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Studies on 2,5-Disubstituted-1,3,4-oxadiazoles. Part-II. Preparation and Antimicrobial Activity of 2-Arylsulphonamido /α-carbamylarylmethylamino-5-(4′-pyridyl)-1,3,4-oxadiazoles

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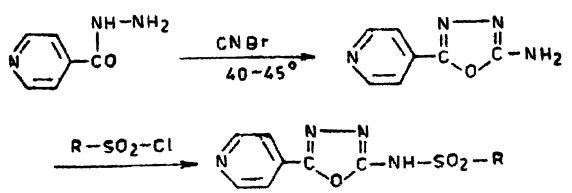
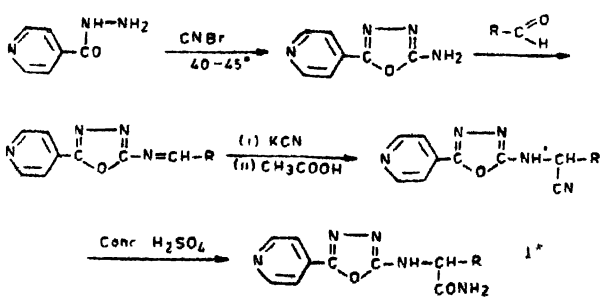
Some new 2,5-disubstituted-1,3,4-oxadiazoles have been prepared having 2-arylsulphonamido and 2-α-carbamylarylmethylamino moieties. Structures of the compounds have been supported by ir spectral data The products were screened for their antimicrobial activity.

2,5-DISUBSTITUTED-1,3,4-oxadiazoles are known to exhibit a wide spectrum of physiological properties[1]. Acetamide derivatives have also been reported to possess good therapeutic activities[2]. With a view to achieve a better therapeutic agent, 1,3,4-oxadiazole derivatives of types **1** and **2** are synthesised. Isoniazide was condensed with cyanogen bromide to get 2-amino-5-(4′-pyridyl)-1,3,4-oxadiazole. It was treated with different aromatic sulphonyl chloride to get the respective sulphonamido derivatives of type **1**. 2-α-Carbamylarylmethylamino-5-(4′-pyridyl)-1,3,4-oxadiazole derivatives of type **2** were synthesised by the action of 2-amino-5-(4′-pyridyl)-1,3,4-oxadiazole with different aromatic aldehydes to get the Schiff's bases. The products were then treated with glacial acetic acid and potassium cyanide to get the respective nitriles. The nitriles were mixed with concentrated sulphuric acid to get the respective amides. The constitution of the product was supported by ir spectral data.



(1)



(2)

Experimental

The ir spectra (KBr) was taken on a Spektromon-2000 spectrophotometer. The oxadiazole derivatives of type **1** gave the characteristic ir bands at 1 580 (C=N), 1 100 (C–O–C), 3 225 (N–H), 1 340 (SO_2–N asym.), 1 160 (SO_2–N sym.) and 1 310 cm^{-1} (C–N). The oxadiazole derivatives of type **2** gave the characteristic ir bands at 1 590 (C=N), 1 140 (C–O–C), 1 680 (C=O), 3 300 (N–H asym.), 3 180 (N–H sym.), 1 365 (C–N) and 735 cm^{-1} (N–H wag).

2-Arylsulphonamido-5-(4′-pyridyl)-1,3,4-oxadiazoles (**1**) *:*

2-Amino-5-(4′-pyridyl)-1,3,4-oxadiazole : To a methanolic solution (100 ml) of isoniazide (13.7 g, 0.1 mol), cyanogen bromide (11.6 g, 0.1 mol) was added. The reaction mixture was warmed at 40–5° for 1 h and then cooled and neutralised with ammonia solution till just alkaline. The resulting solid was filtered, washed with water, dried and crystallised from 1 : 4 dioxan (11.2 g, 70%), m.p. 221° (Found . C, 51.82; H, 3.68; N, 34.52. $C_7H_6N_4O$ calcd. for : C, 51.85; H, 3.70; N, 34.56%).

2-Arylsulphonamido-5-(4′-pyridyl)-1,3,4-oxadiazole : A mixture of 2-amino-5-(4′-pyridyl)-1,3,4-oxadiazole (1 62 g, 0.01 mol), benzenesulphonyl chloride (1.76 g, 0.01 mol) and pyridine (1.0 ml) was refluxed on an oil-bath at 120° for 3 h. The resulting solid was isolated and crystallised from DMF (2.12 g, 70%), m.p. 165° (Found : C, 51.56 ;

H, 3 25 ; N, 18.45. $C_{18}H_{10}N_4O_3S$ calcd. for : C, 51.65 ; H, 3.31 ; N, 18.54%).

