium as catalyst[5] Fig.3

Scheme 3

Compound (3) were synthesized by Suzuki coupling reaction using palladium catalyst from 6 bromo-2-hydroxy-3-methoxybenzaldehyde (2). PdCl2(P(o-tol)3) was a good catalyst for the reaction. The 4-aryl benzofurans (6) were obtained[6]. Fig.4

Scheme 4

For the preparation of 4-thiazolyl benzofurans, compound (2) was bromoacetylated by Friedel Crafts reaction, then cyclization using thioamide to give compound 9 Subsequent hydrolysis and amidation gave the desired compound 10[6]. Fig5

Scheme 5

1-(2-benzofuryl)-3-aryl-2-propen-1-ones 12a-c were prepared by reaction of 2-acetylbenzofuran 11 with aromatic aldehyde. The 1-(benzofuran-2-yl)-4-nitro-3-arylbutan-1-ones 39a-c were prepared by reacting equimolecular amount of 38a-c with nitromethane in

boiling ethanol and in the presence of basic catalyst[7] Fig.6

Scheme 6

Direct reduction of conjugated ester 13 to eganol 15 was performed by using LiAlH4 or LiBH4 as shown in scheme.[8] Fig.7

Scheme 7

Khan isolated a new egonol derivative, 5-(3-propanoyl-oxypropyl)-7-methoxy-2-(3,4-methylenedioxyphenyl) benzofuran 43 fromStyraxobassia[8] Fig8

BIOLOGICAL ACTIVITY

Antibacterial Activity

Hatem A. Abdel-Aziz et al synthesized compound that showed a variable potencies against tested bacteria. The tested compound (1E-2E)-1-(Piperidin-1-yl)-1-[(4-nitrophenyl hydrazonal]-2-[(3-methylbenzofuran-2-oyl)hydrazono] propane exhibited weak inhibitory effect against the Gram-negative bacterium E.Coli (1) whereas they revealed no effect, or very weak against P.aerogenosa[9] Fig.9

Anticonvulsant

Dawood newly synthesized benzotriazole derivatives were screened for anticonvulsant activity in maximal electroshock seizure (MES) and subcutaneous metrazole test in mice.The test compound 2-(5-Acetyl-3-phenyl-1,3,4-thiadiazole-2-ylidene)-1-(2-benzofuryl)-2-(1-benzotriazolyl)-ethanone were found to be active in subcutaneous metrazole[8] Fig.10

Antinociceptive Effect

Dawood newly synthesized benzotriazole derivative to show antinociceptive effect.The pyrazole derivative 3-acetyl-1-aryl-5-(benzofuran-2-yl)-4-(benzotriazol-1-yl) pyrazoles showed a higher antinociceptive activity. It was assessed by three different models:the acetic acid induced writhing test,hot plate test and tail flick test. Some benzotriazole derivative exhibited antinociceptive effect as shown in compound 3[8] Fig.11

Antifungal activity

Abdel-Aziz AAI Mekawey in 2009 synthesize various compound like (1Z,2E)-N- (aryl)propanehydrazonoyl chloride bearing active methyl group used as C-nucleophiles.The newly synthesized benzofuran–based (1E)-1-(Piperidine-1-yl)-N2-arylamidrazones have significant antifungal activity[11]. Fig.12

Antitumor Activity

Galal synthesize a new series benzofuran derivative by the reaction of the furochromone-carboxaldehydes with differentheterocyclic amines to yield the benzofuran-5-carbonyl derivative. The synthesized compound were tested against twelve differenthuman cancer cell lines and all of the compound were more potent than the comparative standard[12]. Fig 13

Antiviral

Galal et al. 2009 synthesized derivatives can serve as lead compound for further investigation and act as antiviral activity. Compound (11 H- Benzo[4,5] imidazol[1,2-a] [1,4] diazepin-4-yl) (6-hydroxy-4,7-dimethoxy- benzofuran-5-yl) methanone[13]. Fig 14

Antiimflammatory

Dawood synthesized benzofuran-benzotriazole-based heterocycles compound. The thiadiazole derivative 2-(5-Acetyl-3-phenyl-1,3,4-thiadiazole-2-ylidene)-1-(2-benzofuryl)-2 (1 benzo tria zolyl) ethanono was the most potent anti-inflammatory compound.The anti inflammation effect of the thiazolidine ester derivative is higher than that of it acetyl derivative[10]. Fig.15

CONCLUSION

Different Derivatives of furan were synthesized and characterized by the spectral method such as IR & NMR The pyrazole derivative 3-acetyl-1-aryl-5-(benzofuran-2-yl)-4-(benzotriazol-1-yl) pyrazoles showed a higher antinociceptive activity.and The test compound 2-(5-Acetyl-3-phenyl-1,3,4-thiadiazole-2-ylidene)-1-(2-benzofuryl)-2-(1-benzotriazolyl)-ethanone were found to be active in subcutaneous metrazole and show a anticonvulsant activity. So these derevatives/compound can be used as potent antinociceptive agents and anticonvulsant activity.

