Synthesis and Antibacterial Activity Study of 2-[(2,6 -dichlorophenyl amino)-phenyl]-acetic acid Derivatives with Various Sulfonamides

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Abstract

Various 30 sulfonamides derivatives of 2-[(2,6-dichlorophenylamino)- phenyl]-acetic acid **(5)** have been prepared via two steps. The antibacterial activity studies for all new derivatives have been performed on both Gram positive *S. aureus, B. subtilis* and Gram negative *E. coli, P. vulgaris* bacteria, when compared with the results obtained from standard drugs penicillin, chloramphenicol, and ampicillin. The antibacterial obtained results were found to be quite satisfactorily compared with the standard drugs. The final compounds were characterized by IR, ^{1}H-NMR spectra and elemental analysis.

Keywords: Phenyl acetic acid; Sulfonamide; Antibacterial.

Introduction

The development of sulfonamide is one of the most fascinating and important parts in medicinal chemistry. Sulfonamides have wide range of antimicrobial activity against both gram-positive and gram-negative bacteria. Sulfonamides continue to be used because they are effective, inexpensive and free of super infection problem. Literature survey reveals that substituted sulfonamides are found to be biologically active viz. analgesic [1], anti-inflammatory [2,3], anticancer [4], antitumor [5,6], antibacterial [7,8], antilukemic [9], carbonic anhydrase inhibitory [10,11], anticonvulsant and analgesic [12], COX-2 inhibitor [13] and antiHIV [14].

Parent compound, 2-[(2,6-dichlorophenylamino)-phenyl]-acetic acid **(5)** is a well known potent non-steroidal anti-inflammatory analgesic agents. It is widely used in the long-term treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondilities [15]. Antibacterial activity of non-steroidal anti-inflammatory drugs (NSAID) 2-[(2,6-dichloro phenylamino)-phenyl]-acetic acid **(5)** was studied by Annadurai and his co-workers [16]. The antibacterial activity of this NSAID would have added advantages, as an infection is often associated with inflammatory process, especially post surgical process.

Recently we have studied the antibacterial activity of cyclized quinazolinone derivatives of 2-[(2,6-dichlorophenylamino)phenyl]acetic acid with anthranilic acid and arylamines [17]. The biological importance of 2-[(2,6-dichlorophenylamino)-phenyl]-acetic acid and the limited work that has been carried out as antibacterial agents prompted us to study antibacterial activity of various sulfonamides with (**5).** The

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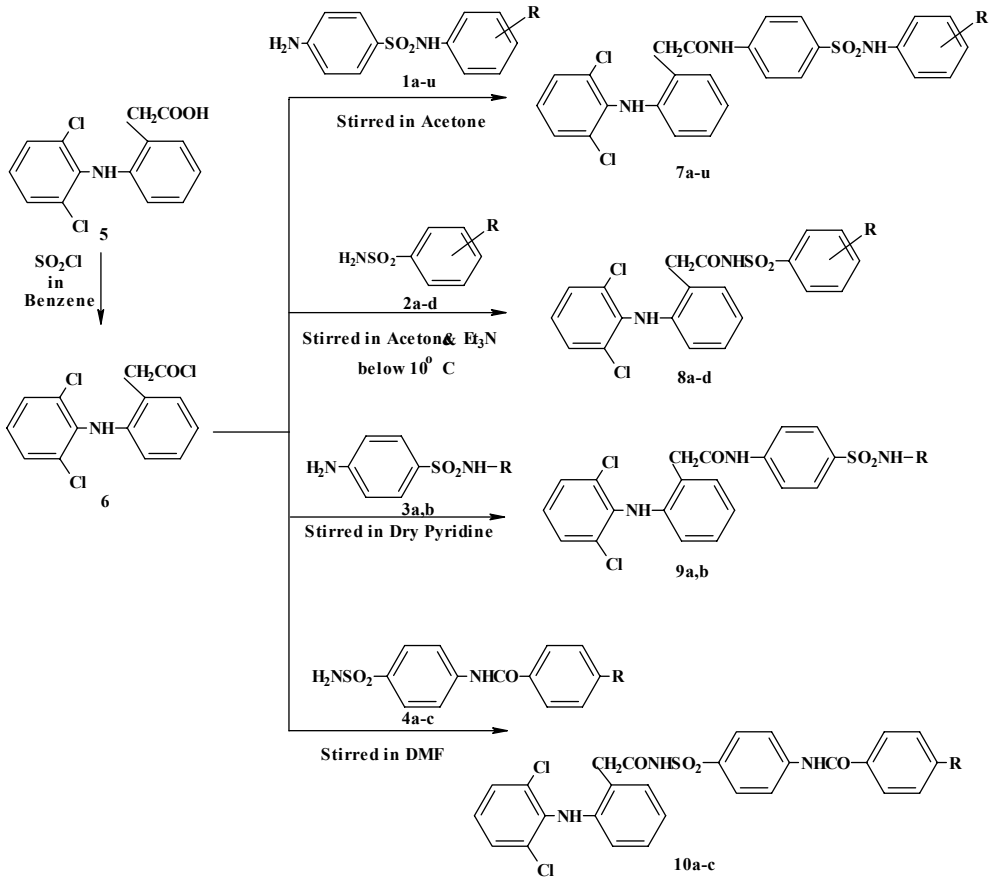
synthesis of new derivatives has been outlined in scheme-1. The antibacterial activity was compared with standard drug penicillin, chloramphenicol and ampicillin. The antibacterial testing was carried out by ***cup-plate*** method**.**