Similarly, other aromatic sulphonyl chloride was condensed with 2-amino-5-(4'-pyridyl)-1,3,4-oxadiazole to get other 2-arylsulphonamido-5-(4'-pyridyl)-1,3,4-oxadiazoles (Table 1).

2-α-Carbamylarylmethylamino-5-(4'-pyridyl)-1,3,4-oxadiazoles (2) :

2-Benzalamino-5-(4'-pyridyl)-1,3,4-oxadiazoles : A mixture of methanolic solution (100 ml) of 2-amino-5-(4'-pyridyl)-1,3,4-oxadiazole (4.86 g, 0.03 mol) and benzaldehyde (3.3 ml, 0 03 mol) in methanol (25 ml) was refluxed for 4 h at 120 – 25° on an oil-bath. The resulting solid was isolated and crystallised from glacial acetic acid (80%), m p. 265° (Found : C, 67.15 ; H, 3 95 ; N, 22.20. $C_{14}H_{10}N_4O$ calcd. for : C, 67.20 ; H, 4.00 ; N, 22 40%).

Similarly, other compounds were prepared (Table 2).

2-(α-Cyanobenzylamino)-5-(4'-pyridyl)-1,3,4-oxadiazole : 2-Benzalamino-5-(4'-pyridyl)-1,3,4-oxadiazole (2.5 g, 0.01 mol) was dissolved in metha-

TABLE 1—ANALYTICAL, PHYSICAL AND ANTIMICROBIAL DATA OF 2-ARYLSULPHONAMIDO-5-(4'-PYRIDYL)-1,3,4-OXADIAZOLES

Sl. no.	R	Mol. formula	M p. °C	Yield %	% N : Found/ (Calcd.)	Zone of inhibition (mm)*						
						S.c	*E.c*	*S.a*	*S.al*	*S.t*	*P.*	*A.n*
1.	Phenyl	$C_{13}H_{10}N_4O_3S$	165	70	18.45 (18.54)	12	12	18	24	18	18	19
2.	4-Acetamidophenyl	$C_{15}H_{13}N_5O_4S$	272	70	19 40 (19.49)	10	15	17	12	17	22	18
3.	4-Chlorophenyl	$C_{13}H_9ClN_4O_3S$	256	72	16.60 (16.64)	12	12	15	14	14	18	18
4.	4-Bromophenyl	$C_{13}H_9BrN_4O_3S$	230	70	14.64 (14.69)	12	10	16	14	18	16	19
5.	4-Iodophenyl	$C_{13}H_9IN_4O_3S$	217	69	13.00 (13.08)	14	10	16	14	10	17	14
6.	4-Hydroxy-3-carboxy-phenyl	$C_{14}H_{10}N_4O_6S$	150	68	15.40 (15.46)	10	25	16	10	16	14	16
7.	4-Tolyl	$C_{14}H_{12}N_4O_3S$	258	75	17.65 (17.72)	14	24	12	15	20	27	15
8.	1-Naphthyl	$C_{17}H_{12}N_4O_3S$	236	72	15.80 (15.90)	14	17	11	13	15	17	13
9.	2-Naphthyl	$C_{17}H_{12}N_4O_3S$	210	70	15.85 (15.90)	14	13	10	10	16	16	15

S.c = S. citrus, E.c = E. coli, S.a = S. aureus, S.al = S. albus, S.t = S. typhosa, P. = Penicillium, A.n = A. niger.

