Indian Journal of Chemistry
Vol. 58B, December 2019, pp 1375-1383

Synthesis, spectral characterization and bioactivity evaluation of sulfonamide derivatives of *p*-nitrobenzene sulfonylchloride

D B Janaki Ramudu[a], C H Subramanyam[c], S K NayabRasool[c], P SeenivasaMurthy[b], M NagalakshmiDevamma[c], C H Venkataramaiah[d], W Rajendra[d], Chamarthi Naga Raju[c] & Ponne Venkata Chalapathi*[a]

[a] Department of Chemistry, Sri Venkateswara Arts College (TTDs), Tirupati 517 502, India

[b] Department of Botany, Sri Venkateswara University, Tirupati 517 502, India

[c] Department Chemistry, Sri Venkateswara University, Tirupati 517 502, India

[d] Department of Zoology, Sri Venkateswara University, Tirupati 517 502, India

E-mail: pvchalapathisumathi@gmail.com; rajuchamarthi10@gmail.com

Received 6 July 2018; accepted (revised) 17 June 2019

A simple and convenient method for the synthesis of biologically active sulfonamide derivatives of *p*-nitrobenzene sulfonylchloride has been achieved. All the title compounds have been characterized by spectral and elemental analysis. They have been further screened *in vitro* for their antibacterial and antifungal activities. All the compounds show good to moderate activity against both bacteria and fungi when compared with standard bactericide, Streptomycin and fungicide, Nystatin.

Keywords: Sulfonamide, *p*-nitrobenzene sulfonylchloride, Streptomycin, Nystatin, anti-microbial agents

The treatment of bacterial infections remains a therapeutic challenge because of emerging infectious diseases and the increasing number of multidrug-resistant microbial pathogens. Inspite of the many antibiotics and chemotherapeutics available, the emergence of old and new antibiotic-resistant bacterial strains in the last two decades has led to a substantial need for new classes of anti-microbial agents.

The discovery of sulfonamides as antibacterials in the early 1930s was the beginning of the most fascinating era of chemotherapeutic agents[1-4]. Since drugs have been widely used to treat a broad spectrum of microbial diseases[5].

However, due to the rapid emergence of sulfonamide resistant organisms and the development of more potent drugs have limited their clinical use. Sulfonamide derivatives exhibit various types of pharmacological activities such as antibacterial[6], antiprotozoal[7], antifungal[8], antiinflammatory[9], nonpeptidic vasopressin receptor antagonists[10] and translation initiation inhibitors[11]. Some important sulfonamide derivatives have been used as carbonic anhydrase inhibitors of commercial importance[12]. They are also effective for the treatment of urinary, intestine, and ophthalmic infections, scalds, ulcerative colitis[13], rheumatoid arthritis[14], male erectile dysfunction as the phosphodiesterase-5 inhibitor sildenafil – better known under its commercial name, Viagra[15], and obesity[16]. More recently, sulfonamides are being used as anticancer agents[17], as the antiviral HIV protease inhibitor amprenavir[18] and in Alzheimer's disease[19].

Some organisms are resistant to all approved antibiotics and can only be treated with experimental and potentially toxic drugs. Therefore, there is an overwhelming need to develop more effective infections caused by antibiotic resistant bacterial pathogens. Sulfonamides exert their effect by targeting on dihydropteroate synthase (DHPS) enzyme, which catalyzes folic acid pathway in bacteria and some eukaryotic cells[20] but is not present in human cells[21]. This is the basis for the selective effect of sulfonamides on bacteria and for their broad spectrum of antibacterial activity.

Due to the broad applicability of sulfonamides, it is desirable to find general and effective methods for their synthesis. Thus synthesis of these compounds is of continuing interest. To date many synthetic methods have been reported. Motivated by the afore-

mentioned literature and in persistence of our earlier work on different sulfonamide derivatives[22], we envision our approach towards the design and synthesis of structurally diverse series of sulfonamide derivatives for their antimicrobial activity.

Results and Discussion

Chemistry

The synthesis of sulfonamide derivatives **3a-j** was performed by reaction between *p*-nitrobenzene sulfonyl chloride **1** and various primary **2a-f**, secondary **2g-j** bioactive amines in the presence of triethylamine as a base with high yields in short reaction time. The synthetic protocol for the title compounds was presented in Scheme I.

The chemical structures of all the title compounds **3a-f** were characterized by spectral data (^{1}H, ^{13}C, IR and LC-MS), elemental analyses and the results were presented in experimental section. The structure of **3a** is interpreted from spectroscopic data. IR spectra of compound **3a** reveals absorption band in the region 3448 cm^{-1} corresponding to -NH stretching vibrations in indole ring. The absorption band in the region 3382 cm^{-1} corresponding to aliphatic-NH stretching vibrations for the compound **3a**. Two absorption bands at 1318, 1173 cm^{-1}corresponds to SO_2 stretchingvibrations. The absorption at 934 cm^{-1} is due to S–N stretching vibrations. In the ^{1}H NMR spectra of **3a**, displayed multiplets in the region δ 7.60-7.11 due to aromatic protons. The indolic-NH proton was highly deshielded and appeared at δ 10.1.

