Review 7

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5-Phenyl-2-furaldehyde: Synthesis, Reactions and Biological Activities

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5 -PHENYL-2-furaldehyde is a good starting material for designing of polyfunctionalized heterocyclic compounds with pharmacological interest such as antimicrobial and antitumor activities. This review article focused on some synthetic methods, reactions and biological activities of 5-phenyl-2-furaldehyde.

Keywords: 5-Phenyl-2-furaldehyde, Synthesis, Palladium-catalyzed, Chemical reactions and Biological activities.

Compounds bearing oxygen heterocycles are well known to be biologically important⁽¹⁾. On the other side, compounds containing furan moiety show a diverse array of favorable pharmacological properties and have consequently been used as medicines in a variety of different diseases areas⁽²⁾. Furan derivatives obtained from natural and synthetic sources have been a subject of considerable interest for their wide range of pharmaceutical applications⁽³⁻⁶⁾. A large number of naturally occurring compounds bearing furan have shown interesting biological activities such as antimicrobial^(7,8), cytotoxic and antitumor properties⁽⁹⁾, as well as of other potentially useful activities^(10,11).

Literature survey, as far as we are aware, revealed that some drugs bearing furan moiety are considered as the most active in manufactured drugs such as Dantrolene (Muscle relaxant), Furosemide (Antihypertensive), Nifurtimox (Antiprotozoal), Nifuroxazide (antibiotic), Nifurprazine (Antibacterial), Furfenorex (Anorexic), Dormovit (Sedative, hypnotic) and Methafurylene (Antihistaminic). The structures of these drugs are shown in Fig. 1.

5-Phenyl-2-furaldehyde (Fig. 2) and its derivatives have been reported for their interesting pharmacological activities *e.g.* antibacterial⁽¹²⁾, antitumor⁽¹³⁾, inhibitors of phosphoinositide 3-Kinase $\gamma^{(14)}$, HCV NS5B polymerase⁽¹⁵⁾ and non-thiol farnesyltransferase⁽¹⁶⁾.

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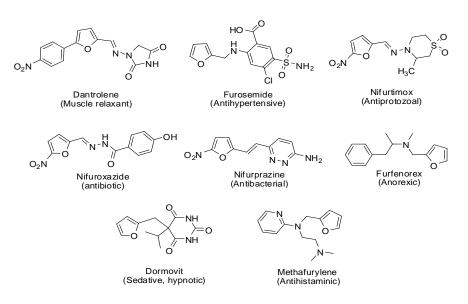


Fig. 1. The structures of some drugs bearing furan moiety.

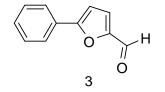


Fig. 2. The structure of 5-phenyl-2-furaldehyde 3.

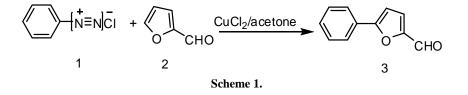
Therefore, the objective of the present work is to shed more light on the synthesis, reactions and biological activities of 5-phenyl-2-furaldehyde.

Synthetic Methods

5-Phenyl-2-furaldehyde can be synthesized via the following reactions:

The coupling reaction with copper(II)-catalyzed (Meerwein arylation)

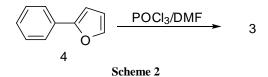
5-Phenyl-2-furaldehyde 3 was prepared by coupling benzene diazonium chloride 1 with 2-furaldehyde 2 in the presence of cupric chloride (Scheme 1) $^{(17-18)}$.



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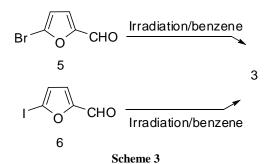
Vilsmeier-Haack reaction

5-Phenyl-2-furaldehyde (3) (yield: 60%) was synthesized from 2-phenylfuran (4) *via* a Vilsmeier-Haack reaction (Scheme 2)⁽¹⁹⁾.



Photochemical reaction

Irradiation of 5-bromofuran-2-carbaldehyde (5) in benzene solution furnished 3 in yield 64%,⁽²⁰⁾ but using 5-iodofuran-2-carbaldehyde (6) gave yield 91% (Scheme 3)⁽²¹⁾.



Palladium(II) acetate catalyzed reaction

Oxidation of 2-furaldehyde (2) by palladium(II) acetate in acetic acid containing benzene at reflux temperature gave 3 (Scheme 4) $^{(22)}$.

$$2 \qquad \frac{[O] / Pd(OAc)_2 / AcOH}{benzene} \qquad 3$$

Scheme 4

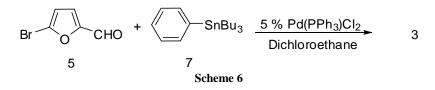
Moreover, the coupling of phenyl boronic acid with 5 in water, in the presence of tetrabutylammonium bromide and palladium(II) acetate at room temperature (RT) yielded 5-phenyl-2-furaldehyde 3 (yield: 74%) (Scheme 5)⁽²³⁾.

