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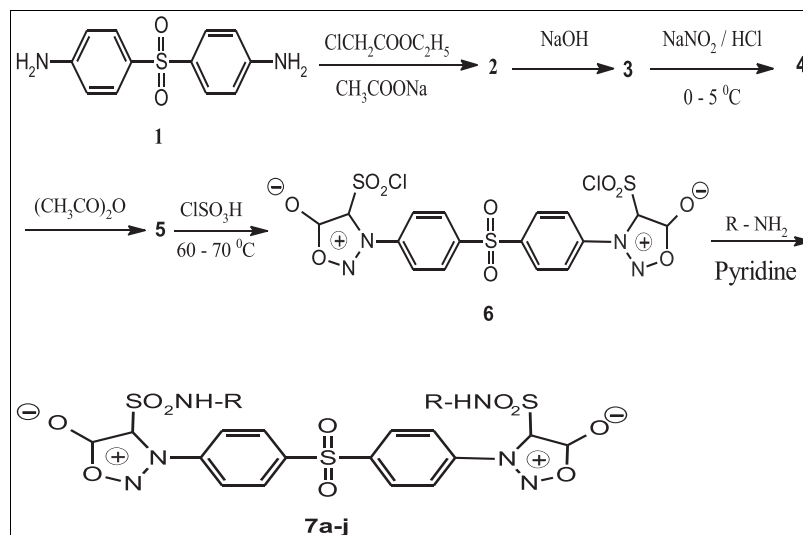
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3,3'-(Sulfonyldi-1,4-phenylene)bis(4-substituted aminosulfonyl)sydnone (**7a-j**) were synthesized from the starting material 4,4'-diaminodiphenylsulfone. The synthesized compounds were characterized by IR, NMR, and elemental analysis. Some of the compounds were effectively active against Gram-positive bacteria (*Streptococcus pneumoniae* and *Staphylococcus aureus*) and Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*).

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INTRODUCTION

Sydnone have continued to attract a widespread interest for a long time because of their unusual structure, chemical properties, and synthetic utility [1]. Kier and Roche [2] had reviewed in detail the biological importance of various mesoionic compounds. Since their discovery, sydnone have shown varieties of biological activities such as anticonvulsant [3], antioxidant [4], analgesic [5], antitumor [6], anti-inflammatory [7], antifungus [8], and antibacterial activity [9]. Sydnone are used as a versatile synthon in many heterocyclic syntheses [10]. Besides, sulfonamides are also an important class of compounds exhibiting interesting biological as well as medical applications [11]. Compounds related to 4,4'-diaminodiphenylsulfone have been proved to be important therapeutic agents [12]. Recently, various bis-sydnone sulfonamide derivatives have been synthesized from our laboratory. To extend the work, we report the synthesis and characterization of novel 3,3'-(sulfonyldi-1,4-phenylene)bis(4-primary substituted aminosulfonyl)sydnone **7(a-j)** and evaluated their antibacterial activity.

RESULTS AND DISCUSSION

Replacement of chlorine atom of sulfonyl chloride by an amino group is a well-established strategy for the synthesis of sulfonamides. Herein, we have described the synthesis, characterization, and biological evaluation of 3,3'-(sulfonyldi-1,4-phenylene)bis(4-substituted aminosulfonyl)sydnone (**7a-j**). Commercially available 4,4'-diaminodiphenylsulfone (**1**) was taken as the starting material. 3,3'-(Sulfonyldi-1,4-phenylene)bissydnone (**5**) has been prepared in moderate yield in four steps through conventional route [13]. Bissydnone derivative (**5**) has been prepared by the cyclodehydration of compound (**4**). The nitroso glycine has to be dried to remove traces of water before it reacted with the cyclization reactant acetic anhydride. The motivating force for the formation of sydnone ring may be the nucleophilicity of the oxygen atom of nitroso group for the carbon atom of carboxylic group. As sydnone compounds are unstable toward both acidic and basic media, the synthesis must be carried out carefully. The carbon atom at the fourth position of sydnone ring bears a fractional negative charge, and therefore, electrophilic substitution takes place with reaction of chlorosulfonic acid. Compound (**5**) on chlorosulfonation followed by condensation

