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Synthesis of new β-D-glucuronides: β-D-glucuronosyl-5- (3-aryl-1*H*-pyrazol-5-yl)-1,2-benzisoxazole-3-carboxylates

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ABSTRACT

*1-(3-Methylbenzo isoxazol-5-yl)-3-phenyl prop-2-en-1-one **1** undergoes interaction with hydrazine hydrate to yield 3-methyl-5-(3-phenyl-1H-pyrazol-5-yl)-1,2-benzisoxazole **2**, which on oxidation with $KMnO_4$ gives 5-(3-phenyl-1H-pyrazol-5-yl)-1,2-benzisoxazole-3-carboxylic acid **3**. Glucuronidation of these 5-(3-phenyl-1H-pyrazol-5-yl)-1,2- benzisoxazole-3-carboxylic acid **3** with free glucuronic acid afforded β-D-glucuronosyl-5-(3-phenyl-1H-pyrazol-5-yl)-1,2-benzisoxazole-3-carboxylate **4**. The structures of the products have been assigned on the basis of ^1H NMR, ^{13}C NMR, FAB-MS, optical activity, and elemental analysis. The title compounds are found to have antibacterial and antifungal activities.*

Keywords: Chalcones, Pyrazoles, Carboxylic acids, β-D-Glucuronides.

INTRODUCTION

The development of new methods for the synthesis of β-D-glucuronides have attracted a current interest in the organic synthesis due to biological, pharmaceutical importance that some compounds of this class have shown. β-D-Glucuronides are the conjugation products of compounds possessing a carboxylic acid functional group with free glucuronic acid[1]. β-D-Glucuronides are polar and chemically reactive metabolites[2-4] it form covalent adduct with protein, generating increasing interest as potential mediator of hypersensitivity reaction, and it shows profound effect on drug metabolism[5-8]. Continuing our studies about heterocyclic β-D-glucuronides, herein we want to describe the synthesis of chalcones and pyrazoles

respectively. The activities of pyrazole derivatives include main topics like remarkable antimicrobial, antioxidant, fungicidal, bacteriocidal, bacteriostatic, sedative, antipyretic, analgesic, anti-inflammatory, muscle relaxant, hypoglycemic and sex stimulating agents[9-17].

EXPERIMENTAL SECTION

General Methods

Chalcones **1** were prepared as described in the literature[18]. Melting points were determined in open glass capillaries and are uncorrected. Optical activity was measured at 29^0C. FT-IR spectra were recorded using KBr disk on Perkin-Elmer spectrum Rx-I spectrometer. ^{1}H NMR and ^{13}C NMR were recorded on Brucker AC-300 F (300MHz) NMR spectrometer by using DMSO and $CDCl_3$ as solvent and tetramethylsilane as an internal standard. Mass spectra were recorded on 70-S Mass spectrometer using *m*-nitro benzyl alcohol (NBA) matrix. Elemental analysis was determined using the Perkin Elmer 2400 CHN analyzer.

3-Methyl-5-(3-phenyl-1*H*-pyrazol-5-yl)-1,2-benzisoxazole 2a. Reaction of 1-(3-methyl benzoisoxazol-5-yl)-3-phenylprop-2-en-1-one **1a** (2.6g, 0.01 mol), hydrazine hydrate (0.5 mL), ethyl alcohol (15 mL) and KOH (0.6g) was refluxed on water bath for 5 h. It was cooled and acidified with glacial acetic acid (1.5 mL), and was poured on ice-cold water (50 mL). The colorless solid was filtered, washed with cold water, dried and crystallized with alcohol (yield 68.5%). IR (KBr): 903 (pyrazole ring streaching), 3305 (C-H, CH_3), 1562 (C=C), and 1715 cm^{-1} (C=N). ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 6.81 (C-H, pyrazole), 13.7 (s, N-H), 2.35 (CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 121-145 (C-2, C-3), 189 (C-1), 155 (s, benzisoxazole), 99 (s, pyrazole), 15.9 (s, CH_3, singlet) and 127.5-133.1 (m, benzene); Anal. Calcd. for C, 74.17; H, 4.76; N, 15.26. Found: C, 74.15; H, 4.75; N, 15.25%.

