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SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF 2-ARYL-3-[5'-ARYL-1', 3', 4'-THIADIAZOL-2[1]-YL)-5-OXAZOLIDINONE AND 2-ARYL-3-[5'-ARYL-1', 3', 4'-OXADIAZOL-2'-YL)-5-OXAZOLIDINONES

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ABSTRACT

The 2-amino-5-aryl-1,3,4 thiadiazoles 1 have been prepared by dehydrative cyclisation of appropriate 1-aryl-3-thiosemicarbazide with conc H_2 SO_4 in cold. 2-Amino-5-aryl-1, 3, 4-oxadiazoles 2 have been prepared by oxidative cyclisation of appropriate aldehyde thiosemicarbazones with bromine in anh sodium acetate and glacial acetic acid. These 2-amino-1, 3, 4-oxa (thià) diazoles were condensed with aromatic aldehydes in methanol to furnish the corresponding Schiffs bases 3 & 4. Schiff's bases of 5-aryl-2-amino-1, 3, 4-oxa (thia) diazoles react with chloroacetyl chloride and water in molar ratio in dioxane to furnish the title compounds 5-oxazolidinones 5 & 6 (Scheme 1, Table 1). The representative samples of the title compounds were assayed against *E. coli* and *A. niger* at 50 µg / m L concentration and have been found to exhibit significant antibacterial and antifungal activities.

KEYWORDS: 5-Aryl-2-Amino-1, 3, 4-Oxadiazole, 5-Aryl-2-Amino-1, 3, 4-Thiadiazole, 5-Oxazolidinone, Bactericidal and Fungicidal Activities

Thiadiazole nucleus is associated with diverse biological activities like fungicidal, insecticidal (Zheng *et al*. 2003, Cao *et al*. 2002, Shi *et a*l. 2000), anticancer (Rzeski *et al*. 2007), antitubercular (Kolavi *et al*. 2006), analgesic and many others (KucuKguzed *et al*. 2006, Burkholder *et al*. 2000, Khennum *et al*. 2005, Demirbas *et al*. 2004, Castro *et al*. 2006) and oxadiazole nucleus is also exhibit biocidal properties (Ismail 2002, Bravo *et al*. 1999, Weidner *et al*. 2002, Das *et al*. 2006, Rensio *et al*. 2006, Lohray *et al*. 2004, Weidner *et al*. 2002, Philips *et al*. 2005, Janin & Bioorg *et al*. 2007). Likewise oxazolidino nucleus is well known for its medicinal use and patented as agrochemicals. In view of these facts, it is worthwhile to unite these two biolabile nuclei together to see the additive effect in biocidal properties. With this objective in mind, we synthesized the title compounds 5 & 6. We considered it worthwhile to continue our investigation on some oxazolidinones incorporating various substituted thiadiazole / oxadiazole moieties.

The required 2-amino-5-aryl-1,3, 4-thiadiazoles 1 have been prepared by dehydrative cyclisation of appropriate 1-aryl-3-thiosemicarbazides with con H_2SO_4, in cold and 2-amino-5-aryl- 1, 3, 4-oxadiazoles 1 have been prepared by oxidative cyclisation of appropriate aldehyde thiosemicarbzones with bromine in anh. Sodium acetate and glacial acetic acid. These 2-amino-1, 3, 4-oxa (thia) diazoles were condensed with aromatic aldehydes in methanol to furnish their corresponding schiff's bases 3 & 4. These schiff's bases, water and chloroacertylchloride react together in molar ratio in dioxane to give title compounds 5-oxazolidinones (Heggelund *et al*. 2007) 5 & 6 (Scheme 1 and Table l).

ANTIMICROBIAL ACTIVITY

Some of the synthesised compounds 5 a-f and 6 a-f are assayed for their antibacterial activity against *E. coli* and antifungal activity against. *A. niger* using DMF as a solvent at 50 µg / mL concentration by filter paper disc method (Bauer *et al*. 1966). After 24 hours of incubation at 37°C, the zone of inhibition were measured in mm. Known antibiotics norfloxacin and griseofulvin are used for comparison at same concentration. Antimicrobial activities are recorded in Table 2.

EXPERIMENTAL SECTION

Melting points are taken in open capillaries and are uncorrected. IR spectra ($y\frac{cm}{max}$) were recorded on PE 781 IR spectrophotometer using KBr disc. 'H NMR spectra max in DMSO - d6 on a varian EM 390 - CW Spectrometer at 90 MHz using TMS as internal reference (chemical shift in δ ppm.) The purity of the compounds were checked by the TLC.

2-(4-Chlorophenyl)-3-[5[1]-phenyl-1[1], 3[1], 4[1]- thiadiazol-2[1]-yl)--5- oxa zolidinone-5a.

