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Synthesis and Biological Evaluation of Some Sulfonamide Schiff's Bases

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ABSTRACT
Substituted sulfonamides were reacted with different aromatic aldehydes to form Schiff's bases. TLC ascertained the purity of synthesized compounds on silica gel G coated plates and visualized by using iodine vapour. The structures of synthesized compounds were confirmed by their IR, ^{1}H NMR spectroscopic data. The derivatives were subjected to antimicrobial activity using different bacterial strains (*Klebsiella pneumoniae*, gram negative bacteria and *Staphylococcus epidermidis*, *Bacillus subtilis* as gram positive bacteria with respect to Ciprofloxacin as standard antibiotics.

Keywords: substituted sulfonamide, Ciprofloxacin, Schiff's bases, antimicrobial activity.

INTRODUCTION

Schiff's bases derived from aromatic amines and aromatic aldehyde have a wide variety of applications in many fields as sulfonamide Schiff's bases have been reported to posses-antimicrobial activity [1-8], anti-inflammatory activity [9-10], antikinetoplastid antimitotic activity [11], antitumor activity [12] and anticonvulsant activity. [13]

MATERIAL AND METHOD

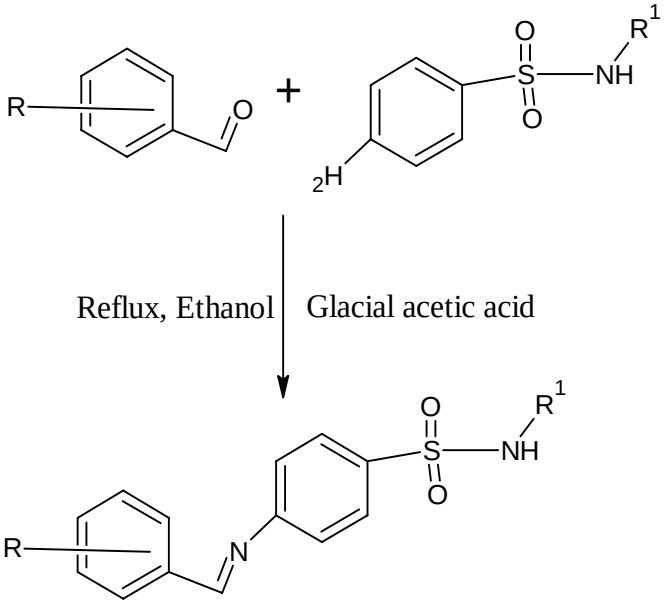
Melting points were determined on a capillary melting point apparatus. Infrared spectra were recorded in Shimadzu FTIR spectrophotometer (KBr) and ^{1}H NMR spectra in DMF-d6 on Brucker spectrospin-300 MHz using TMS internal standard. Elemental analysis (CHN) was performed on Carlo Erba 1108 and was within ±4% of theoretical value.

Synthesis of Schiff's bases (SKS-1 –SKS11):

General method- Equimolar quantities (0.01 moles) of substituted sulfonamide and different aromatic aldehydes were dissolved in 40 ml ethanol. Glacial acetic acid (2 ml) was added and refluxed for about 8-12 h. The content was poured on crushed ice. The crystalline product was collected by filtration, dried and recrystallized.

4- {[(*E*)-phenylmethylidene]amino}benzenesulfonamide (SKS – 1)

IR (KBr): 3230 (NH_2 str), 3100 (CH-Ar str), 1650 (C=N str), 1470 (C=C Ar str), 1320 (O=S=O str), 820 (C-S str)
^{1}H-NMR (DMF)ppm: 7.323-7.965 (m, 9H, Ar-H), 8.620 (s, 1H, NH)



R= H, 4-OCH3, 2-OH, 2-Cl,4-Cl, 3-Br

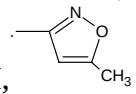
R'= H, 

Fig 1: Synthesis of Schiff's bases

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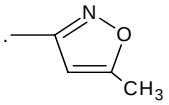
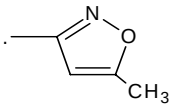
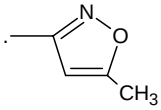
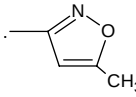
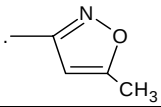
Table 1: Physical constants of synthetic compounds