In the same way, other 3-methyl-5-(3-aryl-1*H*-pyrazol-5-yl)-1,2-benzisoxazoles **2a-o** were prepared by the reaction of **1a-o** with hydrazine hydrate and compounds gave satisfactory C, H, and N analysis **Table 1**.

3-Methyl-5-[3-(4-hydroxy)phenyl-1*H*-pyrazol-5-yl]-1,2-benzisoxazole 2c. mp 120^0C (yield 53.7%); IR (KBr): 3421 (OH), 903 (pyrazole ring streaching), 3305 (C-H, CH_3), 1562 (C=C), and 1715 cm^{-1} (C=N). ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 5.0 (C-OH,), 11.0 (COOH), 6.81 (C-H, pyrazole), 13.7 (s, N-H, pyrazole), 2.35 (CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 121-145 (C-2, C-3), 189 (C-1), 155 (s, benzisoxazole), 99 (s, pyrazole), 173 (carboxyl), 15.9 (s, CH_3, singlet). Anal. Calcd. for C, 70.09; H, 4.49; N, 14.42. Found: C, 70.11; H, 4.50; N, 14.43%.

3-Methyl-5-[3-(2,4-dihydroxy)phenyl-1*H*-pyrazol-5-yl]-1,2-benzisoxazole 2d. mp 187^0C (yield 61.0%); IR (KBr): 3500 and 3480 (OH), 308 (pyrazole ring streaching), 3309 (C-H, CH_3), 1560 (C=C), and 1710 cm^{-1} (C=N). ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 4.9 and 5.2 (C-OH,), 11.0 (COOH), 6.80 (C-H, pyrazole), 13.8 (s, N-H, pyrazole), 2.31 (CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 120-145 (C-2, C-3), 190 (C-1), 155 (s, benzisoxazole), 98 (s, pyrazole), 172 (carboxyl), 15.7 (s, CH_3, singlet). Anal. Calcd. for C, 66.44; H, 4.70; N, 14.93. Found: C, 66.41; H, 4.26; N, 14.93%.

3-Methyl-5-[3-(4-chloro)phenyl-1*H*-pyrazol-5-yl]-1,2-benzisoxazole 2g. mp 218^0C (yield 74.0%); IR (KBr): 780 (C-Cl), 902 (pyrazole ring streaching), 3309 (C-H, CH_3), 1560 (C=C), and 1710 cm^{-1} (C=N). ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 7.42 (C-Cl,), 10.5 (COOH), 6.81 (C-H, pyrazole), 13.7 (s, N-H, pyrazole), 2.35 (CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 134.3 (C-Cl), 122 (C-H, benzisoxazole), 148 (pyrazole), 175 (carboxyl), 15.9 (s, CH_3, singlet). Anal. Calcd. for C, 65.92; H, 3.90; N, 13.57. Found: C, 65.91; H, 3.87; N, 13.57%.

5-(3-Phenyl-1*H*-pyrazol-5-yl)-1,2-benzisoxazole-3-carboxylic acid 3a. 3-Methyl-5-(3-phenyl-1*H*-pyrazol-5-yl)-1,2-benzisoxazole **2a** (2.7g, 0.01 mol), $KMnO_4$ (1.5g), sodium carbonate (1.2g) and H_2O (100mL) was refluxed under water bath for 4h, until the purple color of the permanganate has disappeared. It was acidified with dilute H_2SO_4, the excess manganese dioxide was removed by adding sodium metabisulphite (0.1g), filtered, washed and crystallized with distilled water (yield 50.9%). IR (KBr): 903 (pyrazole ring streaching), 3094 (C-H, CH_3), 1591 (C=N), and 1688 cm^{-1} (C=O). ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 6.81 (C-H, pyrazole), 13.7 (s, N-H), 2.36 (CH_3), 10.7 (s, COOH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 126-147 (benzisoxazole), 99.7 and 148 (C-H, pyrazole), 167.5 (s, COOH), and 127.5-133.1 (m, benzene); Anal. Calcd. for C, 66.88; H, 3.63; N, 13.76. Found: C, 66.87; H, 3.63; N, 13.75%.