5 $\frac{PhB(OH)_2}{Pd(OAc)_2 / H_2O / RT}$ 3 tetrabutylammonium bromide

Scheme 5

5% Pd(PPh₃)₂Cl₂ catalyzed

5-Phenyl-2-furaldehyde (3) was prepared from 5 and phenyl tributyl tin (7) in the presence of 5% Pd(PPh₃)₂Cl₂ in refluxing dichloroethane (yield: 61%) (Scheme 6)⁽²⁴⁾.



Pd(*dppf*)*Cl*₂: [1,1'-Bis(*diphenylphosphino*) *ferrocene*] *dichloropalladium catalyzed* 5-Phenyl-2-furaldehyde 3 was prepared from bromobenzene (8) and organozinc reagents (9a-c) in the presence of Pd(dppf)Cl₂ as a catalyst (yields 9a: 77%, 9b: 76%, 9c: 71%) (Scheme 7)⁽²⁵⁾.

Br +
$$\begin{pmatrix} EtO \\ EtO \end{pmatrix}$$
 ZnLix $Pd(dppf)Cl_2$ 3
8 9a-c
9a: x=0; 9b: x=1; 9c: x=2

Scheme 7

Palladium catalyst

The *cis,cis,cis*,*cis*,1,2,3,4-tetrakis (diphenylphosphinomethyl) cyclopentane/ [PdCl(C₃H₅)]₂ complex catalyzed the Suzuki cross-coupling of 5 with phenyl boronic acid in dry xylene under argon to afford 3 (Scheme 8)^(26,27).



Also, the Suzuki coupling of 5 with phenylboronic acid was catalyzed by trans-(Cy₂NH)₂Pd(OAc)₂(DAPCy) in EtOH under aerobic conditions to afford the coupled product 3 in yield 91% (Scheme 9)⁽²⁸⁾.

Catalyst= trans-(Cy₂NH)₂Pd(OAc)₂(DAPCy)

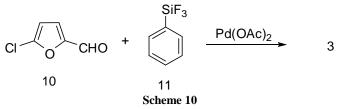
Scheme 9

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Palladium-catalyzed Hiyama cross-coupling

5-Chlorofuran-2-carbaldehyde (10) was coupled with phenyltrifluorosilane (11) in the presence of $Pd(OAc)_2$ as a catalyst to afford the coupled product, 5-phenyl-2-furaldehyde (3) (yield: 74%) (Scheme 10)⁽²⁹⁾.



Suzuki coupling reaction

5-Chlorofuran-2-carbaldehyde (10) can be arylated with phenylboronic acid in the presence of the PAP ligand [2-(di-*tert*-butylphosphino)-1-phenyl-1*H*-pyrrole] as a catalyc to form 3 (yield > 99%) (Scheme 11)⁽³⁰⁾.

PAP ligand = 2-(di-tert-butylphosphino)-1-phenyl-1H-pyrrole

Scheme 11

Suzuki-Miyaura reaction

5-Phenyl-2-furaldehyde (3) can be prepared by reacting 5-bromo-2-furaldehyde (5) with phenylboronic acid in the presence of $Pd(OAc)_2$ and ligand 1 [glyoxal *bis*(*N*-methyl-*N*-phenyl-hydrazone)] as a catalyst under aerobic conditions (yield: 83%) (Scheme 12)⁽³¹⁾.

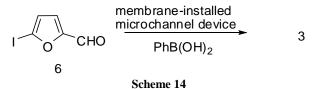
$$Br \xrightarrow{O} CHO \xrightarrow{Pd(OAc)_2/\text{ ligand 1}}{PhB(OH)_2} 3$$

Scheme 12

Also, 5-phenyl-2-furaldehyde 3 can be prepared by reacting 5 with phenylboronic acid *via* Suzuki-Miyaura reaction in the continuous flow reactor with using the palladium resin catalyst, *N*,*N*-diisopropyl ethyl amine in DMF/water at 100 °C, (yield: 91%) (Scheme 13)⁽³²⁾.

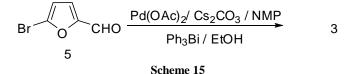
Scheme 13

Moreover, the Suzuki-Miyaura reaction of 6 and phenylboronic acid catalyzed with using the membrane-installed microchannel device furnished 3 in high yield (99%) (Scheme 14)⁽³³⁾.



*The coupling reaction of Ph*₃*Bi with 5-bromo-2-furaldehyde*

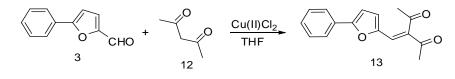
The coupling reaction of 5 with Ph₃Bi furnished 5-phenyl-2-furaldehyde (3) in high yield (89%) with using Pd(OAc)₂ as a catalyst and Cs₂CO₃ base in *N*-methylpyrrolidone (NMP) solvent (Scheme 15) ⁽³⁴⁾.