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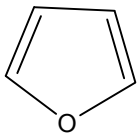
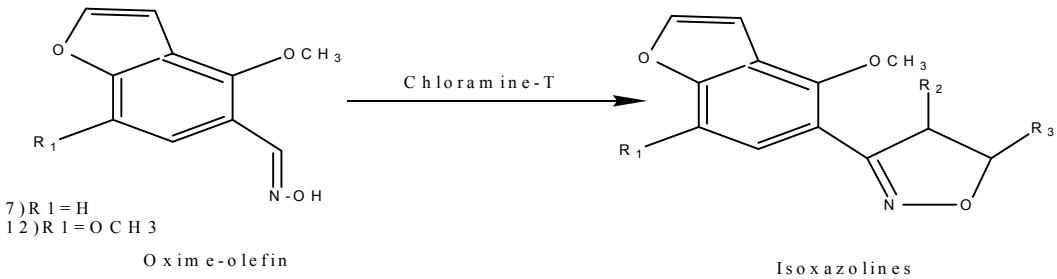


Fig.1



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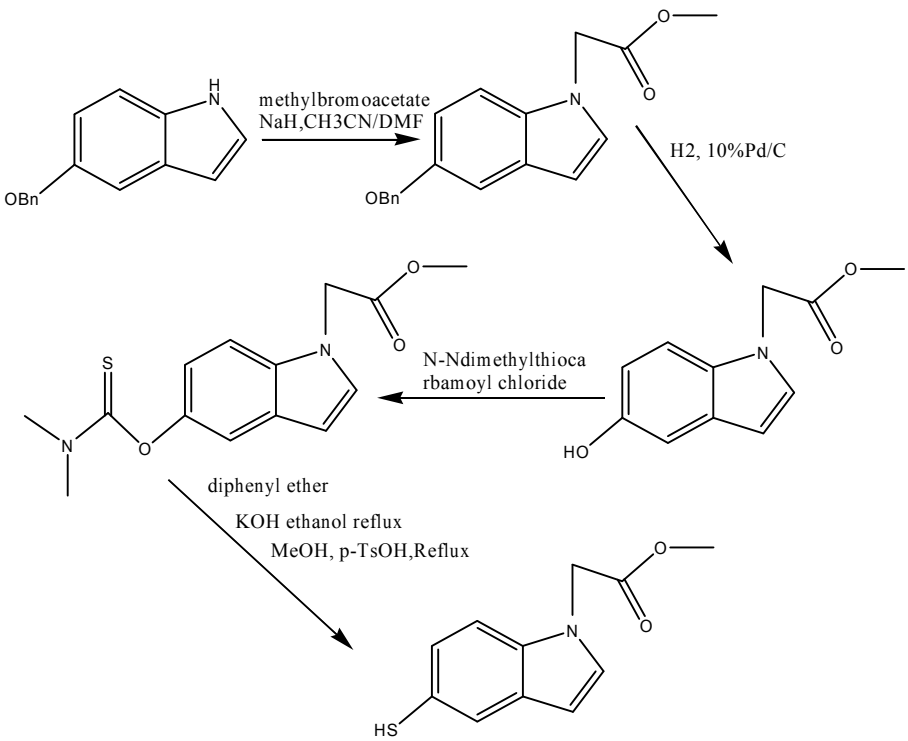
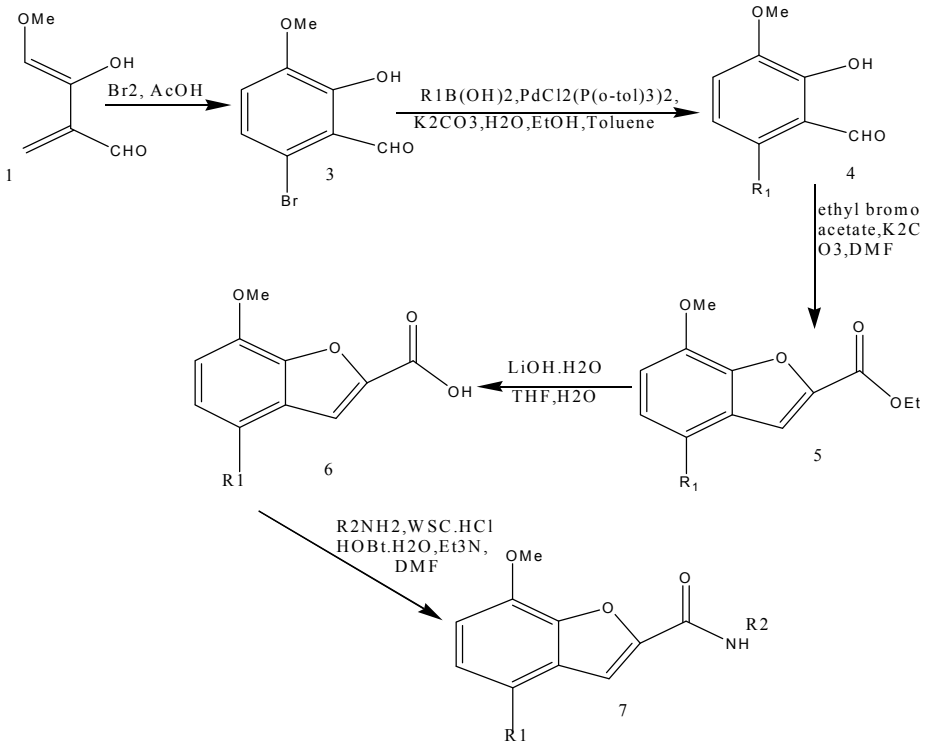