Similarly, various other 5-(3-aryl-1*H*-pyrazol-5-yl)-1,2-benzisoxazole-3-carboxylic acids **3a-o** were prepared by the oxidation of 3-methyl-5-(3-aryl-1*H*-pyrazol-5-yl)-1,2-benzisoxazoles **2a-o** with alkaline $KMnO_4$ solution and compounds gave satisfactory C, H, and N analysis.

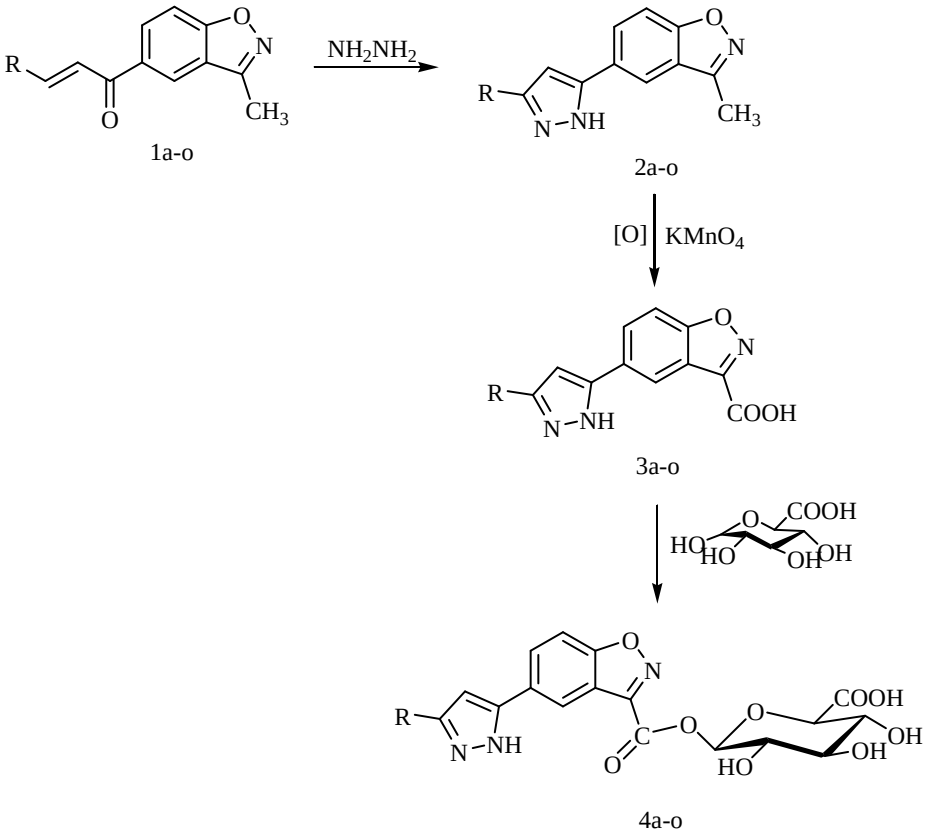
β-D-Glucuronosyl-5-(3-phenyl-1*H*-pyrazol-5-yl)-1,2-benzisoxazole-3-carboxylate 4a Dissolved 5-(3-phenyl-1*H*-pyrazol-5-yl)-1,2-benzisoxazole-3-carboxylic acid **3a** (3.05g, 0.01 mol) in dry pyridine (4mL), which was kept at 0^0C, D-glucuronic acid (1.94g) was added in portion with constant stirring and the solution was left at room temperature for 18h. The solution was poured over crushed ice, the resulting colorless solid was filter and washed with ice-cold water to obtain β-D-glucuronosyl-5-(3-phenyl-1*H*-pyrazol-5-yl)-1,2-benzisoxazole-3-carboxylate **4a** $[D]_D^{29}$ 41.27, (yield 52.4%). IR (KBr): 1263 cm^{-1} (C-O-C), 3135 (OH), 3063 (NH), 1714 (C=O), 1152 cm^{-1} (C-O); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 13.7 (s, NH), 11.0 (s, COOH), 3.73-6.15 (m, OH), 2.0 ppm (OH); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 167.9 (C=O), 173.2 ppm (COOH); FAB-MS: m/z 481 (M^+, $C_{23}H_{19}N_3O_9$), 305 ($C_{17}H_{11}N_3O_3$, M^+-$C_6H_8O_6$); Anal. Calcd. for C, 57.30; H, 3.98; N, 8.73. Found: C, 57.32; H, 3.99; N, 8.71%.

