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3-(Substituted Aryl)-1-benzofuranyl-2-propenones: Antimicrobial Properties of Some Chalcones-Type Compounds and their 2-Pyrazoline Derivatives

DEMET COŞKUN[§*], MISIR AHMEDZADE[§] and SEVDA KIRBAĞ

[§]University of Fırat, Faculty of Science and Arts
Department of Chemistry, 23119 Elazığ-Turkey

University of Fırat, Faculty of Science and Arts
Department of Biology, 23119 Elazığ-Turkey

dcoskun@firat.edu.tr

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Abstract: 2-Acetylbenzofuran on condensation with furan-2-carboxaldehyde and pyrrole-2-carboxaldehyde in methanolic KOH solution yielded the corresponding benzofuran chalcones. These two compounds and nine benzofuran chalcones were synthesized before, were further reacted with hydrazine hydrate in ethanol which led to the formation of 2-pyrazoline derivatives. All the synthesized compounds were characterized by elemental analysis, melting point determination, infrared spectroscopy and nuclear magnetic resonance spectroscopy. Nine chalcone-type compounds and eleven 2-pyrazolines were evaluated for their biological activities against the six bacteria and the three yeast and it was seen that thirteen compounds showed activity. Four of them are chalcone-type compounds showed more or less activity

Keywords: Benzofuran, Chalcone, Pyrazoline, Antimicrobial, Antifungal

Introduction

The various activities of the compounds possessing benzofuran, chalcone and pyrazoline moiety are well known. The pyrazoline function is quite stable and has inspired chemists to utilize this stable fragment in bioactive moieties to synthesize new compounds possessing biological activities. Chalcones have various biological activities such as antioxidant[1,2], cytotoxic[3], antiviral[4,5], tyrosinase inhibitory[6], antimalarial[7,8], antibacterial[9,10] and anti-inflammatory[11,12]. Pyrazolines have been also reported to show a broad spectrum of biological activities including antibacterial[13,14], antifungal[15], antioxidant[14], anti-inflammatory[15,16], cytotoxic[17], antidepressant[18], anti-tumoral[19] and hypotensive[20] activities.

There are lots of environmental bacteria capable of causing a variety of life threatening human infections. In this study, synthesis and characterization of two newly synthesized chalcone-type compouns, 1-(benzofuran-2-yl)-3-(furan-2-yl)-2-propenone **(1j)** and 1-(benzofuran-2-yl)-3-(pyrrol-2-yl)-2-propenone **(1k)** are described. Preparation of 2-pyrazolines derivatives (**2a-k**) of these two compounds and the previously synthesized nine chalcone-type compounds[21] are reported. These chalcones and their 2-pyrazoline derivatives were screened for their biological activities against six bacteria and three yeast.

Experimental

All chemicals were purchased from Fluka and Aldrich. All melting points were measured using a differential scanning calorimeter (Shimadzu DSC-50) and are uncorrected. Elemental analyses were performed on a Leco CHNS-932 apparatus. ^{1}H- and ^{13}C NMR spectra were recorded on a Bruker AC 300 (300 MHz) and a Varian Mercury-Plas NMR (400 MHz) in the specified deuterated solvents. Chemical shifts were expressed in ppm from internal tetramethysilane. Infrared (IR) spectra were recorded as KBr pellets on a Perkin-Elmer Spectrum One FTIR spectrometer.

*General method for the synthesis of 3-(substituted aryl and heteroaryl)-1-benzofuranyl-2-propenones (**1j** and **1k**)*

To a mixture of 2-acetylbenzofuran (2.187 g, 13.6 mmol) and the appropriate aldehyde (13.6 mmol) in methanol (25 mL) a solution of sodium hydroxide (1 M, 18 mL) was added. The reaction mixture was stirred for 3 h on a magnetic stirrer at room temperature and was allowed to stand in refrigerator for overnight. The product was precipitated by pouring to 250 mL of cold water, was filtered and dried and crystallized from ethanol.

