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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF 3-(2'-n-BUTYLBENZOFURAN-3'-YL)-5-ARYL-4, 5-DIHYDRO-1*H*-PYRAZOLES

RAKESH P.N.ROSHAN[1], D.M.PUROHIT[2], SANDIP K.MATARIYA[*]

1. R.K.University, Rajkot, (Guj), India
2. Shri M&N. Virani Science College, Department of Chemistry, Kalawad Road, Rajkot-390005, (Guj), India

* Smt.S.M.Panchal Science College, Department of Chemistry , Talod, (Guj), India

Email: rroshansrs@gmail.com

ABSTRACT:

3-(2'-n-butylbenzofuran-3'-yl)-5-aryl-4, 5-dihydro-1*H*-pyrazoles (4a-4k) have been synthesized. The synthesized products have been assayed for their antimicrobial activity against Gram+ve, Gram-ve bacteria and fungi. All the synthesized products were assigned with IR, ^{1}HNMR, Mass Spectra, TLC, and elemental analysis. Some of the products showed moderate activity, compare with known standard drugs.

INTRODUCTION:

Pyrazolone derivatives showed a vital role largely due to the wide ranging of biological activities. Taking into consideration diverse biodynamic activities such as antimicrobial[1] , antiinflammatory[2-3] , antiallegic[4],anticonvulsant[5],antidiabetic[6] ,antiimplantation[7], antitumor[8], antineoplastic[9],analgesic[10-11],fungicidl[12-13],bactericidal[14-15],herbicidal[16],cardiovascular[17], antiamoebic[18],tranquiliser[19] etc. In this fact to interesting biological activities, it appeared to interest to synthesized some new Pyrazolines (4a-4k)have been synthesized by the condensation

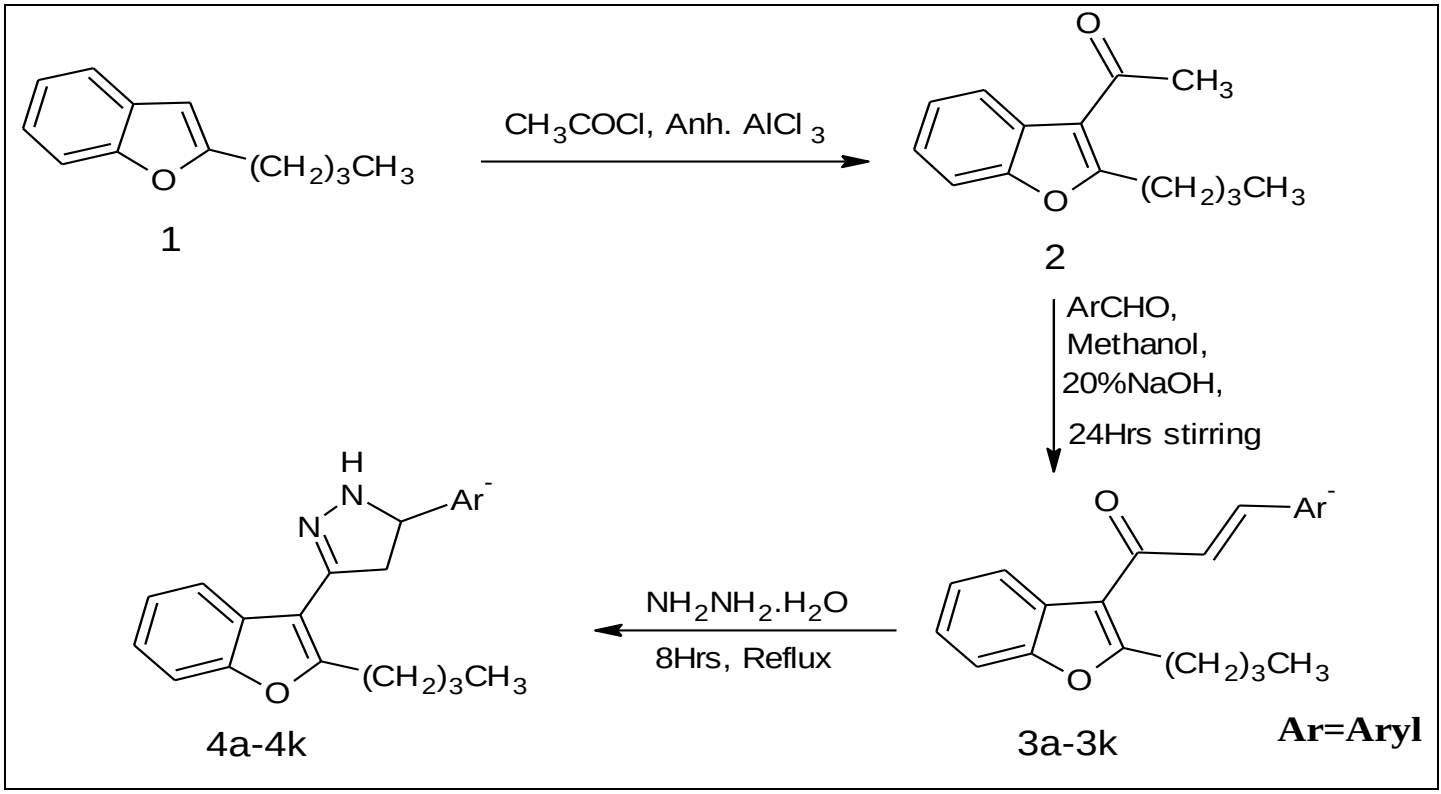
of (E)-1-(2'-n-butylbenzofuran-3'-yl)-3-aryl-prop-2-ene-1- ones with hydrazine hydrate. Chalcones (3a-3k) have been synthesized by the condensation of 1-(2'-n-butylbenzofuran-3'-yl)ethanone with aromatic aldehyde in the presence of aqueous NaOH, 1-(2'-n-butylbenzofuran-3'-yl)ethanone have been synthesized by the acetylation of 2-n-butylbenzofuran with acetyl chloride in the presence of anhydrous $AlCl_3$. The products (4a-4k) were assigned with IR, ^{1}HNMR, Mass Spectra, TLC and Elemental analysis. The physical data recorded in Table no: I. Antimicrobial activity of synthesized compounds represented in Table no: II and comparable antimicrobial compared with known standard drugs represented in Table no: III.