Chemical Reactions

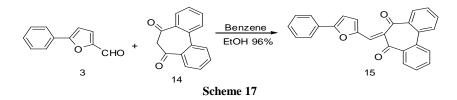
Formation of furfurylidene derivatives

The condensation of 3 and pentan-2,4-dion (12) in THF in the presence of $Cu(II)Cl_2$ as a catalyst formed 3-[(5-phenylfuran-2-yl)methylene]pentane-2,4-dione 13 in moderate yield (Scheme 16)⁽³⁵⁾.



Scheme 16

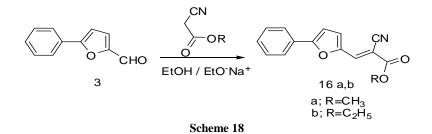
6-(5-Phenyl-2-furfurylidene)-dibenzo[*a*,*c*]cyclohepten-5,7-dione (15) was prepared by the reaction of 6,6-dihydro-dibenzo[*a*,*c*]cyclohepten-5,7-dione (14) with **3** in benzene and 96% ethanol (yield 70%) (Scheme 17)⁽³⁶⁾.



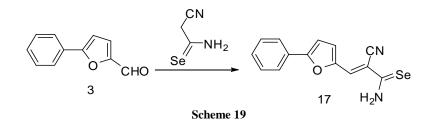
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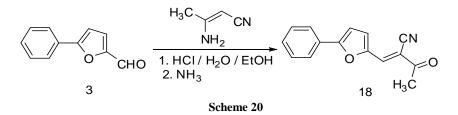
Methyl-2-cyano-3-(5-phenyl-2-furyl)acrylate (16a) $(92\%)^{(37)}$ or ethyl 2-cyano-3-(5-phenyl-2-furyl)acrylate 16b $(72\%)^{38}$ were prepared by the reaction of 3 with methyl cyanoacetate or ethyl cyanoacetate, respectively, *via* using the Knoevenagel reaction conditions, in dry ethanol with adding sodium ethoxide as a catalytic (Scheme 18).



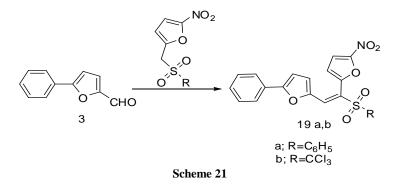
Reaction of 5-phenyl-2-fural dehyde 3 with cyanoselenoacetamide gave 2-cyano-3-(5-phenyl-2-furyl) prop-2-eneselenoamide (17) (yield: 83%) (Scheme 19) $^{(39,40)}$.



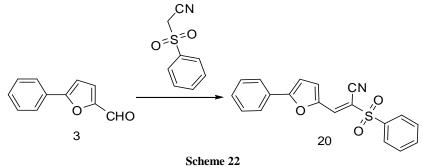
3-Amino-2-butanenitrile was first hydrolyzed by dilute HCl in ethanol to yield cyanoacetone, which, upon Knoevenagel condensation with 3 and then neutralization afforded 3-oxo-2-[(5-phenylfuran-2-yl)methylene]butanenitrile (18) in yield 91% (Scheme 20)⁽⁴¹⁾.



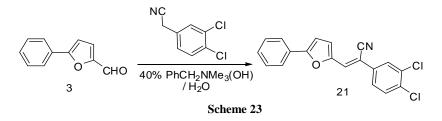
Condensation of 5-phenyl-2-furaldehyde (3) with 5-nitrofurfuryl phenyl sulfone or 5-nitrofurfuryl trichloromethyl sulfone afforded 1-(5-nitro-2-furyl)-1-phenyl sulfonyl-2-(5-phenyl-2-furyl) ethylene $(19a)^{(42)}$ r 1-(5-nitro-2-furyl)-1-trichloromethyl sulfonyl-2-(5-phenyl-2-furyl) ethylene $(19b)^{(43)}$, respectively (Scheme 21).



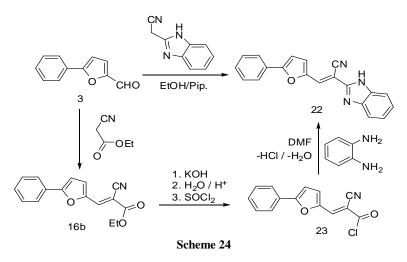
1-Phenyl sulfonyl-1-cyano-2-(5-phenyl-2-furyl) ethylene (20) (yield: 68%) was prepared by the condensation of 3 with phenyl sulfonyl acetonitrile (Scheme 22)⁽⁴⁴⁾.