When the reaction of 5-(3-aryl-1*H*-pyrazol-5-yl)-1,2-benzisoxazole-3-carboxylic acids **3a-o** with D-glucuronic acid using dry pyridine afforded several β-D-glucuronosyl-5-(3-aryl-1*H*-pyrazol-5-yl)-1,2-benzisoxazole-3-carboxylates **4a-o**. Compounds gave satisfactory C, H, and N analysis (Table 2).

β-D-Glucuronosyl-5-[3-(4-hydroxy)phenyl-1*H*-pyrazol-5-yl]-1,2-benzisoxazole-3-carboxylate 4c. (Yield 51.5%); IR (KBr): 1263 cm-^{1} (C-O-C), 3540 (OH), 3062 (NH), 1715 (C=O), 1151 cm^{-1} (C-O); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 13.7 (s, NH), 11.2 (s, COOH), 3.72-6.16 (m, OH), 2.0 ppm (OH); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 167.8 (C=O), 173.5 ppm (COOH); FAB-MS: m/z 497 (M^+, $C_{23}H_{19}N_3O_{10}$), 321 ($C_{17}H_{11}N_3O_4$, M^+-$C_6H_8O_6$); Anal. Calcd. for C, 55.54; H, 3.85; N, 8.45. Found: C, 55.53; H, 3.83; N, 8.44%.

β-D-Glucuronosyl-5-[3-(2,4-dihydroxy)phenyl-1*H*-pyrazol-5-yl]-1,2-benzisoxazole-3-carboxylate 4d. (Yield 42.3?%); IR (KBr): 1262 cm-^{1} (C-O-C), 3540 and 3510 (2OH), 3061 (NH), 1712 (C=O), 1151 cm^{-1} (C-O); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 13.8 (s, NH), 11.2 (s, COOH), 3.75-6.16 (m, OH), 2.0 ppm (OH); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 167.9 (C=O), 173.5 ppm (COOH); FAB-MS: m/z 513 (M^+, $C_{23}H_{19}N_3O_{11}$), 337 ($C_{17}H_{11}N_3O_5$, M^+-$C_6H_8O_6$); Anal. Calcd. for C, 53.81; H, 3.73; N, 8.18. Found: C, 53.80; H, 3.72; N, 8.18%.

β-D-Glucuronosyl-5-[3-(4-chloro)phenyl-1*H*-pyrazol-5-yl]-1,2-benzisoxazole-3-carboxylate 4g. (Yield 48.5%); IR (KBr): 780 (C-Cl), 902 (pyrazole ring stretching), 1565 (C=C), 1712 (C=N), 3062 (NH), 1745 (C=O), and 1151 cm^{-1} (C-O); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 13.7 (s, NH), 11.3 (s, COOH), 3.72-6.18 ppm (m, OH); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 167.7 (C=O), 173.5 ppm (COOH); FAB-MS: m/z 515 (M^+, $C_{23}H_{18}ClN_3O_9$), 339 ($C_{17}H_{11}N_3O_4$, M^+-$C_6H_8O_6$); Anal. Calcd. for C, 53.55; H, 3.52; N, 8.15. Found: C, 53.53; H, 3.51; N, 8.14%.



