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Synthesis and Antibacterial Activity of *N*-(un)substituted-*N*-((3,4-Methylenedioxyphenyl)methyl)arylsulfonamides

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ABSTRACT
Sulfonamides belong to an active group with biological activities and these activities can be enhanced by introducing heterocyclic moiety. *N*-((3,4-methylenedioxyphenyl)methyl) arylsulfonamides **(3a-f)** were synthesized by gearing up (3,4-methylenedioxyphenyl)methyl amine **(1)** and arylsulfonyl chlorides **(2a-f)** in a weak basic aqueous medium. The target molecules, **6a-f** and **7a-f** were yielded by the reaction of **3a-f** with ethyl iodide **(4)** and 4-flourobenzyl chloride **(5)** respectively in a weak basic aprotic polar medium. Structural analysis of the synthesized molecules was processed through the spectral data of IR, ^{1}H-NMR, ^{13}C-NMR and EIMS. All the synthesized molecules were evaluated for the antibacterial activity and remained moderately better inhibitors.

Keywords: (3,4-methylenedioxyphenyl)methylamine, antibacterial activity and arylsulfonyl chlorides.

1. INTRODUCTION
All the sulfonamides bear sulfamoyl group (-NSO_2) in common and have an importance in medicinal chemistry owing to their biological activities. These are widely employed as the carbonic anhydrase inhibitors; anticancer, anti-inflammatory, antiviral agents; antimicrobial drugs and antitumor drugs, plausibly because of reasonable cost, decremented toxicity and incremented activities[1-5]. The sulfonamides have been evaluated for a number of biological activities including antibacterial activities[6-7]. The benzodioxol moiety has much importance in the field of biological active compounds. The various natural products like narciclasine, lycoricidine and pancratistatin bear benzodioxole moiety and have been employed for anticancer etc. Some other drugs like the antidepressant including paroxetine, escitalopram etc also possess this moiety[8-9].

The synthesis of different sulfonamides is the interesting part of research because of their ease of formation and attractive biological activities. We have synthesized different sulfonamides including heterocyclic moieties[10-13] for the evaluation of their various biological activities, as synthesis followed by biological activities is the ongoing methodology of the researchers. This is crucial as the need of hour is to inaugurate new potent molecules with great resistance against the existing microbes. This prompted us to develop new potent molecules and the attempt remained moderately fruitful in this regard.

2. RESULTS AND DISCUSSION

2.1 *Chemistry*
A number of compounds of sulfonamide class are synthesized by the protocol outlined in scheme-1 including reagents and conditions. The various synthesized compounds were evaluated for their antibacterial activity against different bacterial strains of gram-positive and gram-negative bacteria. The theme of the synthesis was to find new potent candidates that might be used as precursors in the drug development programme in the pharmacological industries.

The parent molecules, *N*-((3,4-methylenedioxyphenyl)methyl)arylsulfonamides **(3a-f)** were yielded by reacting (3,4-methylenedioxyphenyl)methylamine **(1)** with arylsulfonyl chlorides **(2a-f)** under basic pH control in an aqueous medium. The products were separated after acidification by dil. HCl. The small amount of acid enhances the yield because of decrease in salt form in the reaction mixture but excess decrements the yield. The parent molecules were further treated with the electrophiles, alkyl/aralkyl halides **(4-5)** to synthesize the products, **6a-f** and **7a-f**, in the presence of NaH as weak base and activator in a polar aprotic solvent using DMF. The sodium hydride detaches the acidic proton to attach the alkyl/aralkyl groups. The structures of all the synthesized molecules were corroborated by spectral data as described in experimental section.

The molecule **3a** exhibited the $[M]^+$ peak at *m/z* 293 and the nominating peaks at *m/z* 141 for phenylsulfonyl cation, at *m/z* 77 for phenyl cation after the loss of SO_2 and at *m/z* 135 for the (3,4-methylenedioxyphenyl)methyl cation, in EI-MS spectrum. Two absorption bands for sulfamoyl group appeared in the IR spectrum at 3310 cm^{-1} and 1350 cm^{-1} due to N-H (stretching) and -SO_2 (stretching of sulfonyl group), respectively. In the ^{1}H-NMR spectrum, the signals resonating at δ 6.67 (d, J = 8.0 Hz, 1H, H-6), 6.64 (s, 1H, H-2), 6.61 (d, J = 8.0 Hz, 1H, H-5), 5.90 (s, 2H, H-8) and 4.02 (s, 2H, H-7) affirmed the presence of (3,4-methylenedioxyphenyl)methyl group attached at nitrogen of sulfamoyl group. The three signals resonating at δ 7.85 (d, J = 7.2 Hz, 2H, H-2', H-6'), 7.57 (t, J = 7.2 Hz, 1H, H-4')

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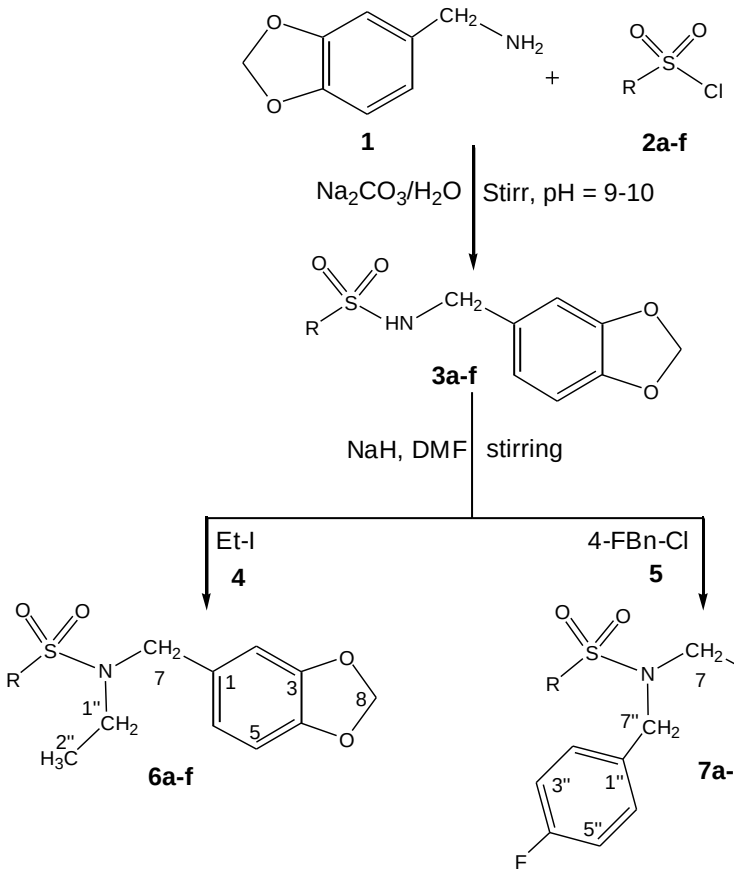
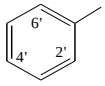
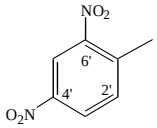
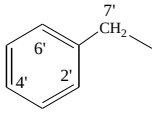
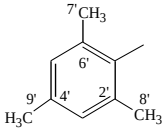
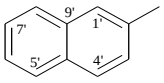
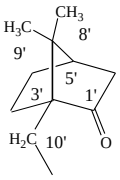