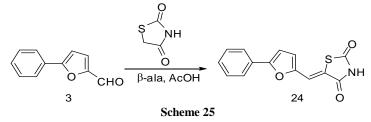
3,4-Dichlorophenylacetonitrile treated with 5-phenyl-2-furaldehyde (3) in water with adding 40% PhCH₂NMe₃(OH) as a catalyst at 50 °C for 5 hr gave (*Z*)-2-(3,4-dichlorophenyl)-3- (5-phenyl-2-furyl) acrylonitrile (21) in yield 94% (Scheme 23)⁽¹³⁾.



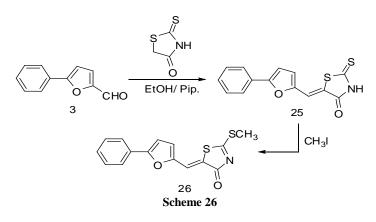
2-Cyanomethylbenzimidazole reacted with 5-phenyl-2-furaldehyde (3) to afford a condensation product, 3-(5-phenyl-2-furyl)-2-(2- enzimidazolyl) crylonitrile 22 in a high yield. The carboxylic acid chloride (23) was prepared from ethyl 2-cyano-3-(5-phenyl-2-furyl)acrylate (16b) which was in turn synthesized by condensation of 5-phenyl-2-furaldehyde (3) with ethyl cyanoacetate. Compound 23 and *o*-phenylenediamine when heated in DMF formed 22 (Scheme 24)⁽⁴⁵⁾.



5-[(5-Phenyl-2-furyl)methylene]thiazolidine-2,4-dione (24) was prepared by the condensation of 5-phenyl-2-furaldehyde (3) with thiazolidine-2,4-dione in the presence of β -alanine in acetic acid (Scheme 25)⁽¹⁴⁾.

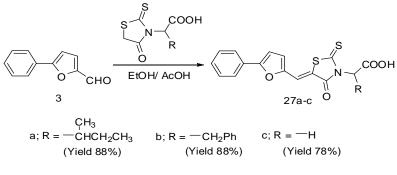


Rhodanine was condensed with 5-phenyl-2-furaldehyde (3) in the presence of piperidine in ethanol to afford (*Z*)-5-((5-phenylfuran-2-yl) methylene)-2-thioxothiazolidin-4-one (25), which then reacted with CH_3I to form the methyl thio-derivative (26) (Scheme 26)⁽⁴⁶⁾.



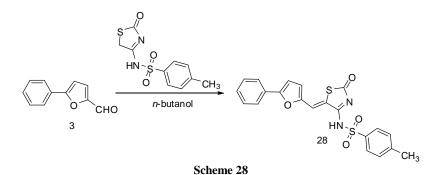
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(*Z*)-3-Methyl-2-(4-oxo-5- ((5-phenylfuran-2-yl) methylene)-2-thioxothiazolidin-3-yl) pentanoic acid (27a)⁽⁴⁷⁾, (*Z*)-2-(4-oxo-5- ((5-phenylfuran-2-yl) methylene)-2thioxothiazolidin-3-yl) -3-phenyl propanoic acid (27b)⁽⁴⁷⁾ and (*Z*)-2-(4-oxo-5- ((5phenylfuran-2-yl)methylene)-2 -thioxothiazolidin-3-yl) acetic acids (27c)⁽⁴⁸⁾ were obtained *via* the Knoevenagel condensation reaction of the 5-phenyl-2- furaldehyde (3) with the *N*-substituted rhodanine, *e.g.* (2*S*)-3-methyl-2- (4-oxo-2thioxothiazolidin-3-yl) pentanoic acid, (*S*)-2-(4-oxo-2-thioxo-thiazolidin-3-yl)-3phenylpropanoic acid and rhodanine-3-acetic acid, respectively (Scheme 27).

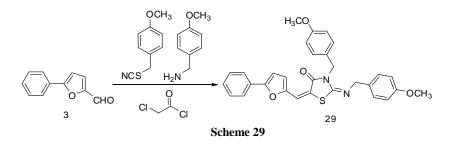


Scheme 27

5-Phenyl-2-furaldehyde (3) condensed with 4-methyl -N-(2-oxo-2,5-dihydrothiazol-4-yl) benzenesulfonamide in *n*-BuOH to form (*Z*)-4- methyl-*N*-{2-oxo-5- [(5-phenylfuran-2-yl) methylene] -2,5-dihydrothiazol-4-yl} benzenesulfonamide (28) in yield 75% (Scheme 28)⁽¹⁵⁾.

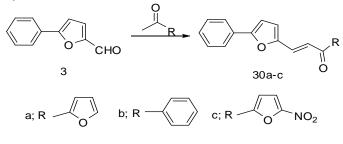


3-(4-Methoxybenzyl)-2- (4-methoxybenzylimino)-5- [(5-phenylfuran-2-yl)methylene] thiazolidin-4-one (29) (yield: 51%) was synthesized by one-pot reaction of 4-methoxybenzylamine, 4-methoxybenzylisothiocyanate with chloroacetyl chloride and 5-phenylfuran-2-carbaldehyde (3) (Scheme 29)⁽⁴⁹⁾.