*General method for the synthesis of 3-(2-benzofuranyl)-5-aryl and heteroaryl-2-pyrazolines (**2a-k**)*

The pyrazolines were synthesized as follow; Compounds **2a-k**: The required chalcone-type compound (example, **1a**, 1.320 g, 5 mmol) was suspended in absolute ethanol (10 mL) and stirred at room temperature. hydrazine hydrate (0.375 g, 7.5 mmol) was added and the mixture stirred at reflux for 30 min. Upon cooling, the mixture was poured to cold water (500 mL) and the precipitate was filtered off and washed with water and dried. The product (**2a**) was crystallized from ethanol solution, yield: 1.029 g, 74%, mp: 211 ^{o}C.

The reflux time in the transformation of the chalcones to the pyrazolines varied from 10 to 60 min according to the kinds of the chalcones (10 min for **2j** and **2e,** 15 min for **2k**, 30 min **2c** and **2i**, 40 min for **2a,2b,2d**, **2f** and **2 h** and 60 min for **2g**).

Evaluation of biological action

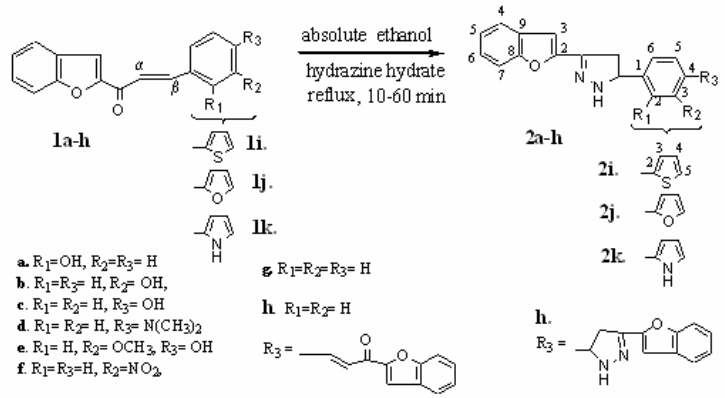
Six bacteria and three yeast were used as test organisms. These bacteria were *Staphylococcus aureus* COWAN 1, *Pseudomonas aeruginosa* DMS 50071 SCOTTA, *Proteus vulgaris* FMC 1, *Escherichia coli* ATCC 25922, *Klebsiella pneumoniae* FMC, *Bacillus megaterium* DMS 32, and the yeasts were *Candida albicans* FMC 17, *Candida glabrata* ATCC 66032 and *Candida tropicalis* ATCC 13803.

All of the synthesized compounds were screened against six bacteria and three yeasts using the method given in literature[22]. The bacteria strains were inoculated into nutrient broth and yeast strain inoculated into malt extract broth for 24 and 48 h, respectively. In the disc- diffusion method, sterile Mueller-Hinton agar for bacteria and Malt extract agar for yeasts

were separately inoculated with the test bacteria (10^5 bacteria per mL) and yeasts (10^4 yeast per mL). In order to prepare the disc a part containing 1000 μg of compound from its solution in DMSO was added onto the discs. In addition, disk containing DMSO were placed (10 μL). Discs were applied on the solid agar medium by pressing slightly. Petri dishes were placed at 4 °C for 2 h. The bacteria samples were incubated at 35±0.1 °C for 24 h and yeast samples were incubated at 25±0.1 °C for 72 h. At the end of the period, inhibition zones were measured in millimeter. The inhibition zone of compound was calculated by subtracting that of pure DMSO from the zone of solution in DMSO of the compound.

Results and Discussion

This work is the second part of the studies on 3-(substituted aryl)-1-benzofuranl-2-propenones and describes the synthesis and characterization of 2–pyrazoline derivatives (**2a-k**) from the chalcones (**1a-i**) given previously[21] and two new chalcones (**1j** and **1k**) (Scheme 1) and the biological activities of the twenty products. The synthesized chalcones compounds were suspended in absolute ethanol, hydrazine hydrate was added and the mixture stirred at reflux for a period of 10-60 min as depending on the kind of chalcones. The cyclization of chalcones were carried out at a short period of time[13,14]. The cyclization of some chalcones with hydrazine hydrate was required to make a reflux of 7 h in ethanol[13]. 2-Pyrazoline derivatives were formed in 74-90 % yields[13]. The yields in formation of 3-(benzofuran-2-yl)-5-(3-nitrophenyl)-2-pyrazoline (**2f**) and bispyrazoline (**2h**) are 60% and 45%, respectively and relatively low.