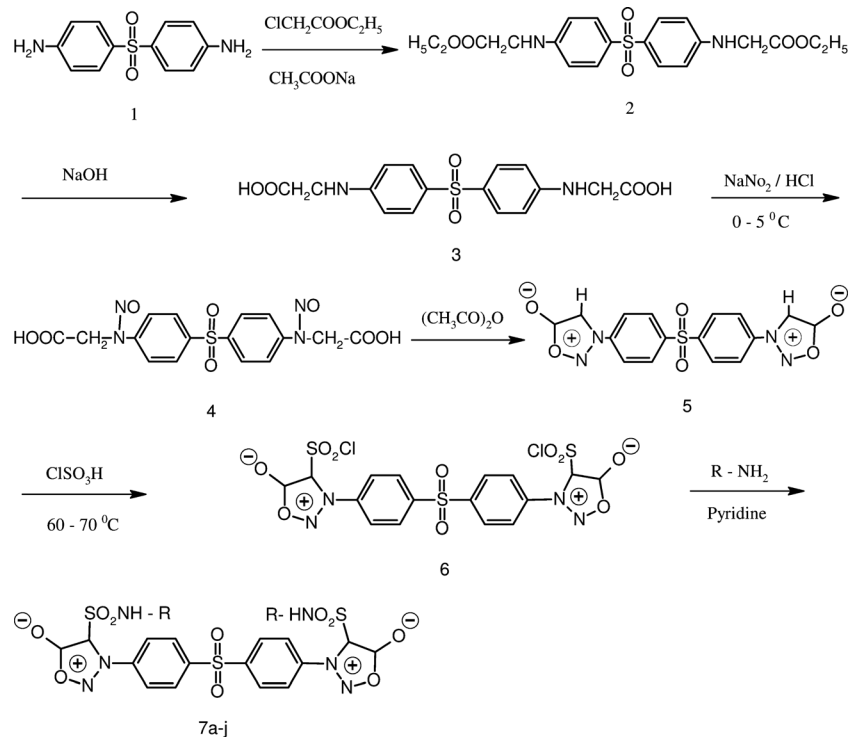


Figure 1. 3,3'-(Sulfonyldi-1,4-phenylene)bis(4-substituted aminosulfonyl)sydnone (**7a-j**). (a) R = 4-ClC₆H₄; (b) R = CH₂(CH₂)₄CH₃; (c) R = CH₃; (d) R = C₆H₅; (e) R = 3-ClC₆H₄; (f) R = 2-FC₆H₄; (g) R = CH₂(CH₂)₂CH₃; (h) R = 3-CH₃C₆H₄; (i) R = CH₂-C₆H₅; (j) R = 2-CH₃C₆H₄.

with different amines formed final compounds 3,3'-(sulfonyldi-1,4-phenylene)bis(4-substituted aminosulfonyl)sydnone (**7a-j**). Figure 1 shows the synthetic route of compounds (**7a-j**). Thin layer chromatography (TLC) of compounds **6** and (**7a-j**) showed that single compounds were produced. The solvent system used for TLC was toluene:ethyl acetate:isopropyl alcohol (7:2:1). The structures of synthesized compounds were deduced from elemental analysis and spectral data. IR spectrum shows characteristic band for C=O group of sydnone between 1727 and 1750 cm⁻¹. Sometimes multiple peaks of carbonyl group occur due to the Fermi resonance splitting [14]. The SO₂ stretching was observed between 1336–1350 cm⁻¹ and 1129–1168 cm⁻¹. Sulfonamide group of compound **7a-j** also shows N-H stretching band near 3260 cm⁻¹. The IR spectrum of **7a** is shown in Figure 2. The ¹H-NMR spectrum of each compound in the series shows characteristic singlet for sulfonamide group about δ = 8.96–10.25 and δ = 4.65–5.75. In the mesoionic structure of sydnone, the positive charge associated with the ring exerts a very marked deshielding effect, and therefore, high field for the ring proton of sydnone ring in compound (**5**) is observed at δ = 7.80. Figure 3 shows the ¹H-NMR spectrum of compound **7a**. ¹³C-NMR of sydnone carbon at the fourth position resonance near δ = 90.00 and carbonyl carbon of sydnone ring near δ = 161.00. ¹³C-NMR spectrum of the compound **7a** is depicted in Figure 4. Characterization data of the compounds **7(a-j)** obtained are given in Table 1.

The antibacterial screening results have shown that this activity varies with the substitution on sulfonamide group (Table 2). Compound **7d** possessing phenyl substitution showed highest activity, whereas compounds **7g**, **7i**, and **7j** having butyl, benzyl, and 2-methylphenyl substituent, respectively, showed good activity against *Streptococcus pneumoniae*. Compound **7i** containing benzyl ring as substituent showed highest activity against rest of the tested bacterial organisms. Compounds **7g**, **7h**, and **7j** containing butyl, 3-methylphenyl, and 2-methylphenyl substituents, respectively, were found to show good activity against *Staphylococcus aureus*. Compounds **7a** and **7j** possessing 4-chlorophenyl and 2-methylphenyl substituents displayed pronounced activity against *Escherichia coli*, whereas compound **7g** having butyl substitution was found to possess higher activity against *Pseudomonas aeruginosa*. The rest of the compounds were found to possess moderate to poor activity against tested organisms. It shows how biological properties influence by minor structural modification. In general, most of the compounds were found to possess antibacterial activity. It is noted that larger zones are co-related with smaller minimum inhibitory concentration.