Compd.	R	Compd.	R	Compd.	R
3a,6a,7a		**3c,6c,7c**		**3e,6e,7e**	
3b,6b,7b		**3d,6d,7d**		**3f,6f,7f**	

Scheme-1: Synthesis of *N*-alkyl/aralkyl-*N*-((3,4-methylenedioxyphenyl)methyl) arylsulfonamides

And 7.50 (t, *J* = 8.0 Hz, 2H, H-3', H-5') confirmed the phenyl ring attached to the sulfur of sulfamoyl group. In BB (broad band) and DEPT (distorsionless enhancement by polarization transfer) of ^{13}C-NMR, twelve signals resonated for four quaternary, eight methine and two methylene carbons. Eight signals of three quaternary, three methine and two methylene carbons of (3,4-methylenedioxyphenyl)methyl group appeared at δ 150.2 (C-3), 144.3 (C-4), 135.6 (C-1), 121.7 (C-6), 108.7 (C-5), 108.3 (C-2), 101.0 (C-8) and 48.5 (C-7). Four signals of one quaternary and five methine carbons of phenyl sulfonyl group appeared at δ 141.6 (C-1'), 132.1 (C-4'), 129.4 (C-3' & C-5') and 127.5 (C-2' & C-6'). All these manifests corroborated the structure of *N*-((3,4-methylenedioxyphenyl)methyl)benzenesulfonamide **(3a)**. The mass fragmentation pattern of *N*-(4-flourobenzyl)-*N*-((3,4-methylenedioxyphenyl)methylbenzenesulfonamide **(7a)** is sketched in Figure-1. In the same way, the structures of other synthesized compounds were corroborated by ^{1}H-NMR, ^{13}C-NMR, IR and mass spectral data as described in experimental section.

2.1 *Antibacterial activity*

The results of antibacterial study of the synthesized compounds are listed in Table-1 as their %age inhibition and MIC values. The series of synthesized molecules has been shown to be potentially active against the five bacterial strains of Gram-bacteria.

Among the Gram-negative bacterial strains, the molecules **3f** and **7b**; **6c**, **7d** and **7e**; and **6c**, **6d** and **7a** remained inactive against *Salmonella typhi*, *Escherichia coli* and *Pseudomonas aeruginosa*, respectively. The molecules **6b** showed the most potential activity (with MIC values of 10.90±2.88 µM) relative to the reference standard, ciprofloxacin (with MIC value of 9.42±1.09 µM) against *Salmonella typhi*. The most potent molecules against *Escherichia coli* were **3d** and **3e** with MIC values of 8.70±1.00 and 8.66±4.54 µM,

much comparable to that of ciprofloxacin i.e. 8.02±2.17 µM. Only **3c** exhibited the prominent activity against *Pseudomonas aeruginosa*, comparable to the reference. Among the Gram-positive bacterial strains, only parent molecules i.e. **3a** to **3f** and some derivatives showed the activity against *Bacillus subtilis*. The only two molecules, **3b** and **6a** executed the same activity as that of ciprofloxacin against *Staphylococcus aureus*, evident from their MIC values. Almost the whole series remained active against all the bacterial strains, credibly, because of the heterocyclic moiety attached to the sulfamoyl group and whose interaction was extended by substitution of acidic proton at nitrogen of sulfamoyl group.

