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Preparation and Antimicrobial Activity of 2-Phenyl-3-Aryl Sulphonamido Indoles and N′-Benzothiazol-2-yl-Thioacetyl-N^2-Arylsuphonyl Hydrazines

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A series of 2-phenyl-3-arylsulphonamido indoles (3a-1) and N^1-benzothiazol-2-yl-thioacetyl-N^2-aryl sulphonyl hydrazines (5a-1) have been prepared and screened for their antibacterial and antifungal activity. Most of them exhibited moderate to good activity. The structures of the compounds have been elucidated by IR and PMR and mass spectral data.

INTRODUCTION

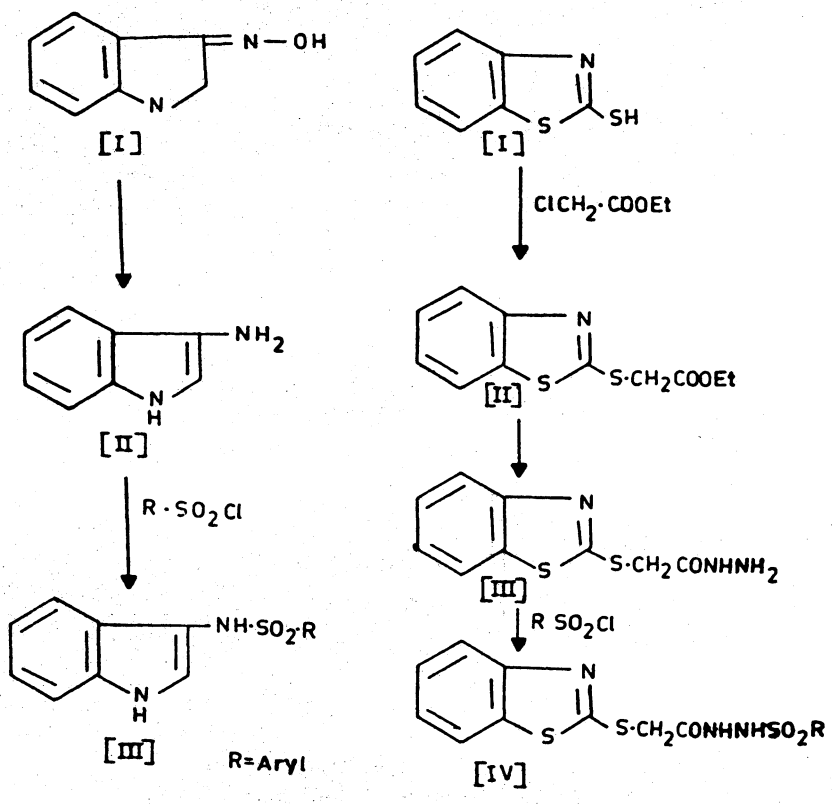
Indole and its derivatives represent one of the most active classes of compounds possessing a wide spectrum of biological activity[1–6]. 2-Mercaptobenzothiazole derivatives have a prominent place in heterocyclic chemistry largely due to the wide ranging biological activity[7–9]. It is reported that sulphonamides exhibit varied biological activity[10,11]. In view of these studies, it was considered of interest to synthesize sulphonamides bearing indole and benzothiazole moieties. The compounds were screened for their antimicrobial activity.

The required 2-phenyl-3-amino indole[12,13] was obtained by the condensation of 2-phenyl indole followed by alkaline dithionite reduction. This amino indole and S-(benzothiazolyl-2′)-mercapto-acetyl hydrazide[14] when treated with different aromatic sulphonyl chlorides in pyridine yielded 2-phenyl-3-aryl sulphonamido indole (3a-1) and N^1-benzothiazol-2-yl-thioacetyl-N^2-aryl-sulphonyl hydrazines (5a-1) respectively. The aryl sulphonyl chlorides[15] were obtained by reported method.

EXPERIMENTAL

All the melting points were determined in sealed evacuated capillary tubes and are uncorrected. IR spectra were determined in KBr on 435-IR Shimadzu spectrophotometer. PMR spectra were taken on 60 MHz Hitachi R-1200 spectrometer using TMS as standard. Elemental analyses were quite comparable with their structures. The purity of compounds was routinely checked by TLC using silica gel G (Merck).

