REPORT

Synthesis and screening of some new *N*-alkyl/aralkyl-*N*-(3,4-methylenedioxybenzyl)-4-substituted benzenesulfonamides as potential antibacterial agents

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Abstract: The various *p*-substituted benzenesulfonyl chlorides (2a-e) were treated with (3,4-methylenedioxy) benzylamine (1) in the presence of aqueous Na_2CO_3 solution to synthesize *N*-(3,4-methylenedioxybenzyl)-4-substitutedbenzenesulfonamides (3a-e). The synthesized molecules were further converted into corresponding *N*-ethyl/benzyl/4-flourobenzyl-*N*-(3,4-methylenedioxybenzyl)-4-substitutedbenzenesulfonamides (7a-e, 8a-e, 9a-e) on reaction with ethyl iodide (4), benzyl chloride (5) and 4-flourobenzyl chloride (6) in the presence of sodium hydride using *N*,*N*-dimethylformamide as solvent. The structure elucidation was processed through different spectral techniques including IR, ^{1}H-NMR and EIMS. The screening of the synthesized molecules against Gram-bacterial strains, to evaluate antibacterial activity, showed them moderately good inhibitors as shown by their low MIC values.

Keywords: (3,4-Methylenedioxy)benzylamine, antibacterial activity, *p*-substituted benzenesulfonamides.

INTRODUCTION

Sulfonamides (R-NH-SO_2-R) are gaining interest of organic synthetic chemists plausibly because of a range of biological activities and have been employed as drugs in numerous forms e.g. as inhibitors of carbonic anhydrase and as part of anti microbial & anti-tumor drugs etc(Alsughayer *et al.,* 2011, Baskin *et al.,* 2002. Kumar *et al.,* 2010, Ozbek *et al.,* 2007, Shi *et al.,* 2009). The previous research work by our group has also revealed the antibacterial potential of the various classes of sulfonamides (Aziz-ur-Rehman *et al.,* 2012a, Aziz-ur-Rehman *et al.,* 2013). The benzodioxol moiety employed in this synthetic work, is biologically active compound because of its considerable anticancer and antidepressant activities (Bar-Oz *et al.,* 2007, in Grassia *et al.,* 2008).

A series of *p*-substituted benzenesulfonyl chlorides were employed to evaluate the effect of structural modification on the antibacterial potential of heterocyclic moiety, (3,4-methylenedioxy) benzylamine. The results inaugurated the valuable information about the antibacterial activities of the synthesized molecules. This research project was in protraction of our last work for the evaluation of antibacterial and anti-enzymatic activities of various sulfonamides bearing (non) heterocyclic moieties (Khalid H *et al.,* 2013, Khalid H *et al.,* 2012, Aziz-ur-Rehman *et al.,* 2012b, Abbasi *et al.,* 2013). The synthesized derivatives of sulfonamides were screened against different bacterial strains to find out their potential for antibacterial activity. The low MIC values were rendered them potent antibacterial active molecules.

MATERIALS AND METHODS

General

The chemicals employed in the synthesis were purchased from Merck and Alfa Aesar through local suppliers along with the analytical grade solvents. Thin layer chromatography (TLC) was a valuable source to check out the purity of the synthesized molecules utilizing a solvent system of EtOAc and *n*-C_6H_6 followed by visualization under UV at 254 nm. Griffin-George apparatus with open capillary tube was used for the computation of melting points, which were uncorrected. Jasco-320-A spectrophotometer was employed to record the I.R. spectra by KBr pellet method and results were expressed in wave number (cm^{-1}). Bruker spectrometers were functionalized for ^{1}H-NMR (at 400 MHz) and for ^{13}C-NMR (at 100 MHz) using $CHCl_3$-$d_1$as solvent, δ-values (ppm) for chemical shift, tetramethylsilane as internal reference standard and the *J*-values (Hz) for coupling constant. JMS-HX-110 spectrometer was utilized for recording of Mass spectra (EIMS), with data system.

Procedure for the synthesis of N-(3,4-methylenedioxybenzyl)-4-substitutedbenzenesulfonamides (3a-e)

(3,4-methylenedioxy) benzylamine (**1**; 0.03mol) was suspended in an aqueous medium containing 35 mL

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distilled water and 5mL 10% sodium carbonate solution in a round bottom (RB) flask (250 mL). The *p*-substitutedbenzenesulfonyl chlorides (2a-e; 0.03mol) were poured into the suspension under continuous stirring. The pH of reaction mixture was maintained up to 8-10 by the addition of solid sodium carbonate time by time until there was no pH change. The stirring of reaction mixture was continued for 2-4 hrs. The reaction progress was monitored by TLC plates. After confirmation by single spot, few drops of concentrated HCl were used to acidify the reaction contents up to pH of 5-6 accompanied by vigorous shaking till the persistence of pH. Filtration followed by washing with distilled water was processed for the collection of solid precipitates (Aziz-ur-Rehman *et al.,* 2013).

N-(3,4-methylenedioxybenzyl)-4-methylbenzenesulfonamide (3a)

White amorphous solid; Yield: 89%; M.P.: 84-86^{o}C; Mol. Formula: $C_{15}H_{15}NO_4S$; Mol. Mass: 305 gmol^{-1}; IR (KBr, v_{max} (cm^{-1})): 3323 (N-H), 3076 (Ar C-H), 1616 (Ar C=C), 1348 (S=O), 1227 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.73 (d, *J*=8.0 Hz, 2H, H-2', H-6'), 7.29 (d, *J*=8.0 Hz, 2H, H-3', H-5'), 6.67 (d, *J*=8.0 Hz, 1H, H-6), 6.63 (d, *J*=8.8 Hz, 1H, H-5), 6.60 (s, 1H, H-2), 5.90 (s, 2H, H-8), 3.99 (s, 2H, H-7), 2.42 (s, 3H, CH_3-7'); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 149.6 (C-3), 143.9 (C-4), 140.3 (C-1'), 138.5 (C-4'), 133.9 (C-1), 129.7 (C-2' & C-6'), 127.1 (C-3' & C-5'), 121.3 (C-6), 108.4 (C-5), 108.2 (C-2), 101.1 (C-8), 47.1 (C-7), 20.5 (C-7'); EIMS (*m/z*): 305 $(M)^+$, 155 $((C_7H_7SO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 121 $(C_7H_5O_2)^+$, 91 $(C_7H_7)^+$, 76 $(C_6H_4)^+$, 51 $(C_4H_3)^+$.