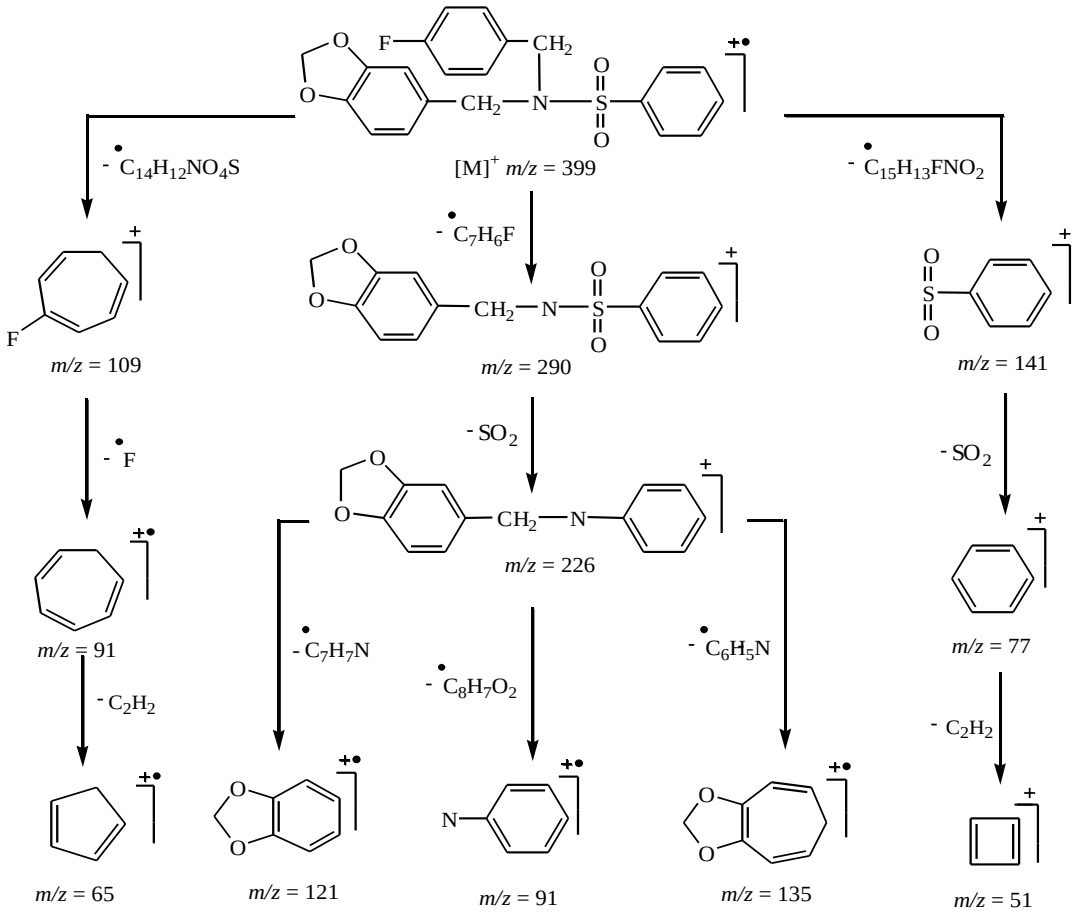


Fig-1: Mass fragmentation pattern of *N*-(4-flourobenzyl)-*N*-((3,4-methylenedioxyphenyl) methyl)benzenesulfonamide **(7a)**

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	66.41±2.18	11.47±2.91	77.25±4.63	11.08±2.41	63.67±2.92	12.74±3.75	69.10±3.10	12.66±2.14	64.05±0.85	14.95±1.86
3b	60.12±5.00	15.09±1.55	64.88±2.25	13.04±1.90	62.50±2.00	13.16±2.00	63.50±2.00	13.07±1.99	76.80±1.60	10.85±1.47
3c	63.53±2.12	12.05±1.64	59.94±5.00	14.60±1.57	70.83±2.33	8.50±1.42	64.60±0.60	11.82±3.02	56.55±0.55	15.95±1.33
3d	63.71±1.82	12.19±1.37	83.81±1.19	8.70±1.00	53.79±1.29	17.93±3.58	66.85±0.95	11.48±2.15	62.05±2.75	14.52±2.47
3e	64.76±2.29	13.17±1.44	82.25±2.38	8.66±4.54	62.50±3.58	12.34±3.42	65.35±1.45	11.69±2.74	64.00±1.00	13.07±3.02
3f	47.47±5.00	-	59.19±1.56	11.12±3.14	50.17±5.00	19.85±4.42	60.45±2.45	14.36±1.61	50.70±5.00	19.26±2.68
6a	63.67±4.44	13.92±1.07	50.63±4.32	19.75±1.20	69.65±2.70	11.00±1.25	59.41±5.00	13.99±5.00	60.41±4.29	10.76±3.17
6b	75.33±1.56	10.90±2.88	85.84±2.47	10.73±1.15	61.65±2.87	16.23±4.83	65.00±1.55	14.69±1.37	58.01±2.50	16.18±2.63
6c	59.33±2.00	15.37±1.76	41.16±5.00	-	49.91±1.65	-	50.82±2.14	19.63±1.81	55.61±4.59	16.92±1.32
6d	66.78±3.33	12.58±0.87	70.47±0.58	13.58±1.15	48.91±1.99	-	29.82±4.00	-	53.67±1.84	17.56±2.40
6e	59.28±1.28	15.15±1.13	86.11±1.26	10.66±3.75	63.26±2.65	13.53±3.92	43.77±2.59	-	52.60±3.32	18.64±1.47
6f	74.94±2.28	11.08±1.67	57.95±5.00	14.11±2.11	74.26±1.43	10.76±2.00	68.18±1.36	15.65±2.94	68.32±1.36	11.89±2.52
7a	62.50±3.83	13.27±3.47	58.00±4.53	16.04±1.44	46.78±2.96	-	55.55±2.36	18.37±1.19	58.98±3.57	16.14±1.75
7b	46.22±0.78	-	53.11±3.74	17.14±2.75	57.26±4.22	16.09±4.17	42.45±4.70	-	40.66±1.89	-
7c	69.11±69.11	11.29±1.93	78.84±3.52	11.08±4.00	67.39±1.99	16.12±3.83	36.91±4.00	-	62.81±2.70	11.46±2.25
7d	57.67±2.32	15.95±2.58	20.84±4.56	-	53.13±2.09	17.15±2.15	39.55±3.23	-	59.18±2.00	15.98±1.00
7e	70.61±0.17	11.08±1.27	47.20±3.05	-	53.43±2.57	15.93±1.33	35.32±5.00	-	59.64±2.91	15.73±1.47
7f	64.89±3.12	12.81±2.41	77.26±1.58	11.02±1.75	64.39±3.43	13.78±1.78	49.18±3.65	-	60.31±3.57	12.17±1.18
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

3. EXPERIMENTAL

3.1 *General*

Purity of the synthesized molecules was analyzed by thin layer chromatography (TLC) using EtOAc and *n*-hexane as solvent systems, followed by visualization under UV at 254 nm. Melting points of all synthesized compounds were recorded on a Griffin-George melting point apparatus by open capillary tube and were uncorrected. The I.R. spectra were recorded in KBr pellet method on a Jasco-320-A spectrophotometer (wave number in cm^{-1}). ^{1}H-NMR and ^{13}C-NMR spectra were recorded in $CHCl_3$-d_1 on a Bruker spectrometers at 400 MHz and 100 MHz respectively, with chemical shift in δ-values, tetramethylsilane as reference standard, and the coupling constants (*J*) in Hz. Mass spectra (EIMS) were recorded on a JMS-HX-110 spectrometer. (3,4-methylenedioxyphenyl)methylamine, arylsulfonyl chlorides and alkyl/aralkyl halides were purchased from Merck and Alfa Aeser through local suppliers. The solvents used, were of analytical grade.

3.2 *Procedure for the synthesis of N-((3,4-methylenedioxyphenyl)methyl)arylsulfonamides (3a-f)*

(3,4-methylenedioxyphenyl)methylamine (0.01 mol; **1**) was suspended in 50 mL water using 200 mL round bottom (RB) flask. The pH of reaction mixture was strictly maintained 9.0-10.0 by using aqueous Na_2CO_3 solution (20%). Arylsulfonyl chlorides (0.01 mol; **2a-f**) were poured into the flask in short time duration along with stirring. The reaction contents were kept on stirring for 2-3 hours and monitored by TLC till the single spot. At the completion of reaction, dil. HCl (2.0-3.0 mL) was added slowly along with shaking to make the pH slightly acidic. The reaction mixture was kept undisturbed for 0-5 minutes and then shaken to get the precipitates.