Scheme 1. **2-**Pyrazoline derivatives of some chalcone-type compounds

Structural characterization (FTIR, ^{1}H- and ^{13}C-NMR)

The newly synthesized two benzofuran chalcones (**1j** and **1k**) showed the characteristic absorption bands at 1659 cm^{-1} (C=O stretching in **1j**), at 1648 cm^{-1} (C=O stretching in **1k**), at 3000-3150 cm^{-1} (=C-H stretching in furan ring) and at 3284 cm^{-1} (N-H stretching vibration in pyrrole ring) in FTIR spectra. In ^{1}H-NMR, the signals of olefinic β-H and α-H on double bond conjugated to the carbonyl group were seen at 7.68 and 7.46 ppm as the both doublet (J≈15.02 Hz) for **1j** and at 7.68 and 7.52 ppm as the both doublet (J≈15.60 Hz) for **1k**.

The disappearance of carbonyl absorptions between 1660-1640 cm^{-1} in FT-IR spectra of chalcones[21] and arising a new band between 3290-3360 cm^{-1} (NH stretching vibration) confirm the cyclization to 2-pyrazoline derivatives of the chalcones. ^{1}H-NMR spectra of 2-pyrazolines derivatives show a signal due to NH proton between 8.09-6.92 ppm as depending on substituted aromatic group bonded to pyrazoline ring at 5-position.

Vicinal coupling constants of NH proton with pyrazoline ring proton at 5-position were in the range of 1.60-2.54 Hz. ^{13}C NMR spectra of two pyrazolines (**2b** and **2i**) have also been taken and they show characteristic signals for 2-pyrazoline ring carbons at about 151 ppm (C=N carbon), at about 41 ppm (CH_2 ring carbon) and at about 60 ppm (CH ring carbon).

Biological activity

All the synthesized chalcones and pyrazolines, except **1j** and **1k**, were screened *in vitro* for antibacterial activity against *Staphylococcus aureus COWAN 1*, *Pseudomonas aeruginosa DMS 50071 SCOTTA*, *Proteus vulgaris FMC 1*, *Escherichia coli ATCC 25922*, *Klebsiella pneumoniae FMC*, *Bacillus megaterium DMS 32* at absorbed 1000 µg per disc and for antifungal activity against *Candida albicans* FMC 17, *Candida glabrata* ATCC 66032 and *Candida tropicalis* ATCC 13803 at 1000 µg per disc by agar diffusion method[22] given in detail in experimental section .

Antibacterial and antifungal activities of the obtained compounds were measured as a function of diameter of zone of inhibition (mm). DMSO used as control showed activity at different ratios against the strains of all the bacteria and yeast. The results were compared with standard drugs amoksilin for antibacterial activitiy and nystatin for antifungal activity by measuring the zone of inhibition in mm at 1000 µg. Compound **2j** was found most effective of the synthesized compounds against *S. aureus* with zone of inhibition 23 mm, compound **1a** is the most effective against *P. aeruginosa* and *P. vulgaris* with zone of inhibition 16 mm, **2k** is the most effective against *K. pneumoniae* and *E. coli* with zone of inhibition 18 mm and 17 mm, respectively, and compound **1a** is the most effective among the synthesized compounds against *B. megaterium* with zone of inhibition 27 mm. The compound **2j** exhibited the maximum diameter of zone of inhibition against *C. albicans*, *C. glabrata* and *C. tropicalis* (21 mm, 23 mm and 20 mm, respectively). Compounds **1d**, **1f**, **1g**, **1h**, **1i**, **2d** and **2h** showed no activity against the strains of all the bacteria and the yeast used in the work. Although compounds **1a**, **2f**, **2g** and **2i** showed an activity against most bacteria, they showed no activity against the yeast. The results of the antibacterial and antifungal activity are given in Table 1.