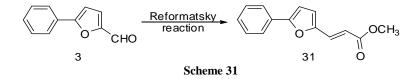
Chalcone derivatives

 $1-(2-Furoyl)-2-(5-phenylfuran-2-yl)ethylene (30a)^{(50)}$, $1-benzoyl-2-(5-phenylfuran-2-yl)ethylene (30b)^{(50)}$ and $1-(5-nitro-2-furoyl)-2-(5-phenylfuran-2-yl)ethylene (30c)^{(51)}$ have been synthesized by the condensation of 5-phenyl-2-furaldehyde (3) with 2-acetylfuran, acetophenone and 5-nitro-2-acetylfuran, respectively (Scheme 30).

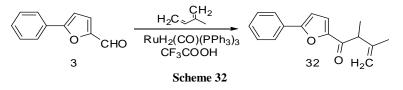


Scheme 30

Methyl 3-(5-phenylfuran-2-yl)acrylate 31 (yield: 80%) was prepared from 5-phenyl-2-furaldehyde (3) by Reformatsky reaction (Scheme 31)⁽⁵²⁾.



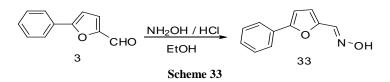
5-Phenyl-2-furaldehyde (3) was coupled with isoprene to form 2,3-dimethyl-1-(5-phenylfuran-2-yl)but-3-en-1-one (32) in good yield (90%). This coupling reaction was accamplished using ruthenium dihydride complex $RuH_2(CO)(PPh_3)_3$ catalyst activated by trifluoroacetic acid (Scheme 32)⁽⁵³⁾.



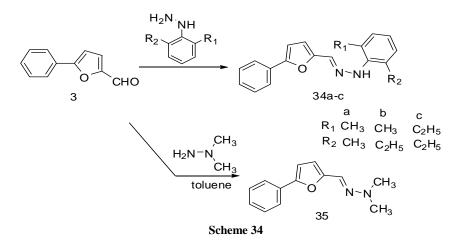
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Hydrazide and hydrazone derivatives

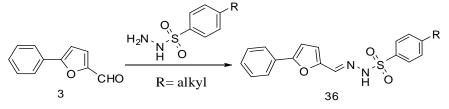
5-Phenyl-2-furaldehyde (3) reacted with hydroxylamine hydrochloride in the presence of sodium acetate in ethanol to yield (*E*)-5-phenylfuran-2-carbaldehyde oxime (33) (Scheme 33)⁽⁵⁴⁾.



A series of 5-phenyl-2-furancarbaldehyde 2,6-dialkylphenylhydrazone (34ac) was prepared in excellent yield by the reaction of 5-phenyl-2-furaldehyde (3) with 2,6-dialkylphenylhydrazine. On the other hand, 5-phenyl-2furancarbaldehyde dimethylhydrazone (35) was prepared by the reaction of 3 with *N*,*N*-dimethylhydrazine in refluxing toluene in the presence of catalytic amount of 4-methylbenzenesulfonic acid (Scheme 34)⁽⁵⁵⁾.

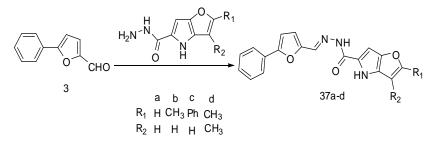


Reaction of 5-phenyl-2-furaldehyde (3) with arylsulfonohydrazides in anhydrous ethanol afforded a series of the corresponding arylsulfonylhydrazones (36) (Scheme 35)⁽⁵⁶⁾.



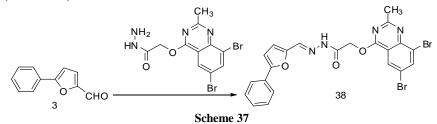
Scheme 35

The reaction of 5-phenyl-2-furaldehyde (3) with substituted furo[3,2-b]pyrrole-5-carbohydrazide in the presence of *p*-toluenesulfonic acid led to *N'*-[(5-phenylfuran-2-yl) methylene] -4*H*-furo[3,2-*b*] pyrrole-5- carbohydrazide derivatives (37a-d) (Scheme 36)⁽⁵⁷⁾.

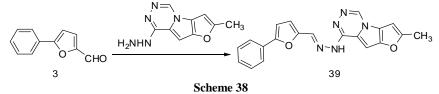


Scheme 36

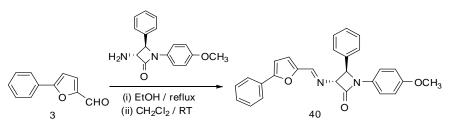
2-[(6,8-Dibromo-2-methylquinazolin -4-yl)oxy]-*N*- [(5-phenylfuran-2-yl) methylene] acetohydrazide (38) was obtained by treatment of 5-phenyl-2-furaldehyde (3) with 4-(acetohydrazide)-6,8- dibromo-2- methylquinazoline (Scheme 37)⁽¹²⁾.