ANTIMICROBIAL ACTIVITY:

All the products (4a-4k) were tested for their antimicrobial activity by Cup-plate method[20] against the Gram positive Bacteria *Bacillus megaterium*; *S.aureus*, Gram negative bacteria *Escherichia coli*, *S.Taphimarium* and for antifungal activity against *Aspergillus niger*, *Anrobacter awamori* at a concentration of 50µg/ml, using DMF as a solvent. After 24hrs of incubation at 37°C, the zone of inhibition were measured in mm. The activity was compared with known standard drugs viz. Ampicillin, Chloramphenicol, Norfloxacin, Fluconazole at the same concentration (50µg/ml) which is represented in Table no II.

All the synthesized compounds (4a-4k) showed moderate to good and remarkable activities with compared to known standard drugs at same concentration which is represented in Table no III.

REACTION SCHEME



EXPERIMENTAL SECTION:

All the melting points were measured in open glass capillary method and are uncorrected. IR absorption Spectra (in cm^{-1}) were recorded on a SHIMADZU IR-435 spectrophotometer using KBr pellet method , ^{1}HNMR spectra on BRUKER (300mHz) spectrometer using DMSO as internal standard (chemical shift in δppm) and Mass spectra on a Jeol-JMSD 300 Mass spectrometer at 70ev. The purity of compounds were routinely checked by TLC method using silica gel G.

(1) Synthesis of 1-(2'-n-butylbenzofuran-3'-yl)ethanone

Methylene dichloride (20ml) was chilled to 0-5°C. Anhydrous Aluminium chloride (2.0gm, 0.015mol) and acetyl chloride (1.0ml, 0.15mol) were added slowly drops by drops at 0-5°C. Reaction mixture was stirred at 0-5°C for 30minutes. 2'-n-butylbenzofuran (1.74gm, 0.01mol)was added slowly to the reaction mass at 0-5°C. After completion of addition, temperature of reaction mass was raised up to 30-35°C. Reaction mixture was stirred at 30-35°C for 4hrs. After completion of the reaction, the reaction mixture was poured in to ice cold water.