Table 1. Antimicrobial and antifungal studies of synthesized compounds

Bacteria/Yeast	Zone of inhibition/ mm														
	Compound numbers														
	1a	**1b**	**1c**	**1e**	**2a**	**2b**	**2c**	**2e**	**2f**	**2g**	**2i**	**2j**	**2k**	**S***	**D**
S. aureus	13	10	-	-	13	13	13	10	9	12	10	23	19	38	10
P. aeruginosa	16	15	10	10	12	15	9	14	9	14	10	9	10	28	8
P. vulgaris	16	15	11	9	13	13	11	9	-	-	9	10	14	30	8
E. coli	12	10	10	11	15	10	13	10	-	-	13	-	17	34	8
K. pneumoniae	15	11	9	-	10	11	13	9	9	9	10	-	18	25	9
B. megaterium	27	13	10	10	13	15	12	10	9	11	11	20	19	30	9
C. albicans	-	11	10	10	10	9	11	11	-	-	-	21	20	27	9
C. glabrata	-	-	10	11	10	9	15	14	-	-	-	23	19	32	10
C. tropicalis	-	18	10	10	10	9	11	11	-	-	-	20	18	32	9

**Antiacterial Standard Drag: Amoksilin 1000 µg, Antifungal Standard Drag: Nystatin 1000 µg D: DMSO*

Another striking result is to show more or less activity against all the bacteria and the yeast of compounds **2a**, **2b**, **2c**, **2e** and **2k** which are pyrazolines with hydroxyl group moiety on the phenyl ring of their first four and the last is a pyrazoline having pyrrole ring. Compound **1a** possessing hydroxyl group on *ortho* position of phenyl ring has shown very good antibacterial activity against *B. megaterium* and the activity is comparable with that of the standard drug (amoksilin) (with 90% inhibition of that of the standard). Compound **1a** against other bacteria and compounds **1b**, **2a**, **2b**, **2c**, **2i** and **2k** against all the bacteria showed moderate activity with 30-63% inhibition of that of the standard drug. While compound **2j** and **2k** showed high antifungal activity against *Candida albicans, Candida glabrata* and *Candida tropicalis*, with 56-78% inhibition of that of the standard drug (nystatin), compounds **1c**, **1e**, **2a**, **2b**, **2c** and **2e** showed moderate activity against all of the three yeast, with 28%-47% inhibition of that of the standard. The results obtained for antibacterial and antifungal activities of 2-pyrazoline derivatives used in this study are comparable with the values given in literature for some 2-pyrazolines[23].

Spectral Analysis of Compounds

1-(Benzofuran-2-yl)-3-(furan-2-yl)-2-propenon ***(1j)***

Yield: 77%; m.p.122-124 ^{o}C. FTIR (KBr, cm^{-1}): 3000-3150 (=C-H stretching in furan), 1659 (C=O), 1597, 1563, 743; ^{1}H-NMR (300 MHz, DMSO-d$_6$), ppm : 7.71 (d, J= 7.3 Hz, 1H, b4-H), 7.68 (d, J= 14.9 Hz, 1H, β-H), 7.62 (d, J= 1.8 Hz, 1H, f5-H), 7.61 (d, J= 8.5 Hz, 1H, b7-H), 7.55 (s, 1H, b3-H), 7.47 (dt, J= 8.5 and 1.2 Hz, 1H, b6-H), 7.46 (d, J= 15.1 Hz, 1H, α-H), 7.31 (t, J= 8.2 Hz, 1H, b-5H), 6.76 (d, J= 3.5 Hz, 1H, f3-H), 6.52 (dd, J= 3.4 and 1.8 Hz, 1H, f4-H). ^{13}C-NMR, ppm : 178.6 (C=O), 155.7 (b8-C), 153.6 (b2-C), 151.4 (f2-C), 147.0 (f5-C), 130.4 (β-C), 129.0 (b6-C), 127.5 (b5-C) , 124.6 (b4-C), 124.2 (α-C), 121.1 (b9-C), 118.9 (b3-C), 118.3 (f3-C), 114.8 (b7-C), 112.7 (f4-C). Anal. Calcd. For $C_{15}H_{10}O_3$: C, 75.62; H, 4.23% Found C, 75.32; H, 4.27%.