Scheme 1

Materials and Methods

Experimental

Melting points were measured by open capillary method and all were uncorrected. IR absorption spectra were recorded on Parkin Elmer-838 FT IR spectrometer using KBr pellet and ^{1}H-NMR spectra were recorded in DMSO-d_6 / D_2O on Bruker DRX-300 (300 MHz FT NMR) instrument (chemical shifts in δppm). The purity of products was routinely checked by TLC using silica gel in benzene: ethyl acetate, benzene: ethanol, acetone: ethanol & ethyl acetate: ethanol solvents.

The compound 2-[(2,6-dichlorophenylamino)-phenyl]-acetyl chloride (**6)** was prepared from 2-[(2,6-dichlorophenylamino)-phenyl]-acetic acid **(5)** by reported method [18]. The intermediate *N*^{1}-(substituted aryl)-*p*-aminobenzenesulfonamide **(1a-u)** was prepared by reported method [19,20]. The synthetic route of the final compounds has been shown in Scheme-1. Characterization data of all derivatives is given in Table-1.

Table 1. Physical and analytical data of synthesized compounds 7a-u, 8a-d, 9a,b and 10a-c

Compd.	R	Molecular Formula	M.P. (°C)	Yield (%)	Elemental analysis Calculated (found)		
					%C	%H	%N
7a	H	$C_{26}H_{21}N_3O_3SCl_2$	135	75	59.32 (59.28)	3.98 (3.91)	7.98 (7.89)
7b	2-NO_2	$C_{26}H_{20}N_4O_5SCl_2$	140	66	54.65 (54.57)	3.50 (3.44)	9.81 (9.72)
7c	3-NO_2	$C_{26}H_{20}N_4O_5SCl_2$	188	58	54.65 (54.55)	3.50 (3.45)	9.81 (9.70)
7d	4-NO_2	$C_{26}H_{20}N_4O_5SCl_2$	110	72	54.65 (54.60)	3.50 (3.41)	9.81 (9.74)
7e	2-CH_3	$C_{27}H_{23}N_4O_3SCl_2$	137	56	60.01 (59.96)	4.25 (4.19)	7.78 (7.67)
7f	3-CH_3	$C_{27}H_{23}N_4O_3SCl_2$	156	66	60.01 (59.92)	4.25 (4.20)	7.78 (7.70)
7g	4-CH_3	$C_{27}H_{23}N_4O_3SCl_2$	180	71	60.01 (59.99)	4.25 (4.17)	7.78 (7.75)
7h	2-OCH_3	$C_{27}H_{23}N_4O_4SCl_2$	177	77	58.28 (58.20)	4.13 (4.09)	7.55 (7.50)
7i	4-OCH_3	$C_{27}H_{23}N_4O_4SCl_2$	190	61	58.28 (58.22)	4.13 (4.06)	7.55 (7.45)
7j	2-Cl	$C_{26}H_{20}N_3O_3SCl_3$	186	58	55.68 (55.61)	3.56 (3.50)	7.49 (7.40)
7k	3-Cl	$C_{26}H_{20}N_3O_3SCl_3$	168	56	55.68 (55.66)	3.56 (3.48)	7.49 (7.39)
7l	4-Cl	$C_{26}H_{20}N_3O_3SCl$	220	61	55.68 (55.60)	3.56 (3.51)	7.49 (7.41)
7m	2,6-$(Cl)_2$,4-NO_2	$C_{26}H_{18}N_4O_5SCl_4$	185	57	48.76 (48.71)	2.81 (2.77)	8.75 (8.68)
7n	6-Cl,2,4-$(NO_2)_2$	$C_{26}H_{18}N_5O_7SCl_3$	235	60	47.98 (47.91)	2.76 (2.70)	10.76 (10.66)