Scheme

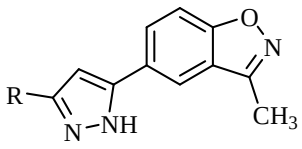
R =	a; C_6H_5	f; *o*-ClC_6H_4	k; 3-C_5H_4N
	b; *o*-OHC_6H_4	g; *p*-ClC_6H_4	l; 4-C_5H_4N
	c; *p*-OHC_6H_4	h; *o*-$NO_2C_6H_4$	m; 3-C_4H_3O
	d; 2,4-$(OH)_2C_6H_3$	i; *m*-$NO_2C_6H_4$	n; 3-C_8H_5N
	e; *p*-OH-*m*-$OCH_3C_6H_3$	j; 2-C_5H_4N	o; *p*-*N*$(CH_3)_2C_6H_4$

RESULTS AND DISCUSSION

The 1-(3-methyl benzoisoxazol-5-yl)-3-phenyl prop-2-en-1-one **1** were prepared by the Claisen-Schmidt method[18-19] by the condensation of 1-(3-methyl benzisoxazol-5-yl) ethanone with different aldehydes. In the ^{1}H NMR spectrum, **1a** exhibited a multiplet for ethylene at δ 7.56-7.90 and CH_3 (aliphatic) at δ 2.35 ppm, while the ^{13}C NMR spectrum showed peaks at 121-145 (C-2, C-3), 189 (C-1) and 15.9 ppm (CH_3). The IR spectrum showed absorption bands at 1562 (C=C) and 1715 cm^{-1} (C=O). The reaction of 1-(3-methyl benzoisoxazol-5-yl)-3-phenyl prop-2-en-1-one **1a** with hydrazine hydrate cyclization occurred to furnish the 3-methyl-5-(3-phenyl-1*H*-pyrazol-5-yl)-1,2-benzisoxazole **2a**. The ^{1}H NMR spectrum for 2a exhibited a singlet for NH at δ 13.7, CH_3 δ 2.35 ppm and ^{13}C NMR spectrum showed peak for CH_3 at 15.9 ppm. Oxidation of above **2a** with $KMnO_4$ afforded 5-(3-phenyl-1*H*-pyrazol-5-yl)-1,2-benzisoxazole-3-carboxylic acid **3a**. The ^{1}H NMR spectrum for **3a** exhibited singlet for NH at δ 13.7, OH at δ 11.0 ppm, and the ^{13}C NMR spectrum showed peaks at 167.5 for COOH. The IR spectrum showed broad absorption bands at 3468 (OH). In view of pronounced biological and pharmacological applications of β-D-glucuronides, β-D-glucuronosyl-5-(3-phenyl-1*H*-pyrazol-5-yl)-1,2-benzisoxazole-3-carboxylate **4a** have been synthesized by the glucuronidation of 5-(3-phenyl-1*H*-pyrazol-5-yl)-1,2-benzisoxazole-3-carboxylic acid **3a** with free D-glucuronic acid using dry pyridine. The absence of -OH absorption broadband in the spectrum, and the presence of strong band at 1263cm^{-1} for C–O–C are fully constituent with structure of **4a**. The IR spectrum showed characteristic bands at 3135 (OH), 3063 (NH), 1714 (C=O), and 1152 cm^{-1} (C–O) groups. The ^{1}H NMR spectrum of **4a** showed signals at δ 13.7 (s, 1H, NH), 11.0 (s, COOH), 3.73-6.15 (m, OH), and 2.0 ppm (OH). The ^{13}C NMR spectrum showed peaks at 167.9 (C=O) and 173.2 ppm (COOH). The FAB-MS spectrum showed a molecular ion peak at 481 (M^+) and base peak appearing at m/z 309 ($C_{17}H_{11}N_3O_3$, M^+-$C_6H_8O_6$) was due to the simultaneous transfer of hydrogen atom and loss of a D-glucuronic acid moiety confirms the molecular formula $C_{23}H_{19}N_3O_9$.

All the compounds gave satisfactory C, H, and N elemental analysis **Table 2**.

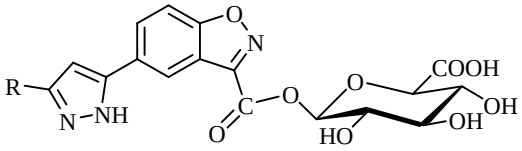
Table 1: Characterization data of compounds 2a-o.