Code	R	R'	Mp(^{0}C)	Mol. Formula	Yield	Rf*
SKS-1	H	H	174	$C_{13}H_{12}N_2O_2S$	41.15	0.56
SKS-2	OCH3	H	157	$C_{14}H_{14}N_2O_3S$	39.65	0.60
SKS-3	CH	H	208	$C_{13}H_{12}N_2O_3S$	68.84	0.69
SKS-4	2-Cl	H	175	$C_{13}H_{11}N_2O_2SCl$	69.72	0.55
SKS-5	4-Cl	H	172	$C_{13}H_{11}N_2O_2SCl$	61.35	0.62
SKS-6	3-Br	H	153	$C_{13}H_{11}N_2O_2SBr$	44.24	0.41
SKS-7	H		98	$C_{17}H_{15}N_3O_3S$	51.61	0.72
SKS-8	OCH3		167	$C_{18}H_{17}N_3O_4S$	55.79	0.70
SKS-9	OH		203	$C_{17}H_{15}N_3O_4S$	53.22	0.71
SKS-10	2-Cl		182	$C_{17}H_{14}N_3O_3SCl$	72.07	0.55
SKS-11	4-Cl		132	$C_{17}H_{14}N_3O_3SCl$	80.85	0.60

Solvent system: Methanol: Chloroform (1:9)v\v

4-{[(*E*)-(4-methoxyphenyl)methylidene]amino}benzenesulfonamide (SKS – 2)

IR (KBr): 3270 (NH_2 str), 2980 (CH-Ar str), 1630 (C=N str), 1480 (C=C Ar str), 1340 (O=S=O str), 1260 (OCH_3 str), 770 (C-S str);

^{1}H-NMR (DMF)ppm: 7.052 –7.901 (m, 8H,Ar-H), 8.525 (s, 1H, NH), 3.838 (t, 9H, OCH_3)

4-{[(*E*)-(2-hydroxyphenyl)methylidene]amino}benzenesulfonamide (SKS – 3):

IR (KBr): 3350 (OH str), 3250 (NH_2 str), 3040 (CH-Ar str), 1700 (C=N str), 1455 (C=C Ar str), 1325 (O=S=O str), 755 (C-S str);

^{1}H-NMR (DMF)ppm: 6.847 –8.007(m, 8H, Ar-H), 10.239 (s, 1H, NH), 12.599 (s, 1H, OH)

4-{[(*E*)-(2-chlorophenyl)methylidene]amino}benzenesulfonamide (SKS – 4):

IR (KBr): 3297 (NH_2 str), 3068 (CH-Ar str), 1616 (C=N str), 1486 (C=C Ar str), 1375 (O=S=O str), 754 (C-S str), 682 (C-Cl str)

^{1}H-NMR (DMF)ppm: 7.363-8.178 (m, 8H, Ar-H), 8.861 (s, 1H, NH)

4-{[(*E*)-(4-chlorophenyl)methylidene]amino}benzenesulfonamide (SKS – 5):

IR (KBr): 3305 (NH_2 str), 3013 (CH-Ar str), 1684 (C=N str), 1493 (C=C Ar str), 1331 (O=S=O str), 762 (C-S str), 670 (C-Cl str)

^{1}H-NMR (DMF)ppm: 7.345-7.974 (m, 8H, Ar-H), 8.641(s, 1H, NH)

4-{[(*E*)-(3-bromophenyl)methylidene]amino}benzenesulfonamide (SKS – 6):

IR (KBr): 3150 (NH_2 str), 2950 (CH-Ar str), 1650 (C=N str), 1470 (C=C Ar str), 1210 (O=S=O str), 720 (C-S str) 580 (C-Br str)

^{1}H-NMR (DMF)ppm: 6.573-7.921 (m, 8H, Ar-H), 8.014 (s, 1H, NH)

N-(5-methylisoxazol-3-yl)-4-{[(*E*)-phenylmethylidene]amino}benzenesulfonamide (SKS -7):

IR (KBr): 3250 (NH_2 str), 3050 (CH-Ar str), 1730 (C=N str), 1445 (C=C Ar str), 1310 (O=S=O str), 1300 (N-O str), 700 (C-S str)