N-(3,4-methylenedioxybenzyl)-4-ter-butylbenzenesulfonamide (3b)

Cream white amorphous solid; Yield: 72%; M.P.: 104-106 ^{o}C; Mol. Formula: $C_{18}H_{21}NO_4S$; Mol. Mass: 347 gmol^{-1}; IR (KBr, v_{max} (cm^{-1})): 3365 (N-H), 3049 (Ar C-H), 1613 (Ar C=C), 1367 (S=O), 1238 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.94 (d, *J*=8.8 Hz, 2H, H-2', H-6'), 7.59 (d, *J*=8.4 Hz, 2H, H-3', H-5'), 6.68 (s, 1H, H-2), 6.66 (d, *J*=7.6 Hz, 1H, H-6), 6.62 (d, *J*=7.2 Hz, 1H, H-5), 5.90 (s, 2H, H-8), 4.03 (s, 2H, H-7), 1.35 (s, 9H, CH_3-8' to CH_3-10'); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 151.3 (C-4'), 149.6 (C-3), 143.5 (C-4), 141.3 (C-1'), 133.8 (C-1), 129.2 (C-2' & C-6'), 126.9 (C-3' & C-5'), 122.5 (C-6), 108.7 (C-5), 108.2 (C-2), 100.9 (C-8), 45.4 (C-7), 32.1 (C-7'), 30.4 (C-8', C-9' & C-10'); EIMS (*m/z*): 347 $(M)^+$, 197 $(C_{10}H_{13}SO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 133 $(C_{10}H_{13})^+$, 121 $(C_7H_5O_2)^+$, 76 $(C_6H_4)^+$.

N-(3,4-methylenedioxybenzyl)-4-acetylbenzenesulfonamide (3c)

Light brown amorphous solid; Yield: 82%; M.P.: 102-104 ^{o}C; Mol. Formula: $C_{16}H_{15}NO_5S$; Mol. Mass: 333 gmol^{-1}; IR (KBr, v_{max} (cm^{-1})): 3345 (N-H), 3090 (Ar C-H), 1619 (Ar C=C), 1349 (S=O), 1229 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 8.04 (d, *J*=8.4 Hz, 2H, H-2', H-6'), 7.91 (d, *J*=8.4 Hz, 2H, H-3', H-5'), 6.67 (d, *J*=8.0 Hz, 1H, H-6), 6.62 (s, 1H, H-2), 6.60 (d, *J*=8.0 Hz, 1H, H-5), 5.89 (s, 2H, H-8), 4.06 (s, 2H, H-7), 2.64 (s, 3H, CH_3-7'); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 171.1 (C-7'), 149.3 (C-3), 147.8 (C-1'), 143.1 (C-4), 138.6 (C-4'), 133.9 (C-1), 130.7 (C-3' & C-5'), 128.8 (C-2' & C-6'), 122.7 (C-6), 108.7 (C-5), 108.2 (C-2), 100.6 (C-8), 50.2 (C-7), 23.3 (C-8'); EIMS (*m/z*): 333 $(M)^+$, 183 $(C_8H_7OSO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 121 $(C_7H_5O_2)^+$, 119 $(C_8H_7O)^+$, 76 $(C_6H_4)^+$.

N-(3,4-methylenedioxybenzyl)-4-acetamidobenzenesulfonamide (3d)

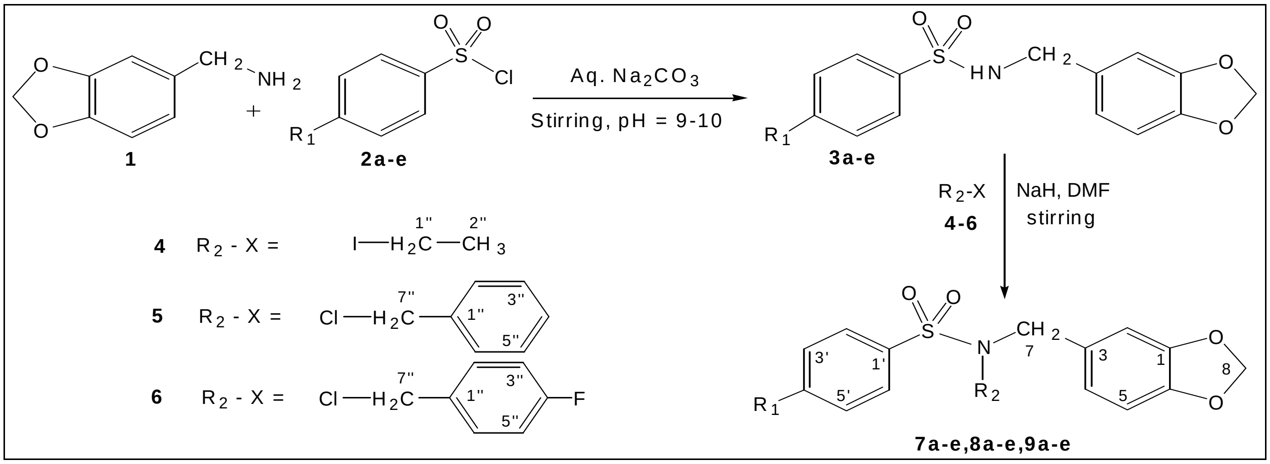
Cream white amorphous solid; Yield: 86%; M.P.: 98-100 ^{o}C; Mol. Formula: $C_{16}H_{16}N_2O_5S$; Mol. Mass: 348 gmol^{-1}; IR (KBr, v_{max} (cm^{-1})): 3312 (N-H), 3070 (Ar C-H), 1620 (Ar C=C), 1340 (S=O), 1245 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.75 (d, *J*=8.8 Hz, 2H, H-3', H-5'), 7.60 (d, *J*=8.4 Hz, 2H, H-2', H-6'), 6.73 (s, 1H, H-2), 6.70 (d, *J*=8.0 Hz, 1H, H-6), 6.61 (d, *J*=8.0 Hz, 1H, H-5), 5.93 (s, 2H, H-8), 4.11 (s, 2H, H-7), 2.20 (s, 3H, CH_3-8'); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 161.3 (C-7'), 149.6 (C-3), 143.9 (C-4), 138.5 (C-4'), 137.8 (C-1'), 133.9 (C-1), 130.4 (C-2' & C-6'), 122.4 (C-6), 113.9 (C-3' & C-5'), 109.0 (C-5), 108.7 (C-2), 100.9 (C-8), 49.3 (C-7), 23.6 (C-8'); EIMS (*m/z*): 348 $(M)^+$, 198 $(C_8H_8NOSO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 134 $(C_8H_8NO)^+$, 121 $(C_7H_5O_2)^+$, 76 $(C_6H_4)^+$, 51 $(C_4H_3)^+$.

N-(3,4-methylenedioxybenzyl)-4-methoxybenzenesulfonamide (3e)

White amorphous solid; Yield: 88%; M.P.: 88-90^{o}C; Mol. Formula: $C_{15}H_{15}NO_5S$; Mol. Mass: 321 gmol^{-1}; IR (KBr, v_{max} (cm^{-1})): 3356 (N-H), 3087 (Ar C-H), 1601 (Ar C=C), 1398 (S=O), 1251 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.78 (d, *J*=9.2 Hz, 2H, H-2', H-6'), 6.95 (d, *J*=8.8 Hz, 2H, H-3', H-5'), 6.67 (d, *J*=8.0 Hz, 1H, H-6), 6.64 (s, 1H, H-2), 6.62 (d, *J*=8.0 Hz, 1H, H-5), 5.91 (s, 2H, H-8), 3.99 (s, 2H, H-7), 3.86 (s, 3H, CH_3O-4'); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 157.5 (C-4'), 148.3 (C-3), 144.1 (C-4),139.1(C-1'), 134.2 (C-1), 129.8 (C-2' & C-6'), 122.8 (C-6), 116.1 (C-3' & C-5'), 109.0 (C-5), 108.4 (C-2), 100.7 (C-8), 57.1 (C-7'), 47.6 (C-7); EIMS (*m/z*): 321 $(M)^+$, 171 $(C_7H_7OSO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 121$(C_7H_5O_2)^+$,107$(C_7H_7O)^+$,76$(C_6H_4)^+$,51$(C_4H_3)^+$.