2a-o

Product	R	Mol. Formula	mp (^{0}C)	Yield (%)	% Found (Calcd) C	H	N
2a	C_6H_5	$C_{17}H_{13}N_3O$	105	68.5	(74.17)	74.15 (4.76)	4.75 (15.26)	15.25
2b	*o*-OHC_6H_4	$C_{17}H_{13}N_3O_2$	120	53.7	(70.09)	70.11 (4.49)	4.50 (14.42)	14.43
2c	*p*-OHC_6H_4	$C_{17}H_{13}N_3O_2$	117	71.6	(70.09)	70.13 (4.25)	4.50 (13.67)	13.66
2d	2,4-$(OH)_2C_6H_3$	$C_{17}H_{13}N_3O_3$	187	61.0		66.41 (66.44)	4.26 (4.70)	14.93 (14.93)
2e	*p*-OH*m*-OCH_3 C_6H_3	$C_{18}H_{15}N_3O_3$	241	83.0		67.26 (67.28)	4.70 (4.71)	14.93 (14.94)
2f	*o*-ClC_6H_4	$C_{17}H_{12}ClN_3O$	99	67.5	(65.92)	65.90 (3.90)	3.89 (13.57)	13.56
2g	*p*-ClC_6H_4	$C_{17}H_{12}ClN_3O$	218	74.0	(65.92)	65.91 (3.90)	3.87 (13.57)	13.57
2h	*o*-$NO_2C_6H_4$	$C_{17}H_{12}N_4O_3$	156	74.0	(63.75)	63.74 (3.78)	3.78 (17.49)	17.48
2i	*m*-$NO_2C_6H_4$	$C_{17}H_{12}N_4O_3$	159	82.0	(63.75)	63.75 (3.78)	3.76 (17.49)	17.47
2j	2-C_5H_4N	$C_{16}H_{12}N_4O$	101	57.0	(69.55)	69.54 (4.38)	4.37 (20.28)	20.19
2k	3-C_5H_4N	$C_{16}H_{12}N_4O$	97	68.5	(69.55)	69.38 (4.38)	4.36 (20.28)	20.27
2l	4-C_5H_4N	$C_{16}H_{12}N_4O$	100	77.7	(69.55)	69.53 (4.38)	4.30 (20.28)	20.24
2m	3-C_4H_3O	$C_{15}H_{11}N_3O_2$	190	79.0	(67.92)	67.92 (4.18)	4.35 (15.84)	15.83
2n	3-C_8H_5N	$C_{19}H_{14}N_4O$	259	66.0	(72.60)	72.59 (4.49)	4.48 (17.82)	17.81
2o	*p*-*N*$(CH_3)_2C_6H_4$	$C_{19}H_{18}N_4O$	119	81.0	(71.68)	71.67 (5.70)	5.69 (17.60)	17.58

Table 2: Characterization data of compounds 4a-o.