IR spectra of compound **3i** gave absorption band the absorption bands at 1346, 1169 cm^{-1} were due to SO_2 stretching vibrations. The band at 887 $cm^{-1}$was due to S–N stretching. In ^{1}H NMR spectra of **3i**, aromatic protons resonated in the range δ 8.42-6.79 as doublets. The triplet at δ 3.22 was due to proton in piperazine moiety.

In ^{13}C NMR spectra, chemical shifts for the title compounds were observed in the expected regions. In their mass spectra, $M^{+\cdot}$ions were observed in the expected *m/z* values.

Biological activity

Molecular docking analysis

In order to provide strength to the synthesized compounds, docking analysis was carried out for compounds **3a-j** with selective pharmacological target such as DNA Gyrase A protein (Figure 1, **A**) of *E. coli* which is a suitable target for anti-bacterial activity. The crystal structure of DNA Gyrase A (PDB id: 3LPX) was retrieved from the protein data bank, and the reference drug Streptomycin Figure 1, **B**) (**PC ID 19649)** Pub Chem Drug bank.The docking results of DNA Gyrase A showed that compounds **3j**, **3h**, **3f**, **3i** and **3a** have significant binding modes, with dock scores (Table I) of **-8.2**, **-8.1**, **-7.7**, **-7.5** and **-7.2** k cal/mol when compared with the control drug Streptomycin (-6.9) respectively. The H-bonds, binding affinities and energy profiles of compounds **3a-j** along with reference drug, towards the active site amino acids of the enzyme are summarized in Table I. The binding modes of compounds **3j**, **3h**, **3f**, **3i** and **3a** suggested that they fitted more stably into the DNA Gyrase A binding pocket. Hence, the present investigation demonstrate that the synthesised compounds will be the promising next generation anti-microbial drugs, which can be effectively used in the treatment of microbial and other related infections.

Antibacterial activity

The title compounds **3a-j** were screened for antibacterial activityat two different concentrations, 100 and 200 μg/mL, against two Gram positive (*B. subtilis*, *S. aureus)* and two Gram negative bacteria (*E. coli*, *P. aeruginosa)* using disc diffusion method. The bactericide, Streptomycin was used as a standard to compare the activity of the title compounds. The results revealed that all the title compounds exhibited moderate to good activity against both Gram-positive and Gram-negative bacteria (Table II).

Especially the compounds **3j** bearing 4-fluorophenyl piperazine moiety, **3h** incorporated with 4-nitrophenyl piperazine moiety, **3f** having 1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl moiety, **3i** bearing 4-chlorophenyl piperazine moiety, **3a** linked withindole moiety; exhibited good activity against both Gram-positive and Gram-negative bacteria. The remaining compounds displayed moderate activity against Gram-positive bacteria and Gram negative bacteria.

Antifungal activity

The title compounds were also evaluated for their antifungal activityat two different concentrations, 150 and 250 μg/mL, against four fungi, *Aspergillus niger*, *Aspergillus flavus*, *Penicilliumnotatum* and *Fusarium solani*. The fungicide Nystatin was used as a standard to compare the activity of the title compounds. The