1-(Benzofuran-2-yl)-3-(pyrrol-2-yl)-2-propenon ***(1k)***

Yield: 50%; m.p.196-198 ^{o}C. FTIR (KBr, cm^{-1}): 3284 (N-H stretching), 1648 (C=O), 1579, 1550, 740 ;^{1}H-NMR (300 MHz, DMSO-d$_6$), ppm: 7.86-7.90 (m, 2H, b3, b4-H), 7.74 (dd, J= 8.3 and 0.8 Hz, 1H, b7-H), 7.68 (d, J= 15.7 Hz, 1H, β-H), 7.55 (dt, J= 7.8 and 1.2 Hz, 1H, b6-H), 7.5 (d, J= 15.5 Hz, 1H, α-H), 7.4 (dt, J= 7.5 and 0.8 Hz, 1H, b5-H), 7.19 (broad signal, 1H, pyrrole-5-H), 6.81 (dd, J= 1.8 and 1.5 Hz, 1H, pyrrol-4-H), 6.27 (broad signal, 1H, pyrrole-3-H). Anal. Calcd. For $C_{15}H_{11}NO_2$: C, 75.94; H, 4.67; N, 5.90% Found C, 75.55; H, 4.70; N, 6.20%.

3-(Benzofuran-2-yl)-5-(2-dihydroxphenyl)-2-pyrazoline ***(2a)***

Yield: 74%; m.p.210-212 ^{o}C. FTIR (KBr, cm^{-1}) : 3437 (O-H), 3335 (N-H), ; ^{1}H-NMR (300 MHz, DMSO-d$_6$), ppm: 9.64 (s, 1H, OH), 7.81 (d, J= 2.0 Hz, ,1H,NH), 7.56-7.63 (m, 2H, b4, b7-H), 7.32 (dt, J= 7.7 and 1.4 Hz, 1 H, b6-H), 7.25 (m, 2H, b5, 6-H), 7.09 (dt, J= 7.7 and 1.7 Hz, 1H, 4-H), 7.02 (s, 1H, b3-H), 6.85 (dd, J= 8.0 and 1.0 Hz, 1H, 3-H), 6.67 (ddd, J= 8.0 , 2.4 and 0.6 Hz, 1H, 3-H), 5.08 (dt, J= 10.3 and 1.9 Hz, 1H, p5-H), 3.45 (dd, J= 16.1 and 10.8 Hz, 1H, p4-H), 2.78 (dd, J= 16.1 and 9.7 Hz, 1H, p4-H). ^{13}C-NMR, ppm : 155.1 (b8-C), 154.8 (2-C), 151.1 (p3-C), 140.6 (b2-C), 128.7 (6-C), 128.7 (1-C), 128.5 (b9-C), 126.9 (4-C), 125.3 (b6-C), 123.7 (b5-C), 121.6 (b4-C), 119.4 (5-C), 115.5 (3-C), 111.5 (b7-C), 105.4 (b3-C), 58.8 (p5-C), 39.5 (p4-C). Anal. Calcd. For $C_{17}H_{14}N_2O_2$: C, 73.37; H, 5.07; N, 10.07% Found C, 73.75; H, 4.85; N, 9.88%.

3-(Benzofuran-2-yl)-5-(3-dihydroxphenyl)-2-pyrazoline ***(2b)***

Yield: 80%; m.p.219-221 ^{o}C. FTIR (KBr, cm^{-1}):3410 (O-H), 3335 (N-H); ^{1}H-NMR (300 MHz, DMSO-d$_6$), ppm: 9.41 (s, 1H, OH), 7.85 (d, J= 2.0 Hz, 1H,NH), 7.57-7.64 (m, 2H,

b4, b7-H), 7.35 (dt, J= 7.6 and 1.4 Hz, 1 H, b6-H), 7.25 (dt, J= 7.5 and 1.1 Hz, 1H, b5-H), 7.14 (t, J= 7.9 , 1H, 5-H), 7.02 (s, 1H, b3-H), 6.78-6.80 (m, 2H, 2,5-H), 6.67 (ddd, J= 8.0 , 2.4 and 0.6 Hz, 1H, 6-H), 4.83 (dt, J= 10.4 and 2.2 Hz, 1H, p5-H), 3.45 (dd, J= 16.1 and 10.8 Hz, 1H, p4-H), 2.86 (dd, J= 16.2 and 10.0 Hz, 1H, p4-H). ^{13}C-NMR, ppm : 157.1 (3-C), 154.8 (b8-C), 151.0(p3-C), 144.6 (b2-C), 140.1 (1-C), 129.9 (5-C), 128.7 (b9-C), 125.4 (b6-C), 123.7 (b5-C), 121.6 (b4-C), 117.6 (6-C), 114.7 (2-C), 113.6 (4-C), 111.5 (b7-C), 105.4 (b3-C), 64.0(p5-C), 40.8(p4-C). Anal. Calcd. For $C_{17}H_{14}N_2O_2$: C, 73.38; H, 5.04; N, 10.07% Found C, 73.82; H, 5.15; N, 9.97%.