A solution of chloroacetyl chloride 1.2ml (0.012M) in dioxane (5ml) was added dropwise to a well strirred solution of 2-(4-chloro benzylidene) amino-5 phenyl -1, 3, 4 -thiadiazole 3.0 gm (0.01M) and 0.2 ml water in dioxane (50ml) at room temperature. The solution was stirred for an hour then refluxed for another hour. The excess of dioxane was removed and the residue was poured into water. The resulting solid mass was filtered, washed with water and purified by washing with ethanol and recrystallised in dioxane (5a), m.p. 184 ° C, yield 86.7% , IR (KBr cm[31]) 3010 (C-H aromatic), 2860(C-H aliphatic) 1730 (C=O), 1590 (C=N), 1240,

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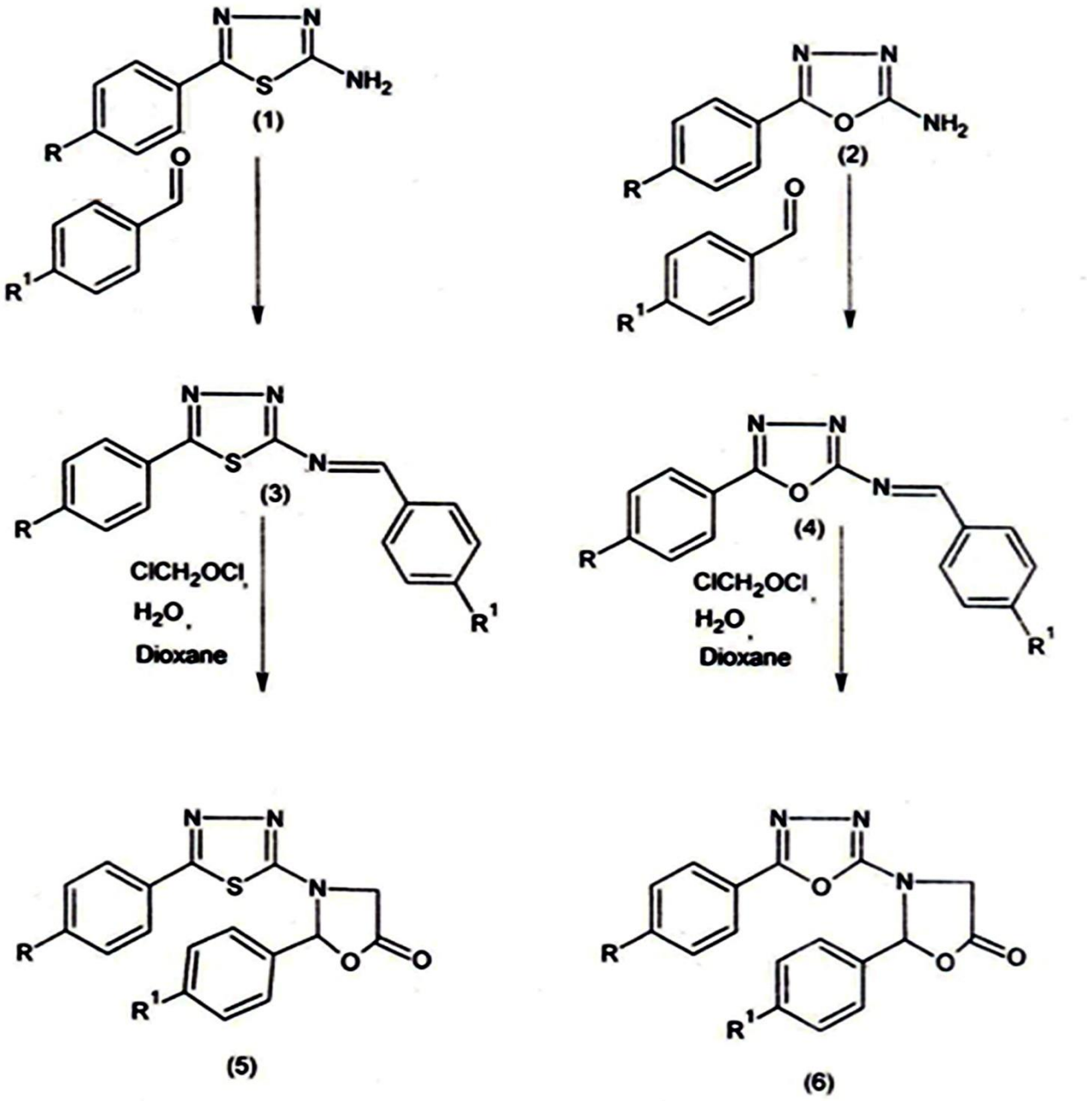
1010, (C-O-C),' H NMR (DMSO-d6) 3.6 (s, 2H, CH2), 4.8 (s. 1H, CH), 7.8-8.5 (m. 9H, Ar H)

The compounds 5b - f were prepared from 3b - f using similar procedure.