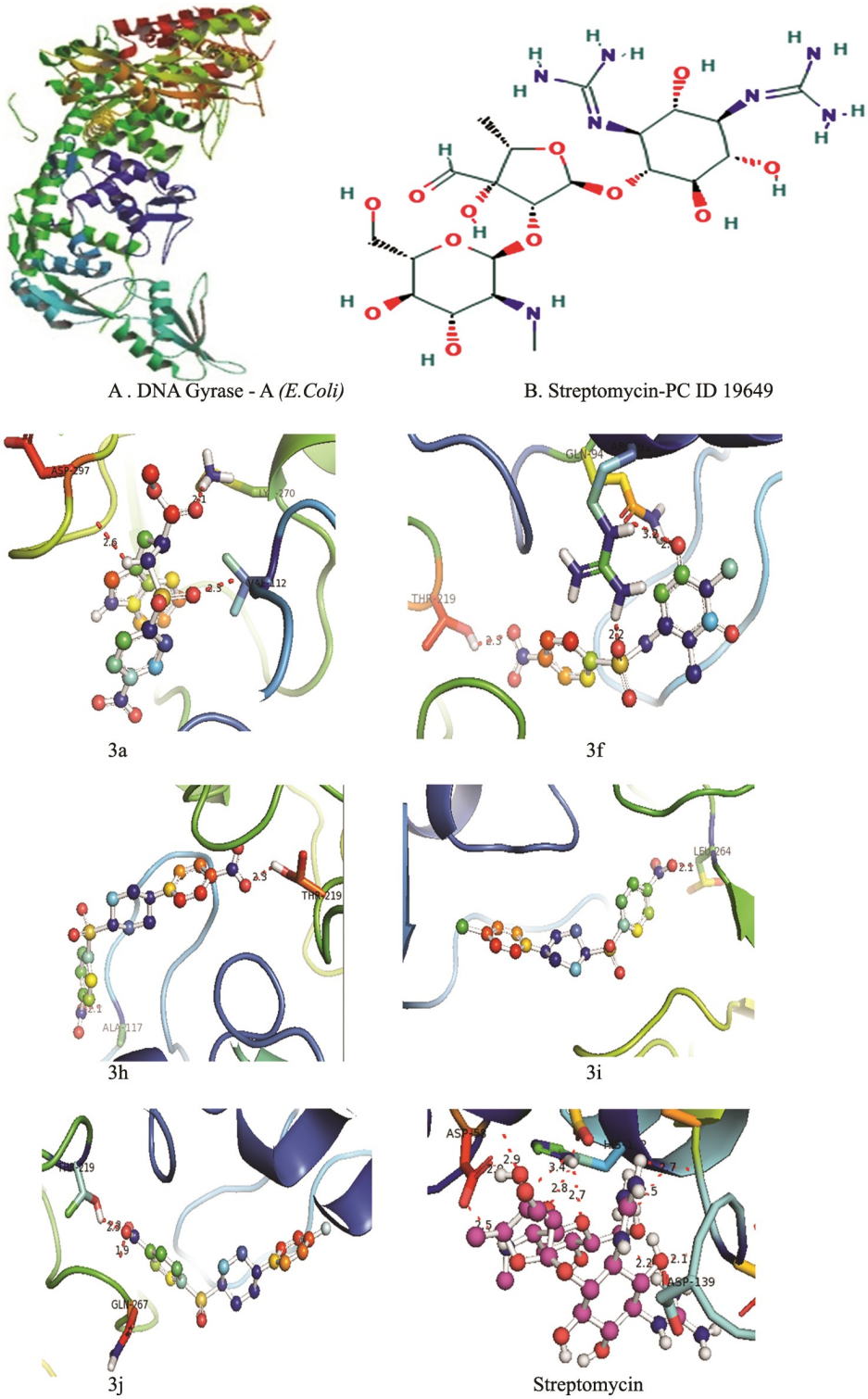


Figure 1 — Docking structures of the compounds

observed results on the antifungal activity of the title compounds and control drug are given in Table III.

Especially the compounds **3g** bearing propanoate moiety, **3j** linked with 4-fluorophenyl piperazine moiety, **3b** incorporated with pentanoate moiety, **3d** having 3,4-dihydroxyphenethyl moiety and**3i** bearing 4-chlorophenyl piperazine moiety exhibited good activity against fungi when compared with the

Table I — Bonding characterization of synthesized compounds **3a-j** and STM (A), Reference drug) against *E. coli* DNA Gyrase A protein

S. No.	Compd	Rank	Binding energy (K cal mol^{-1})	Binding interaction	Bond Length(Å)	Bond Angle (°)	Bond Type
A	Streptomycin	R	−6.9	Arg 139 CG…HN	2.2	124.4	H- don
				Leu 135 CD…HN	2.7	125.7	H- don
				His 132 CB…OH	2.5	125.0	H- acc
				Asp 53 CG…OC	3.4	116.7	H- acc
				Asp 53 OC…OC	2.9	118.9	H- acc
				Asp 58 OD…OH	2.0	118.6	H- acc
				Asp 58 OD…HN	2.5	116.4	H- don
				His 132 ND…OC	2.8	126.2	H- acc
				His 132 ND…OC	2.7	120.0	H- acc
				His 132 OC…OH	2.5	119.8	H- acc
1	**3a**	5.0	−7.2	Asp 297 CA ….HN	2.6	112.4	H- don
				Val 112 CA ….OS	2.3	114.3	H- acc
				Lys 270 NZ ….OC	2.1	110.3	H- acc
2	**3b**	9.0	−5.9	Lys 270 NC ….OC	2.4	124.6	H- acc
3	**3d**	7.0	−6.3	Asp 297 CA ….HN	2.4	122.4	H- don
				Leu 264 CA …..ON	2.2	114.7	H- acc
4	**3e**	8	−6.1	Asp 297 CB ….HN	2.6	122.2	H- don
				Val 112 CB ….OC	2.2	73.6	H- acc
5	**3f**	3	−7.7	Gln 94 CG …..OC	3.2	99.6	H- acc
				Gln 94 CG …..OC	2.4	65.6	H- acc
				Arg 91 CZ …..OS	2.2	119.0	H- acc
				Thr 219 CB ….ON	2.3	109.6	H- acc
6	**3g**	6	−6.5	Asp 297 CA ….HN	2.0	122.4	H- don
				Lys 270 NZ …..OC	2.3	110.3	H- acc
7	**3h**	2	−8.1	Ala 117 CA …..ON	2.1	114.9	H- acc
				Met 301 CA ….ON	2.3	115.2	H- acc
8	**3i**	4	−7.5	Leu 264 NN …..ON	2.1	90.6	H- acc
9	**3j**	1	−8.2	Thr 219 CB …..ON	2.3	109.6	H- acc
				Thr 219 CB …..ON	2.3	109.6	H- acc
				Gln 267 CB …..ON	1.9	129.4	H- acc