3-(Benzofuran-2-yl)-5-(4-dihydroxphenyl)-2-pyrazoline ***(2c)***

Yield: 76%; m.p.182-184 °C. FTIR (KBr, cm^{-1}) :3430 (O-H), 3358 (N-H), 1610, 808, 750; ^{1}H-NMR (400 MHz, $CDCl_3$), ppm: 7.56 (d, 1H, J= 8.5 Hz, b4-H), 7.51 (d,1H, J= 7.2, b7-H), 7.31 (dt, J= 8.2 and 1.3 Hz, 1H, b6-H), 7.20-7.24 (m,5H, b3,b5,NH,2-H), 6.78-6.84 (m, 3H, OH, 3,5-H), 4.92 (dt, J= 9.6 and 1.8 Hz, 1H, p5-H), 3.45 (dd, J= 16.3 and 10.7 Hz, 1H, p4-H), 3.05 (dd, J= 16.3 and 9.9 Hz, 1H, p4-H). Anal. Calcd. For $C_{17}H_{14}N_2O_2$: C, 73.38; H, 5.04; N, 10.07% Found C, 73.25; H, 5.12; N, 9.78%.

3-(Benzofuran-2-yl)-5-(4-N,N-dimethylaminophenyl)-2-pyrazoline ***(2d)***

Yield: 78%; m.p.161-163 °C. FTIR (KBr, cm^{-1}) :3343 (N-H), 1611, 829; ^{1}H-NMR (300 MHz, DMSO-d_6), ppm: 7.83 (d, J= 2.3 Hz, ,1H,NH), 7.63 (d, J= 7.5 Hz , 1H,b4-H), 7.57 (d, J= 7.8 Hz, 1H, b7-H), 7.32 (dt, J= 7.8 and 1.5 Hz, 1 H, b6-H), 7.25 (dt, J= 7.5 and 1.1 Hz, 1H, b5-H), 7.18 (d, J= 8.7 , 2H, 2,6-H), 7.01 (s, 1H, b3-H), 6.70(d, J= 8.8 Hz, 2H, 3,5-H), 4.81 (dt, J= 10.5 and 2.3 Hz, 1H, p5-H), 3.38 (dt, J= 16.1 and 10.7 Hz, 1H, p4-H), 2.85 (dd, J= 16.3 and 10.5 Hz, 1H, p4-H). Anal. Calcd. For $C_{19}H_{19}N_3O$: C, 74.73; H, 6.27; N, 13.76% Found C, 75.05; H, 6.05; N, 13.90%.

3-(Benzofuran-2-yl)-5-(3-methoxy-4-dihydroxphenyl)-2-pyrazoline ***(2e)***

Yield: 76%; m.p.123-125 °C. FTIR (KBr, cm^{-1}) :3526 (OH), 3227 (NH), 1595, 1524, 1258 (C-O-C), 751 ; ^{1}H-NMR (400 MHz, $CDCl_3$), ppm : 7.56 (d, 1H, J= 7.5 Hz, b4-H), 7.51 (d,1H, J= 7.6, b7-H), 7.40 (s, 1H, b3-H), 7.30 (t, J= 7.7 Hz, 1H, b6-H), 7.22 (t, J= 7.5 Hz, 1H, b5-H), 6.92(d, J= 1.6 Hz, 1H, NH), 6.82-6.88 (m, 4H,OH, 2,3,6-H), 4.92 (dt, J= 9.4 and 1.4 Hz, 1H, p5-H), 3.47 (dd, J= 16.3 and 10.8 Hz, 1H, p4-H), 3.06 (dd, J= 16.2 and 9.5 Hz, 1H, p4-H). Anal. Calcd. For $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09% Found C, 70.35; H, 5.08; N, 9.27%.