3.2.1 *N-((3,4-methylenedioxyphenyl)methyl)benzenesulfonamide (3a)*

White amorphous solid; Yield: 70%; M.P.: 80-82 ^{o}C; Mol. Formula: $C_{14}H_{13}NO_4S$; Mol. Mass: 293 $gmol^{-1}$; IR (KBr, ν_{max} (cm^{-1})): 3310 (N-H), 3080 (Ar C-H), 1610 (Ar C=C), 1350 (S=O), 1235 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.85 (d, *J* = 7.2 Hz, 2H, H-2', H-6'), 7.57 (t, *J* = 7.2 Hz, 1H, H-4'), 7.50 (t, *J* = 8.0 Hz, 2H, H-3', H-5'), 6.67 (d, *J* = 8.0 Hz, 1H, H-6), 6.64 (s, 1H, H-2), 6.61 (d, *J* = 8.0 Hz, 1H, H-5), 5.90 (s, 2H, H-8), 4.02 (s, 2H, H-7); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 150.2 (C-3), 144.3 (C-4), 141.6 (C-1'), 135.6 (C-1), 132.1 (C-4'), 129.4 (C-3' & C-5'), 127.5 (C-2' & C-6'), 121.7 (C-6), 108.7 (C-5), 108.3 (C-2), 101.0 (C-8), 48.5 (C-7); EIMS (*m/z*): 293 $[M]^+$, 150 $[C_8H_8NO_2]^+$, 141 $[C_6H_5SO_2]^+$, 135 $[C_8H_7O_2]^+$, 121 $[C_7H_5O_2]^+$, 77 $[C_6H_5]^+$, 51 $[C_4H_3]^+$.

3.2.2 *N-((3,4-methylenedioxyphenyl)methyl)-2,4,6-trimethylbenzenesulfonamide (3b)*

White amorphous solid; Yield: 82%; M.P.: 100-102 ^{o}C; Mol. Formula: $C_{17}H_{19}NO_4S$; Mol. Mass: 333 $gmol^{-1}$; IR (KBr, ν_{max} (cm^{-1})): 3323 (N-H), 3055 (Ar C-H), 1621 (Ar C=C), 1365 (S=O), 1225 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 6.94 (s, 2H, H-3', H-5'), 6.66 (d, *J* = 8.4 Hz, 1H, H-6), 6.60 (s, 1H, H-2), 6.57 (d, *J* = 8.8 Hz, 1H, H-5), 5.90 (s, 2H, H-8), 3.95 (s, 2H, H-7), 2.60 (s, 6H, CH_3-7', CH_3-8'), 2.29 (s, 3H, CH_3-9'); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 148.7 (C-1'), 146.9 (C-3), 145.2 (C-2' & C-6'), 142.0 (C-4), 138.9 (C-4'), 135.3 (C-3' & C-5'), 133.8 (C-1), 122.9 (C-6), 108.5 (C-5), 107.6 (C-2), 101.4 (C-8), 50.0 (C-7), 21.4 (C-7' & C-8'), 18.9 (C-9'); EIMS (*m/z*): 333 $[M]^+$, 183 $[C_9H_{11}SO_2]^+$, 150 $[C_8H_8NO_2]^+$, 135 $[C_8H_7O_2]^+$, 121 $[C_7H_5O_2]^+$, 119 $[C_9H_{11}]^+$, 74 $[C_6H_2]^+$.

3.2.3 *N-((3,4-methylenedioxyphenyl)methyl)-2,4-dinitrobenzenesulfonamide (3c)*

Yellow amorphous solid; Yield: 81%; M.P.: 96-98 ^{o}C; Mol. Formula: $C_{14}H_{11}N_3O_8S$; Mol. Mass: 381 $gmol^{-1}$; IR (KBr, ν_{max} (cm^{-1})): 3376 (N-H), 3057 (Ar C-H), 1607 (Ar C=C), 1367 (S=O), 1219 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 8.58 (d, *J* = 2.0 Hz, 1H, H-3'), 8.37 (dd, *J* = 8.8, 2.4 Hz, 1H, H-5'), 8.10 (d, *J* = 8.8 Hz, 1H, H-6'), 6.65 (d, *J* = 7.2 Hz, 1H, H-6), 6.63 (d, *J* = 2.4 Hz, 1H, H-2), 6.60 (d, *J* = 7.2 Hz, 1H, H-5), 5.85 (s, 2H, H-8), 4.25 (s, 2H, H-7); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 153.2 (C-4'), 149.4 (C-3), 143.2 (C-4), 141.7 (C-1'), 139.8 (C-2'), 133.4 (C-1), 129.3 (C-6'), 128.6 (C-5'), 122.6 (C-6), 120.7 (C-3'), 109.4 (C-5), 108.6 (C-2), 101.0 (C-8), 45.4 (C-7); EIMS (*m/z*): 381 $[M]^+$, 231 $[C_6H_3N_2O_4SO_2]^+$, 167 $[C_6H_3N_2O_4]^+$, 150 $[C_8H_8NO_2]^+$, 135 $[C_8H_7O_2]^+$, 121 $[C_7H_5O_2]^+$, 75 $[C_6H_3]^+$.