Table II — Antibacterial activity of the title compounds **3a-j**

Compd	Zone of Inhibition in mm							
	Bacillus subtilis		*Pseudomonas aeruginosa*		*Staphylococcus aureus*		*Escherichia coli*	
	150 µg/mL	250 µg/mL	150 µg/mL	250 µg/mL	150 µg/mL	250 µg/mL	150 µg/mL	250 µg/mL
3a	9	13	11	13	18	20	15	18
3b	8	10	8	10	11	14	11	14
3c	0	0	9	13	9	12	10	13
3d	8	11	11	14	14	17	9	13
3e	8	11	15	17	11	13	18	21
3f	10	13	9	12	8	11	15	18
3g	0	9	12	15	10	12	8	10
3h	12	14	10	13	18	21	16	19
3i	10	13	9	13	09	12	12	15
3j	12	15	12	15	11	14	14	17
Std	14	16	12	15	13	15	16	20

Std: Streptomycin

standard fungicide, Nystatin. All the remaining compounds showed moderate activity.

Biological assay

Molecular docking analysis

Molecular docking studies[23,24]were carried against DNA Gyrase A protein with compounds **3a-j**, and the reference drug Streptomycin (A), using the docking module implemented in Pyrx 2010.12. Initially the protein structures were protonated with the addition of polar hydrogens, followed by energy minimization with the MMFF94x force field, in order to get the stable conformer of the protein. Flexible docking was

Table III — Antifungal activity of the title compounds **3a-j**

Compd	Percent Inhibition of Fungal growth							
	Aspergillus niger		*Aspergillus flavus*		*Penicilliumnotatum*		*Fusarium solani*	
	150 µg/mL	250 µg/mL	150 µg/mL	250 µg/mL	150 µg/mL	250 µg/mL	150 µg/mL	250 µg/mL
3a	53	67	59	65	58	65	55	69
3b	66	75	67	78	67	79	67	73
3c	54	66	56	69	56	65	59	67
3d	66	72	65	72	65	70	68	73
3e	55	68	54	66	57	67	59	68
3f	42	60	43	55	45	60	46	59
3g	75	80	72	80	66	82	70	82
3h	62	75	65	76	60	78	62	72
3i	65	76	62	73	65	75	64	78
3j	69	70	69	75	69	77	63	73
Blank (DMSO)	00	00	00	00	00	00	00	00
Std	60	75	65	75	62	76	60	75

Std: Nystatin

employed, the inhibitor binding site residues were softened and highlighted through the "Site Finder" module implemented in the Pymol software. The grid dimensions were predicted as ˚ X: 28.27, Y: 27.13, Z: 28.51 for DNA Gyrase Arespectively. The docking was carried out with the default parameters *i.e*., placement: triangle matcher, recording 1: London dG, refinement: force field, and a maximum of 10 conformations of each compound were allowed to be saved in a separate database file in a. mdb format. After the docking process, the binding energy and binding affinity of the protein-ligand complexes were calculated using Pymol viewer tool (www.pymol.org).[25]

Antibacterial activity

All the newly synthesized compounds were screened for their antibacterial activity against Gram positive bacteria, *Bacillus subtilis* (MTCC- 441), *Staphylococcus aureus* (MTCC-737) and Gram negative bacteria, *Escherichia coli* (MTCC- 443), *Pseudomonas aeruginosa* (MTCC-741) using a disk diffusion method. 2 mg of the title compounds and the standard drug were dissolved in 10 mL of dimethylsulphoxide (DMSO) and further diluted to a concentration of 100 and 200 µg /mL of the tested samples. The sterile nutrient agar medium was pored into a set of petri plates and allowed few minutes for solidification after 20 µL of respective bacterial culture was uniformly spread on the surface of the nutrient agar medium with sterile inocula or 'L' shape glass rod. The sterile disks (6 mm diameter) previously soaked in 150 and 250 µg/mL test solutions were placed on petri plates and incubated for 24 h at 37±1°C. The zone of inhibition around the disc was measured. Streptomycin was used as a positive control and DMSO was used as a negative control. For each treatment, triplicate experiments were carried out and the average zone of inhibition was calculated in mm (Table II).

Antifungal activity

Antifungal activity of the synthesized compounds was screened against *Aspergillus niger*, *Aspergillus flavus*,*Penicilliumnotatum*and *Fusarium solani* by the poison food technique. 2 mg of the synthesized and of the standard (Nystatin) compounds were dissolved in 10 mL of dimethylsulphoxide (DMSO) and their concentrations were adjusted to 150 and 250 µg/mL by dilution before mixing with potato dextrose agar medium (PDA). 5 mm of mycelia disc was cut from the respected culture medium with a sterilized cork borer, inoculated in the center of the PDA plate and incubated for 5 days at 26±2°C. Nystatin was used as a positive control while a disk dipped in DMSO was used as a negative control. Triplicate experiments were carried out for each treatment and results were expressed in mm (Table II). The inhibiting activity of the title compounds was calculated by the formula I=C-T/C, where 'I' indicates the rate of inhibition, 'C' indicates the diameter of fungi growth in the control and 'T' indicates the diameter of fungi growth in treatment.