3-(Benzofuran-2-yl)-5-(3-nitrophenyl)-2-pyrazoline ***(2f)***

Yield: 60%; m.p.125-127 °C. FTIR (KBr, cm^{-1}) :3348 (N-H), 1523 (NO_2) , 1350 (NO_2), ^{1}H-NMR (400 MHz, $CDCl_3$), ppm : 8.35 (s, 1H, 2-H), 8.15 (d, J= 8.6 Hz, 1H, 4-H), 7.60-7.75 (m, 2H, 5,6-H), 7.45-7.55 (m, 2H, b4,b7-H), 7.20-7.35 (m, 3H, b5,b6-H,NH), 7.05 (s, 1H, b3-H), 5.20 (t, J= 10.1 Hz, 1H, p5-H), 3.52 (dd, J= 16.8 and 10.0 Hz, 1H, p4-H), 3.05 (dd, J=16.8 and 10.0 Hz, 1H, p4-H). Anal. Calcd. For $C_{17}H_{13}N_3O_3$: C, 66.44; H, 4.26; N, 13.67% Found C, 67.01; H, 4.15; N, 14.20%.

3-(Benzofuran-2-yl)-5-phenyl-2-pyrazoline ***(2g)***

Yield: 81%; m.p.113-115 °C, FTIR (KBr, cm^{-1}) :3347 (N-H), 3100-3000, 1610, 1587, 747, 698; ^{1}H-NMR (300 MHz, DMSO-d_6), ppm: 8.01 (d, J= 2.6 Hz, 1H, p-NH), 7.58-7.65 (m, 2H, b4,b7-H), 7.22-7.40 (m, 7H, 2-6,b5,b6-H), 7.02 (s, 1H, b3-H), 4.92 (dt, J= 10.7 and 2.6 Hz, 1H, p5-H), 3.48 (dd, J= 16.1 and 10.4 Hz, 1H, p4-H), 2.90 (dd, J= 16.1 and 10.9 Hz, 1H, p4-H). Anal. Calcd. For $C_{17}H_{14}N_2O$: C, 77.84; H, 5.38; N, 10.68% Found C, 78.22; H, 5.25; N, 10.98%.

1,4-Bis[3-(benzofuran-2-yl)-2-pyrazoline-5-yl] benzene **(2h)**.

Yield: 45%; m.p.254-256 °C. FTIR (KBr, cm^{-1}): ^{1}H-NMR (300 MHz,DMSO-d_6), ppm: 7.99 (broad, 2H, p-NH), 7.62 (d, J= 7.2 Hz, 2H, b4-H), 7.58 (d, J= 7.8 Hz, 2H, b7-H), 7.38 (s, 4H, 2,3,5,6-H), 7.32 (t, J= 8.6 Hz,1H, b6-H), 7.29 (t, J= 7.5 Hz,1H, b5-H), 7,02 (s, 2H, b3-H), 4.92 (broad, t, J= 10.2 Hz, 2H, p5-H), 3.47 (dd, J= 16.2 and 10.9 Hz, 2H, p4-H), 2.89 (dd, J= 16.1 and 10.4 Hz, 2H, p4-H). Anal. Calcd. For $C_{28}H_{22}N_4O_2$: C, 75.34; H, 4.93; N, 12.56% Found C, 76.12; H, 5.20; N, 11.96%.

3-(Benzofuran-2-yl)-5-(thiophene-2-yl)-2-pyrazoline ***(2i)***

Yield: 90%; m.p.114-116 °C. FTIR (KBr, cm^{-1}): 3296 (N-H), 1601, 808, 750, 700; ^{1}H-NMR (300 MHz, DMSO-d_6), ppm: 8.09 (d, J= 2.5 Hz, 1H, NH), 7.58-7.66 (m, 2H, b4,b7-H), 7.44 (dd, J= 5.0 and 1.1 Hz, 1H, t3-H), 7.34 (dt, J= 7.5 Hz and 1.0 Hz, 1H, b5-H), 7.26 (dt, J= 7.3 Hz and 1.4 Hz, 1H, b6-H), 7.08-7.10 (m, 2H, t5,b3-H), 7.00 (dd, J= 5.1 and 3.47 Hz, 1H, t4-H), 5.18 (dt, J= 10.3 and 2.5 Hz, 1H, p5-H), 3.49 (dd, J= 16.1 and 10.6 Hz), 2.95 (dd, J= 16.1 and 10.2 Hz). ^{13}C-NMR, ppm : 154.9 (b8-C), 150.6 (p3-C), 146.4 (b2-C), 141.0 (t2-C), 128.6 (b9-C), 127.3 (t4-C), 125.5 (t3-C), 125.4 (b6-C), 125.3 (t5-C), 123.7 (b5-C), 121.7 (b4-C), 111.6 (b7-C), 105.9 (b3-C), 59.8 (p5-C), 41.5 (p4-C). Anal. Calcd. For $C_{15}H_{12}N_2OS$: C, 67.16; H, 4.48; N, 10.45; S, 11.94% Found C, 67.23; H, 4.32; N, 10.63; S, 11.76%.