Fig.3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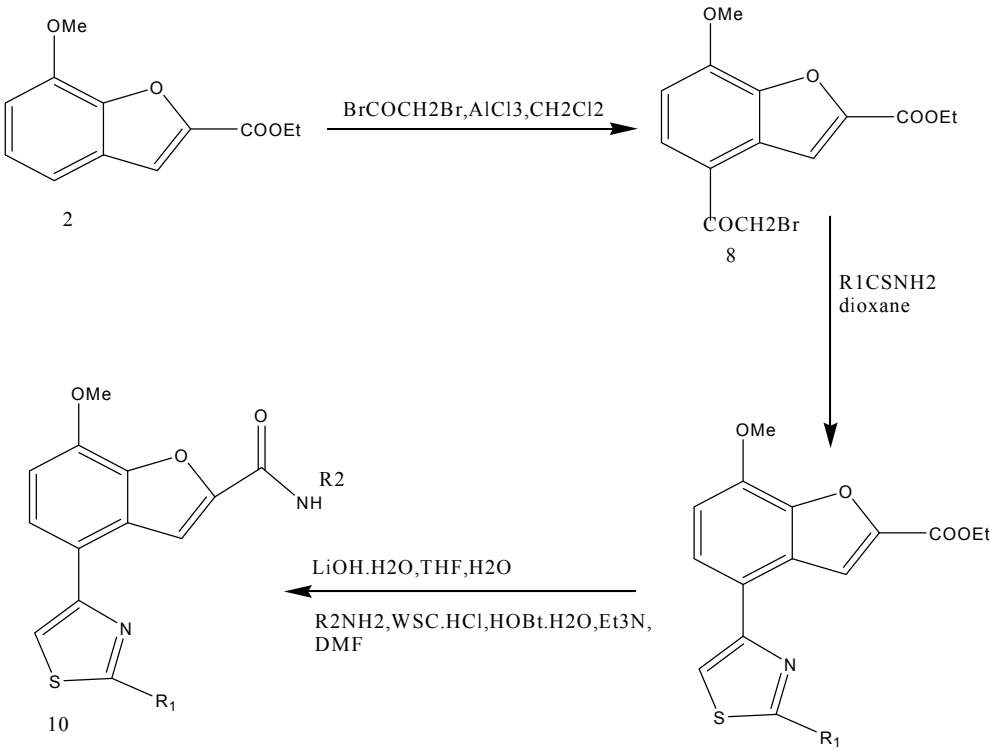
R1
ethyl bromo
acetate,K2C
O3,DMF
OEt
LiOH.H2O
THF,H2O
R2NH2,WSC.HCl
HOBt.H2O,Et3N,
DMF
NH
R2
1
3
4
5
6
7

Fig.4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R2
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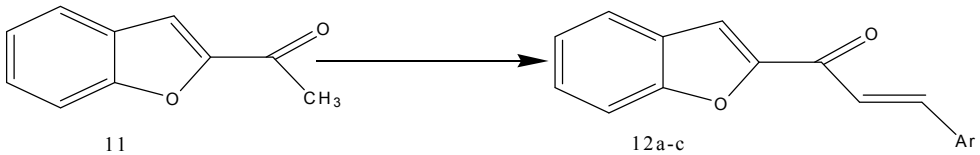
DMF
N
S
R1
2
8
9
10