7o	2-Cl,4-NO_2	$C_{26}H_{19}N_4O_5SCl_3$	135	58	51.54 (50.48)	3.14 (3.10)	9.24 (9.19)
7p	2,6-$(Br)_2$,4-CH_3	$C_{26}H_{21}N_3O_3SCl_2Br_2$	130	61	46.43 (46.37)	3.01 (2.96)	6.02 (5.93)
7q	2,6-$(Br)_2$,4-NO_2	$C_{26}H_{18}N_4O_5SCl_2Br_2$	185	55	42.81 (42.79)	2.46 (2.40)	7.68 (7.61)
7r	2,6-$(NO_2)_2$-	$C_{26}H_{19}N_5O_7SCl_2$	125	53	50.66 (50.60)	3.08 (3.01)	11.36 (11.28)
7s	2-CN,4-NO_2-	$C_{27}H_{19}N_5O_5SCl_2$	180	69	54.37 (54.29)	3.18 (3.10)	11.74 (11.67)
7t	2-SO_3H,4-NO_2	$C_{26}H_{20}N_3O_6SCl_2$	260	58	51.58 (51.52)	3.30 (3.24)	6.94 (6.87)
7u	2-SO_3K,4-NO_2	$C_{26}H_{19}N_3O_6SCl_2K$	deco. 300	56	48.52 (48.49)	2.95 (2.90)	6.53 (6.48)
8a	4-CH_3	$C_{21}H_{18}N_2O_3SCl_2$	95	61	56.14 (56.09)	4.01 (3.97)	6.24 (6.19)
8b	4-OCH_3	$C_{21}H_{18}N_2O_4SCl_2$	260	66	54.21 (54.19)	3.86 (3.80)	6.02 (5.96)
8c	4-OCH_3,3-Cl	$C_{21}H_{17}N_2O_4SCl_3$	270	58	50.46 (50.38)	3.40 (3.31)	5.60 (5.51)
8d	4-$NHCOCH_3$	$C_{22}H_{19}N_3O_4SCl_2$	185	68	53.66 (53.61)	3.85 (3.79)	8.54 (8.49)
9a	H	$C_{20}H_{17}N_3O_3SCl_2$	215	66	53.34 (53.29)	3.78 (3.69)	9.33 (9.26)
9b	4,6-$(CH_3)_2$-pyrimidine	$C_{26}H_{28}N_5O_3SCl_2$	285	61	56.12 (56.10)	4.13 (4.13)	12.59 (12.46)
10a	4-Cl	$C_{27}H_{20}N_3O_4SCl_3$	105	66	55.06 (55.00)	3.39 (3.30)	7.14 (7.00)
10b	4-NO_2	$C_{27}H_{20}N_4O_6SCl_2$	135	60	54.10 (54.01)	3.34 (3.29)	9.34 (9.25)
10c	4-$NHCOCH_3$	$C_{29}H_{24}N_4O_5SCl_2$	190	59	56.88 (56.88)	3.92 (3.92)	9.16 (9.08)

General procedure for preparation of 2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(substitutedphenyl)sulfamoyl-phenyl]-acetamide (7a-u)

To a cooled suspension of N^1-(substituted aryl) *p*-aminobenzenesulfonamide **1a-u** (0.005 mol) in dry acetone (25 ml) was added pyridine (5 ml), followed by the addition of the appropriate 2-[(2,6-dichlorophenylamino)-phenyl]-acetyl chloride **6** (0.005 mol) in one portion with constant stirring for 2 hr below 10 ºC. The reaction mixture was stirred further for 4 hr at room temperature and under reflux in water bath for 8-9 hr. The solvent was removed under reduced pressure and the residue was poured into cold water, followed by thoroughly washing with aqueous $NaHCO_3$ (10%) solution. The resulted precipitate was filtered and crystallized from ethanol. Reaction time and purity of the compound was checked by TLC using benzene:ethyl acetate (1:1).