Biological activity. The preliminary antibacterial testing has been carried out by Kirby-Bauer Technique [16] to estimate the minimum inhibitory concentration of the test compounds. The following dilutions of compounds were selected: 400, 200, and 100 μg/mL. The antimicrobial

Table 1
Characterization data of 3,3'-(sulfonyl-di-1,4-phenylene)bis(4-substituted aminosulfonyl)sydnone (7a-j).

Compd. no.	R	Molecular formula (molecular weight)	Yield (% w/w)	M.P. (°C)	Analysis (%)				
					C (%)	H (%)	O (%)	N (%)	S (%)
7a	4-Cl-C ₆ H ₄	C ₂₈ H ₁₈ Cl ₂ N ₆ O ₁₀ S ₃ (765.52)	63	89-92	43.93 (43.90)	2.37 (2.34)	20.90 (20.93)	10.98 (10.92)	12.57 (12.59)
7b	-CH ₂ (CH ₂) ₄ CH ₃	C ₂₈ H ₃₆ O ₁₀ N ₆ S ₃ (712.86)	59	149-151	47.18 (47.13)	5.09 (4.95)	22.45 (22.40)	11.79 (11.65)	13.50 (13.47)
7c	-CH ₃	C ₁₈ H ₁₆ N ₆ O ₁₀ S ₃ (572.54)	65	182-184	37.76 (37.72)	2.82 (2.79)	27.94 (27.98)	14.68 (14.63)	16.80 (16.75)
7d	C ₆ H ₅	C ₂₈ H ₂₀ N ₆ O ₁₀ S ₃ (696.68)	58	167-169	48.27 (48.23)	2.89 (2.85)	22.96 (22.93)	12.06 (12.01)	13.81 (13.75)
7e	3-Cl-C ₆ H ₄	C ₂₈ H ₁₈ Cl ₂ N ₆ O ₁₀ S ₃ (765.57)	60	149-151	43.93 (43.87)	2.37 (2.33)	20.90 (20.84)	10.98 (10.95)	12.57 (12.54)
7f	1-F-C ₆ H ₄	C ₂₈ H ₁₈ F ₂ N ₆ O ₁₀ S ₃ (732.66)	63	176-178	45.90 (45.82)	2.48 (2.37)	21.84 (21.75)	11.47 (11.44)	13.13 (13.11)
7g	-CH ₂ (CH ₂) ₂ CH ₃	C ₂₄ H ₂₈ O ₁₀ N ₆ S ₃ (656.75)	65	151-153	43.89 (43.85)	4.30 (4.27)	24.36 (24.33)	12.80 (12.74)	14.65 (14.68)
7h	3-CH ₃ -C ₆ H ₄	C ₃₀ H ₂₄ N ₆ O ₁₀ S ₃ (724.73)	59	155-157	49.72 (49.68)	3.34 (3.31)	21.08 (21.03)	11.60 (11.56)	13.27 (13.23)
7i	-H ₂ C-C ₆ H ₅	C ₃₀ H ₂₄ N ₆ O ₁₀ S ₃ (724.73)	59	154-156	49.72 (49.65)	3.34 (3.30)	22.08 (22.11)	11.60 (11.62)	13.27 (13.24)
7j	2-CH ₃ -C ₆ H ₄	C ₃₀ H ₂₄ N ₆ O ₁₀ S ₃ (724.73)	64	157-159	49.72 (49.69)	3.34 (3.28)	22.08 (22.11)	11.60 (11.54)	13.27 (13.22)

activity was done against Gram-positive bacterial strains *Streptococcus pneumoniae* and *Staphylococcus aureus* and against Gram-negative bacterial strains *Escherichia coli* and *Pseudomonas aeruginosa*. The reference drugs used were streptomycin and penicillin-G. The sample drugs were screened at 200 µg/mL under identical conditions, and the zone of inhibition was measured in millimeters. A reading of 10 mm indicates no zone. The activity of the compounds (7a-j) as spectrum is depicted in Figure 5.

CONCLUSIONS

The sulfonyl chloride derivative of sydnone was reacted with various amines. Their analytical data provide adequate results. Many of the new products exhibited splendid activity against tested organisms.