TABLE 2—ANALYTICAL, PHYSICAL AND ANTIMICROBIAL DATA OF 2-BENZALAMINO-5-(4'-PYRIDYL)-1,3,4-OXADIAZOLE

Sl. no.	R	Mol. formula	M.p. °C	Yield %	% N : Found/ (Calcd.)	Zone of inhibition (mm)*						
						S.c	*E.c*	*S.a*	*S.al*	*S.t*	*P.*	*A.n*
1.	Phenyl	$C_{14}H_{10}N_4O$	265	80	22.20 (22.40)	12	16	19	17	18	13	13
2.	3-Aminophenyl	$C_{14}H_{11}N_5O$	255	82	26.35 (26.41)	10	18	19	10	20	12	13
3.	4-Aminophenyl	$C_{14}H_{11}N_5O$	233	80	26.36 (26.41)	10	16	18	13	18	12	15
4.	2-Chlorophenyl	$C_{14}H_9ClN_4O$	238	84	24.52 (24.60)	10	11	23	13	14	12	15
5.	4-Chlorophenyl	$C_{14}H_9ClN_4O$	235	80	24.50 (24.60)	10	14	15	12	15	11	11
6.	2-Hydroxyphenyl	$C_{14}H_{10}N_4O_2$	213	85	21.00 (21.05)	11	14	26	12	15	11	13
7.	4-Hydroxyphenyl	$C_{14}H_{10}N_4O_2$	278	85	21.02 (21.05)	10	12	19	17	14	11	13
8.	3-Nitrophenyl	$C_{14}H_9N_5O_3$	250	82	23.68 (23.73)	10	10	14	19	12	11	11
9.	4-Nitrophenyl	$C_{14}H_9N_5O_3$	234	78	23.70 (23.73)	10	14	19	12	18	11	13
10.	4-Dimethylaminophenyl	$C_{16}H_{15}N_5O$	210	86	19.05 (19.11)	10	11	19	11	15	12	17
11.	3,4-Dimethoxyphenyl	$C_{16}H_{14}N_4O_3$	225	85	18.02 (18.06)	10	13	19	15	16	14	15
12.	2,4-Dichlorophenyl	$C_{14}H_8Cl_2N_4O$	70	85	17.48 (17.55)	10	16	19	18	18	18	13
13.	3,5-Dichloro-2-hydroxy-phenyl	$C_{14}H_8Cl_2N_4O_2$	80	80	16.65 (16.71)	12	26	22	17	22	34	30

(Table 2 contd.)

14.	2-Hydroxy-3-methoxyphenyl	$C_{16}H_{12}N_4O_3$	126	85	18.83 (18.92)	10	15	22	14	16	14	18
15.	3-Hydroxy-4-methoxyphenyl	$C_{16}H_{12}N_4O_3$	208	82	18.86 (18.92)	10	16	17	22	13	17	17
16.	4-Hydroxy-3-methoxyphenyl	$C_{16}H_{12}N_4O_3$	240	80	18.85 (18.92)	10	15	19	18	16	11	15
17.	4-Methoxyphenyl	$C_{16}H_{12}N_4O_2$	238	82	19.94 (20.00)	15	13	22	17	16	13	14
18.	3,4,5-Trimethoxyphenyl	$C_{17}H_{16}N_4O_4$	262	75	16.40 (16.47)	11	19	18	13	22	19	13
19.	2-Hydroxynaphthyl	$C_{19}H_{12}N_4O_2$	90	86	17.70 (17.72)	10	17	15	18	18	23	11
20.	Cinnamyl	$C_{18}H_{14}N_4O$	228	85	20.25 (20.29)	12	10	17	13	12	13	14
21.	4'-Pyridyl	$C_{14}H_9N_5O$	285	80	27.82 (27.88)	11	16	26	18	18	18	12

*Explanation as in Table 1.

nol (50 ml). Potassium cyanide (1.3 g, 0.02 mol in 10 ml water) was then added to it followed by glacial acetic acid (1.2 g. 0.02 mol). The mixture was stirred mechanically and allowed to stand for 24 h at 25 – 30°. The resulting solid was isolated and crystallised from glacial acetic acid (70%), m.p. 270° (Found : C, 64.90 ; H, 3.94 ; N, 25.22. $C_{16}H_{11}N_5O$ calcd. for : C, 64.95 ; H, 3.97 ; N, 25.26%).

Similarly, other α-cyano-2-benzylamino-5-(4'-pyridyl)-1,3,4-oxadiazoles were prepared (Table 3).

2-α-Carbamylarylmethylamino-5-(4'-pyridyl)-1,3,4-oxadiazoles : 2-(α-Cyanobenzylamino)-5-(4'-pyridyl)-1,3,4-oxadiazole (1.385 g, 0.005 mol) was treated with an excess of concentrated sulphuric acid at 0° and allowed to stand at room temperature for 48 h. The resulting solid was isolated and crystallised from dioxan (70%), m.p. 215° (Found :