^{1}H-NMR (DMF)ppm: 6.038-7.458 (m, 9H, Ar-H), 10.900 (s, 1H, NH)

4-{[(*E*)-(4-methoxyphenyl)methylidene]amino}-*N*-(5-methylisoxazol-3-yl)benzenesulfonamide (SKS – 8):

IR (KBr): 3400 (NH_2 str), 3200 (CH-Ar str), 1625 (C=N str), 1455 (C=C Ar str), 1370 (O=S=O str), 1300 (N-O str), 1220 (OCH_3 str), 760 (C-S str)

^{1}H-NMR (DMF)ppm: 6.050-7.894 (m, 8H, Ar-H), 8.522 (s, 1H, NH), 3.850 (t, 9H, OCH_3)

4-{[(*E*)-(2-hydroxyphenyl)methylidene]amino}-*N*-(5-methylisoxazol-3-yl)benzenesulfonamide (SKS – 9):

IR (KBr): 3500 (OH str), 3400 (NH_2 str), 3100 (CH-Ar str), 1620 (C=N str), 1455 (C=C Ar str), 1355 (O=S=O str), 1300 (N-O str), 720 (C-S str);

^{1}H-NMR (DMF)ppm: 6.056-8.950 (m, 8H, Ar-H), 10.693 (t, 1H, NH), 12.429 (s, 1H, OH)

4-{[(*E*)-(2-chlorophenyl)methylidene]amino}-*N*-(5-methylisoxazol-3-yl)benzenesulfonamide (SKS – 10):

IR (KBr): 3160 (NH_2 str), 2980 (CH-Ar str), 1615 (C=N str), 1479 (C=C Ar str), 1346 (O=S=O str), 1300 (N-O str), 756 (C-S str), 674 (C-Cl str)

^{1}H-NMR (DMF)ppm: 6.062-7.867 (m, 8H, Ar-H), 10.322 (s, 1H, NH)

4-{[(*E*)-(4-chlorophenyl)methylidene]amino}-*N*-(5-methylisoxazol-3-yl)benzenesulfonamide (SKS – 11):

IR (KBr): 3381 (NH_2 str), 3056 (CH-Ar str), 1686 (C=N str), 1454 (C=C Ar str), 1343 (O=S=O str), 1300 (N-O str), 743 (C-S str), 668 (C-Cl str)

^{1}H-NMR (DMF)ppm: 6.048-8.606 (m, 8H, Ar-H), 10.911(s, 1H, NH)

Table 2: *In vitro* antibacterial activity (cup plate method)

Compounds Code	Antibacterial activity (µg/ml)					
	B. subtilis		***K. pneumonia***		***S. epidermididis***	
Conc.(in µg/ml)	**50**	**100**	**50**	**100**	**50**	**100**
SKS-1	12	13	13.5	14	13	14.5
SKS-2	---	10	---	---	11.5	12
SKS-3	10.5	11	---	10.5	13.5	14.5
SKS-4	10	10.5	---	10	12	13
SKS-5	---	10	10	10.5	12.5	13
SKS-6	---	10	10.5	11	13	13.5
SKS-7	---	10.5	---	10	14	14.5
SKS-8	10	11	10	10.5	16	17
SKS-9	10	10.5	10.5	11	13	14
SKS-10	---	10	13	14.5	16	17
SKS-11	10.5	11	16	17.5	17.5	19
Std. Ciprofloxacin	20	22	21.5	24	15	21

Antimicrobial screening

All the synthesized compounds were evaluated for their antimicrobial activity against *Klebsiella pneumoniae*, gram negative bacteria and *Staphylococcus epidermidis*, *Bacillus subtilis* as gram positive bacteria. The antimicrobial activity was carried out by the agar diffusion method. Here responses of organisms to the synthesized compounds were measured (zone of inhibition) and compared with the response of standard reference drug. The standard reference drugs used in the present work was Ciprofloxacin. [14]

RESULT AND DISCUSSION

It has been observed that all compounds tested showed good to moderate antibacterial activity, but compounds SKS-8, SKS-10 and SKS-11 showed very significant results against *S. epidermidis*.

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