Synthesis of 2-phenyl-3-phenyl sulphonamido indole (3a): A mixture of 2-phenyl-3-amino indole (0.01 mol), benzene sulphonyl chloride (0.01 mol) and pyridine (8 mL) was refluxed for 8 h. After cooling content was poured on crushed ice containing small amount of HCl (2 mL), filtered, washed and dried. The solid obtained was recrystallised from 95% ethanol. Yield 66%, m.f. $C_{20}H_{16}N_2O_2S$; m.p. 182°C; % found (calcd.): C = 68.93 (68.95) H = 4.57 (4.59) N = 8.01 (8.04).



IR (KBr) (cm^{-1}) ν_{max}: 3400 (—N—H str.), 3240 (—N—H str. of R—SO_2 NH—R), 1330 (S=O str. asym.), 1150 (S=O str. sym. of R—SO_2NH—R). PMR ($CDCl_3$) δ: 6.8 to 7.7 (M, 14H, Ar—H), 7.9 (S, 1H, —SO_2NH), 9.9 (S, 1H, —NH indole). m/z: 348 (M^+), 270, 269, 207 (base peak), 205, 194, 179, 104, 77.

Similarly other sulphonamides were prepared. The analytical data are recorded in Table-1.

Synthesis of N^1-benzothiazol-2-yl-thioacetyl-N^2-phenyl sulhonyl hydrazine (*5a*): A mixture of S-(benzothiazolyl-2′)-mercapto-acetyl hydrazide (0.01 mol), benzene sulphonyl chloride (0.01 mol) and pyridine (10 mL) was refluxed for 6 h. After cooling the content was poured on crushed ice containing small amount of HCl (2 mL), filtered, washed and dried. The solid obtained was recrystallised from 1:4 dioxane 95% ethanol (2:1) solvent. Yield 54%; m.f. $C_{15}H_{13}N_3O_3S_3$; m.p. 156°C; % found (calcd.): C = 47.47 (47.49), H = 3.41 (3.43), N = 11.06 (11.08).

IR (KBr) (cm^{-1}) ν_{max}: 3400 (—NH str. of C—NH), 3200 (—NH str. of R—SO_2—NH—R), 1660 (C=O str. of C—NH), 1330 (S=O str. asym. of R—SO_2NH—R), 1150 (S=O str. sym. of R—SO_2NH—R). PMR δ: 3.7 (2H, S, S—CH_2), 6.7 (1H, S, —SO_2 NH), 7.0 to 7.8 (9H, M, Ar—H), 8.25 (1H, S, —CONH). m/z: 380 (M^{+1}), 397 (M^+), 238, 208, 180, 167 (base peak), 135, 136, 109, 77.

Similarly other compounds were prepared and their analytical data are recorded in Table-2.

TABLE-1
ANALYTICAL DATA OF 2-PHENYL-3-SUBSTITUTED SUPHONAMIDO INDOLES (3a–k)

S. No.	R	m.f.	m.p. (°C)	% Nitrogen found (calcd.)	Antibacterial activity			Antifungal activity	
					Zones of inhibition in mm.				
					S. aureus.	*S. pyogens*	*E. coli*	*K. pneumoniae*	*A. niger*
3a	Phenyl	$C_{20}H_{16}N_2O_2S$	182	8.01 (8.04)	15	16	18	15	17
3b	3-Carboxyphenyl	$C_{21}H_{16}N_2O_4S$	125	7.14 (7.17)	13	13	19	10	16
3c	3-Carboxy-4-bromophenyl	$C_{21}H_{15}N_2O_4SBr$	199	5.91 (5.95)	13	20	19	18	14
3d	3-Carboxy-4-chlorophenyl	$C_{21}H_{15}ClN_2O_4S$	155	6.51 (6.56)	19	13	15	10	18
3e	3-Carboxy-6-chlorophenyl	$C_{21}H_{15}ClN_2O_4S$	149	6.53 (6.56)	11	19	20	10	15
3f	3-Carboxy-4-hydroxyphenyl	$C_{21}H_{16}N_2O_5S$	241	6.83 (6.86)	18	15	16	15	19
3g	3-Carboxy-4-methoxyphenyl	$C_{22}H_{18}N_2O_5S$	206	6.61 (6.63)	10	15	11	13	10
3h	3-Carboxy-6-methoxyphenyl	$C_{22}H_{18}N_2O_5S$	231	6.60 (6.63)	16	18	13	19	11
3i	3-Carboxy-4-methylphenyl	$C_{22}H_{18}N_2O_4S$	167	6.85 (6.89)	18	20	15	18	11
3j	3-Carboxy-6-methylphenyl	$C_{22}H_{18}N_2O_4S$	137	6.83 (6.89)	20	19	11	18	13
3k	4-(α′-Carboxy) styryl	$C_{23}H_{18}N_2O_4S$	229	6.68 (6.69)	10	10	11	11	17
3l	4-Methylphenyl	$C_{21}H_{18}N_2O_2S$	163	7.71 (7.73)	19	15	20	17	16