3.2.4 *N-((3,4-methylenedioxyphenyl)methyl)-2-naphthalenesulfonamide (3d)*

White amorphous solid; Yield: 77%; M.P.: 104-106 ^{o}C; Mol. Formula: $C_{18}H_{15}NO_4S$; Mol. Mass: 341 $gmol^{-1}$; IR (KBr, ν_{max} (cm^{-1})): 3316 (N-H), 3078 (Ar C-H), 1614 (Ar C=C), 1347 (S=O), 1227 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 8.38 (s, 1H, H-8'), 7.95 (d, *J* = 8.4 Hz, 1H, H-3'), 7.91 (d, *J* = 8.4 Hz, 1H, H-2'), 7.86 (d, *J* = 8.4 Hz, 1H, H-4'), 7.80 (d, *J* = 8.4 Hz, 1H, H-7'), 7.64 (t, *J* = 7.2 Hz, 1H, H-6'), 7.60 (t, *J* = 7.2 Hz, 1H, H-5'), 6.65 (d, *J* = 7.2 Hz, 1H, H-6), 6.62 (s, 1H, H-2), 6.59 (d, *J* = 7.2 Hz, 1H, H-5), 5.82 (s, 2H, H-8), 4.06 (s, 2H, H-7); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 149.9 (C-3), 144.2 (C-4), 140.5 (C-2'), 138.7 (C-10'), 129.1 (C-5'), 128.8 (C-7'), 128.7 (C-1), 128.4 (C-8'), 127.9 (C-4'), 127.5 (C-6'), 127.1 (C-9'), 126.7 (C-1'), 123.3 (C-3'), 121.5 (C-6), 109.2 (C-5), 108.4 (C-2), 100.7 (C-8), 50.3 (C-7); EIMS (*m/z*): 341 $[M]^+$, 191 $[C_{10}H_7SO_2]^+$, 150 $[C_8H_8NO_2]^+$, 135 $[C_8H_7O_2]^+$, 127 $[C_{10}H_7]^+$, 121 $[C_7H_5O_2]^+$, 102 $[C_8H_6]^+$.

3.2.5 *N-((3,4-methylenedioxyphenyl)methyl)-1-phenylmethanesulfonamide (3e)*

White amorphous solid; Yield: 91%; M.P.: 80-82 ^{o}C; Mol. Formula: $C_{15}H_{15}NO_4S$; Mol. Mass: 305 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3345 (N-H), 3065 (Ar C-H), 1604 (Ar C=C), 1375 (S=O), 1249 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.36-7.32 (m, 5H, H-2' to H-6'), 6.82 (d, *J* = 2.0 Hz, 1H, H-2), 6.74 (d, *J* = 7.6 Hz, 1H, H-6), 6.69 (d, *J* = 8.0 Hz, 1H, H-5), 5.94 (s, 2H, H-8), 4.20 (s, 2H, H-7'), 4.08 (s, 2H, H-7); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 150.3 (C-3), 143.5 (C-4), 133.4 (C-1), 130.6 (C-2' & C-6'), 128.8 (C-3' & C-5'), 128.4 (C-1'), 127.5 (C-4'), 121.5 (C-6), 108.6 (C-5), 108.3 (C-2), 101.2 (C-8), 59.4 (C-7'), 47.5 (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 $[C_7H_7]^+$, 65 $[C_5H_5]^+$.

3.2.6 *N-((3,4-methylenedioxyphenyl)methyl)-1-((1R,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1] heptan-1-yl)methanesulfonamide (3f)*

White amorphous solid; Yield: 77%; M.P.: 110-112 ^{o}C; Mol. Formula: $C_{18}H_{23}NO_5S$; Mol. Mass: 365 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3345 (N-H), 3057 (Ar C-H), 1622 (Ar C=C), 1378 (S=O), 1241 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 6.85 (d, *J* = 1.2 Hz, 1H, H-2), 6.81 (d, *J* = 8.0 Hz, 1H, H-6), 6.74 (d, *J* = 8.0 Hz, 1H, H-5), 5.92 (s, 2H, H-8), 4.23 (s, 2H, H-7), 3.11 (s, 2H, H-10'), 2.39-2.37 (m, 2H, H-3'), 2.12-2.07 (m, 2H, H-6'), 2.00-1.96 (m, 2H, H-4'), 1.44-1.39 (m, 1H, H-5'), 0.94 (s, 6H, CH_3-8', CH_3-9'); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 210.7 (C-1'), 148.4 (C-3), 141.3 (C-4), 137.6 (C-1), 123.1 (C-6), 111.2 (C-5), 108.9 (C-2), 100.6 (C-8), 55.2 (C-2'), 52.9 (C-10'), 45.3 (C-7'), 43.2 (C-5'), 41.9 (C-6'), 40.4 (C-7), 29.4 (C-3'), 28.1 (C-4'), 20.3 (C-8'), 18.7 (C-9'); EIMS (*m/z*): 365 $[M]^+$, 215 $[C_{10}H_{15}OSO_2]^+$, 151 $[C_{10}H_{15}O]^+$, 150 $[C_8H_8NO_2]^+$, 135 $[C_8H_7O_2]^+$, 121 $[C_7H_5O_2]^+$.

3.3 *Procedure for the synthesis of N-alkyl/aralkyl-N-((3,4-methylenedioxyphenyl)methyl) arylsulfonamides (6a-f, 7a-f)*

Compounds **3a-f** (0.01 mol) was homogeneously dissolved in 10 mL *N*,*N*-dimethyl formamide (DMF) in a 100 mL RB flask along with the addition of sodium hydride (0.01 mol) at room temperature (RT). The reaction contents were stirred for 30-45 min and then the electrophiles; ethyl iodide (0.01 mol; **4**) and 4-flourobenzyl chloride (0.01 mol; **5**) were added to yield the target molecules **6a-f** and **7a-f** respectively after stirring for 3-4 hours. After complete reaction as per single spot on TLC, the reaction mixture was quenched with ice cold distilled water (200 mL) along with hand shaking. The formed precipitates were kept undisturbed for 10-15 minutes and then were filtered, washed with water and dried to yield the corresponding molecules **6a-f** and **7a-f**.

3.3.1 *N-ethyl-N-((3,4-methylenedioxyphenyl)methyl)benzenesulfonamide (6a)*

White amorphous solid; Yield: 73%; M.P.: 76-78 ^{o}C; Mol. Formula: $C_{16}H_{17}NO_4S$; Mol. Mass: 319 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3065 (Ar C-H), 1603 (Ar C=C), 1339 (S=O), 1241 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.83 (d, *J* = 7.6 Hz, 2H, H-2', H-6'), 7.55 (t, *J* = 7.6 Hz, 1H, H-4'), 7.51 (t, *J* = 7.6 Hz, 2H, H-3', H-5'), 6.69 (d, *J* = 8.0 Hz, 1H, H-6), 6.67 (s, 1H, H-2), 6.63 (d, *J* = 8.0 Hz, 1H, H-5), 5.89 (s, 2H, H-8), 4.05 (s, 2H, H-7), 3.21 (q, *J* = 7.2 Hz, 2H, H-1"), 0.95 (t, *J* = 7.2 Hz, 3H, CH_3-2"); EIMS (*m/z*): 319 $[M]^+$, 150 $[C_8H_8NO_2]^+$, 141 $[C_6H_5SO_2]^+$, 135 $[C_8H_7O_2]^+$, 121 $[C_7H_5O_2]^+$, 77 $[C_6H_5]^+$, 51 $[C_4H_3]^+$, 29 $[C_2H_5]^+$.