Procedure for the synthesis of N-ethyl/benzyl/4-flourobenzyl-N-(3,4-methylenedioxybenzyl)-4-substitutedbenzenesulfonamides (7a-e, 8a-e, 9a-e)

10mL *N,N*-Dimethylformamide (DMF) was employed to completely dissolve the molecules3a-e(0.06mmol), synthesized in the last step, in a 100mL RB flask. Sodium hydride was used to activate these molecules in this medium after stirring for 45-50mins. *N*-substitution was carried out by the treatment of these dissolved molecules with 0.06 mmol of each of the three electrophiles; ethyl iodide (4), benzyl chloride (5) and 4-flourobenzyl



Compd.	R_1	Compd.	R_1	Compd.	R_1
3a,7a,8a,9a	7' CH_3—	3c,7c,8c,9c	H_3C—C(=O)— (8', 7')	3e,7e,8e,9e	7' H_3CO—
3b,7b,8b,9b	H_3C—C(CH_3)(CH_3)— (9', 7', 8', 10')	3d,7d,8d,9d	H_3C—C(=O)—NH— (8', 7')		

Scheme 1: Protocol for synthesis of *N*-(un)substituted-*N*-(3,4-methylenedioxybenzyl)-4-substituted benzene sulfonamides

chloride (6). The reaction mixture was stirred for 3-5hrs till the single spot on TLC plate. The title compounds (7a-e, 8a-e and 9a-e) were collected through filtration and solvent extraction (using chloroform), depending upon the nature of the products, after the addition of ice cold distilled water (Aziz-ur-Rehman *et al.,* 2013).

N-ethyl-N-(3,4-methylenedioxybenzyl)-4-methylbenzenesulfonamide (7a)

Cream white amorphous solid; Yield: 63%; M.P: 80-82^{o}C; Mol. Formula: $C_{17}H_{19}NO_4S$; Mol. Mass: 333 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3062 (Ar C-H), 1612 (Ar C=C), 1343 (S=O), 1214 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.72 (d, *J*=8.4 Hz, 2H, H-2', H-6'), 7.31 (d, *J*=8.0 Hz, 2H, H-3', H-5'), 6.70 (d, *J*=3.6 Hz, 1H, H-2), 6.68 (d, *J*=7.6 Hz, 1H, H-6), 6.64 (d, *J*=8.8 Hz, 1H, H-5), 5.91 (s, 2H, H-8), 3.99 (s, 2H, H-7), 3.25 (q, *J*=7.2 Hz, 2H, H-1"), 2.42 (s, 3H, CH_3-7'), 0.95 (t, *J*=7.2 Hz, 3H, CH_3-2"); EIMS (*m/z*): 333 $(M)^+$, 155 $(C_7H_7SO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 121 $(C_7H_5O_2)^+$, 91 $(C_7H_7)^+$, 76 $(C_6H_4)^+$, 51 $(C_4H_3)^+$, 29 $(C_2H_5)^+$.

N-ethyl-N-(3,4-methylenedioxybenzyl)-4-ter-butylbenzenesulfonamide (7b)

White amorphous solid; Yield: 88%; M.P.: 98-100 ^{o}C; Mol. Formula: $C_{20}H_{25}NO_4S$; Mol. Mass: 375 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3057 (Ar C-H), 1601 (Ar C=C), 1347 (S=O), 1236 (C-O); ^{1}H-NMR ($CDCl_3$, 400MHz, δ/ppm): 7.97 (d, *J*=8.4 Hz, 2H, H-2', H-6'), 7.63 (d, *J*=8.4 Hz, 2H, H-3', H-5'), 6.70 (s, 1H, H-2), 6.67 (d, *J*=7.6 Hz, 1H, H-6), 6.64 (d, *J*=7.2 Hz, 1H, H-5), 5.91 (s, 2H, H-8), 4.17 (s, 2H, H-7), 3.38 (q, *J*=7.2 Hz, 2H, H-1"), 1.41 (s,9H,CH_3-8' to CH_3-10'), 1.01 (t, *J*=7.2 Hz, 3H, CH_3-2"); EIMS (*m/z*): 375 $(M)^+$, 197 $(C_{10}H_{13}SO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$,133$(C_{10}H_{13})^+$,121 $(C_7H_5O_2)^+$, 76 $(C_6H_4)^+$, 29 $(C_2H_5)^+$.

N-ethyl-N-(3,4-methylenedioxybenzyl)-4-acetylbenzenesulfonamide (7c)

Yellow amorphous solid; Yield: 78%; M.P.: 106-108 ^{o}C; Mol. Formula: $C_{18}H_{19}NO_5S$; Mol. Mass: 361 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3090 (Ar C-H), 1601 (Ar C=C), 1370 (S=O), 1231 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.98 (d, *J*=8.4 Hz, 2H, H-2', H-6'), 7.85 (d, *J*=8.4 Hz, 2H, H-3', H-5'), 6.74 (s, 1H, H-2), 6.69 (d, *J*=7.6 Hz, 1H, H-6), 6.64 (d, *J*=7.2 Hz, 1H, H-5), 5.90 (s, 2H, H-8), 4.19 (s, 2H, H-7), 3.40 (q, *J*=7.6 Hz, 2H, H-1"), 2.15 (s, 3H, CH_3-7'), 1.05 (t, *J*=7.6 Hz, 3H, CH_3-2"); EIMS (*m/z*): 361 $(M)^+$, 183 $(C_8H_7OSO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 121 $(C_7H_5O_2)^+$, 119 $(C_8H_7O)^+$, 76 $(C_6H_4)^+$, 29 $(C_2H_5)^+$.