EXPERIMENTAL

Melting points were determined by open capillary method and are uncorrected. All compounds were analyzed satisfactorily for C, H, O, N, and S. IR spectra (KBr) were recorded on Shimadzu FTIR spectrophotometer (Japan). ¹H-NMR and ¹³C-NMR spectra were recorded on Bruker spectrometer at 400 MHz using dimethyl sulfoxide (DMSO)-d₆ as a solvent and TMS as an internal standard. Elemental analysis was carried out on a Vairo-EL (Elementa) model. Purity of the compounds was checked by TLC on silica gel plates. Analytical TLC was carried out with Merck silica gel 60 F₂₅₄ aluminum sheets.

Typical procedure for the synthesis of 3,3'-sulfonyldi-1,4-phenylene)bis(4-primary substituted aminosulfonyl)sydnones (7a-j). *Synthesis of 2,2'-(sulfonylbis(1,4-phenylene imino))diethyl acetate (2).* To a mixture of 4,4'-diaminodiphenylsulfone (2.48 g, 0.01 mol) and double molar quantity of ethylchloroacetate in dry ethanol (10 mL), freshly dried sodium acetate (3.28 g, 0.04 mol) was added, and then the mixture was heated under reflux for 4-5 h. The mixture was diluted with water and kept in refrigerator overnight. Crystalline esters were obtained and purified by recrystallization from ethanol. The reaction was monitored by TLC.

Synthesis of 2,2'-(sulfonylbis(1,4-phenylene imino))diacetic acid (3). 2,2'-(Sulfonylbis(4,1-phenyleneimino))diethylacetate (4.20 g, 0.01 mol) and sodium hydroxide (1.2 g, 0.03 mol) were dissolved in distilled water: absolute alcohol (36.0:4.0 mL) in a flat-bottomed flask. The mixture was stirred at reflux temperature for 30 min. The resultant mixture was cooled and acidified with hydrochloric acid to get the final product. Pure product was obtained by recrystallization from ethanol.

Synthesis of 2,2'-(sulfonylbis(1,4-phenylene(nitrosoimino)))diacetic acid (4). To a well-stirred solution of 2,2'-(sulfonylbis(4,1-phenylene-imino))diacetic acid (5.82 g, 0.016 mol) in water (40 mL), freshly prepared sodium nitrate solution (3.32 g, 0.049 mol) was added dropwise at 0-5°C over a period of 40 min [15]. Concentrated hydrochloric acid was added until pH becomes 2-3. The nitroso compound was filtered with suction and washed with cold water and then was dried and recrystallized from ethanol.

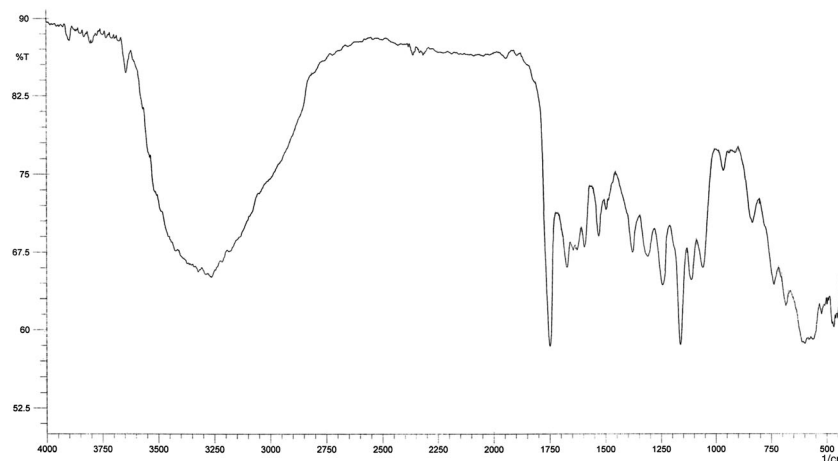


Figure 2. IR spectrum of 3,3'-(sulfonyldi-1,4-phenylene)bis(4-((4-chlorophenyl)amino)sulfonyl)sydnone (**7a**).