3.3.2 *N-ethyl-N-((3,4-methylenedioxyphenyl)methyl)-2,4,6-trimethylbenzenesulfonamide (6b)*

White crystalline solid; Yield: 89%; M.P.: 104-106 ^{o}C; Mol. Formula: $C_{19}H_{23}NO_4S$; Mol. Mass: 361 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3075 (Ar C-H), 1613 (Ar C=C), 1359 (S=O), 1231 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 6.93 (s, 2H, H-3', H-5'), 6.71 (s, 1H, H-2), 6.67 (d, *J* = 8.4 Hz, 1H, H-6), 6.57 (d, *J* = 8.0 Hz, 1H, H-5), 5.93 (s, 2H, H-8), 4.18 (s, 2H, H-7), 3.34 (q, *J* = 7.2 Hz, 2H, H-1"), 2.55 (s, 6H, CH_3-7', CH_3-8'), 2.23 (s, 3H, CH_3-9'), 0.96 (t, *J* = 7.2 Hz, 3H, CH_3-2"); EIMS (*m/z*): 361 $[M]^+$, 183 $[C_9H_{11}SO_2]^+$, 150 $[C_8H_8NO_2]^+$, 135 $[C_8H_7O_2]^+$, 121 $[C_7H_5O_2]^+$, 119 $[C_9H_{11}]^+$, 74 $[C_6H_2]^+$, 29 $[C_2H_5]^+$.

3.3.3 *N-ethyl-N-((3,4-methylenedioxyphenyl)methyl)-2,4-dinitrobenzenesulfonamide (6c)*

Light brown sticky solid; Yield: 76%; Mol. Formula: $C_{16}H_{15}N_3O_8S$; Mol. Mass: 409 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3062 (Ar C-H), 1604 (Ar C=C), 1379 (S=O), 1281 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 8.51 (d, *J* = 2.4 Hz, 1H, H-3'), 8.45 (dd, *J* = 8.4, 2.0 Hz, 1H, H-5'), 8.19 (d, *J* = 8.4 Hz, 1H, H-6'), 6.71 (d, *J* = 8.4 Hz, 1H, H-6), 6.66 (s, 1H, H-2), 6.63 (d, *J* = 8.4 Hz, 1H, H-5), 5.92 (s, 2H, H-8), 4.19 (s, 2H, H-7), 3.45 (q, *J* = 7.2 Hz, 2H, H-1"), 1.03 (t, *J* = 7.2 Hz, 3H, CH_3-2"); EIMS (*m/z*): 409 $[M]^+$, 231 $[C_6H_3N_2O_4SO_2]^+$, 167 $[C_6H_3N_2O_4]^+$, 150 $[C_8H_8NO_2]^+$, 135 $[C_8H_7O_2]^+$, 121 $[C_7H_5O_2]^+$, 75 $[C_6H_3]^+$, 29 $[C_2H_5]^+$.

3.3.4 *N-ethyl-N-((3,4-methylenedioxyphenyl)methyl)-2-naphthalenesulfonamide (6d)*

White amorphous solid; Yield: 75%; M.P.: 100-102 ^{o}C; Mol. Formula: $C_{20}H_{19}NO_4S$; Mol. Mass: 369 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3053 (Ar C-H), 1617 (Ar C=C), 1347 (S=O), 1223 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 8.38 (d, *J* = 4.0 Hz, 1H, H-8'), 7.95 (dd, *J* = 8.4, 3.6 Hz, 1H, H-2'), 7.90 (d, *J* = 7.6 Hz, 1H, H-3'), 7.80 (dd, *J* = 7.6, 1.6 Hz, 1H,

H-4'), 7.78 (d, *J* = 7.6 Hz, 1H, H-7'), 7.63-7.59 (m, 2H, H-5', H-6'), 6.72 (s, 1H, H-2), 6.65 (d, *J* = 8.0 Hz, 1H, H-6), 6.62 (d, *J* = 8.0 Hz, 1H, H-5), 5.90 (s, 2H, H-8), 4.29 (s, 2H, H-7), 3.23 (q, *J* = 7.2 Hz, 2H, H-1"), 0.92 (t, *J* = 7.2 Hz, 3H, CH_3-2"); EIMS (*m/z*): 369 $[M]^+$, 191 $[C_{10}H_7SO_2]^+$, 150 $[C_8H_8NO_2]^+$, 135 $[C_8H_7O_2]^+$, 127 $[C_{10}H_7]^+$, 121 $[C_7H_5O_2]^+$, 102 $[C_8H_6]^+$, 29 $[C_2H_5]^+$.

3.3.5 *N-ethyl-N-((3,4-methylenedioxyphenyl)methyl)-1-phenylmethanesulfonamide (6e)*

White amorphous solid; Yield: 83%; M.P.: 84-86 °C; Mol. Formula: $C_{17}H_{19}NO_4S$; Mol. Mass: 333 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3075 (Ar C-H), 1621 (Ar C=C), 1381 (S=O), 1248 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.39-7.30 (m, 5H, H-2' to H-6'), 6.78 (s, 1H, H-2), 6.73 (d, *J* = 7.2 Hz, 1H, H-6), 6.69 (d, *J* = 7.2 Hz, 1H, H-5), 5.94 (s, 2H, H-8), 4.21 (s, 2H, H-7'), 4.00 (s, 2H, H-7), 3.05 (q, *J* = 7.2 Hz, 2H, H-1"), 0.94 (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 $[C_7H_7]^+$, 65 $[C_5H_5]^+$, 29 $[C_2H_5]^+$.