3-(Benzofuran-2-yl)-5-(furan-2-yl)-2-pyrazoline ***(2j)***

Yield: 77%; m.p.92-94 °C. FTIR (KBr, cm^{-1}): 3318, 3150-3000, 1605, 1258, 1154, 747; ^{1}H-NMR (400 MHz, $CDCl_3$), ppm: 7.91 (d,J= 2.1 Hz, 1H, NH), 7.57-7.67 (m, 3H, b4,b7, f5-H), 7.33 (dt, J= 8.3 and 1.4 Hz, 1H, b5-H), 7.26 (dt, J= 7.3 and 1.1 Hz, 1H, b6-H), 7.07 (s, 1H, b3-H), 6.38-6.43(m, 2H, f3,f4-H), 4.95 (dt, J= 10.1 and 2.1 Hz, 1H, p5-H), 3.37 (dd, J= 15.6 and 11.5 Hz, 1H, p4-H), 3.14 (dd, J= 16.2 and 9.2 Hz, p4-H). Anal. Calcd. For $C_{15}H_{12}N_2O_2$: C, 71.43; H, 4.76; N, 11.11% Found C, 71.27; H, 4.55; N, 11.04%.

3-(Benzofuran-2-yl)-5-(pyrrol-2-yl)-2-pyrazoline ***(2k)***

Yield: 93%; m.p.175-177 °C. FTIR (KBr, cm^{-1}): 3312, 3190, 3130, 1610, 1541; ^{1}H-NMR (400 MHz, $CDCl_3$), ppm: 11.81 (broad, 1H, NH), 8.50 (broad, 1H, pyrrole-NH), 7.56 (d, J= 8.7 Hz, 1H, b4-H), 7.53 (d, J= 8.6 Hz, 1H, b7-H), 7.32 (t, J= 8.5 Hz, 1H, b6-H), 7.24 (t, J= 8.6 Hz, 1H, b5-H), 6.82 (s, 1H, b3-H), 6.76 (m, 1H, pyrrole-5-H), 6.13-6.17 (m, 3H, p-NH, pyrrole-3,4-H), 5.05 (t, J= 10.2 Hz, 1H, p5-H), 3.41 (dd, J= 16.3 and 10.3 Hz, 1H, p4-H), 3.09 (dd, J= 16.30and 10.1 Hz, 1H, p4-H). Anal. Calcd. For $C_{15}H_{13}N_3O$: C, 71.71; H, 5.18; N, 16.73% Found C, 71.52; H, 5.20; N, 17.02%.

Conclusion

Syntheses and structural characterizations of two new chalcones and eleven pyrazolines were given in this study. The cyclization of the chalcones, given 2-pyrazoline was carried out at a shorter period of time than that of the some other chalcones given in literature using absolute ethanol in reflux. Antibacterial and antifungal activities of twenty compounds from this new class of benzofurane chalcones and pyrazoline derivatives against the six bacteria and three yeast were investigated. Seven compounds (**1d**, **1f**, **1g**, **1h**, **1i**, **2d** and **2h**) showed no activity against any bacteria and any yeast. Five compounds (**2a**, **2b**, **2c**, **2e** and **2k**) which are the all pyrazoline derivatives have exhibited an activity against all of the bacteria and yeast. Compound **1a** possessing hydroxyl group on ortho position of phenyl ring has exhibited a comparable antibacterial activity against *B. megaterium* with that of the standard drug (amoksilin). While the compounds **1b**, **1c, 1e** and **2j** are effective against most of bacteria and yeast used in this work, the compounds **2f**, **2g** and **2i** are effective against most bacteria but no yeast.

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