Experimental Section

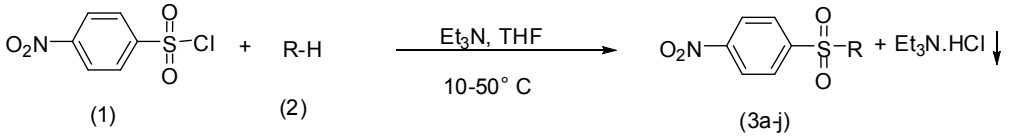
Chemicals were purchased from Sigma-Aldrich, Merck and Lancaster, and were used as received without further purification. All solvents used for spectroscopic and other physical studies were of reagent grade and were further purified by literature methods. Melting points were determined using a calibrated thermometer by Guna Digital Melting Point apparatus. IR spectra were recorded as KBr discs on a Nicolet 380 FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded as solutions in DMSO-d_6 on a Bruker AMX 500 MHz spectrometer operating at 500 MHz for ^{1}H and 500 MHz for ^{13}C. The ^{1}H and ^{13}C chemical shifts were referenced to tetramethylsilane. Electrospray ionization mass spectrometry (ESI-MS) was performed on a Bruker electrospray mass spectrometer. Elemental analyses were performed on a ThermoFinnigan Instrument at University of Hyderabad, Hyderabad, India.

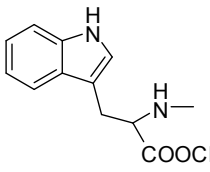
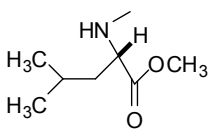
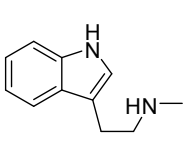
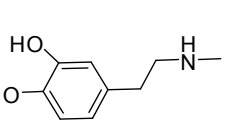
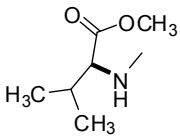
General procedure for the synthesis of title compounds, 3a-j

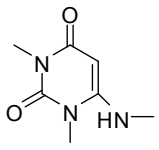
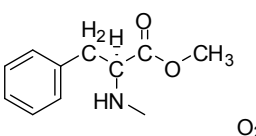
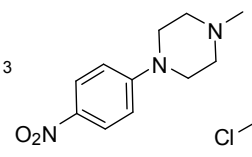
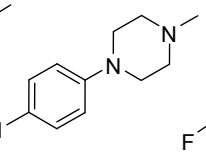
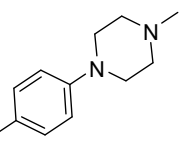
To a stirred solution of methyl 2-amino-3-(1*H*-indol-3-yl) propanoate **2a** (1 mmol) in dry THF, *p*-nitrobenzene sulfonyl chloride **1** (1 mmol) was added at 0°C in the presence of triethylamine (1.2 mmol) as a base in THF (20 mL). After the addition, the reaction mixture temperature was slowly raised to 40-45°C and stirred for 4 h. The progress of the reaction was monitored by TLC using ethyl acetate: hexane (3:2). After completion of the reaction, the triethylamine hydrochloride salt was filtered off and the solvent was removed in a rotary evaporator. The residue was purified by washing with hexane and recrystallization from ethanol. The resulting compound Methyl 3-(1*H*-indol-3-yl)-2-(4-nitrophenyl-sulfonamido)propanoate **3a** was obtained in good yield (86%). The same procedure was adopted for the synthesis of the remaining title compounds **3b-j** (Scheme I).

Spectral data of title compounds, 3a-j

Methyl 3-(1*H*-indol-3-yl)-2-(4-nitrophenyl-sulfonamido)propanoate, 3a: Yield 86%. m.p.173-174°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.1 (s, 1H, Indololic-NH), 8.42 (d, 2H, J = 8.5 Hz, Ar-H), 7.99 (d, 2H, J = 8.5 Hz, Ar-H), 7.74 (s, 1H, NH), 7.60-7.11 (m, 5H, Ar-H), 3.81 (t, 1H, J = 6.0 Hz, -C*H*-COO), 3.68 (s, 3H, -OCH_3), 3.42 (m, 1H, -CH_2-), 3.17 (m, 1H, -CH_2-); ^{13}C NMR (500 MHz, $CDCl_3$): δ 171.5, 151.1, 150.6, 136.5, 128.2, 127.4, 124.2, 123.0, 121.7, 119.8, 118.8, 111.1, 109.7, 59.5, 51.9, 29.6; IR (KBr): 3448



Compd.	3a	3b	3c	3d	3e
R					

Compd.	3f	3g	3h	3i	3j
R					

Scheme I — Synthesis of sulfonamide derivatives of *p*-nitrobenzene sulfonyl chloride

(Indole-NH), 3382 (NH), 1318, 1173 (SO_2 str.), 934 cm^{-1} (S-N str,); EI-MS: *m/z* 403. Anal. Calcd for $C_{18}H_{17}N_3O_6S$: C, 53.59; H, 4.25; N, 10.42. Found: C, 53.54; H, 4.20; N, 10.37%.