Table 1: %age inhibition and MIC values of antibacterial activity

Compound	*S. typhi (-)*		*E. coli (-)*		*P. aeroginosa (-)*		*B. subtilis (+)*		*S. aureus (+)*	
	%age inhibition	MIC	%age inhibition	MIC	%age inhibition	MIC	%age inhibition	MIC	%age inhibition	MIC
3a	58.76±1.35	16.25±5.00	67.31±5.00	14.00±1.54	65.17±2.67	12.38±5.00	51.50±3.00	17.96±1.14	50.60±3.70	19.74±2.76
3b	71.00±3.59	10.66±3.45	79.63±5.00	12.37±2.89	70.25±3.12	9.15±1.92	61.10±2.23	13.43±2.47	79.45±0.65	12.17±3.17
3c	61.82±4.06	14.93±3.12	80.50±1.63	8.88±3.84	65.42±0.58	11.84±3.67	67.45±1.15	11.02±3.24	67.65±1.55	11.58±2.88
3d	62.18±3.82	11.34±2.27	86.81±1.56	8.80±4.12	66.79±1.13	11.94±3.33	65.70±1.10	11.62±1.54	74.75±2.45	12.16±1.61
3e	64.65±3.59	12.85±2.78	84.31±1.44	8.60±1.74	55.04±0.29	12.08±2.48	64.45±0.15	11.71±1.26	66.50±2.40	12.66±1.58
7a	73.28±1.83	11.07±3.87	81.37±0.53	10.92±3.03	63.78±1.09	12.98±4.00	59.41±3.87	13.70±2.81	63.88±3.57	12.56±4.24
7b	67.28±1.94	12.24±2.04	71.89±4.84	12.45±2.04	58.87±4.43	14.74±4.67	56.91±1.73	16.34±3.50	53.78±1.10	17.25±1.83
7c	69.61±1.61	11.02±2.07	79.84±4.79	11.00±2.20	69.17±1.91	14.66±3.42	57.05±2.50	18.43±4.44	38.37±5.00	-
7d	75.56±1.78	11.01±2.07	73.11±5.00	13.24±4.00	56.83±1.17	10.50±1.17	65.77±3.50	13.62±1.06	61.48±1.46	14.79±1.88
7e	72.11±1.56	12.36±3.73	76.58±0.79	11.11±2.75	67.04±5.00	12.81±3.58	64.86±1.86	14.66±3.13	59.85±3.62	15.34±2.95
8a	65.72±1.28	12.65±1.43	75.32±1.00	11.16±2.60	57.43±1.22	15.71±2.90	57.45±2.45	16.95±5.00	42.91±1.99	-
8b	53.76±0.82	13.47±2.18	70.81±4.94	12.77±3.45	57.04±4.71	15.56±3.33	59.45±1.25	10.35±1.02	51.35±1.15	19.29±3.33
8c	62.94±1.06	12.36±1.00	73.16±2.95	12.23±4.09	55.61±2.80	17.82±3.54	52.86±2.59	19.40±1.31	53.47±3.88	18.22±1.76
8d	68.83±1.61	11.29±1.04	63.11±2.79	12.77±3.00	55.61±3.43	14.71±4.33	46.55±1.82	-	61.38±2.19	16.20±1.66
8e	53.82±0.53	14.04±2.43	74.75±1.50	11.18±1.45	56.67±0.83	16.47±5.00	58.15±2.15	15.26±0.96	65.80±1.40	11.13±1.60
9a	68.33±1.67	11.73±1.73	76.00±0.74	11.28±3.83	65.39±4.52	13.12±4.83	42.68±5.00	-	47.09±0.56	-
9b	64.17±0.39	13.24±1.13	71.47±3.05	12.41±3.75	62.48±4.13	13.80±5.00	56.68±3.21	17.32±4.38	52.19±1.17	17.58±1.76
9c	44.33±1.67	-	46.26±2.68	-	57.87±4.83	16.49±1.75	11.27±4.45	-	51.68±3.93	19.05±2.11
9d	70.06±0.39	11.24±1.13	73.74±4.16	12.20±5.00	64.17±1.26	13.48±4.08	48.23±4.50	-	48.72±0.77	-
9e	60.50±3.28	12.40±3.47	61.16±4.00	15.08±2.22	49.74±4.52	-	26.41±1.14	-	41.28±1.48	-
Ciprofloxacin	91.19±2.10	9.42±1.09	90.44±1.23	8.02±2.17	92.00±2.76	8.11±1.32	89.98±2.07	8.88±2.00	92.21±1.59	9.23±1.87

NOTE**:** Minimum inhibitory concentration (MIC) was measured with suitable dilutions (5-30 µg/well) and results were calculated using EZ-Fit Perrella Scientific Inc. Amherst USA software, and data was expressed as MIC.

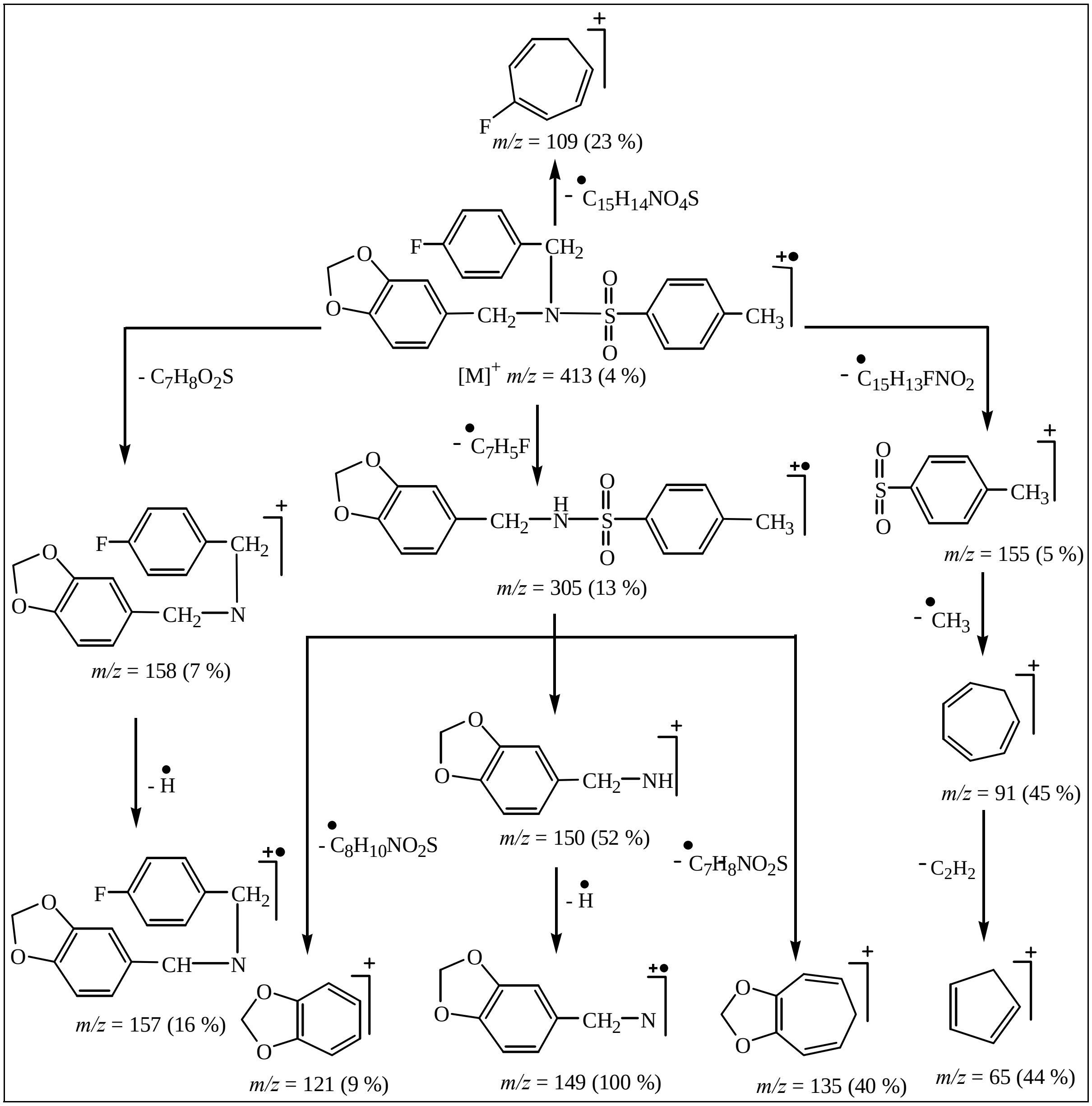


Fig. 1: Mass fragmentation pattern of *N*-(4-flourobenzyl)-*N*-((3,4-methylenedioxybenzyl)-4-methylbenzenesulfonamide (9a)