TABLE 3—ANALYTICAL, PHYSICAL AND ANTIMICROBIAL DATA OF 2-(α-CYANOBENZYLAMINO)-5-(4'-PYRIDYL)-1,3,4-OXADIAZOLES

Sl. no.	R	Mol. formula	M.p. °C	Yield %	% N : Found/ (Calcd.)	Zone of inhibition (mm)*						
						S.c	*E.c*	*S.a*	*S.al*	*S.t*	*P.*	*A.n*
1.	Phenyl	$C_{16}H_{11}N_5O$	270	70	25.22 (25.27)	10	18	18	17	18	17	18
2.	3-Aminophenyl	$C_{16}H_{12}N_6O$	235	69	28.71 (28.76)	13	18	18	14	19	15	20
3.	4-Aminophenyl	$C_{16}H_{12}N_6O$	330	68	28.70 (28.76)	15	17	19	20	18	16	10
4.	2-Chlorophenyl	$C_{16}H_{10}ClN_5O$	260	73	22.42 (22.47)	13	26	17	16	21	24	20
5.	4-Chlorophenyl	$C_{16}H_{10}ClN_5O$	96	74	22.44 (22.47)	11	22	19	15	22	13	12
6.	2-Hydroxyphenyl	$C_{16}H_{11}N_5O_2$	120	72	23.85 (23.89)	12	24	22	18	22	14	21
7.	4-Hydroxyphenyl	$C_{16}H_{11}N_5O_2$	200	70	23.83 (23.89)	10	17	15	22	20	10	14
8.	3-Nitrophenyl	$C_{16}H_{10}N_6O_3$	200	68	26.02 (26.08)	11	23	21	18	19	11	10
9.	4-Nitrophenyl	$C_{16}H_{10}N_6O_3$	90	71	26.03 (26.08)	11	21	23	15	16	24	11
10.	4-Dimethylaminophenyl	$C_{17}H_{16}N_6O$	62	75	26.15 (26.25)	15	19	18	15	18	14	17
11.	3,4-Dimethoxyphenyl	$C_{17}H_{15}N_5O_3$	240	73	20.67 (20.77)	12	20	17	20	19	24	19
12.	2,4-Dichlorophenyl	$C_{16}H_9Cl_2N_5O$	55	69	20.14 (20.23)	11	26	18	14	22	18	18
13.	3,5-Dichloro-2-hydroxyphenyl	$C_{16}H_9Cl_2N_5O_2$	128	68	19.25 (19.33)	13	24	24	16	23	20	13
14.	2-Hydroxy-3-methoxyphenyl	$C_{16}H_{10}N_5O_2$	118	73	22.68 (22.72)	10	23	16	16	21	21	11
15.	3-Hydroxy-4-methoxyphenyl	$C_{16}H_{10}N_5O_2$	265	71	22.70 (22.72)	10	24	19	17	25	19	18
16.	4-Hydroxy-3-methoxyphenyl	$C_{16}H_{10}N_5O_2$	222	67	22.65 (22.72)	16	25	16	18	21	23	13
17.	4-Methoxyphenyl	$C_{16}H_{12}N_5O_2$	200	72	22.70 (22.80)	10	16	18	13	16	14	13

(Table 3 contd.)

18.	3,4,5,-Trimethoxyphenyl	$C_{19}H_{17}N_5O_4$	—	73	19.02 (19.07)	11	20	16	14	20	14	11
19.	2-Hydroxynaphthyl	$C_{19}H_{13}N_5O_2$	116	75	20.32 (20.40)	11	26	14	13	24	17	17
20.	Cinnamyl	$C_{17}H_{13}N_5O$	240	70	23.20 (23.25)	10	20	20	15	18	23	11
21.	4'-Pyridyl	$C_{14}H_{10}N_6O$	300	69	30.14 (30.21)	10	17	17	14	16	16	16

*Explanation same as in Table 1.