Fig.5



12	Ar
a	Ph
b	4-Cl-C6H4
c	4-MeO-C6H4

Fig.6

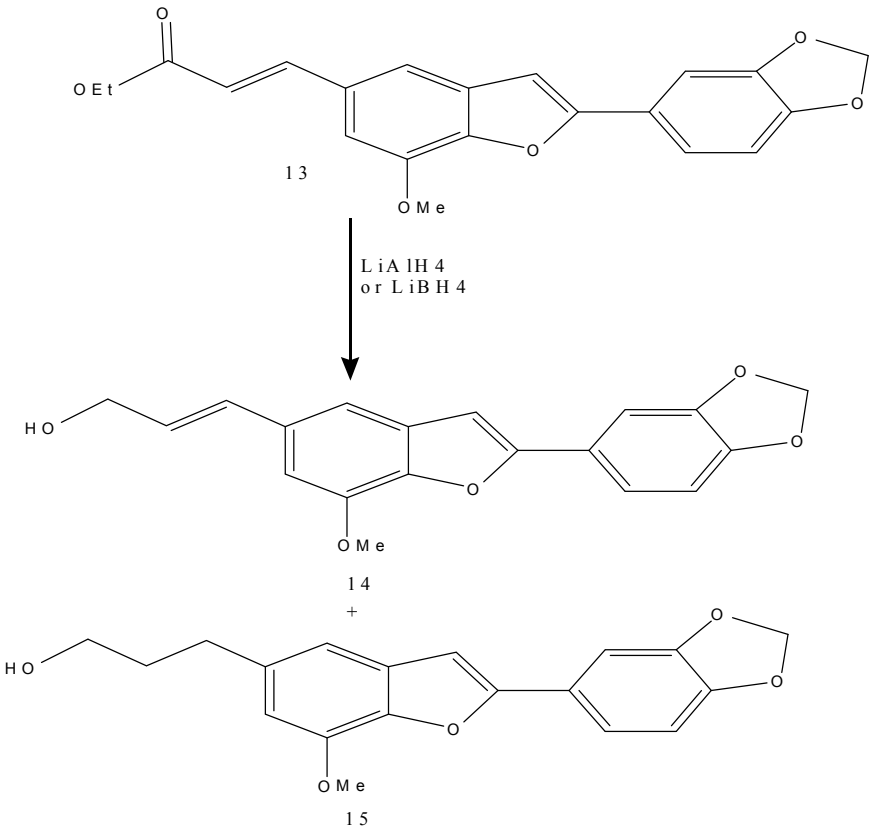


Fig.7

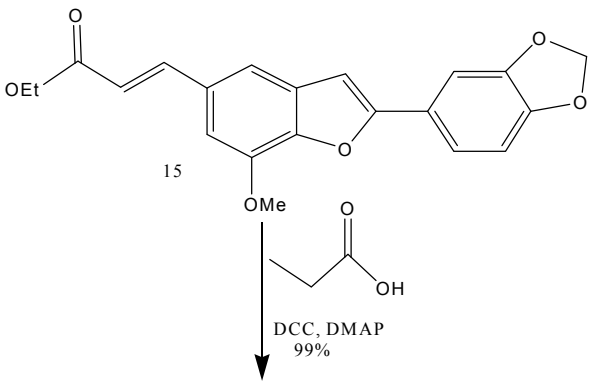


Fig.8

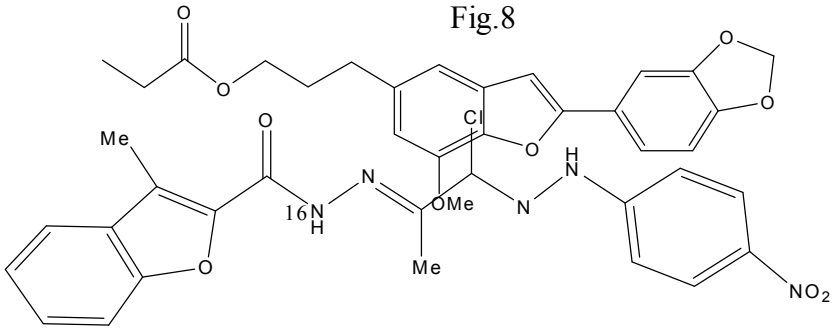


Fig 9

N'-{(2*E*)-1-chloro-1-[2-(4-nitrophenyl)hydrazinyl]propan-2-ylidene}-3-methyl-1-benzofuran-2-carbohydrazide