% of yield varing from 55 to 70%

TABLE-2

ANALYTICAL DATA OF N^1-BENZOTHIAZOL-2-YL-THIOACETYL-N^2-ARYLSULPHONYL HYDRAZINES

S. No.	R	m.f.	m.p. (°C)	% Nitrogen found (Calcd.)	Antibacterial activity		Antifungal activity		
					Zones of inhibition in mm.				
					S. aureus.	*S. pyogens*	*E. coli*	*K. Pneumoniae*	*A. niger*
5a	Phenyl	$C_{15}H_{13}N_3O_3S_3$	156	11.06 (11.08)	15	16	11	11	10
5b	3-Carboxyphenyl	$C_{16}H_{13}N_3O_5S_3$	127	9.91 (9.92)	13	11	13	11	10
5c	3-Carboxy-4-chlorophenyl	$C_{16}H_{12}N_3O_5S_3Br$	191	8.35 (8.38)	19	21	18	20	19
5d	3-carboxy-4-chlorophenyl	$C_{16}H_{12}ClN_3O_5S_3$	205	9.17 (9.18)	11	15	14	11	15
5e	3-Carboxy-6-chlorophenyl	$C_{16}H_{12}ClN_3O_3S_3$	135	9.14 (9.18)	16	13	13	17	13
5f	3-Carboxy-4-hydroxyphenyl	$C_{16}H_{13}N_3O_6S_3$	224	9.51 (9.56)	18	17	17	19	10
5g	3-Carboxy-4-methoxyphenyl	$C_{17}H_{15}N_3O_6S_3$	138	9.26 (9.27)	20	10	19	15	17
5h	3-Carboxy-6-methoxyphenyl	$C_{17}H_{15}N_3O_6S_3$	127	9.23 (9.27)	18	15	21	18	19
5i	3-Carboxy-4-methylphenyl	$C_{17}H_{15}N_3O_5S_3$	192	9.60 (9.61)	17	19	15	16	18
5j	3-Carboxy-6-methylphenyl	$C_{17}H_{15}N_3O_5S_3$	125	9.58 (9.61)	10	18	14	10	10
5k	4-(2′-Carboxy) styryl	$C_{18}H_{15}N_3O_5S_3$	200	9.31 (9.35)	15	13	18	11	15
5l	4-Methylphenyl	$C_{16}H_{15}N_3O_3S_3$	132	10.65 (10.68)	19	20	17	19	10

RESULTS AND DISCUSSION

Antimicrobial Activity

The *in vitro* antimicrobial activity of all the purified products was tested for their antibacterial activity against gram +ve bacteria such as *S. aureus*, *S. pyogens* and gram –ve bacteria such as *E. coli*, *K. pneumoniae* and antifungal activity against *A. niger* using the cup-plate method[16] at 50 μg concentration using DMF as solvent. After incubation for 24 h at 37°C, the zones of inhibition were measured in mm. The activity was compared with that of displayed by known antibiotics as standard at the same concentration. The activity data are recorded in Tables 1 and 2.

From the screening results, it was evident that, on the whole, the compounds showed moderate activity against bacteria strains. However, some of the compounds of 3j, c, e, i and showed comparable activity with standard norfloxacin (21), chloramphanicol (22) against *S. pyogens*, *S. aureus* and *E. coli* respectively and 4g, c, l, h, c showed, comparable activity with standard norfloxacin (21), chloramphanicol (22) against *S. aureus*, *S. pyogens* and *K. pneumoniae* respectively.

In case of antifungal activity, most of the compounds showed low activity as compared to standard griseofulvin against *A. niger*.

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