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-(4-phenylsulfamoyl-phenly)-acetamide (7a)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(2-nitrophenyl)sulfamoyl-phenyl]-acetamide (7b)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(3-nitrophenyl)sulfamoyl-phenyl]-acetamide (7c)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(4-nitrophenyl)sulfamoyl-phenyl]-acetamide (7d)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(2-methylphenyl)sulfamoyl-phenyl]-acetamide (7e)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(3-methylphenyl)sulfamoyl-phenyl]-acetamide (7f)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(4-methylphenyl)sulfamoyl-phenyl]-acetamide (7g)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(2-methoxylphenyl)sulfamoyl-phenyl]-acetamide (7h)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(4-methoxylphenyl)sulfamoyl-phenyl]-acetamide (7i)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(2-chlorophenyl)sulfamoyl-phenyl]-acetamide (7j)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(3-chlorophenyl)sulfamoyl-phenyl]-acetamide (7k)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(4-chlorophenyl)sulfamoyl-phenyl]-acetamide (7l)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(2,6-dichloro-4-nitrophenyl)sulfamoyl-phenyl]-acetamide (7m)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(6-chloro-2,4-dinitrophenyl)sulfamoyl-phenyl]-acetamide (7n)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(2-chloro-4-nitrophenyl)sulfamoyl-phenyl]-acetamide (7o)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(2,6-dibromo-4-methylphenyl) sulfamoyl-phenyl]-acetamide (7p)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(2,6-dibromo-4-nitrophenyl)sulfamoyl-phenyl]-acetamide (7q)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(2,6-dinitrophenyl)sulfamoyl-phenyl]-acetamide (7r)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(2-cyano-4-nitrophenyl)sulfamoyl-phenyl]-acetamide (7s)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(2-sulphonicacid-4-nitrophenyl) sulfamoyl-phenyl]-acetamide (7t)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(2-potassiumsulphonate-4-nitrophenyl) sulfamoyl-phenyl]-acetamide (7u)

General procedure for preparation of N-{2-[2-(2,6-Dichloro-phenylamino)-phenyl]-acetyl}-substituted-benzenesulfonamide(8a-d)

To a solution of **6** (0.005 mol) in acetone (25 ml), the appropriate sulfonamide **2a-d** (0.005 mol) in acetone (25 ml) was added at 10 ºC and stirred for 3 hr. Meanwhile triethyl amine (0.005 mole) was added portion wise with constant stirring. The reaction mixture was removed from the ice bath and stirred further for 4 hr at room temperature, refluxed for 10 hr in water bath and allowed to stand overnight. The residue was washed with ethanol, filtrate was concentrated under reduced pressure and the solid obtained was washed successively with water and 10% $NaHCO_3$ solution. The product was filtered, dried and recrystallised from $CHCl_3$: ethanol (1:2). The reaction time and purity of the compound were checked by TLC using acetone: ethanol (1:1).

N-{2-[2-(2,6-Dichloro-phenylamino)-phenyl]-acetyl}-p-toluenesulfonamide(8a)

N-{2-[2-(2,6-Dichloro-phenylamino)-phenyl]-acetyl}-4-methoxy-benzenesulfonamide (8b)

N-{2-[2-(2,6-Dichloro-phenylamino)-phenyl]-acetyl}-3-chloro-4-methoxy-benzene sulfonamide (8c)

N-{2-[2-(2,6-Dichloro-phenylamino)-phenyl]-acetyl}-4-acetamido-benzenesulfonamide (8d)

General procedure for preparation of 2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(Substitutedsulfamoyl)-phenyl]-acetamide (9a,b)

To a well stirred cooled solution of compound **3a,b** (0.005 mol) dissolved in dry pyridine (15 ml) compound **6** (0.005 mol) in dry acetone (20 ml) was added under stirring. The temperature of the reaction mixture was maintained below 10 ºC for 2 hr, then was kept at room temperature for 4 hr. The reaction was heated under refluxed in water bath for 6-8 hr. The solvent was removed under reduced pressure. The crude product was treated with ice cold water and little amount of HCl. The product was

filtered, washed with water and aqueous $NaHCO_3$ (10%) solution, dried and recrystallised from ethanol. The reaction time and purity of the compound was checked by TLC using benzene: ethanol (1:1).

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-(4--sulfamoyl-phenyl)-acetamide (9a)

2-[2-(2,6-Dichloro-phenylamino)-phenyl]-N-[4-(4,6-dimethyl-2-pyrimidinysulfamoy)l-phenyl]-acetamide (9b)

General procedure for preparation of N-{2-[2-(2,6-Dichloro-phenylamino)-phenyl]-acetyl}-4-(substitutedbenzamido)-benzenesulfonamide (10a-c)

A solution of acid chloride **6** (0.005 mol) in DMF (15 ml) was added dropwise into the ice cold mixture of N^4-(*p*-substituted benzoylamino)benzene- sulfonamide **4a-c** (0.05 mol) dissolved in DMF (25ml) with vigorous stirring. The temperature of the reaction mixture was maintained for 2 hr at 10 ºC; then stirring for 6 hr at room temperature. Then the reaction mixture was heated to 120-130 ºC for 16 hr in an oil bath and was kept at room temperature for 2 days. The whole content was poured into ice cold water with vigorous shaking. The obtained solid was filtered, washed thoroughly with cold water and 5% aqueous $NaHCO_3$ solution. The crude product was dried and recrystallised from ethanol.