3.3.6 *N-ethyl-N-((3,4-methylenedioxyphenyl)methyl)-1-((1R,4R)-7,7-dimethyl-2-oxobicyclo [2.2.1]heptan-1-yl)methanesulfonamide (6f)*

Light yellow liquid; Yield: 79%; Mol. Formula: $C_{20}H_{27}NO_5S$; Mol. Mass: 393 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3058 (Ar C-H), 1609 (Ar C=C), 1357 (S=O), 1235 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 6.80 (s, 1H, H-2), 6.69 (d, *J* = 8.4 Hz, 1H, H-6), 6.64 (d, *J* = 8.4 Hz, 1H, H-5), 5.93 (s, 2H, H-8), 4.20 (s, 2H, H-7), 3.29 (q, *J* = 7.2 Hz, 2H, H-1"), 3.16 (s, 2H, H-10'), 2.45-2.42 (m, 2H, H-3'), 2.13-2.06 (m, 2H, H-6'), 2.01-1.98 (m, 2H, H-4'), 1.56-1.47 (m, 1H, H-5'), 0.99 (t, *J* = 7.2 Hz, 3H, CH_3-2"), 0.92 (s, 6H, CH_3-8', CH_3-9'); EIMS (*m/z*): 393 $[M]^+$, 215 $[C_{10}H_{15}OSO_2]^+$, 151 $[C_{10}H_{15}O]^+$, 150 $[C_8H_8NO_2]^+$, 135 $[C_8H_7O_2]^+$, 121 $[C_7H_5O_2]^+$, 29 $[C_2H_5]^+$.

3.3.7 *N-(4-fluorobenzyl)-N-((3,4-methylenedioxyphenyl)methyl)benzenesulfonamide (7a)*

Grey amorphous solid; Yield: 69%; M.P.: 88-90 °C; Mol. Formula: $C_{21}H_{18}FNO_4S$; Mol. Mass: 399 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3066 (Ar C-H), 1601 (Ar C=C), 1332 (S=O), 1248 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.80 (d, *J* = 8.0 Hz, 2H, H-2', H-6'), 7.65 (d, *J* = 7.6 Hz, 2H, H-2", H-6"), 7.50 (t, *J* = 8.0 Hz, 1H, H-4'), 7.45 (t, *J* = 8.0 Hz, 2H, H-3', H-5'), 7.27 (t, *J* = 7.6 Hz, 2H, H-3", H-5"), 6.64 (d, *J* = 7.6 Hz, 1H, H-6), 6.62 (s, 1H, H-2), 6.59 (d, *J* = 7.6 Hz, 1H, H-5), 5.85 (s, 2H, H-8), 4.12 (s, 2H, H-7), 3.89 (s, 2H, H-7"); EIMS (*m/z*): 399 $[M]^+$, 150 $[C_8H_8NO_2]^+$, 141 $[C_6H_5SO_2]^+$, 135 $[C_8H_7O_2]^+$, 121 $[C_7H_5O_2]^+$, 109 $[C_7H_6F]^+$, 90 $[C_7H_6]^+$, 83 $[C_5H_4F]^+$, 77 $[C_6H_5]^+$, 64 $[C_5H_4]^+$, 51 $[C_4H_3]^+$.

3.3.8 *N-(4-flourobenzyl)-N-((3,4-methylenedioxyphenyl)methyl)-2,4,6-trimethylbenzene sulfonamide (7b)*

Cream white amorphous solid; Yield: 86%; M.P.: 114-116 °C; Mol. Formula: $C_{24}H_{24}FNO_4S$; Mol. Mass: 441 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3090 (Ar C-H), 1612 (Ar C=C), 1347 (S=O), 1232 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.40 (d, *J* = 8.4 Hz, 2H, H-2", H-6"), 7.15 (t, *J* = 8.4 Hz, 2H, H-3", H-5"), 6.95 (s, 2H, H-3', H-5'), 6.79 (s, 1H, H-2), 6.76 (d, *J* = 8.0 Hz, 1H, H-6), 6.69 (d, *J* = 7.6 Hz, 1H, H-5), 5.87 (s, 2H, H-8), 4.19 (s, 2H, H-7), 3.71 (s, 2H, H-7"), 2.50 (s, 6H, CH_3-7', CH_3-8'), 2.25 (s, 3H, CH_3-9'); EIMS (*m/z*): 441 $[M]^+$, 183 $[C_9H_{11}SO_2]^+$, 150 $[C_8H_8NO_2]^+$, 135 $[C_8H_7O_2]^+$, 121 $[C_7H_5O_2]^+$, 119 $[C_9H_{11}]^+$, 109 $[C_7H_6F]^+$, 90 $[C_7H_6]^+$, 83 $[C_5H_4F]^+$, 74 $[C_6H_2]^+$, 64 $[C_5H_4]^+$.

3.3.9 *N-(4-flourobenzyl)-N-((3,4-methylenedioxyphenyl)methyl)-2,4-dinitrobenzene sulfonamide (7c)*

Light brown sticky solid; Yield: 77%; Mol. Formula: $C_{21}H_{16}FN_3O_8S$; Mol. Mass: 489 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3059 (Ar C-H), 1598 (Ar C=C), 1343 (S=O), 1221 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 8.54 (d, *J* = 2.4 Hz, 1H, H-3'), 8.46 (dd, *J* = 8.0, 2.0 Hz, 1H, H-5'), 8.33 (d, *J* = 8.4 Hz, 1H, H-6'), 7.51 (d, *J* = 8.0 Hz, 2H, H-2", H-6"), 7.17 (t, *J* = 8.0 Hz, 2H, H-3", H-5"), 6.75 (s, 1H, H-2), 6.71 (d, *J* = 8.4 Hz, 1H, H-6), 6.68 (d, *J* = 8.4 Hz, 1H, H-5), 5.89 (s, 2H, H-8), 4.44 (s, 2H, H-7), 3.81 (s, 2H, H-7"); EIMS (*m/z*): 489 $[M]^+$, 231 $[C_6H_3N_2O_4SO_2]^+$, 167 $[C_6H_3N_2O_4]^+$, 150 $[C_8H_8NO_2]^+$, 135 $[C_8H_7O_2]^+$, 121 $[C_7H_5O_2]^+$, 109 $[C_7H_6F]^+$, 90 $[C_7H_6]^+$, 83 $[C_5H_4F]^+$, 75 $[C_6H_3]^+$, 64 $[C_5H_4]^+$.