N-ethyl-N-(3,4-methylenedioxybenzyl)-4-acetamidobenzenesulfonamide (7d)

White amorphous solid; Yield: 88%; M.P.: 102-104 °C; Mol. Formula: $C_{18}H_{20}N_2O_5S$; Mol. Mass: 376 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3045 (Ar C-H), 1617 (Ar C=C), 1379 (S=O), 1245 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.73 (d, *J*=8.4 Hz, 2H, H-3', H-5'), 7.55 (d, *J*=8.4 Hz, 2H, H-2', H-6'), 6.69 (s, 1H, H-2), 6.64 (d, *J*=7.6 Hz, 1H, H-6), 6.61 (d, *J*=7.2 Hz, 1H, H-5), 5.92 (s, 2H, H-8), 4.09 (s, 2H, H-7), 3.37 (q, *J*=7.2 Hz, 2H, H-1''), 2.25 (s, 3H, CH_3-8'), 1.03 (t, *J*=7.2 Hz, 3H, CH_3-2''); EIMS (*m/z*): 376 $(M)^+$, 198 $(C_8H_8NOSO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 134 $(C_8H_8NO)^+$, 121 $(C_7H_5O_2)^+$, 76 $(C_6H_4)^+$, 51 $(C_4H_3)^+$, 29 $(C_2H_5)^+$.

N-ethyl-N-(3,4-methylenedioxybenzyl)-4-methoxybenzenesulfonamide (7e)

Cream white crystalline solid; Yield: 81%; M.P.: 84-86 °C; Mol. Formula: $C_{17}H_{19}NO_5S$; Mol. Mass: 349 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3047 (Ar C-H), 1602 (Ar C=C), 1375 (S=O), 1234 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.77 (d, *J*=8.4 Hz, 2H, H-2', H-6'), 7.03 (d, *J*=8.4 Hz, 2H, H-3', H-5'), 6.69 (s, 1H, H-2), 6.63 (d, *J*=7.6 Hz, 1H, H-6), 6.56 (d, *J*=7.6 Hz, 1H, H-5), 5.90 (s, 2H, H-8), 4.01 (s, 2H, H-7), 3.80 (s, 3H, CH_3O-4'), 3.31 (q, *J*=7.2 Hz, 2H, H-1''), 0.96 (t, *J*=7.2 Hz, 3H, CH_3-2''); EIMS (*m/z*): 349 $(M)^+$, 171 $(C_7H_7OSO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 121 $(C_7H_5O_2)^+$, 107 $(C_7H_7O)^+$, 76 $(C_6H_4)^+$, 51 $(C_4H_3)^+$, 29 $(C_2H_5)^+$.

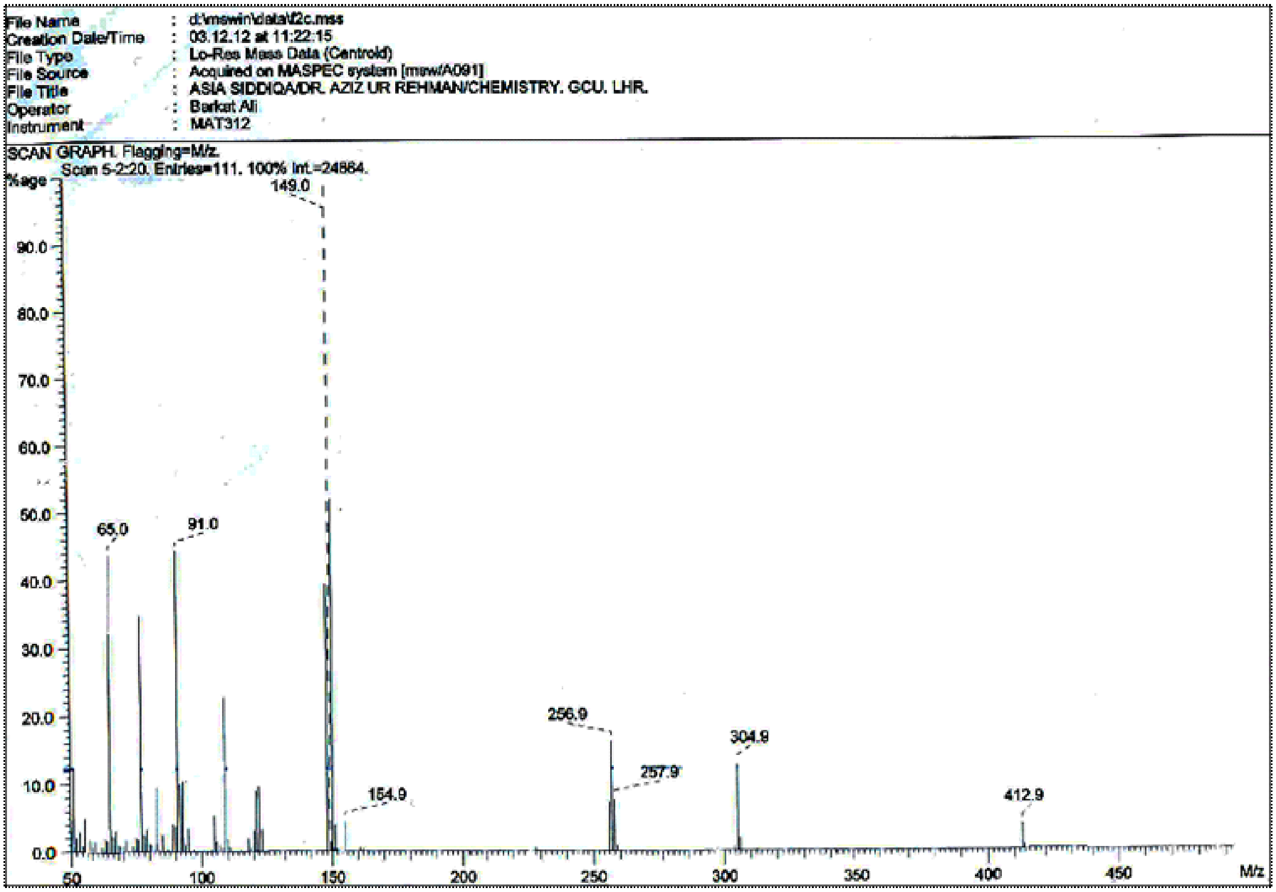


Fig. 2: Mass spectrum of compound **9a.**

N-benzyl-N-(3,4-methylenedioxybenzyl)-4-methylbenzenesulfonamide (8a)