The reaction time and purity of the compounds was checked by TLC using ethyl acetate:ethanol (1:1).

N-{2-[2-(2,6-Dichloro-phenylamino)-phenyl]-acetyl}-4-(4-chlorobenzamido)-benzene sulfonamide(10a)

N-{2-[2-(2,6-Dichloro-phenylamino)-phenyl]-acetyl}-4-(4-nitrobenzamido)-benzene sulfonamide(10b)

N-{2-[2-(2,6-Dichloro-phenylamino)-phenyl]-acetyl}-4-(4-acetamidobenzamido)-benzene sulfonamide (10c)

Result and Discussion

The structures of the synthesized compounds were assigned based on the IR and ^{1}H NMR spectra along with elemental CHN-analyses data for unknown compounds. The absorption band of carboxylic acid group of lead molecule observed at 1730 cm^{-1}, which sifted to 1670 cm^{-1} after the formation of amides. The IR spectra (cm^{-1}) of compounds **7a-u** exhibited absorption band at 3442 (-NH), 2925, 2845 (C-H), 1678 (amide-I), 1565 (amide-II), 1355, 1160 (S=O), 1245 (amide-III), 1310 (C-N), 781 (C-Cl). Some additional peaks appeared due to substitution in aromatic ring showed absorption band at 1320, 1553 (-NO_2 sym, asym), 643 (C-Br). The ^{1}H NMR spectra of compounds 7a-u showed a singlet peak at δ 3.62 for –CH_2-, singlet peak at δ 8.27 for –CONH-, singlet at δ 10.07 for –SO_2NH-, singlet at δ 10.51 for –NH-, multiplet at δ 6.37 to 7.92 for aromatic proton. A singlet at δ 2.30 for –CH_3 and singlet at δ 3.41 for –OCH_3 due to the substitution on aromatic ring were observed.

Table 2. IR and ^{1}H NMR spectral data of synthesized compounds 7a-u, 8a-d, 9a,b and 10a-c