Layers were separated. Methylene dichloride layer was washed with water. To get required product from Methylene dichloride layer, Methylene dichloride distilled out under reduced pressure. 2-n-butylbenzofuran-3-yl ethanone oily product is formed. Yield: 85.00%, B.P.:87°C

(2) Synthesis of (E)-1-(2'-n-butylbenzofuran-3'-yl)-3-(4''-methoxyphenyl)-prop-2-ene-1-one (3e).

1-(2'-n-butylbenzofuran-3'-yl)ethanone (2.16gm, 0.01m),4-Methoxybenzaldehyde (1.36gm, 0.01m), methanol(20ml), 20% NaOH (20ml). The reaction mixture was stirred for 24 hrs. at room temperature. Completion of reaction checked with TLC. The reaction mixture was poured into crushed ice, filtered and dried. Yield:78.28% ; M.P.:161°C; (Required: C:79.04;H:6.58%; , $C_{22}H_{22}O_3$; Found: C:79.04 ;H:6.58%;). IR(KBr)(cm^{-1}): 2968(C-H Str. Asym);2832(C-H Str. Sym);1457(C-H Str. Def); 3047(C-H Str., aromatic);1537(C=C-Ring skeletal);1189(C-H Str., i.p.def);728(C-H Str., o.o.P.def); 1680 (C=0 str.); 1138(C-O-C); 1620(-CH=CH Str.); ^{1}HNMR: (δ ppm^{1}HNMR (δ ppm):0.85-0.89(3H,t,-C<u>H</u>$_3$);1.22-1.30(2H,m,-C<u>H</u>$_2$-CH$_3$);1.32-1.66(2H,q,-C<u>H</u>$_2$-CH$_2$-CH$_3$);2.51-2.66(2H,t,C<u>H</u>$_2$-CH$_2$-CH$_2$-CH$_3$);3.84(3H,s,-OC<u>H</u>$_3$);6.97-7.86(10H,m,Ar-<u>H</u>).

m/z:334,327,311,301,281,269,246,230,210,209,183,167,144,139,121,108,91,77,64,44,41.

Similarly other Chalcones (3a-3k)have been synthesized.

(3) Synthesis of 3-(2'-n-butylbenzofuran-3'-yl)-5-(4''-methoxyphenyl)-4, 5-dihydro-1*H*-pyrazole

(4e).

(E)-1-(2'-n-butylbenzofuran-3'-yl)-3-(4''-methoxyphenyl)-prop-2-ene-1-one (3.34gm, 0.01 mol) in methanol (5 ml) was added hydrazine hydrate (0.8 ml, 0.15 mol) and refluxed in water bath for 8 hrs. After completion of the reaction, the reaction mixture was poured into crushed ice water. The ppts are formed, filter it, dry it. The product is crysrallized in methanol. Yield:88.28% ; M.P.:177°C (Required: C:75.64;H6.87;N:8.04%; $C_{22}H_{24}O_2N_2$; Found: C:75.60 ;H;6.85;N:8.01%). IR(KBr)(cm^{-1}): 2965(C-H Str. Asym);2829(C-H Str. Sym);1459(C-H Str. Def); 3050(C-H Str., aromatic);1535(C=C-Ring skeletal);1248(C-H Str., i.p.def);758(C-H Str., o.o.P.def);1325 (C-N Str.);1177(C-O-C); 1578(C= N Str.); 3311(-N-H Str.); 1628(-N-H bending); ^{1}HNMR (δ ppm): ^{1}HNMR (δ ppm):0.85-0.89(3H,t,-C<u>H</u>$_3$);1.24-1.30(2H,m,-C<u>H</u>$_2$-CH$_3$);1.58-1.64(2H,q,-C<u>H</u>$_2$-CH$_2$-CH$_3$);2.50-2.66(2H,t,C<u>H</u>$_2$-CH$_2$-CH$_2$-CH$_3$);3.82(3H,s,-

OC<u>H</u>$_3$);6.96-7.65(12H,m,Ar-<u>H</u>).

m/z:349,343,327,301,268,237,209,186,171,157,144,144(BP),135,121,108,88,80,64,54,41,40.

Similarly other Pyrazolones (4a-4k) have been synthesized. The physical data of compounds represented in Table-I and antimicrobial activity of compounds (4a-4k) have been represented in Table-II and comparable antimicrobial activity of synthesized compounds represented in Table-III.