(S)-Methyl 4-methyl-2-(4-nitrophenyl-sulfonamido) pentanoate, 3b: Yield 90%. m.p.130-132°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.99 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.74 (s, 1H, NH), 3.68 (s, 3H, -OCH_3), 3.45 (m, 1H, SO_2NH-C*H*-), 1.87 (t, 2H, *J* = 6.1 Hz, -CH_2-), 1.49 (m, 1H, -C*H*(CH_3)$_2$) 0.91 (d, 6H, *J* = 7.6 Hz, -CH(C*H*$_3$)$_2$); ^{13}C NMR (500 MHz, $CDCl_3$): δ 171.5, 151.1, 150.6, 128.2, 124.2, 53.5, 51.9, 39.7, 24.8, 22.9; IR (KBr): 3285 (NH), 1723 (C=O), 1320, 1174 (SO_2 str.), 911 cm^{-1} (S-N Str); EI-MS: *m/z* 330. Anal. Calcd for $C_{13}H_{18}N_2O_6S$: C, 47.26; H, 5.49; N, 8.48. Found: C, 47.21; H, 5.45; N, 8.44%.

N-(2-(1*H*-Indol-3-yl)ethyl)-4-nitrobenzene-sulfonamide, 3c: Yield 89%. m.p.162-163 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.1 (s, 1H, Indololic-NH), 8.42 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.99 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.74 (s, 1H, NH), 7.60-7.11 (m, 5H, Ar-H), 3.43 (t, 2H, methylene-H), 2.71 (t, 2H, *J* = 6.8 Hz, methylene-H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 151.1, 150.6, 136.5, 128.2, 127.4, 124.2, 123.0, 121.7, 119.8, 118.8, 113.0, 111.1, 43.9, 27.9; IR (KBr): 3443 (Indole-NH), 3380 (NH), 1315, 1175 (SO_2 str.), 938 cm^{-1} (S-N str,); EI-MS: *m/z* 345). Anal. Calcd for $C_{16}H_{15}N_3O_4S$: C, 55.64; H, 4.38; N, 12.17. Found: C, 55.60; H, 4.34; N, 12.12%.

N-(3,4-Dihydroxyphenethyl)-4-nitrobenzene-sulfonamide, 3d: Yield 83%. m.p.142-144°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.48 (s, 2H, Ar-OH), 8.42 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.99 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.74 (s, 1H, NH), 6.86-6.68 (m, 3H, Ar-H), 5.35 (1H,OH), 3.49 (t, 2H, *J* = 6.8 Hz, methylene-H), 2.83(t, 2H, *J* = 7.2 Hz, methylene-H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 151.1, 150.6, 145.6, 144.5, 131.5, 128.2, 124.2, 122.8, 116.4, 115.9, 42.8, 34.5; IR (KBr): 3399 (Phenolic-OH), 3222 (-NH), 1314, 1176 (SO_2 str.), 919 cm^{-1} (S-N Stretch); EI-MS: *m/z* 338. Anal. Calcd for $C_{14}H_{14}N_2O_6S$: C, 49.70; H, 4.17; N, 8.28. Found: C, 49.65; H, 4.13; N, 8.24%.

(R)-Methyl 3-methyl-2-(4-nitrophenyl-sulfonamido) butanoate, 3e: Yield 82%. m.p.122-124°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.99 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.74 (s, 1H, NH), 3.68 (s, 3H, -OCH_3), 3.44 (m, 1H, NH-C*H*-), 2.67 (m, 1H, -C*H*(CH_3)$_2$), 0.91 (d, 6H, *J*= 7.2 Hz, -CH(C*H*$_3$)$_2$); ^{13}C NMR (500 MHz, $CDCl_3$): δ 171.5, 151.1, 150.6, 128.2, 124.2, 63.1, 51.9, 29.6, 18.9; IR (KBr): 3334 (NH), 1721 (C=O), 1298, 1164 (SO_2str), 907 cm^{-1} (S-N Stretch); EI-MS: *m/z* 316. Anal. Calcd for $C_{12}H_{16}N_2O_6S$: C, 45.56; H, 5.10; N, 8.86. Found: C, 45.51; H, 5.05; N, 8.82%.

N-(1,3-Dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-pyrimidin-4-yl)-4-nitrobenzenesulfonamide, 3f: Yield 75%. m.p.132-133°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.99 (d, 2H, *J* = 8.5 Hz, Ar-H), 4.50(s, 1H, Pyrimidine-H), 3.16 (s, 3H, -N-CH_3), 3.01 (s, 3H, -N-CH_3), 2.0 (s, 1H, SO_2N*H*); ^{13}C NMR (500 MHz, $CDCl_3$): δ 163.2, 162.3, 151.4, 151.1, 146.9, 128.2, 124.2, 75.5, 30.1, 29.4; IR (KBr): 3385 (NH), 1754 (C=O), 1310, 1166 (SO_2 str.), 912 cm^{-1} (S-N Stretch); EI-MS: *m/z* 340. Anal. Calcd for $C_{12}H_{12}N_4O_6S$: C, 42.35; H, 3.55; N, 16.46. Found: C, 42.31; H, 3.51; N, 16.41%.