Com.	R	IR (KBr) ν_{max} cm^{-1}	^{1}H-NMR (δ ppm) 300 MHz, DMSO-d_6 / D_2O
7a	H	3442 (-NH), 2925, 2845 (C-H), 1678, 1565, 1245 (amide-I, II, III), 1355, 1160 (S=O), 1310 (C-N), 781 (C-Cl)	3.62 (s, 2H, –CH_2-), 8.27 (s, 1H, -CONH-), 10.07 (s, 1H, -SO_2NH-), 10.51 (s, 1H, -NH-), 6.37-7.92 (m, 16H, Ar-H)
7b	2-NO_2	3445 (-NH), 1670, 1560, 1240 (amide-I, II, III), 1553, 1320 (-NO_2), 1350, 1165 (S=O)	3.60 (s, 2H, –CH_2-), 8.22 (s, 1H, -CONH-), 10.02 (s, 1H, -SO_2NH-), 10.62 (s, 1H, -NH-), 6.31-7.95 (m, 15H, Ar-H)
7c	3-NO_2	3442 (-NH), 1674, 1562, 1248 (amide-I, II, III), 1555, 1324 (-NO_2), 1353, 1160 (S=O)	3.60 (s, 2H, –CH_2-), 8.25 (s, 1H, -CONH-), 10.03 (s, 1H, -SO_2NH-), 10.65 (s, 1H, -NH-), 6.33-7.92 (m, 15H, Ar-H)
7d	4-NO_2	3440 (-NH), 1680, 1565 1240 (amide-I, II, III), 1551, 1322 (-NO_2), 1350, 1160 (S=O)	3.67 (s, 2H, –CH_2-), 8.27 (s, 1H, -CONH-), 10.05 (s, 1H, -SO_2NH-), 10.67 (s, 1H, -NH-), 6.30-7.99 (m, 15H, Ar-H)
7e	2-CH_3	3445 (-NH), 1671, 1566, 1240 (amide-I, II, III), 1358, 1168 (S=O)	2.30 (s, 3H, -CH_3), 3.61 (s, 2H, –CH_2-), 8.22 (s, 1H, -CONH-), 10.02 (s, 1H, -SO_2NH-), 10.64 (s, 1H, -NH-), 6.33-7.91 (m, 15H, Ar-H)
7f	3-CH_3	3441 (-NH), 1670, 1560, 1250 (amide-I, II, III), 1355, 1162 (S=O)	2.32 (s, 3H, -CH_3), 3.69 (s, 2H, –CH_2-), 8.25 (s, 1H, -CONH-), 10.07 (s, 1H, -SO_2NH-), 10.68 (s, 1H, -NH-), 6.38-7.92 (m, 15H, Ar-H)
7g	4-CH_3	3445 (-NH), 1680, 1565 1250 (amide-I, II, III), 1360, 1160 (S=O)	2.38 (s, 3H, -CH_3), 3.68 (s, 2H, –CH_2-), 8.20 (s, 1H, -CONH-), 10.01 (s, 1H, -SO_2NH-), 10.65 (s, 1H, -NH-), 6.34-7.98 (m, 15H, Ar-H)
7h	2-OCH_3	3444 (-NH), 1670, 1570, 1243 (amide-I, II, III), 1360, 1170 (S=O)	3.41 (s, 3H, -OCH_3), 3.67 (s, 2H, –CH_2-), 8.27 (s, 1H, -CONH-), 10.05 (s, 1H, -SO_2NH-), 10.67 (s, 1H, -NH-), 6.37-7.98 (m, 15H, Ar-H)
7i	4-OCH_3	3447 (-NH), , 1677, 1568, 1245 (amide-I, II, III), 1352, 1162 (S=O)	3.45 (s, 3H, -OCH_3), 3.61 (s, 2H, –CH_2-), 8.20 (s, 1H, -CONH-), 10.05 (s, 1H, -SO_2NH-), 10.67 (s, 1H, -NH-), 6.38-7.93 (m, 15H, Ar-H)
7j	2-Cl	3441 (-NH), 1671, 1566, 1240 (amide-I, II, III), 1355, 1171 (S=O)	3.62 (s, 2H, –CH_2-), 8.21 (s, 1H, -CONH-), 10.07 (s, 1H, -SO_2NH-), 10.61 (s, 1H, -NH-), 6.38-7.92 (m, 15H, Ar-H)
7k	3-Cl	3445 (-NH), 1677, 1560 1250 (amide-I, II, III), 1355, 1164 (S=O)	3.69 (s, 2H, –CH_2-), 8.22 (s, 1H, -CONH-), 10.01 (s, 1H, -SO_2NH-), 10.65 (s, 1H, -NH-), 6.31-7.98 (m, 15H, Ar-H)
7l	4-Cl	3440 (-NH), 1665, 1570, 1255 (amide-I, II, III), 1350, 1160 (S=O)	3.62 (s, 2H, –CH_2-), 8.24 (s, 1H, -CONH-), 10.07 (s, 1H, -SO_2NH-), 10.61 (s, 1H, -NH-), 6.32-7.94 (m, 15H, Ar-H)
7m	2,6-$(Cl)_2$,4-NO_2	3443 (-NH), 1669, 1565, 1247 (amide-I, II, III), 1550, 1325 (-NO_2), 1356, 1160 (S=O)	3.61 (s, 2H, –CH_2-), 8.23 (s, 1H, -CONH-), 10.07 (s, 1H, -SO_2NH-), 10.61 (s, 1H, -NH-), 6.33-7.91 (m, 13H, Ar-H)
7n	6-Cl,2,4-$(NO_2)_2$	3445 (-NH), 1672, 1562, 1245 (amide-I, II, III), 1555, 1320 (-NO_2), 1358, 1170 (S=O)	3.60 (s, 2H, –CH_2-), 8.22 (s, 1H, -CONH-), 10.08 (s, 1H, -SO_2NH-), 10.66 (s, 1H, -NH-), 6.31-7.95 (m, 13H, Ar-H)
7o	2-Cl,4-NO_2	3441 (-NH), 1677, 1569, 1243 (amide-I, II, III), 1553, 1327 (-NO_2), 1355, 1163 (S=O)	3.66 (s, 2H, –CH_2-), 8.27 (s, 1H, -CONH-), 10.03 (s, 1H, -SO_2NH-), 10.64 (s, 1H, -NH-), 6.34-7.92 (m, 14H, Ar-H)