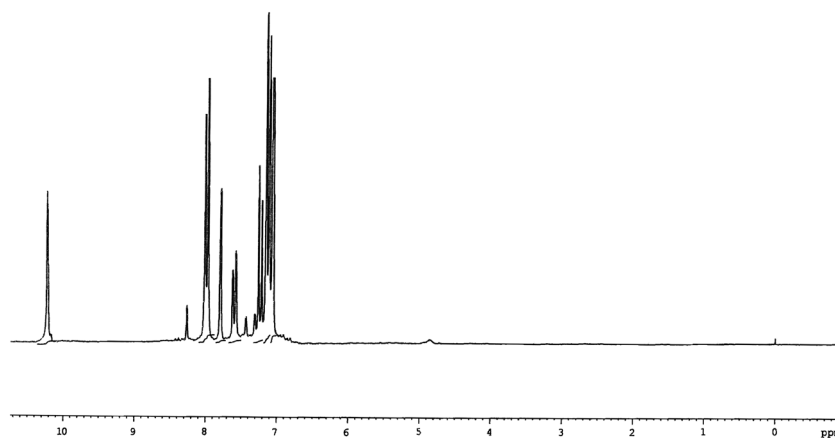


Figure 3. $^1\text{H-NMR}$ spectrum of 3,3'-(sulfonyldi-1,4-phenylene)bis(4-((4-chlorophenyl)amino)sulfonyl)sydnone (**7a**).

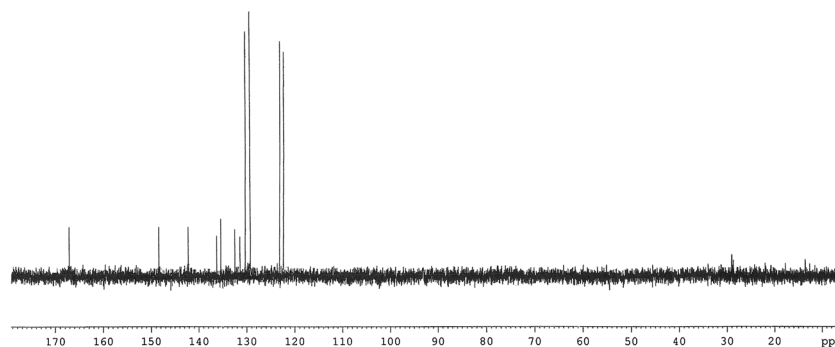


Figure 4. $^{13}\text{C-NMR}$ spectrum of 3,3'-(sulfonyldi-1,4-phenylene)bis(4-((4-chlorophenyl)amino)sulfonyl)sydnone (**7a**).

Synthesis of 3,3'-(sulfonyldi-1,4-phenylene)bissydnone (5). The dried 2,2'-(sulfonylbis{4,1-phenylene(nitrosoimino)}) diacetic acid (**4**) and acetic anhydride were taken in the ratio of 1:5 and stirred for 10 h. The stirred solution was slowly poured into cold water. The content was neutralized by 10% sodium bicarbonate solution and washed well with water and dried. The crude sydnone was recrystallized from benzene–petroleum ether.

Synthesis of 3,3'-(sulfonyldi-1,4-phenylene)bis(4-chlorosulfonyl)sydnone (6). Chlorosulfonic acid (2.32 mL, 0.02 mol) was added dropwise into the mixture of 3,3'-(4,4'-diphenyl)bissydnonyl sulfone (3.86 g, 0.01 mol) and catalytic amount of P_2O_5 over 30 min with constant stirring at 0–5°C. The temperature of the well-stirred mixture was maintained at 5°C. When all the chlorosulfonic acid has been added (about 1 h), the mixture was

Table 2

Antibacterial activity of 3,3'-(sulfonyldi-1,4-phenylene)bis(4-substituted aminosulfonyl)sydnone (7a–j).

Compd. no.	Gram-positive organism				Gram-negative organism			
	<i>Streptococcus pneumoniae</i>		<i>Staphylococcus aureus</i>		<i>Escherichia coli</i>		<i>Pseudomonas aeruginosa</i>	
	IZ	MIC	IZ	MIC	IZ	MIC	IZ	MIC
7a	13	64	12	64	13	32	12	64
7b	10	–	11	128	11	128	12	64
7c	12	64	10	–	14	64	13	64
7d	17	16	14	64	15	64	10	–
7e	13	64	12	128	11	128	10	–
7f	12	64	13	64	12	128	12	64
7g	16	32	16	32	16	16	14	32
7h	10	–	15	32	13	64	10	–
7i	16	32	18	32	16	16	15	32
7j	16	32	17	32	15	32	10	–
Streptomycin	40	0.25	40	0.125	28	1	34	0.5
Penicillin-G	35	0.25	45	0.125	30	0.5	38	0.25

IZ, inhibition of zone; MIC, minimum inhibitory concentration.

refluxed at about 60°C for about 60 min. The solution was then poured into a mixture of crushed ice and water with vigorous stirring. Precipitation was collected by filtration, washed thrice with water and then dried.