3.3.10 *N-(4-flourobenzyl)-N-((3,4-methylenedioxyphenyl)methyl)-2-naphthalene sulfonamide (7d)*

White amorphous solid; Yield: 86%; M.P.: 118-120 °C; Mol. Formula: $C_{25}H_{20}FNO_4S$; Mol. Mass: 449 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3051 (Ar C-H), 1611 (Ar C=C), 1369 (S=O), 1237 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 8.38 (s, 1H, H-8'), 7.95 (d, *J* = 8.4 Hz, 1H, H-3'), 7.91 (d, *J* = 8.4 Hz, 1H, H-2'), 7.89 (d, *J* = 8.4 Hz, 2H, H-2", H-6"), 7.80 (dd, *J* = 8.0, 1.6 Hz, 1H, H-4'), 7.73 (dd, *J* = 8.0, 1.6 Hz, 1H, H-7'), 7.64 (t, *J* = 8.4 Hz, 2H, H-3", H-5"), 7.62 (t, *J* = 8.0 Hz, 1H, H-6'), 7.60 (t, *J* = 8.0 Hz, 1H, H-5'), 6.64 (d, *J* = 7.2 Hz, 1H, H-6), 6.61 (d, *J* = 3.6 Hz, 1H, H-2), 6.59 (d, *J* = 7.2 Hz, 1H, H-5), 5.82 (s, 2H, H-8), 4.05 (s, 2H, H-7), 3.28 (s, 2H, H-7"); EIMS (*m/z*): 449 $[M]^+$, 191 $[C_{10}H_7SO_2]^+$, 150 $[C_8H_8NO_2]^+$, 135 $[C_8H_7O_2]^+$, 127 $[C_{10}H_7]^+$, 121 $[C_7H_5O_2]^+$, 109 $[C_7H_6F]^+$, 102 $[C_8H_6]^+$, 90 $[C_7H_6]^+$, 83 $[C_5H_4F]^+$, 64 $[C_5H_4]^+$.

3.3.11 ***N-(4-flourobenzyl)-N-((3,4-methylenedioxyphenyl)methyl)-1-phenylmethane sulfonamide (7e)***
White crystalline solid; Yield: 86%; M.P.: 90-92 ^{o}C; Mol. Formula: $C_{22}H_{20}FNO_4S$; Mol. Mass: 413 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3085 (Ar C-H), 1600 (Ar C=C), 1382 (S=O), 1251 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.30 (d, J = 8.4 Hz, 2H, H-2", H-6"), 7.18-7.11 (m, 5H, H-2' to H-6'), 6.97 (t, J = 8.4 Hz, 2H, H-3", H-5"), 6.72 (s, 1H, H-2), 6.69 (dd, J = 8.0, 2.4 Hz, 1H, H-6), 6.62 (d, J = 8.0 Hz, 1H, H-5), 5.93 (s, 2H, H-8), 4.15 (s, 2H, H-7'), 4.03 (s, 2H, H-7), 3.99 (s, 2H, H-7"); EIMS (*m/z*): 413 $[M]^+$, 155 $[C_7H_7SO_2]^+$, 150 $[C_8H_8NO_2]^+$, 135 $[C_8H_7O_2]^+$, 121 $[C_7H_5O_2]^+$, 91 $[C_7H_7]^+$, 65 $[C_5H_5]^+$; 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 $[C_5H_4F]^+$, 64 $[C_5H_4]^+$.

3.3.12 ***N-(4-flourobenzyl)-N-((3,4-methylenedioxyphenyl)methyl)-1-((1R,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)methanesulfonamide (7f)***
Colorless liquid; Yield: 86%; Mol. Formula: $C_{25}H_{28}FNO_5S$; Mol. Mass: 473 gmol^{-1}; IR (KBr, ν_{max} (cm^{-1})): 3076 (Ar C-H), 1605 (Ar C=C), 1384 (S=O), 1221 (C-O); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.32 (d, J = 8.0 Hz, 2H, H-2", H-6"), 7.25 (t, J = 8.0 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 = 7.6 Hz, 1H, H-5), 5.89 (s, 2H, H-8), 4.21 (s, 2H, H-7), 3.73 (s, 2H, H-7"), 3.33 (s, 2H, H-10'), 2.41-2.38 (m, 2H, H-3'), 2.17-2.11 (m, 2H, H-6'), 2.09-2.00 (m, 2H, H-4'), 1.38-1.35 (m, 1H, H-5'), 0.95 (s, 6H, CH_3-8', CH_3-9'); EIMS (*m/z*): 473 $[M]^+$, 215 $[C_{10}H_{15}OSO_2]^+$, 151 $[C_{10}H_{15}O]^+$, 150 $[C_8H_8NO_2]^+$, 135 $[C_8H_7O_2]^+$, 121 $[C_7H_5O_2]^+$, 109 $[C_7H_6F]^+$, 90 $[C_7H_6]^+$, 83 $[C_5H_4F]^+$, 64 $[C_5H_4]^+$.

3.4 ***Antibacterial activity***
The antibacterial activity method was based on the principle that microbial cell number or microbial growth was directly related to the log phase of growth with increase in absorbance of broth medium[13-14]. The clinically isolated two gram-positive (*Bacillus subtilis* and *Staphylococcus aureus*) and three gram-negative (*Salmonella typhi*, *Escherichia coli* and *Pseudomonas aeruginosa*) bacteria were stored on stock culture agar medium. 20 µg test samples with dilution by suited solvents and 180 µL overnight maintained fresh bacterial cultures with suited dilution with fresh nutrient broth were mixed. The initial absorbance was crucially between 0.12-0.19 at 540 nm. The incubation was processed at 37 ^{o}C for 16-24 hrs with lid on the micro plate. The absorbance was measured at 540 nm using micro plate reader before and after incubation and the difference was noted as an index of bacterial growth. The percent inhibition was calculated using the formula:

$$\text{Inhibition (\%)} = \frac{\text{Control} - \text{Test}}{\text{Control}} \times 100$$

where Control = Absorbance in control with bacterial culture
Test = Absorbance in test sample

Results are mean of triplicate (n=3, ± sem). Ciprofloxacin was employed as standard. 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.

3.5 Statistical analysis
All the measurements were done in triplicate and statistical analysis was performed by Microsoft Excel 2010. Results are presented as mean ± sem.

4. CONCLUSION
All the compounds of this series were synthesized in good yield and purity. All the structures were well supported by spectral analysis and executed for the antibacterial activity. The results assisted our aim of preparing these molecules i.e. to inaugurate new potent molecules with more potential. The pharmacological industries can further proceed these synthesized molecules to evaluate their *in vivo* activity and toxicity.

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