Com.	R	IR (KBr) ν_{max} cm^{-1}	^{1}H-NMR (δ ppm) 300 MHz, DMSO-d_6 / D_2O
7p	2,6-$(Br)_2$,4-CH_3	3446 (-NH), 1679, 1572, 1245 (amide-I, II, III), 1360, 1167 (S=O)	2.32 (s, 3H, -CH_3), 3.60 (s, 2H, –CH_2-), 8.25 (s, 1H, -CONH-), 10.07 (s, 1H, -SO_2NH-), 10.61 (s, 1H, -NH-), 6.34-7.91 (m, 13H, Ar-H)
7q	2,6-$(Br)_2$,4-NO_2	3442 (-NH), 1670, 1560, 1250 (amide-I, II, III), 1551, 1322 (-NO_2), 1357, 1160 (S=O)	3.69 (s, 2H, –CH_2-), 8.21 (s, 1H, -CONH-), 10.04 (s, 1H, -SO_2NH-), 10.66 (s, 1H, -NH-), 6.34-7.91 (m, 13H, Ar-H)
7r	2,6-$(NO_2)_2$-	3445 (-NH), 1680, 1560, 1260 (amide-I, II, III), 1550, 1326 (-NO_2), 1360, 1180 (S=O)	3.61 (s, 2H, –CH_2-), 8.22 (s, 1H, -CONH-), 10.04 (s, 1H, -SO_2NH-), 10.61 (s, 1H, -NH-), 6.32-7.97 (m, 14H, Ar-H)
7s	2-CN,4-NO_2-	3435 (-NH), 1670, 1560, 1245 (amide-I, II, III), 1555, 1328 (-NO_2), 1360, 1155 (S=O)	3.67 (s, 2H, –CH_2-), 8.21 (s, 1H, -CONH-), 10.03 (s, 1H, -SO_2NH-), 10.64 (s, 1H, -NH-), 6.31-7.90 (m, 14H, Ar-H)
7t	2-SO_3H,4-NO_2	3448 (-NH), 1675, 1575, 1242 (amide-I, II, III), 1557, 1323 (-NO_2), 1360, 1172 (S=O)	3.62 (s, 2H, –CH_2-), 8.23 (s, 1H, -CONH-), 10.05 (s, 1H, -SO_2NH-), 10.66 (s, 1H, -NH-), 6.31-7.94 (m, 14H, Ar-H)
7u	2-SO_3K,4-NO_2	3442 (-NH), 1670, 1568, 1242 (amide-I, II, III), 1551, 1322 (-NO_2), 1354, 1164 (S=O)	3.60 (s, 2H, –CH_2-), 8.22 (s, 1H, -CONH-), 10.07 (s, 1H, -SO_2NH-), 10.60 (s, 1H, -NH-), 6.35-7.91 (m, 14H, Ar-H)
8a	4-CH_3	3440 (-NH), 1680, 1565, 1245 (amide-I, II, III), 1360, 1150 (S=O)	2.10 (s, 3H, -CH_3), 3.75 (s, 2H, –CH_2-), 8.37 (s, 1H, -CONH-), 10.64 (s, 1H, -NH-), 6.57-7.80 (m, 11H, Ar-H)
8b	4-OCH_3	3440 (-NH), 1685, 1565, 1245 (amide-I, II, III), 1355, 1160 (S=O)	2.15 (s, 3H, -CH_3), 3.48 (s, 3H, -OCH_3), 3.77 (s, 2H, –CH_2-), 8.37 (s, 1H, -CONH-), 10.69 (s, 1H, -NH-), 6.50-7.85 (m, 11H, Ar-H)
8c	4-OCH_3,3-Cl	3443 (-NH.), 1670, 1570, 1250 (amide-I, II, III), 1360, 1160 (S=O)	2.10 (s, 3H, -CH_3), 3.44 (s, 3H, -OCH_3), 3.71 (s, 2H, –CH_2-), 8.32 (s, 1H, -CONH-), 10.65 (s, 1H, -NH-), 6.57-7.88 (m, 10H, Ar-H)
8d	4-$NHCOCH_3$	3445 (-NH.), 1679, 1560, 1240 (amide-I, II, III), 1355, 1164 (S=O)	3.77 (s, 2H, –CH_2-), 8.37 (s, 1H, -CONH-), 10.63 (s, 1H, -NH-), 6.59-7.88 (m, 11H, Ar-H)
9a	H	3440 (-NH), 1675, 1565 1240 (amide-I, II, III), 1550, 1325 (-NO_2), 1352, 1170 (S=O)	3.65 (s, 2H, –CH_2-), 8.39 (s, 1H, -CONH-), 10.10 (s, 1H, -SO_2NH-), 10.60 (s, 1H, -NH-), 6.30-7.90 (m, 11H, Ar-H)
9b	4,6-$(CH_3)_2$-pyrimidine	3445 (-NH), 1680, 1565, 1245 (amide-I, II, III), 1555, 1327 (-NO_2), 1350, 1166 (S=O)	2.24 (s, 6H, -CH_3), 3.55 (s, 2H, –CH_2-), 8.30 (s, 1H, -CONH-), 10.10 (s, 1H, -SO_2NH-), 9.07 (s, 1H, -NH-), 6.30-7.90 (m, 12H, Ar-H)
10a	4-Cl	3440 (-NH), 1680, 1560, 1240 (amide-I, II, III), 1355, 1170 (S=O)	3.88 (s, 2H, –CH_2-), 8.34 (s, 1H, -CONH-), 10.31 (s, 1H, -NH-), 6.34-7.91 (m, 15H, Ar-H)
10b	4-NO_2	3445 (-NH), 1673, 1565, 1250 (amide-I, II, III), 1551, 1322 (-NO_2), 1350, 1162 (S=O)	3.80 (s, 2H, –CH_2-), 8.31 (s, 1H, -CONH-), 10.34 (s, 1H, -NH-), 6.38-7.95 (m, 15H, Ar-H)
10c	4-$NHCOCH_3$	3420 (-NH), 1680, 1560, 1245 (amide-I, II, III), 1360, 1160 (S=O)	3.87 (s, 2H, –CH_2-), 8.35 (s, 1H, -CONH-), 10.35 (s, 1H, -NH-), 6.37-7.90 (m, 15H, Ar-H)