Condensation of 3,3'-(sulfonyldi-1,4-phenylene)bis(4-chlorosulfonyl)sydnone with different primary amines (7a–j). 3,3'-(Sulfonyldi-1,4-phenylene)bis(4-chlorosulfonyl)sydnone (0.011 mol) was dissolved in acetone at room temperature. A solution of primary amine (0.022 mol) in acetone was added dropwise into the solution of compound 6 over a period of 5 h with constant stirring. Then 10 mL of pyridine was added to the well-stirred solution after 1 and 2 h during the reaction. The solution was poured into ice with stirring. The precipitate was collected by filtration, washed thrice with water and then dried. The precipitate was recrystallized from benzene.

Following the above procedure, bis-sydnone derivatives (7a–j) were synthesized using *p*-chloroaniline, *n*-hexylamine, *n*-methylamine, aniline, *m*-chloroaniline, *o*-floroaniline, *n*-butylamine, *m*-toluidine, benzylamine, and *o*-toluidine as primary amines. All the synthesized compounds 7(a–j) are recorded in Table 1.

IR, ¹H-NMR (δ, ppm; DMSO), and ¹³C-NMR (δ, ppm; DMSO) of the synthesized compounds. 2,2'-(Sulfonylbis(1,4-phenyleneimino))diethyl acetate (2). IR (KBr): 2955, 2919, 2864, 2845, 1757, 1339, 1320, 1150 cm⁻¹; ¹H-NMR: δ = 1.33 (t, 6H, *J* = 7.10 Hz, CH₃), 3.70 (s, 2H, CH₂), 4.00 (s, 2H, NH), 4.35 (q, 4H, *J* = 7.10 Hz, COO-CH₂), 6.47–7.70 (m, 8H, Ar-H); ¹³C-NMR: δ = 14.46, 44.42, 61.45, 115.08, 128.07, 133.38, 171.49, 149.12.

2,2'-(Sulfonylbis(1,4-phenylene imino))diacetic acid (3). IR (KBr): 3340–2523, 2948, 2914, 1710, 1343, 1320, 1139 cm⁻¹; ¹H-NMR: δ = 4.03 (s, 4H, CH₂), 6.37 (s, 2H, NH), 6.40 (s, 2H,

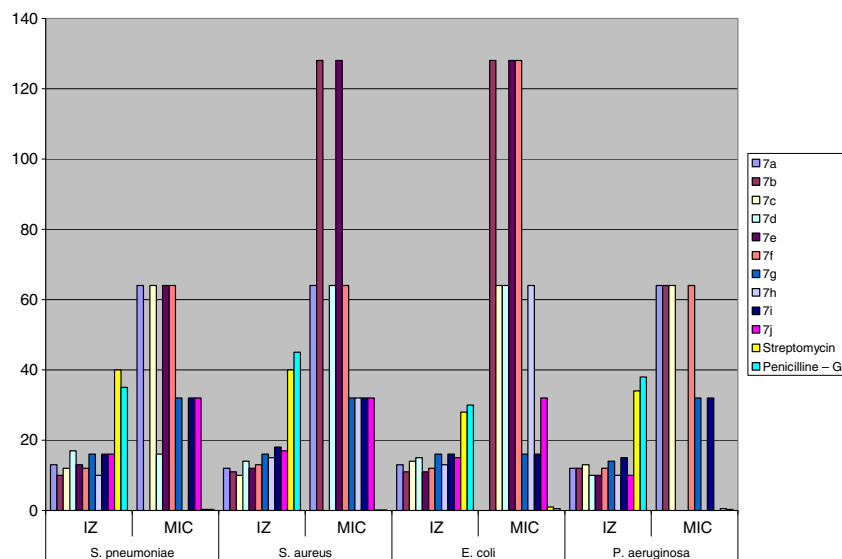


Figure 5. Minimum inhibitory concentration and zone of inhibition of compounds (7a–j). [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://www.wileyonlinelibrary.com).]

COOH), 6.49–7.45 (m, 8H, Ar-H); $^{13}\text{C-NMR}$: δ = 44.77, 114.56, 128.64, 133.57, 148.96, 171.79.

2,2'-(Sulfonylbis[1,4-phenylene(nitrosoimino)]diacetic acid (4). IR (KBr): 2520–3322, 2935, 2917, 1505, 1355, 1347, 1134 cm^{-1} ; $^1\text{H-NMR}$: δ = 4.79 (s, 4H, CH_2), 7.87–8.10 (m, 8H, Ar-H), 11.37 (s, 2H, COOH); $^{13}\text{C-NMR}$: δ = 49.24, 121.40, 128.92, 134.77, 141.33, 167.77.