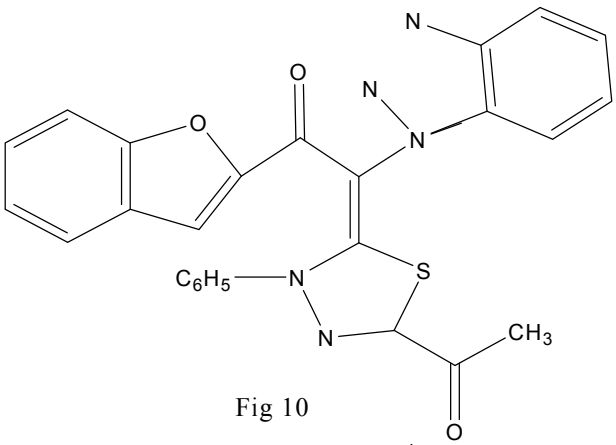


Fig 10

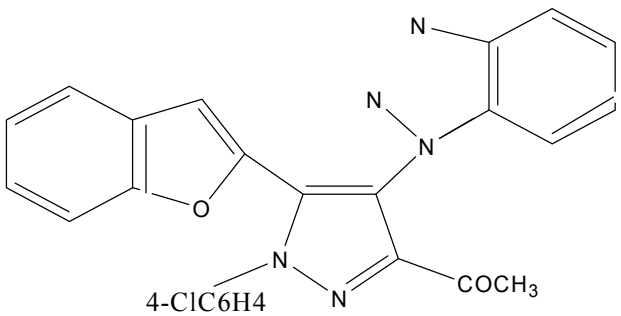


fig. 11

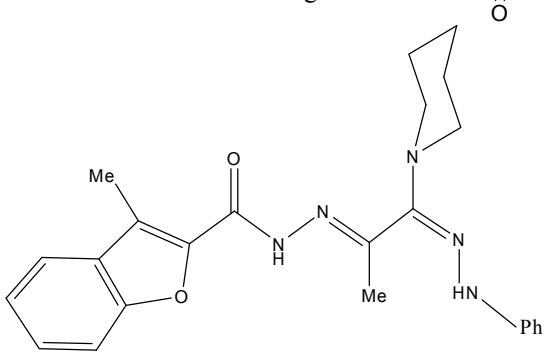


Fig .12

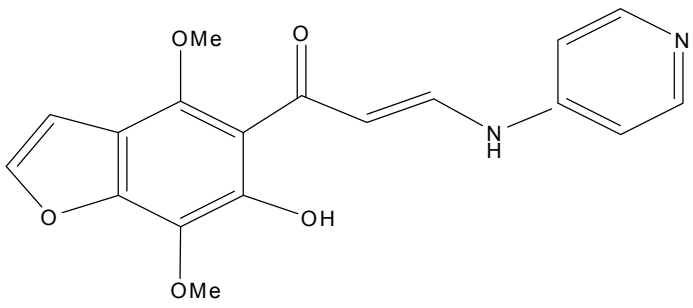


Fig. 13

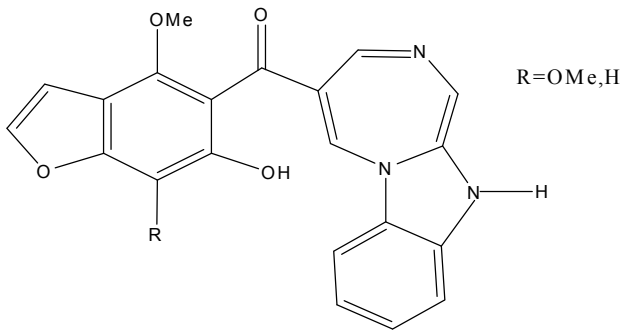


Fig.14

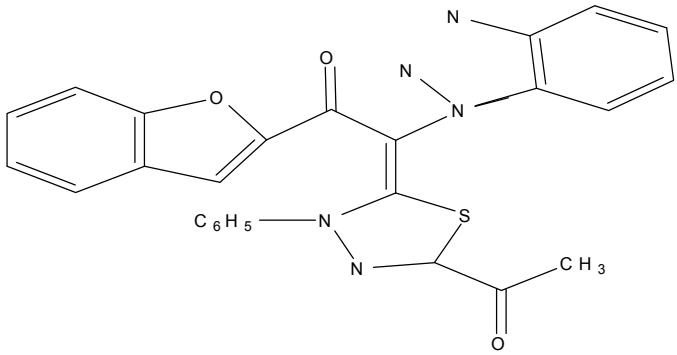


Fig 15