Cream white amorphous solid; Yield: 81%; M.P.: 90-92 ^{o}C; Mol. Formula: $C_{22}H_{21}NO_4S$; Mol. Mass: 395 $gmol^{-1}$; IR (KBr, ν_{max} (cm^{-1})): 3058 (Ar C-H), 1602 (Ar C=C), 1334 (S=O), 1256 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.69 (d, J=8.0 Hz, 2H, H-2', H-6'), 7.29 (d, J=8.0 Hz, 2H, H-3', H-5'), 7.15-7.05 (m, 5H, H-2" to H-6"), 6.80 (d, J=2.8 Hz, 1H, H-2), 6.71 (d, J=7.2 Hz, 1H, H-6), 6.60 (d, J=7.2 Hz, 1H, H-5), 5.88 (s, 2H, H-8), 4.33 (s, 2H, H-7), 3.46 (s, 2H, H-7"), 2.42 (s, 3H, CH_3-7'); EIMS (m/z): 395 $(M)^+$, 155 $(C_7H_7SO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 121 $(C_7H_5O_2)^+$, 91 $(C_7H_7)^+$, 76 $(C_6H_4)^+$, 65 $(C_5H_5)^+$, 51 $(C_4H_3)^+$.

N-benzyl-N-(3,4-methylenedioxybenzyl)-4-ter-butylbenzenesulfonamide (8b)

White amorphous solid; Yield: 86%; M.P.: 108-110 ^{o}C; Mol. Formula: $C_{25}H_{27}NO_4S$; Mol. Mass: 437 $gmol^{-1}$; IR (KBr, ν_{max} (cm^{-1})): 3082 (Ar C-H), 1601 (Ar C=C), 1341 (S=O), 1273 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.93 (d, J=8.4 Hz, 2H, H-2', H-6'), 7.51 (d, J=8.4 Hz, 2H, H-3', H-5'), 7.23-7.17 (m, 5H, H-2" to H-6"), 6.70 (s, 1H, H-2), 6.68 (d, J=8.0 Hz, 1H, H-6), 6.64 (d, J=8.4 Hz, 1H, H-5), 5.93 (s, 2H, H-8), 4.18 (s, 2H, H-7), 3.44 (s, 2H, H-7"), 1.30 (s, 9H, CH_3-8' to CH_3-10'); EIMS (m/z): 437 $(M)^+$, 197 $(C_{10}H_{13}SO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 133 $(C_{10}H_{13})^+$, 121 $(C_7H_5O_2)^+$, 91 $(C_7H_7)^+$, 76 $(C_6H_4)^+$, 65 $(C_5H_5)^+$.

N-benzyl-N-(3,4-methylenedioxybenzyl)-4-acetylbenzenesulfonamide (8c)

Light brown amorphous solid; Yield: 75%; M.P.: 110-112 ^{o}C; Mol. Formula: $C_{23}H_{21}NO_5S$; Mol. Mass: 423 $gmol^{-1}$; IR (KBr, ν_{max} (cm^{-1})): 3079 (Ar C-H), 1605 (Ar C=C), 1389 (S=O), 1233 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.73 (d, J=8.4 Hz, 2H, H-2', H-6'), 7.50 (d, J=8.4 Hz, 2H, H-3', H-5'), 7.15-7.07 (m, 5H, H-2" to H-6"), 6.71 (s, 1H, H-2), 6.66 (d, J=8.4 Hz, 1H, H-6), 6.60 (d, J=8.4 Hz, 1H, H-5), 5.91 (s, 2H, H-8), 4.23 (s, 2H, H-7), 3.31 (s, 2H, H-7"), 2.20 (s, 3H, CH_3-7'); EIMS (m/z): 423 $(M)^+$, 183 $(C_8H_7OSO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 121 $(C_7H_5O_2)^+$, 119 $(C_8H_7O)^+$, 76 $(C_6H_4)^+$, 91 $(C_7H_7)^+$, 65 $(C_5H_5)^+$.

N-benzyl-N-(3,4-methylenedioxybenzyl)-4-acetamidobenzenesulfonamide (8d)

White crystalline solid; Yield: 79%; M.P.: 108-110^{o}C; Mol. Formula: $C_{23}H_{22}N_2O_5S$; Mol. Mass: 438 $gmol^{-1}$; IR (KBr, ν_{max} (cm^{-1})): 3079 (Ar C-H), 1615 (Ar C=C), 1349

(S=O), 1239 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.74 (d, J=8.4 Hz, 2H, H-3', H-5'), 7.52 (d, J=8.4 Hz, 2H, H-2', H-6'), 7.19-7.11 (m, 5H, H-2" to H-6"), 6.72 (s, 1H, H-2), 6.67 (d, J=8.0 Hz, 1H, H-6), 6.61 (d, J=8.0 Hz, 1H, H-5), 5.92 (s, 2H, H-8), 4.15 (s, 2H, H-7), 3.30 (s, 2H, H-7"), 2.19 (s, 3H, CH_3-8'); EIMS (m/z): 438 $(M)^+$, 198 $(C_8H_8NOSO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 134 $(C_8H_8NO)^+$, 121 $(C_7H_5O_2)^+$, 91 $(C_7H_7)^+$, 76 $(C_6H_4)^+$, 65 $(C_5H_5)^+$, 51 $(C_4H_3)^+$.

N-benzyl-N-(3,4-methylenedioxybenzyl)-4-methoxybenzenesulfonamide (8e)

Light grey amorphous solid; Yield: 73%; M.P.: 90-92 ^oC; Mol. Formula: $C_{22}H_{21}NO_5S$; Mol. Mass: 411 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3048 (Ar C-H), 1600 (Ar C=C), 1373 (S=O), 1235 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.83 (d, J 8.0 Hz, 2H, H-2', H-6'), 7.20-7.14 (m, 5H, H-2" to H-6"), 6.93 (d, J=8.0 Hz, 2H, H-3', H-5'), 6.69 (s, 1H, H-2), 6.63 (d, J=8.0 Hz, 1H, H-6), 6.59 (d, J=8.0 Hz, 1H, H-5), 5.89 (s, 2H, H-8), 4.39 (s, 2H, H-7), 3.96 (s, 2H, H-7"), 3.76 (s, 3H, CH_3O-4'); EIMS (m/z): 411 $(M)^+$, 171 $(C_7H_7OSO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 121 $(C_7H_5O_2)^+$, 107 $(C_7H_7O)^+$, 91 $(C_7H_7)^+$, 76 $(C_6H_4)^+$, 65 $(C_5H_5)^+$, 51 $(C_4H_3)^+$.