3,3'-(Sulfonyldi-1,4-phenylene)bissydnone (5). IR (KBr): 1745, 1339, 1129 cm^{-1} ; $^1\text{H-NMR}$: δ = 7.80 (s, 2H, sydnone), 8.54–8.06 (m, 8H, Ar-H); $^{13}\text{C-NMR}$: δ = 95.67, 122.82, 128.70, 131.77, 141.98, 169.13.

3,3'-(Sulfonyldi-1,4-phenylene)bis(4-chlorosulfonyl)sydnone (6). IR (KBr): 1745, 1410, 1336, 1193, 1138 cm^{-1} ; $^1\text{H-NMR}$: δ = 8.22–8.54 (m, 8H, Ar-H); $^{13}\text{C-NMR}$: δ = 123.18, 126.16, 128.36, 139.64, 141.66, 168.47.

3,3'-(Sulfonyldi-1,4-phenylene)bis(4-[(4-chlorophenyl)amino]sulfonyl)sydnone (7a). IR (KBr): 3261, 1750, 1339, 1163, 1055 cm^{-1} ; $^1\text{H-NMR}$: δ = 7.00–8.30 (m, 16H, Ar-H), 10.25 (s, 2H, SO_2NH); $^{13}\text{C-NMR}$: δ = 122.47, 123.11, 129.45, 130.37, 131.26, 132.64, 135.75, 136.30, 142.37, 167.30.

3,3'-(Sulfonyldi-1,4-phenylene)bis[4-(hexylamino)sulfonyl]sydnone (7b). IR (KBr): 3263 (NH), 2965, 2930, 2880, 2865, 1750, 1339, 1164 cm^{-1} ; $^1\text{H-NMR}$: δ = 0.92 (t, 6H, J = 6.72 Hz, CH_3), 1.19–1.75 (m, 16H, CH_2), 2.84 (t, 4H, J = 7.11 Hz, NH-CH_2), 4.98 (s, 2H, SO_2NH), 7.50–8.13 (m, 8H, Ar-H); $^{13}\text{C-NMR}$: δ = 14.97, 22.43, 26.76, 27.65, 30.73, 44.00, 123.87, 128.54, 133.87, 138.53, 143.71, 168.76.

3,3'-(Sulfonyldi-1,4-phenylene)bis[4-(methylamino)sulfonyl]sydnone (7c). IR (KBr): 3262, 2975, 2884, 1727, 1345, 1168 cm^{-1} ; $^1\text{H-NMR}$: δ = 3.10 (s, 6H, CH_3), 4.59 (s, 2H, SO_2NH), 8.22–8.65 (m, 8H, Ar-H); $^{13}\text{C-NMR}$: δ = 31.69, 123.85, 129.75, 131.59, 138.88, 142.83, 168.53.

3,3'-(Sulfonyldi-1,4-phenylene)bis[4-(anilinosulfonyl)]sydnone (7d). IR (KBr): 3260, 1730, 1350, 1161 cm^{-1} ; $^1\text{H-NMR}$: δ = 7.12–8.50 (m, 18H, Ar-H), 9.35 (s, 2H, SO_2NH); $^{13}\text{C-NMR}$: δ = 121.31, 123.76, 124.79, 129.85, 130.97, 133.40, 137.45, 138.21, 142.78, 168.66.

3,3'-(Sulfonyldi-1,4-phenylene)bis(4-[(3-chlorophenyl)amino]sulfonyl)sydnone (7e). IR (KBr): 3260, 1730, 1335, 1162, 1055 cm^{-1} ; $^1\text{H-NMR}$: δ = 7.00–8.30 (m, 16H, Ar-H), 9.12 (s, 2H, $-\text{SO}_2\text{NH}$); $^{13}\text{C-NMR}$: δ = 120.09, 121.43, 123.57, 125.64, 128.52, 131.74, 133.87, 135.75, 138.47, 138.83, 168.13, 142.75.

3,3'-(Sulfonyldi-1,4-phenylene)bis(4-[(2-fluorophenyl)amino]sulfonyl)sydnone (7f). IR (KBr): 3263, 1730, 1350, 1230, 1161 cm^{-1} ; $^1\text{H-NMR}$: δ = 6.94–8.60 (m, 16H, Ar-H), 8.96 (s, 2H, $-\text{SO}_2\text{NH}$); $^{13}\text{C-NMR}$: δ = 115.78, 123.13, 123.81, 124.01, 126.13, 126.97, 129.66, 133.19, 138.72, 142.71, 159.74, 167.89.