Reaction of 5-phenyl-2-furaldehyde (3) with 8-hydrazino-2-methylfuro [2',3':4,5] pyrrolo[1,2-d] [1,2,4]triazine yielded 5-phenylfuran-2-carbaldehyde (2-methylfuro[2',3':4,5]pyrrolo [1,2-d][1,2,4]triazin-8-yl) hydrazone (39) (yield 50%) (Scheme 38)⁽⁵⁸⁾.

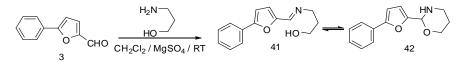


(3R, 4R)-1- (4-methoxyphenyl) -4-phenyl-3- ((5-phenylfuran-2-yl) methyleneamino) azetidin-2-one (40) was obtained by treatment of 5-phenyl-2-furaldehyde (3) with *trans*-3-amino- β -lactam in boiling ethanol followed by stirring in dichloromethane at room temperature in the presence of sodium sulfate (Scheme 39)⁽⁵⁹⁾.



Scheme 39

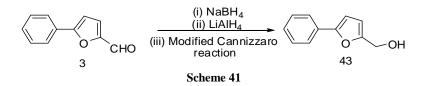
The condensation of 5-phenyl-2-furaldehyde (3) with 3-aminopropanol at room temperature in the presence of a dehydrating agent (MgSO₄) yielded 3-[(5-phenylfuran-2-yl)methyleneamino]propan-1-ol (41) and 2-(5-phenyl-2-furyl)-1,3-oxazinane (42) in an equilibrium mixture (Scheme 40)⁽⁶⁰⁾.



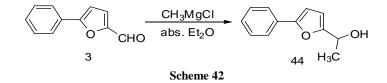
Scheme 40

Furfuryl alcohol derivatives

The preparation of 2-hydroxymethyl-5-phenylfuran (43) from 5-phenyl-2-furaldehyde (3) processed *via* (i) the reduction by using sodium borohydride NaBH₄⁽⁶¹⁾; (ii) the reduction by LiAlH₄ (high yield 96%); (iii) modified Cannizzaro reaction⁽⁶²⁾ (Scheme 41).

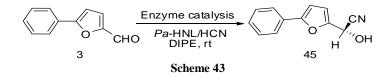


1-(5-Phenylfuran-2-yl)ethanol (44) was prepared by the reaction of 5-phenyl-2-furaldehyde (3) with methyl magnesium bromide CH_3MgCl in absolute Et_2O (yield: 58%) (Scheme 42)⁽⁶³⁾.



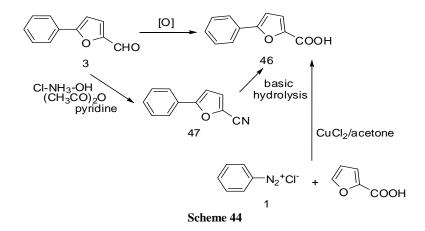
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5-Phenyl-2-furaldehyde (3) was converted to (*S*)-hydroxy(5-phenylfuran-2-yl)acetonitrile (45) by enzyme catalysis (Scheme 43)⁶⁴.

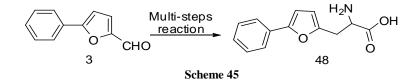


Furancarboxylic acid derivatives

5-Phenyl-2-furancarboxylic acid (46) was prepared *via* the oxidation of 5phenyl-2-furaldehyde (3) or by basic hydrolysis of 5-phenyl-2-furonitrile (47) which was prepared through heating of 3 in pyridine with hydroxyl ammonium chloride in acetic anhydride at temperatures not exceeding $95^{\circ}C^{(65)}$. Also, 5-phenyl-2-furancarboxylic acid (46) can be prepared by coupling of benzene diazonium chloride (1) with 2-furancarboxylic acid in the presence of cupric chloride (Scheme 44)⁽⁶⁶⁾.

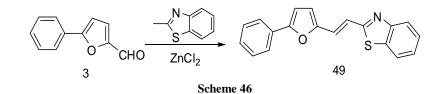


5-Phenyl-2-furaldehyde (3) was transformed into 2-amino-3-(5-phenylfuran-2-yl)propanoic acid (48) *via* multi-steps reaction (Scheme 45)⁽⁶⁷⁾.