N-(4-flourobenzyl)-N-(3,4-methylenedioxybenzyl)-4-methylbenzenesulfonamide (9a)

Cream white amorphous solid; Yield: 81%; M.P.: 94-96 ^oC; Mol. Formula: $C_{22}H_{20}FNO_4S$; Mol. Mass: 413 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3076 (Ar C-H), 1619 (Ar C=C), 1378 (S=O), 1259 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.73 (d, J=8.4 Hz, 2H, H-2', H-6'), 7.69 (d, J=7.6 Hz, 2H, H-2", H-6"), 7.30 (d, J=8.0 Hz, 2H, H-3', H-5'), 6.87 (br.d, J=7.6 Hz, 2H, H-3", H-5"), 6.71 (s, 1H, H-2), 6.66 (d, J=7.2 Hz, 1H, H-6), 6.61 (d, J=7.6 Hz, 1H, H-5), 5.88 (s, 2H, H-8), 4.23 (s, 2H, H-7), 3.99 (s, 2H, H-7"), 2.43 (s, 3H, CH_3-4'); EIMS (m/z): 413 $(M)^+$, 155 $(C_7H_7SO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 121 $(C_7H_5O_2)^+$, 109 $(C_7H_6F)^+$, 90 $(C_7H_6)^+$, 83 $(C_5H_4F)^+$, 76 $(C_6H_4)^+$, 64 $(C_5H_4)^+$, 51 $(C_4H_3)^+$.

N-(4-flourobenzyl)-N-(3,4-methylenedioxybenzyl)-4-ter-butylbenzenesulfonamide (9b)

Cream white amorphous solid; Yield: 79%; M.P.: 112-114 ^oC; Mol. Formula: $C_{25}H_{26}FNO_4S$; Mol. Mass: 455 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3076 (Ar C-H), 1601 (Ar C=C), 1366 (S=O), 1242 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.91 (d, J=8.4 Hz, 2H, H-2', H-6'), 7.83 (d, J=8.0 Hz, 2H, H-2", H-6"), 7.71 (t, J=8.0 Hz, 2H, H-3", H-5"), 7.63 (d, J=8.4 Hz, 2H, H-3', H-5'), 6.68 (s, 1H, H-2), 6.66 (d, J=8.0 Hz, 1H, H-6), 6.63 (d, J=8.0 Hz, 1H, H-5), 5.85 (s, 2H, H-8), 4.31 (s, 2H, H-7), 3.89 (s, 2H, H-7"), 1.41 (s, 9H, CH_3-8' to CH_3-10'); EIMS (m/z): 455 $(M)^+$, 197 $(C_{10}H_{13}SO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 133 $(C_{10}H_{13})^+$, 121 $(C_7H_5O_2)^+$, 109 $(C_7H_6F)^+$, 90 $(C_7H_6)^+$, 83 $(C_5H_4F)^+$, 76 $(C_6H_4)^+$, 64 $(C_5H_4)^+$.

N-(4-flourobenzyl)-N-(3,4-methylenedioxybenzyl)-4-acetylbenzenesulfonamide (9c)

White amorphous solid; Yield: 78%; M.P.: 114-116 ^oC; Mol. Formula: $C_{23}H_{20}FNO_5S$; Mol. Mass: 441 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3088 (Ar C-H), 1607 (Ar C=C), 1378 (S=O), 1246 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.73 (d, J=8.0 Hz, 2H, H-2', H-6'), 7.67 (d, J=8.0 Hz, 2H, H-3', H-5'), 7.62 (d, J=8.4 Hz, 2H, H-2", H-6"), 7.43 (t, J=8.4 Hz, 2H, H-3", H-5"), 6.70 (s, 1H, H-2), 6.65 (d, J=8.0 Hz, 1H, H-6), 6.59 (d, J=8.0 Hz, 1H, H-5), 5.83 (s, 2H, H-8), 4.29 (s, 2H, H-7), 3.85 (s, 2H, H-7"), 2.24 (s, 3H, CH_3-7'); EIMS (m/z): 441 $(M)^+$, 183 $(C_8H_7OSO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 121 $(C_7H_5O_2)^+$, 119 $(C_8H_7O)^+$, 109 $(C_7H_6F)^+$, 90 $(C_7H_6)^+$, 83 $(C_5H_4F)^+$, 76 $(C_6H_4)^+$, 64 $(C_5H_4)^+$.

N-(4-flourobenzyl)-N-(3,4-methylenedioxybenzyl)-4-acetamidobenzenesulfonamide (9d)

White amorphous solid; Yield: 71%; M.P.: 110-112 ^oC; Mol. Formula: $C_{23}H_{21}FN_2O_5S$; Mol. Mass: 456 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3076 (Ar C-H), 1609 (Ar C=C), 1376 (S=O), 1248 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.79 (d, J=8.4 Hz, 2H, H-3', H-5'), 7.69 (d, J=8.4 Hz, 2H, H-2', H-6'), 7.64 (d, J=7.6 Hz, 2H, H-2", H-6"), 7.34 (t, J=7.6 Hz, 2H, H-3", H-5"), 6.73 (s, 1H, H-2), 6.64 (d, J=7.2 Hz, 1H, H-6), 6.60 (d, J=7.2 Hz, 1H, H-5), 5.89 (s, 2H, H-8), 4.19 (s, 2H, H-7), 3.93 (s, 2H, H-7"), 2.27 (s, 3H, CH_3-8'); EIMS (m/z): 456 $(M)^+$, 198 $(C_8H_8NOSO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 134 $(C_8H_8NO)^+$, 121 $(C_7H_5O_2)^+$, 109 $(C_7H_6F)^+$, 90 $(C_7H_6)^+$, 83 $(C_5H_4F)^+$, 76 $(C_6H_4)^+$, 64 $(C_5H_4)^+$, 51 $(C_4H_3)^+$.

N-(4-flourobenzyl)-N-(3,4-methylenedioxybenzyl)-4-methoxybenzenesulfonamide (9e)

White amorphous solid; Yield: 81%; M.P.: 96-98 ^oC; Mol. Formula: $C_{22}H_{20}FNO_5S$; Mol. Mass: 429 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3087 (Ar C-H), 1606 (Ar C=C), 1364 (S=O), 1234 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.80 (d, J=8.0 Hz, 2H, H-2', H-6'), 7.43 (d, J=8.0 Hz, 2H, H-2", H-6"), 7.21 (t, J=7.6 Hz, 2H, H-3", H-5"), 6.98 (d, J=8.0 Hz, 2H, H-3', H-5'), 6.73 (s, 1H, H-2), 6.67 (d, J=8.0 Hz, 1H, H-6), 6.61 (d, J=8.0 Hz, 1H, H-5), 5.92 (s, 2H, H-8), 4.39 (s, 2H, H-7), 3.83 (s, 2H, H-7"), 3.71 (s, 3H, CH_3O-4'); EIMS (m/z): 429 $(M)^+$, 171 $(C_7H_7OSO_2)^+$, 150 $(C_8H_8NO_2)^+$, 135 $(C_8H_7O_2)^+$, 121 $(C_7H_5O_2)^+$, 109 $(C_7H_6F)^+$, 107 $(C_7H_7O)^+$, 90 $(C_7H_6)^+$, 83 $(C_5H_4F)^+$, 76 $(C_6H_4)^+$, 64 $(C_5H_4)^+$, 51 $(C_4H_3)^+$.