3,3'-(Sulfonyldi-1,4-phenylene)bis[4-(butylamino)sulfonyl]sydnone (7g). IR (KBr): 3263, 2965, 2930, 2880, 2865, 1750, 1339, 1164 cm^{-1} ; $^1\text{H-NMR}$: δ = 0.94 (t, 6H, J = 7.15 Hz, CH_3), 1.35–1.69 (m, 8H, CH_2), 3.04 (t, 4H, J = 6.53 Hz, NHCH_2), 4.65 (s, 2H, $-\text{SO}_2\text{NH}$), 8.15–8.73 (m, 8H, Ar-H); $^{13}\text{C-NMR}$: δ = 13.83, 20.16, 29.72, 41.18, 124.12, 129.58, 132.53, 137.54, 142.26, 167.75.

3,3'-(Sulfonyldi-1,4-phenylene)bis(4-[(3-methylphenyl)amino]sulfonyl)sydnone (7h). IR (KBr): 3263, 2968, 2950, 1750, 1339, 1162 cm^{-1} ; $^1\text{H-NMR}$: δ = 2.15 (s, 6H, CH_3), 6.89–8.30 (m, 16H, Ar-H), 9.05 (s, 2H, SO_2NH); $^{13}\text{C-NMR}$: δ = 22.03, 118.57, 122.15, 123.76, 125.97, 129.64, 129.75, 132.54, 137.05, 137.96, 141.21, 142.75, 167.28.

3,3'-(Sulfonyldi-1,4-phenylene)bis[4-(benzylamino)sulfonyl]sydnone (7i). IR (KBr): 3262, 2920, 1750, 1339, 1161 cm^{-1} ; $^1\text{H-NMR}$: δ = 4.85 (s, 4H, CH_2), 5.75 (s, 2H, SO_2NH), 7.35–8.50 (m, 18H, Ar-H); $^{13}\text{C-NMR}$: δ = 45.21, 123.46, 127.28, 127.94, 128.30, 129.76, 132.95, 138.44, 142.35, 142.72, 167.34.

3,3'-(Sulfonyldi-1,4-phenylene)bis(4-[(2-methylphenyl)amino]sulfonyl)sydnone (7j). IR (KBr): 3261, 2968, 2950, 1750, 1339, 1161 cm^{-1} ; $^1\text{H-NMR}$: δ = 2.21 (s, 6H, CH_3), 7.10–8.50 (m, 16H, Ar-H), 8.96 (s, 2H, SO_2NH); $^{13}\text{C-NMR}$: δ = 17.03, 123.42, 124.65, 126.64, 127.79, 129.83, 131.39, 131.94, 132.73, 134.53, 138.27, 143.11, 167.52.

REFERENCES AND NOTES

- [1] Badami, B. V. *Resonance* 2006, 11, 40.
- [2] Kier, L. B.; Roche, E. B. *J Pharm Sci* 1967, 56, 149.
- [3] Goeres, E.; Faehndrich, A. *Acta Biol Med Ger* 1968, 20, 641.
- [4] Shih, M. H.; Ke, F. Y. *Bioorg Med Chem* 2004, 12, 4633.
- [5] Satyanarayana, K.; Rao, M. N. *J Pharm Sci* 1995, 84, 263.
- [6] Dunkley, C. S.; Thoman, C. J. *Bioorg Med Chem Lett* 2003, 13, 2899.
- [7] Satyanarayana, K.; Rao, M. N. *Eur J Med Chem* 1995, 30, 641.
- [8] Kavali, J. R.; Badami, B. V. *IL Farmaco* 2000, 55, 406.
- [9] (a) Moustafa, M. A.; Gineinah, M. M.; Nasr, M. N.; Waleed, A. H. B. *Arch Pharm* 2004, 337, 427; (b) Moustafa, M. A.; Nasr, M. N.; Gineinah, M. M.; Bayoumi, W. A. *Arch Pharm* 2004, 337, 164.
- [10] Jogul, J. J.; Badami, B. V. *J Serb Chem Soc* 2006, 71, 851.
- [11] (a) Supuran, C. T.; Casini, A.; Scozzafava, A. *Med Res Rev* 2003, 23, 535; (b) Moustafa, O. S.; Ahmad, R. A. *Phosphorus Sulfur Silicon Relat Elem* 2003, 178, 475.
- [12] Popoff, I. C.; Singhal, G. H.; Engle, A. R. *J Med Chem* 1971, 14, 550.
- [13] Stewart, F. H. C. *Chem Rev* 1964, 64, 129.
- [14] Daeniker, H. U.; Druey, J. *Helv Chim Acta* 1957, 40, 918.
- [15] Thoman, C. J.; Voaden, D. J. *Org Synth* 1965, 45, 96.
- [16] Bauer, A. W.; Kirby, W. M.; Sherris, J. C.; Turk, M. *Am J Clin Pathol* 1966, 45, 493.