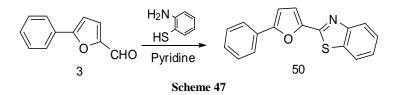


Furyl benzothiazole or benzimidazole derivatives

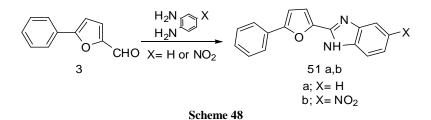
5-Phenyl-2-furaldehyde (3) reacted with 2-methylbenzothiazole in the presence of anhydrous $ZnCl_2$ on heating to 120-180 °C without a solvent to form 2-[2-(5-phenyl-2-furyl)ethenyl]benzothiazole (49) (Scheme 46)⁽⁴⁵⁾.



2-(5-Phenyl-2-furyl)benzothiazole (50) (yield: 25%) was prepared from the reaction of 5-phenyl-2-furaldehyde (3) with *o*-aminothiophenole in pyridine (Scheme 47)⁽⁶⁸⁾.



The cyclization of 5-phenyl-2-furaldehyde (3) with 1,2-phenylenediamine or 4-nitro-1,2-phenylenediamine yielded 2-(5-phenyl-2-furyl)benzimidazole (51a) or 2-(5-phenyl-2-furyl)-5-nitrobenzimidazole (51b), respectively, (Scheme 48)⁽⁶⁹⁾.

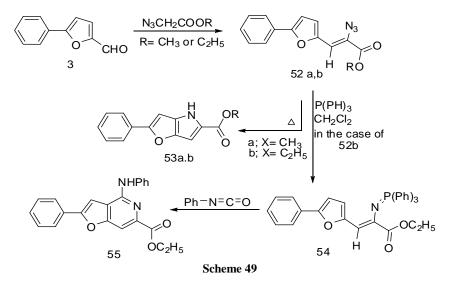


Fused derivatives

The treatment of 5-phenyl-2-furancarbaldehyde (3) with methyl- or ethyl azidoacrylate at 0°C in methanol containing sodium metal gave methyl 2-azido-3- (5-phenyl-2-furyl) acrylate (52a) or ethyl 2-azido-3- (5-phenyl-2-furyl) acrylate (52b), respectively,⁽⁷⁰⁻⁷³⁾. The thermolysis of 52a or 52b in boiling toluene led to methyl 4*H*-2-phenyl-furo [3,2-*b*] pyrrole-5- carboxylate (53a) or ethyl 2-phenyl-furo [3,2-*b*] pyrrole-5-carboxylate (53b), respectively,⁽⁷⁰⁻⁷²⁾. Ethyl 2-azido-3- (5-phenyl-2-furyl) acrylate (52b) reacted with triphenylphosphine in dry dichloromethane to give ethyl 2-triphenylphosphoimino-3-(5-phenyl-2-furyl) acrylate (54) which reacted with phenyl isocyanate in dry toluene under reflux to give ethyl 2-phenyl-4-phenylaminofuro[3,2-*c*]pyridine-6-carboxylate (55) (Scheme 49)⁽⁷³⁾.

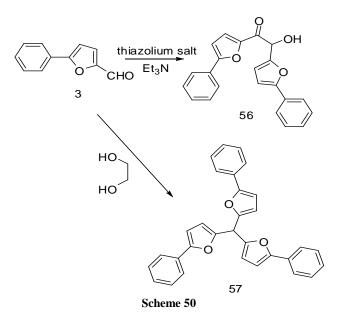
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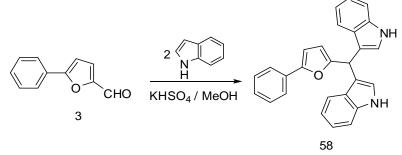
Bis and tris derivatives

The conversion of 5-phenyl-2-furancarbaldehyde (3) into 2-hydroxy-1,2bis(5-phenylfuran-2-yl)ethanone (56) takes place in the presence of a base (Et₃N) and thiazolium salt⁽⁷⁴⁾. Also, 5-phenyl-2-furancarbaldehyde (3) was converted into *tris*(5-phenyl-2-furyl)methane (57) by the reaction with ethylene glycol (Scheme 50)⁽⁷⁵⁾.



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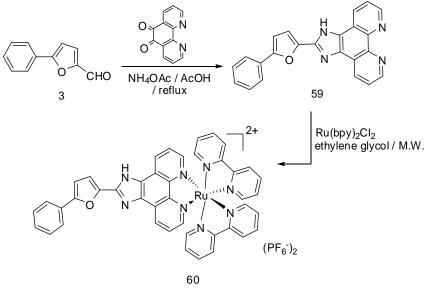
Moreover, 3-((1H-indol-3-yl) (5'-phenylfuran-2'-yl) methyl)-1H-indole (58) (yield: 50%) was obtained by the condensation of 5-phenyl-2-furancarbaldehyde (3) with indole in dry methanol in the presence of potassium hydrogen sulfate (Scheme 51)⁽⁷⁶⁾.