Methyl 2-(4-nitrophenylsulfonamido)-3-phenyl-propanoate, 3g: Yield 77%. m.p.145-147 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.12 (d, 2H, *J* = 7.9 Hz, Ar-H), 7.74 (s, 1H, NH), 7.23-6.60 (m, 5H, Ar-H), 3.68 (s, 3H, -COO-C*H*$_3$), 3.63 (q, 1H, -CH-C*H*$_2$), 1.41 (d, 2H, -CH-C*H*$_2$); ^{13}C NMR (500 MHz, $CDCl_3$): δ 171.5, 151.1, 144.7, 138.8, 138.3, 129.5, 128.2, 124.2, 120.8, 62.1, 51.9, 13.8; IR (KBr): 3389 (NH), 1725 (C=O), 1311, 1170 (SO_2 str.), 914 cm^{-1} (S-N Stretch); EI-MS: *m/z* 364. Anal. Calcd for $C_{16}H_{16}N_2O_6S$: C, 52.74; H, 4.43; N, 7.69. Found: C, 52.71; H, 4.40; N, 7.65%.

1-(4-Nitrophenyl)-4-((4-nitrophenyl)-sulfonyl) piperazine, 3h: Yield 79%. m.p.171 – 172°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.99 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.21 (d, 2H, *J* = 8.5 Hz, Ar-H), 6.79 (d, 2H, *J* = 9.0 Hz, Ar-H), 3.22 (t, 8H, *J* = 5.0 Hz, piperazine-H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 155.7, 151.1, 145.8, 137.4, 128.2, 124.8, 124.2, 112.3, 53.1, 48.4; IR (KBr): 1510, 1325 (NO_2 Str.), 1315, 1168 (SO_2 str.), 918 cm^{-1} (S-N Stretch); EI-MS: *m/z* 392. Anal. Calcd for $C_{16}H_{16}N_4O_6S$: C, 48.97; H, 4.11; N, 14.28. Found: C, 48.93; H, 4.06; N, 14.24%.

1-(4-Chlorophenyl)-4-((4-nitrophenyl)-sulfonyl) piperazine, 3i: Yield 88%. m.p.179-180°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.99 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.21 (d, 2H, *J* = 8.5

Hz, Ar-H), 6.79 (d, 2H, *J* = 9.0 Hz, Ar-H), 3.22 (t, 8H, *J* = 5.0 Hz, piperazine-H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 150.3, 149.0, 141.6, 131.0, 129.1, 128.9, 124.4, 118.2, 49.2, 45.8; IR (KBr): 1346, 1169 (SO_2 str.), 887 (S-N), 765 cm^{-1} (C-Cl); EI-MS (*m/z*, %): 381 $(M)^+$, 383 (M+2). Anal. Calcd for $C_{16}H_{16}ClN_3O_4S$: C, 50.33; H, 4.22; N, 11.00. Found: C, 50.29; H, 4.18; N, 10.95%.

1-(4-Fluorophenyl)-4-((4-nitrophenyl)-sulfonyl) piperazine, 3j: Yield 70%. m.p.175-176°C. ^{1}H NMR (500 MHz, $CDCl_3$)**:** δ 8.42 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.99 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.06 (d, 2H, *J* = 7.9 Hz, Ar-H), 6.74 (d, 2H, *J* = 8.9 Hz, Ar-H), 3.22 (t, 8H, *J* = 5.0 Hz, piperazine-H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 156.8, 151.1, 145.8, 145.2, 128.2, 124.2, 116.4, 115.9, 53.1, 48.4; IR (KBr): 1343, 1177 (SO_2 str.), 1095 (C-F Str.), 917 cm^{-1} (S-N Str.); EI-MS: *m/z* 365. Anal. Calcd for $C_{16}H_{16}ClN_3O_4S$: C, 52.59; H, 4.41; N, 11.50. Found: C, 52.54; H, 4.37; N, 11.45%.

Conclusion

A simple and convenient method was developed for the synthesis of a series of new sulfonamide derivatives of *p*-nitrobenzene sulfonyl chloride with high yields by reacting *p*-nitrobenzene sulfonylchloride with various biologically active amines. These compounds exhibited moderate to good antibacterial and antifungal activities. Especially the compounds **3j** bearing 4-fluorophenyl piperazine moiety, **3h** substituted with 4-nitrophenyl piperazine moiety, **3f** having 1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl moiety, **3i** bearing 4-chlorophenyl piperazine moiety, **3a**incorporated with indole moiety; exhibited good activity against both Gram-positive and Gram-negative bacteria. The compounds **3g** bearing propanoate moiety, **3j** bearing 4-fluorophenyl piperazine moiety, **3b** incorporated with pentanoate moietyexhibited good activity against fungi when compared with the standard fungicide, Nystatin. All the remaining compounds showed moderate activity against both bacteria and fungi.

Acknowledgements

The authors are thankful to Hyderabad Central University, Osmania University and Department of Biochemistry, S. V. University for providing instrumentation facilities to characterize the compounds and for obtaining biological data.