Antibacterial activity

As the number of microbial cell number increases with the logarithm of the rate of growth and that increases with the increment in absorbance of broth medium. This principle is involved in the antibacterial activity method (Kaspady H *et al.,* 2009, Yang CR *et al.,* 2006). After the clinical isolation, the two gram-positive and three gram-negative bacteria were stored in culture agar medium and used for further processing. 180 µL of this stock (after dilutions with fresh nutrient broth) were added to 20 µg test samples (after suitable dilutions) and the initial absorbance was between 0.12-0.19 on measurement at 540 nm. The fluctuation in absorbance, before and after incubation at 37°C for 16-24 hrs with lid on the micro plate, was the index for bacterial growth. The percent inhibition was calculated by the formula:

$$\text{Inhibition (\%)} = \frac{\text{A - B}}{\text{A}} \times 100$$

Where, A=Absorbance in control with bacterial culture
B=Absorbance in test sample

Results are presented as mean of triplicate (n=3, ± SEM) taking Ciprofloxacin as reference standard. Minimum inhibitory concentration (MIC) was computed with suitable dilutions (5-30 µg/well) for each sample and results were calculated using EZ-Fit Perrella Scientific Inc. Amherst USA software.

STATISTICAL ANALYSIS

The measurements were recorded after triplicate experiments along with statistical analysis performed by Microsoft excel 2010 and presentations of results as mean ± SEM.

RESULTS

The *p*-substituted benzenesulfonamides were synthesized according to the protocol sketch in scheme-1. The general reaction conditions and the structure characterization are described in experimental section.

The given research work was an attempt to inaugurate a new series of biological active compounds which may be helpful in drug development program. The *p*-substituted benzenesulfonamides were synthesized in two steps, synthesis of parent molecules and then the target compounds, according to the scheme-1. The reaction was carried out by the coupling of (3,4-methylenedioxy) benzylamine (1) with *p*-substituted benzenesulfonyl chlorides (2a-e) to yield *N*-(3,4-methylenedioxybenzyl)-4-substitutedbenezenesulfonamides (3a-e)in basic medium.
Basic conditions are necessary to keep the reaction in forward direction by consuming generated HCl. The product was separated from reaction mixture after acidification, necessary for better yield but excess should be obviated because of negative effect. The structures of 3a-e were further modified by *N*-substitution with ethyl/benzyl/4-flourobenzyl halides and to yield the target molecules 7a-e, 8a-e and 9a-erespectively.The screening of all these synthesized molecules against the bacterial strains of gram-positive and gram-negative bacteria rendered them as moderately better inhibitors. The best inhibitors among these molecules might be employed for further investigation to be used as or part of new drug candidates, valuable for the remedy of various ailments. The structural elucidation of all the synthesized molecules was progressed by IR, ^{1}H-NMR and EIMS spectral data.

DISCUSSION

The sulfamoyl functional group present in the synthesized molecule3a exhibited two characteristic absorption bands at 3323 cm^{-1} and 1348 cm^{-1} because of stretching of N-H and S=O bonds, in the IR spectrum. The EI-MS spectrum sustained the molecular structure by giving characteristic peaks at *m/z*305 (for molecular ion), at *m/z* 155 and 91(for 4-methylphenylsulfonyl cation & 4-methylphenylcation) and at *m/z* 135 (for the (3,4-methylenedioxy) benzylcation). The ^{1}H-NMR spectrum affirmed the molecular structure by giving the signals at δ6.67 (d, *J*=8.0 Hz, 1H, H-6), 6.63 (d, *J*=8.8 Hz, 1H, H-5), 6.60 (s, 1H, H-2), 5.90 (s, 2H, H-8) and 3.99 (s, 2H, H-7) for 3,4-methylenedioxy) benzyl moiety and at δ7.73 (d, *J*=8.0 Hz, 2H, H-2', H-6') and 7.29 (d, *J*=8.0 Hz, 2H, H-3', H-5') for the *p*-methylphenyl ring. Eleven signals resonated in the combined view of broad band (BB) and distortion less enhancement by polarization transfer (DEPT) of ^{13}C-NMRfor five quaternary, seven methine, two methylene and one methyl carbon(s). The five signals for quaternary carbons resonated at δ 149.6 (C-3), 143.9 (C-4), 140.3 (C-1'), 138.5 (C-4') and 133.9 (C-1); the five signals for methine carbons atδ129.7 (C-2' & C-6'), 127.1 (C-3' & C-5'), 121.3 (C-6), 108.4 (C-5) and 108.2 (C-2); the two signals for methylene carbons atδ5.90 (s, 2H, H-8) and 3.99 (s, 2H, H-7); and one signal for methyl carbon at δ2.42 (s, 3H, CH_3-7').All these manifests of spectral data corroborated the molecular structure of 3a and hence named as *N*-(3,4-methylenedioxybenzyl)-4-methyl benzenesulfonamide. The mass fragmentation pattern of *N*-(4-flourobenzyl)-*N*-(3,4-methylenedioxybenzyl)-4-methylbenzenesulfonamide (9a) is sketched in fig.1 and EI-MS spectrum of same compound is given in fig. 2. Similarly, all the structures of synthesized molecules were confirmed by IR, ^{1}H-NMR and mass spectral data written in experimental section.

Antibacterial activity

The results of antibacterial study of the synthesized compounds are tabulated in table-1 as % age inhibition and MIC values. Almost all the synthesized compounds expressed inhibition potential against the five bacterial strains taken into account.

The compounds, 9a-e, have shown low activity against some bacterial strains otherwise the remaining ones showed better activities against all the bacterial strains. All the molecules expressed better activity except 9c against *Salmonella typhi*, relative to the reference standard, ciprofloxacin. The compounds 3c, 3dand 3e depicted comparable activity, 9e showed 50% activity and 9c exhibited no activity against *Escherichia coli* relative to the reference. All the molecules showed better activity but3bwith promising activity and8c&8ewith 50% activity against *Pseudomonas aeruginosa* with respect to the reference. The molecules also showed better results against *Bacillus subtilis* and *Staphylococcus aureus*. Overall the MIC values rendered these molecules valuable antibacterial active compounds.

CONCLUSION

All the synthesized compounds were prepared in good yields and well characterized by the different spectral techniques like IR, ^{1}H-NMR and EIMS. The aim of this project was to inaugurate new potent molecules with better potential and might be less toxicity. Potential of these molecules has been perfectly analyzed through their comparison with ciprofloxacin, the drug already present in market, against the bacterial strains of Gram bacteria. Therefore, these molecules can be further processed to evaluate their toxicity and reliability for use as new drug candidate.

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