Metal complex

2-(5'-Phenylfuran-2'-yl)-1*H*-imidazo [4,5-*f*][1,1'] phenanthroline (59) (yield: 60%) was prepared by the reaction of 5-phenyl-2-furancarbaldehyde (3) with 1,10-phenanthroline-5,6-dione and ammonium acetate in refluxing glacial acetic acid *via* the Radziszewski reaction. The complex 60 (yield: 96%) was obtained by the direct reaction of the ligand 59 with Ru(bpy)₂Cl₂ in ethylene glycol under microwave irradiation for 2 min (Scheme 52)⁽⁷⁷⁾.



Scheme 52

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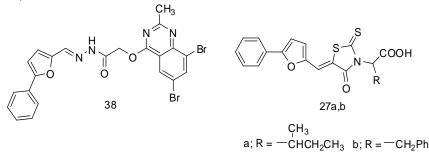
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Biological Activities

5-Phenyl-2-furaldehyde derivatives exhibit a wide spectrum of pharmacological activities.

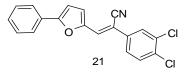
Antibacterial activity

2-[(6,8-Dibromo-2- methylquinazolin-4-yl) oxy]-*N*'- [(5-phenylfuran-2-yl) methylene]acetohydrazide (38) showed good antibacterial activity against Gram positive and Gram negative bacterial species⁽¹²⁾. Also, (*Z*)-3-methyl-2-(4-oxo-5-((5-phenylfuran-2-yl) methylene)-2- thioxothiazolidin-3-yl) pentanoic acid (27a) and (*Z*)-2-(4-oxo-5- ((5-phenylfuran-2-yl) methylene)-2- thioxothiazolidin-3-yl)-3-phenylpropanoic acid (27b), exhibited moderate levels of inhibition against the two Gram-positive bacterial strains (*S. aureus* KCTC 209 and *S. aureus* KCTC 503)⁽⁴⁷⁾.



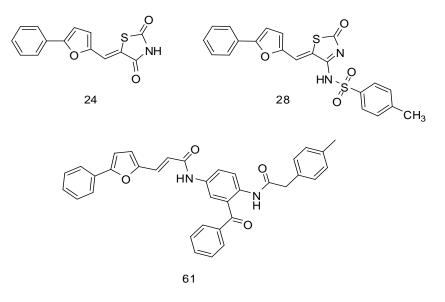
Antitumor activity

(*Z*)-2-(3,4-Dichlorophenyl)-3-(5-phenyl-2-furyl)acrylonitrile (21) was found to have antitumor activity against a panel of eleven cancer cell lines {HT29 and SW480 (colon carcinoma), MCF-7 (breast carcinoma), A2780 (ovarian carcinoma), H460 (lung carcinoma), A431 (skin carcinoma), DU145 (prostate carcinoma), BEC-2 (neuroblastoma), SJ-G2 (glioblastoma), MIA (pancreatic carcinoma) and SMA (spontaneous murine astrocytoma)}⁽¹³⁾.



Inhibition of the enzymes

5-[(5-Phenyl-2-furyl)methylene]thiazolidine-2,4-dione (24) has been found as potent and selective inhibitor of phosphoinositide 3-Kinase $\gamma^{(14)}$. Also, (*Z*)-4-methyl-*N*-(2-oxo-5-((5-phenylfuran-2-yl) methylene)-2,5-dihydrothiazol-4-yl) benzenesulfonamide (28) is an inhibitor of HCV NS5B polymerase⁽¹⁵⁾. Moreover, *N*-[3-benzoyl-4- (4-tolylacetylamino)phenyl]-3-(5-phenyl-2-furyl) acrylic acid amide (61) is an inhibitor of non-thiol farnesyltransferase⁽¹⁶⁾.



Conclusion

5-Phenyl-2-furaldehyde has high chemical reactivity due to the presence of the formyl group. This survey is attempted to summarize the synthetic methods, reactions and pharmacological activities of 5-phenyl-2-furaldehyde from 1950 till 2014. From this review, it can be concluded that 5-phenyl-2-furaldehyde and its derivatives display a wide range of pharmacological activities, *e.g.* antimicrobial and antitumor. They also show inhibition of the enzymes, especially phosphoinositide 3-Kinase γ , HCV NS5B polymerase and non-thiol farnesyltransferase. For that, 5-phenyl-2-furaldehyde and its derivatives have attracted increasing attention of the scientists for the search of new potent pharmacological activity and medicinal activities.

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5-فينيل-2-فيور الدهيد: تحضير وتفاعلات والأنشطة البيولوجية

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نظراً لأهمية المركب 5-فينيل-2-فيورالدهيد فى تحضير المركبات الحلقية غير المتجانسة والتى تتميز بخواصها البيولوجية والطبية المتعددة كمضادات للميكروبات والأورام وغيرها فقد قمنا فى هذا البحث المرجعى بالتركيز على بعض طرق تحضيره وتفاعلاته مع مركبات مختلفة بالإضافة إلى أنشطته البيولوجية.