3- [5[1]- (4 - Chlorophenyl) -1[1], 3 ', 4[1] - oxadiazol - 2[1] - yl] -2- (4-methoxy phenyl) oxazolidinone 6a.

A solution of chloroacetyl chloride 1.2 ml (0.01M) in dioxane (5ml) was added dropwise to a well stirred solution of 2-(4-methoxy benzylidene) amino - 5 (4-chlorophenyl) -1, 3, 4 oxadiazole, 3.1 gm (0.01M) and water 0.2 ml (0.01M) in dioxane (50ml) at room temperature. The solution was stirred for an hour, then refluxed for another hour. The excess of dioxane was evaporated and the residue was poured into water. The resulting solid mass was filtered, washed with water and dried. The compound was purified with ethanol and recrystallised in dioxane (6a). m.p. 220°C , yield 64.6 % IR (KBr cm-[1]) : 3010 (C-H aromatic), 2865 (C-H aliphatic), 1720 (C=O), 1585 (C = N), 1255, 1020 (C - O - C), 1H NMR (DMSO - d6) 3.7 (s, 2H, CH_2), 4.0 (s, 3H, OCH_2), 4.6 (s, H, CH) 7.2-8.2 (m, 8H, ArH).

The compounds 6b - f were prepared from 4b - f using similar procedure (Table l).



Scheme 1

Table 1: Physical Data of compounds 5 and 6

Comp.	R	R_1	m.p.(^{0}C)	Yield (%)	Mol formula	Found (Calc.) %		
						C	H	N
5a	H	4-Cl	184	86.7	$C_{17}H_{12}N_3O_2SCl$	57.00 (57.05)	3.40 (3.36)	11.80 (11.75)
5b	3,4-Cl_2	4-Cl	165	93.5	$C_{17}H_{10}N_3O_2SCl_3$	47.72 (47.83)	2.23 (2.34)	9.96 (9.85)
5c	4-NO_2	4-Cl	197-9	79.5	$C_{17}H_{11}N_4O_4SCl$	50.60 (50.68)	2.80 (2.93)	13.98 (13.91)
5d	2,4-Cl_2	4-OCH_3	163-4	90.4	$C_{18}H_{13}N_3O_3SCl_2$	51.12 (51.18)	3.00 (3.08)	10.03 (9.95)
5e	4-OCH_3	4-OCH_3	167	52.2	$C_{19}H_{17}N_3O_4S$	59.46 (59.53)	4.37 (4.43)	11.16 (10.97)
5f	4-OCH_3	4-Cl	175	59.3	$C_{18}H_{14}N_3O_3SCl$	55.67 (55.74)	3.56 (3.61)	10.92 (10.84)
5g	2-Cl	4-OCH_3	153-5	67.1	$C_{18}H_{14}N_3O_3SCl$	55.65 (55.24)	3.53 (3.61)	10.97 (10.84)
6a	4-Cl	4-OCH_3	220	64.6	$C_{18}H_{14}N_3O_4Cl$	58.05 (58.14)	3.69 (3.77)	11.43 (11.31)
6b	4-OCH_3	4-Cl	218	70	$C_{18}H_{14}N_3O_4Cl$	58.00 (58.14)	3.65 (3.77)	11.46 (11.31)
6c	4-Cl	3,4-$(OCH_3)_2$	198-9	79.7	$C_{19}H_{16}N_3O_5Cl$	56.70 (56.79)	3.91 (3.99)	10.58 (10.46)
6d	4-OCH_3	2-Cl	190-1	75.3	$C_{18}H_{14}N_3O_4Cl$	58.03 (58.14)	3.69 (3.77)	11.40 (11.31)
6e	2-Cl	3,4-$(OCH_3)_2$	165	74.7	$C_{19}H_{16}N_3O_5Cl$	56.70 (56.79)	3.91 (3.99)	10.60 (10.46)
6f	4-OCH_3	3,4-$(OCH_3)_2$	231	75.5	$C_{20}H_{19}N_3O_6$	60.35 (60.45)	4.70 (4.79)	10.68 (10.58)

Table 2: Antibacterial and Antifungal activities of the compounds 5a-f and 6a-f

Compd.	Zone of Inhibition after 24 hours	
	E. coli	***A.niger***
5a	+	4
5b	+++	6
5c	++	5
5d	++	4
5e	+	3
5f	+	3
6a	+	4
6b	++	5
6c	+	5
6d	++	5
6e	++	4
6f	++	4
	Norfloxacin	+++
	Griseofulvin	+++

(-) = Inactive, (+) = weakly active (12-16mm)

(++) = Moderately active (17-21mm) and

(+++) = Highly active (22-30mm)

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