Antibacterial Activity

All the synthesized compounds were screened for their antibacterial properties against *S. aureus, B. subtilis (Gram positive)* and *E. coli*, *P. vulgaris* (Gram negative). The results were compared with the standard drugs penicillin, chloramphenicol and

ampicillin tested under similar condition. The cup-plate method was employed using DMF solution of compounds at 100 μg/ml concentration (Table 3).

Table 3. The *in vitro* antibacterial activity of synthesized compounds 7a-u, 8a-d, 9a,b and 10a-c

Compds.	R	Zone of inhibition in mm.			
		Gram-positive		Gram-negative	
		S. aureus	*B. subtilis*	*E. coli*	*P. vulgaris*
7a	H	13	12	17	16
7b	2-NO_2	12	14	16	14
7c	3-NO_2	14	16	14	14
7d	4-NO_2	13	19	21	16
7e	2-CH_3	12	14	20	14
7f	3-CH_3	14	14	16	13
7g	4-CH_3	15	13	17	14
7h	2-OCH_3	12	16	17	15
7i	4-OCH_3	13	14	18	16
7j	2-Cl	14	13	18	13
7k	3-Cl	16	15	16	14
7l	4-Cl	14	16	18	18
7m	2,6-$(Cl)_2$,4-NO_2	18	17	20	16
7n	6-Cl,2,4-$(NO_2)_2$	16	-	19	-
7o	2-Cl,4-NO_2	16	-	17	14
7p	2,6-$(Br)_2$,4-CH_3	17	19	22	-
7q	2,6-$(Br)_2$,4-NO_2	16	20	19	18
7r	2,6-$(NO_2)_2$	14	14	17	14
7s	2-CN,4-NO_2	17	21	27	20
7t	2-SO_3H,4-NO_2	16	19	19	14
7u	2-SO_3K,4-NO_2	-	-	-	-
8a	4-CH_3	20	11	15	13
8b	4-OCH_3	15	16	20	18
8c	3-Cl,4-OCH_3	19	24	19	20
8d	4-$NHCOCH_3$	10	10	09	16
9a	H	13	12	13	14
9b	4,6-$(CH_3)_2$-2-pyrimidine	12	09	13	12
10a	4-Cl	19	24	20	16
10b	4-NO_2	14	14	14	13
10c	4-$NHCOCH_3$	11	15	16	11
Penicillin		30	28	20	21
Chloramphanicol		28	25	21	20
Ampicillin		26	28	22	21

From the experimental data it has been observed that sulfonamide derivatives were found mild to moderately active. The highest activity was observed in the compounds **7m, 8a, 8c and 10a** against *S. aureus*. While, the compound **8c and 10a** were more effective against *B. subtilis* bacterial species.

In case of gram-negative bacterial strains, compounds **7d, 7e, 7m, 7p, 8b and 10a** exhibited comparable activity with standard drug against *E.coli*. However, compounds **7s and 8c** exhibited comparable activity with standard drug against *P. vulgaris.*

Compound **7s** showed greater activity in comparison to standard drug. Whenever, compounds **7i, 7j, 7l, 7n, 7q, 7t, 8c, 8d** and **7l, 7q, 8b** showed promising activity against gram-negative bacterial strains *E. coli* and *P. vulgaris,* respectively. The remaining compounds exhibited feeble to moderate activity against gram-negative bacterial strains.

Conclusion

From the above result compounds **7s** and **8c** displayed good activity against both gram-positive and gram-negative bacteria.

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