TABLE 4—ANALYTICAL, PHYSICAL AND ANTIMICROBIAL DATA OF 2-α-CARBAMYLARYLMETHYLAMINO-5-(4'-PYRIDYL)-1,3,4-OXADIAZOLES

Sl. no.	R	Mol. formula	M.p. °C	Yield %	% N : Found/ (Calcd.)	Zone of inhibition (mm)*						
						S.c	*E.c*	*S.a*	*S.al*	*S.t*	*P.*	*A.n*
1.	Phenyl	$C_{15}H_{13}N_5O_2$	215	70	23.69 (23.72)	20	22	14	16	20	10	15
2.	3-Aminophenyl	$C_{15}H_{14}N_6O_2$	350	65	27.00 (27.09)	12	28	16	17	13	14	14
3.	4-Aminophenyl	$C_{14}H_{14}N_6O_2$	350	65	27.08 (27.09)	12	28	16	11	19	16	17
4.	2-Chlorophenyl	$C_{15}H_{12}ClN_5O_2$	135	68	21.18 (21.24)	19	27	18	13	19	15	22
5.	4-Chlorophenyl	$C_{15}H_{12}ClN_5O_2$	160	73	21.20 (21.24)	19	26	17	16	20	11	16
6.	2-Hydroxyphenyl	$C_{15}H_{13}N_5O_2$	275	59	22.42 (22.50)	14	26	18	14	22	12	16
7.	4-Hydroxyphenyl	$C_{15}H_{13}N_5O_2$	340	72	22.40 (22.50)	16	18	16	14	18	11	16
8.	3-Nitrophenyl	$C_{15}H_{12}N_6O_4$	126	69	24.62 (24.70)	17	20	17	12	16	15	18
9.	4-Nitrophenyl	$C_{15}H_{12}N_6O_4$	218	72	24.60 (24.70)	15	23	18	15	21	15	17
10.	4-Dimethylaminophenyl	$C_{17}H_{18}N_6O_2$	234	66	24.76 (24.85)	19	30	12	13	14	14	14
11.	3,4-Dimethoxyphenyl	$C_{17}H_{17}N_5O_4$	240	70	19.65 (19.71)	16	22	22	13	18	15	18
12.	2,4-Dichlorophenyl	$C_{15}H_{11}Cl_2N_5O_2$	210	71	19.15 (19.23)	15	29	21	10	24	18	14
13.	3,5-Dichloro-2-hydroxyphenyl	$C_{15}H_{11}Cl_2N_5O_3$	120	71	18.35 (18.42)	16	26	20	16	24	32	15
14.	2-Hydroxy-3-methoxyphenyl	$C_{16}H_{15}N_5O_4$	280	65	20.45 (20.52)	15	28	17	14	19	15	14
15.	3-Hydroxy-4-methoxyphenyl	$C_{16}H_{15}N_5O_4$	250	74	20.42 (20.52)	14	30	18	10	26	18	18
16.	4-Hydroxy-3-methoxyphenyl	$C_{16}H_{15}N_5O_4$	257	73	20.45 (20.52)	19	24	18	17	20	14	19
17.	4-Methoxyphenyl	$C_{16}H_{15}N_5O_3$	250	65	21.45 (21.53)	17	28	19	12	19	15	21
18.	3,4,5-Trimethoxyphenyl	$C_{18}H_{19}N_5O_5$	150	70	18.12 (18.18)	16	23	18	11	22	16	20
19.	2-Hydroxynaphthyl	$C_{19}H_{15}N_5O_2$	330	68	19.30 (19.39)	12	27	20	14	20	16	13
20.	Cinnamyl	$C_{17}H_{15}N_5O_2$	265	70	21.75 (21.80)	17	24	10	15	18	20	17
21.	4'-Pyridyl	$C_{14}H_{13}N_6O_2$	300	65	28.32 (28.37)	10	15	20	14	16	15	20

*Explanation same as in Table 1.

C, 60.95 ; H, 4.35 ; N, 23.69. $C_{15}H_{13}N_5O_2$ calcd. for : C, 61.01 ; H, 4.40 ; N, 23.72%).

Similarly, other compounds were prepared (Table 4).

Antimicrobial activity : The purified products were screened for antimicrobial activity by cup-plate method[8]. The testing was carried out at a concentration of 100 μg using DMF as a solvent for a time period of 24 h. The compounds were tested against gram-positive (*S. citrus, S. aureus* and *S. albus*) and gram-negative (*E. coli* and *S. typhosa*) bacteria. The antifungal testing was carried out with *Penicillium* and *A. niger*. The antimicrobial activity of the compounds was compared with chloromycetin at a same concentration level.

From the experimental data, it was observed that most of the compounds showed good activity against different strains of bacteria and fungi.

The comparable activity was observed in compounds of the type **1/2** when R=4-tolyl, 4-hydroxy-3-carboxyphenyl against *E. coli* and *S. typhosa*/4-methoxyphenyl, 2- and 4-chlorophenyl, 2- and 3-aminophenyl, 2-hydroxyphenyl, 2,4-dichlorophenyl, 3,5-dichloro-2-hydroxyphenyl against *E. coli* and *S. typhosa*. The comparable antifungal activity was observed in compounds **1/2** when R=phenyl, 4-acetamidophenyl, 4-tolyl against *Penicillium* and *A. niger*/4-hydroxyphenyl, 2-chlorophenyl, 3,4,5-trimethoxyphenyl and 4'-pyridyl against *A. niger*.

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