4a-o

Product	R	Mol. Formula	$[\alpha]^{29}_D$ (^{0})	Yield (%)	% Found (Calcd) C	H	N
4a	C_6H_5	$C_{23}H_{19}N_3O_9$	41.27	52.4	(57.30)	57.32 (3.98)	3.99 (8.73)	8.71
4b	*o*-OHC_6H_4	$C_{23}H_{19}N_3O_{10}$	46.44	56.0	(55.54)	55.54 (3.85)	3.83 (8.45)	8.42
4c	*p*-OHC_6H_4	$C_{23}H_{19}N_3O_{10}$	46.54	51.5	(55.54)	55.53 (3.85)	3.83 (8.45)	8.44
4d	2,4-$(OH)_2C_6H_3$	$C_{23}H_{19}N_3O_{11}$	47.13	42.3	(53.81)	53.80 (3.73)	3.72 (8.18)	8.18
4e	*p*-OH*m*-$OCH_3C_6H_3$	$C_{24}H_{21}N_3O_{11}$	49.09	49.8	(54.65)	54.65 (4.01)	4.00 (7.97)	7.96
4f	*o*-ClC_6H_4	$C_{23}H_{18}ClN_3O_9$	47.82	45.3	(53.55)	53.54 (3.52)	3.51 (8.15)	8.15
4g	*p*-ClC_6H_4	$C_{23}H_{18}ClN_3O_9$	47.83	48.5	(53.55)	53.53 (3.52)	3.51 (8.15)	8.14
4h	*o*-$NO_2C_6H_4$	$C_{23}H_{18}N_4O_{11}$	48.32	54.5	(52.48)	52.46 (3.45)	3.44 (10.64)	10.62
4i	*m*-$NO_2C_6H_4$	$C_{23}H_{18}N_4O_{11}$	48.33	54.4	(52.48)	52.47 (3.45)	3.45 (10.64)	10.63
4j	2-C_5H_4N	$C_{22}H_{18}N_4O_9$	45.05	43.4	(54.78)	54.76 (3.76)	3.75 (11.61)	11.60
4k	3-C_5H_4N	$C_{22}H_{18}N_4O_9$	44.09	57.9	(54.78)	54.75 (3.76)	3.75 (11.61)	11.60
4l	4-C_5H_4N	$C_{22}H_{18}N_4O_9$	45.05	54.3	(54.78)	54.75 (3.76)	3.75 (11.61)	11.62
4m	3-C_4H_3O	$C_{21}H_{17}N_3O_{10}$	42.93	52.8	(53.51)	53.50 (3.64)	3.62 (8.91)	8.90
4n	3-C_8H_6N	$C_{25}H_{20}N_4O_9$	50.47	52.0	(57.69)	57.65 (3.87)	3.86 (10.77)	10.75
4o	*p*-*N*$(CH_3)_2C_6H_4$	$C_{25}H_{24}N_4O_9$	51.12	47.1	(57.25)	57.24 (4.61)	4.60 (10.68)	10.68

Microbial activities:

Antimicrobial Activity

The synthesized compounds were tested for their antibacterial activities by the using the cup-plate method against *Bacillus subtilis* (gram-positive) and *Escherichia coli* (gram-negative) at concentration of 100μg/mL in DMF. Pure Norfloxacin was used as standard antibiotic for the comparison of the results. The sterilized Mullier-Hinton agar medium 50mL was inoculated with test organism and poured into petridishes. Then four holes of 6mm were completely filled with different test solution. The plates were then incubated for 24h at 37^0C and zones of inhibitions were measured. Similar procedure was adopted for pure Norfloxacin and the corresponding zone diameters were compared. Screening results indicate that compounds **4a-o** showed to excellent bacteriocidal activities against both organisms **Table 3**.

Table 3: Data for in vitro antibacterial and antifungal activities of compounds 4a-o

	Diameter of Inhibition Zone (in mm) Against			
	Bacterial Strains		Fungal Strain	
Product	***E. Coli***	***B. subtilis***	***A. niger***	***C. albicans***
4a	14	15	16	14
4b	13	14	12	11
4c	15	15	13	16
4d	14	10	08	22
4e	16	11	17	--
4f	--	17	22	24
4g	10	16	11	13
4h	17	14	22	18
4i	13	09	15	28
4j	12	14	23	21
4k	15	15	11	16
4l	10	13	23	23
4m	17	16	--	18
4n	08	12	21	--
4o	11	15	19	22

-- = No inhibition of growth. Diameter of zone of inhibition from 13-16 (in mm) shows excellent activity and that of 9-12 (in mm) exhibit moderate activity for bacterial strains. Diameter of zone of inhibition from 22-28 (in mm) shows excellent activity, that of 15-21 (in mm) exhibits moderate activity and that of 11-14 (in mm) shows poor activity for fungal strains. Norfloxacin 100μg/mL used as standard against E. coli and B. subtilis diameter of zone of inhibition is 20. Griseofulvin 100μm/mL used as standard against A. niger and C. albicans diameter of zone of inhibition is 32.

Antifungal Activity

The antifungal activity of synthesized compounds was evaluated by the using above same procedure (cup-plate) against *Aspergillus niger* and *Candida albicans* at a concentration 100μm/mL in DMF. The plates were incubated for 8 days at 37^0C. The zones of inhibitions were measured. A commercial fungicide griseofulvin was also tested under similar condition with a view of comparing the results. The compounds showed significant fungi toxicity against both the fungi **Table 3**.

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