Table-I

The physical data of compounds (4a-4k)

Compounds	Ar	Molecular formula	M.P. °C	% Yield	%Nitrogen	
					Calculated	Found
4a	C_6H_5-	$C_{21}H_{22}ON_2$	153	78.91	8.79	8.71
4b	2-Cl-C_6H_4-	$C_{21}H_{21}ON_2Cl$	148	82.83	7.94	7.92
4c	4-Cl-C_6H_4-	$C_{21}H_{21}ON_2Cl$	157	83.02	7.94	7.85
4d	4-F-C_6H_4-	$C_{21}H_{21}ON_2F$	162	85.15	8.32	8.26
4e	4-OCH_3- C_6H_4-	$C_{22}H_{24}O_2N_2$	177	88.28	8.04	8.01
4f	2,5-$(OCH_3)_2$- C_6H_3-	$C_{23}H_{26}O_3N_2$	165	79.57	7.40	7.35
4g	3,4-$(OCH_3)_2$- C_6H_3-	$C_{23}H_{26}O_3N_2$	189	82.74	7.40	7.37
4h	3,4,5-$(OCH_3)_3$- C_6H_2-	$C_{24}H_{28}O_4N_2$	208	51.62	6.85	6.81
4i	2-OH-C_6H_4-	$C_{21}H_{22}O_2N_2$	179	91.83	8.37	8.36
4j	3-NO_2-C_6H_4-	$C_{21}H_{21}O_3N_3$	183	92.03	11.55	11.51
4k	4-NO_2-C_6H_4-	$C_{21}H_{21}O_3N_3$	198	90.83	11.55	11.53

Table-II

Compounds	Ar.	Antibacterial activity Zone of inhibition in mm				Antifungal activity Zone of inhibition in mm	
		Gram +ve bacteria		Gram –ve bacteria			
		B.mega	***S.aureus***	***E.coli***	***S.Taphimarium***	***A. niger***	***A. awamori***
4a	C_6H_5-	14	13	16	12	11	13
4b	2-Cl-C_6H_4-	18	**19**	**20**	17	**19**	**20**
4c	4-Cl-C_6H_4-	17	**20**	**22**	18	**21**	17
4d	4-F-C_6H_4-	18	**23**	**21**	**19**	**20**	**21**
4e	4-OCH_3- C_6H_4-	15	15	17	**20**	14	15
4f	2,5-$(OCH_3)_2$- C_6H_3-	**19**	16	15	18	17	16
4g	3,4-$(OCH_3)_2$- C_6H_3-	14	17	16	15	15	18
4h	3,4,5-$(OCH_3)_3$- C_6H_2-	**20**	**19**	18	**19**	16	17
4i	2-OH-C_6H_4-	18	14	13	15	**20**	**21**
4j	3-NO_2-C_6H_4-	17	13	15	18	**22**	**19**
4k	4-NO_2-C_6H_4-	15	17	16	**19**	**23**	**22**

Table-III

Comparable antimicrobial activity:

(Compared with known standard drugs.)

Compounds	Maximum antimicrobial activity Zone of inhibition in mm					
	B.mega	***S.aureus***	***E.coli***	***S.Taphimarium***	***A. niger***	***A. awamori***
(4a-4k) (50µg/ml)	4f,4h	4b,4c,4d, 4h	4b,4c,4d	4d,4e,4h,4k	4b,4c,4d,4 I,4j,4k	4b,,4d,4i,4j,4k
Ampicillin 50µg/ml	22	21	20	21	-	-
Chloramphenicol 50µg/ml	21	22	23	20	-	-
Norfloxacin 50µg/ml	23	20	22	21	-	-
Fluconazole 50µg/ml	-	-	-	-	21	21

CONCLUSION:

The compounds 3-(2'-n-butylbenzofuran-3'-yl)-5-(4''-methoxyphenyl)-4, 5-dihydro-1*H*-pyrazoles (4a-4k) have been synthesized. Some of the compounds **4b, 4c, 4d, 4k** showed good remarkable antibacterial and antifungal activity with compared with known standard drugs e.g: Ampicillin, Chloramphenicol, Norfloxacin and Fluconazole.

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