References

1 Hen N, Bialer M, Wlodarczyk B, Finnell R H &Yagen B, *J Med Chem*,53(10) (2010) 4177.
2 Carta F, Maresca A, Scozzafava A, Vullo D &Supuran C T, *Bioorg Med Chem*, 17(20) (2009) 7093.
3 Namba K, Zheng X, Motoshima K, Kobayashi H, Tai A,Takahashi E, Sasaki K, Okamoto K &Kakuta H, *Bioorg Med Chem*, 16(11) (2008) 6131.
4 Joseph P, Turtaut F, Ouahrani-Bettache S, Montero J L, Nishimori I, Minakuchi T, Vullo D, Scozzafava A, Kohler S, Winum J-Y &Supuran C T, *J Med Chem*, 53(5) (2010) 2277.
5 Wilkinson B L, Bornaghi L F, Wright A D, Houston T A &Poulsen S A, *Bioorg Med ChemLett*,17(5) (2007) 1355.
6 Stokes S S, Albert R, Buurman E T, Andrews B, Shapiro A B, Green O M, McKenzie A R & Otterbein L R, *Bioorg Med Chem Lett*, 22 (2012) 7019.
7 Chibale K, Haupt H, Kendrick H, Yardley V, Saravanamuthu A, Fairlamb A H & Croft S L, *Bioorg Med Chem Lett*, 11 (2001) 2655.
8 RahaviEzabadi I, Camoutsis C, Zoumpoulakis P, Geronikaki A, Soković M, Glamočilija J &Čirič A, *Bioorg Med Chem*, 16 (2008) 1150.
9 Kennedy J F & Thorley M, in *Pharmaceutical Substances*, 3rd edn., edited by Kleeman A, Engel J, Kutscher B and Reichert D (Thieme, Stuttgart) (1999).
10 Serradeil-Le & Gal C, *CardiovascularDrug Rev*, 19 (2001) 201.
11 Natarajan A, Guo Y, Harbinski F, Fan Y-H, Chen H, Luus L, Diercks J, Aktas H, Chorev M &Halperin J A, *J Med Chem*, 47 (2004) 4979.
12 Vullo D, De Luca V, Scozzafava A, Carginale V, Rossi M, Supuran C T &Capasso C, *Bioorg Med Chem*, 21 (2013) 4521.
13 Wilson C O, Gisvold O & Block J H, *Wilson and Gisvold's Textbook of Organic Medicinal and Pharmaceutical Chemistry*, 11th edn., edited by Block J and Beale J M (Lippincott Williams and Wilkins, Philadelphia) (2004).
14 Levin J I, Chen J M, Du M T, Nelson F C, Killar L M, Skala S, Sung A, Jin G, Cowling R, Barone D, March C J, MohlerK M, Black R A &Skotnicki J S, *Bioorg Med Chem Lett*,
12 (2002) 1199.
15 Kim D-K, Lee J Y, Lee N, Ryu D H, Kim J-S, Lee S, Choi J-Y, Ryu J-H, Kim N-H, Im G-J, Choi W-S & Kim T-K, *Bioorg Med Chem*, 9 (2001) 3013.
16 Hu B, Ellingboe J, Han S, Largis E, Lim K, Malamas M, Mulvey R, Niu C, Oliphant A, Pelletier J, Singanallore T, Sum F-W, Tillett J & Wong V, *Bioorg Med Chem*, 8 (2001) 2045.
17 Ma T, Fuld A D, Rigas J R, Hagey A E, Gordon G B, Dmitrovsky E &Dragnev K H, *Chemotherapy*, 58 (2012) 321.
18 *Protease Inhibitors in AIDS Therapy*, edited by Ogden R C and Flexner C W (Marcel Dekker, New York) (2001).
19 Roush W R, Gwaltney S L, Cheng J, Scheidt K A, McKerrow J H &Hansell E, *J Am Chem Soc*, 120 (1998) 10994.
20 Brown G M, *J Biolog Chem*,237 (1962) 536.
21 Huovinen P, Sundström L, Swedberg G &Skold O, *AntimicrobAgents Chemother*, 39(2) (1995) 279.

22 SubramanyamCh, Nayab RasoolSk, JanakiramuduD B, RasheedS, UdaySankar A &Naga RajuC, *Phosphorous Silicon Relat Elem*, 192(7) (2017) 845.
23 Morris G M, Huey R, Lindstrom W, Sanner M F, Belew R K, Goodsell D S & Olson A J, *J Comput Chem*, 30 (2009) 2785.
24 Ter Haar E, Coll J T, Austen D A, Hsiao H M, Swenson L & Jain J, *Nature* (*Struct Biol*) 8 (2001) 593.
25 Pettersen E F, Goddard T D & Huang C C, *J Comput Chem*, 25 (2004) 1605.
26 Nandhakumar R, Viswanathan H, Suresh T & Mohan P S, *Fitoterapia*, 73(2002)734; (b) Karvembu R & Natarajan K, *Polyhedron*, 21(2002) 219; (c) BonjarShahidi G H, *Asian J Plant Sci*, 3(2004) 82.
27 Song S, Zhou L, Li D, Tang D, Li J & Jiang W, *Nat Prod Res Dev*, 16 (2004) 157.