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Synthesis and Biocidal Activity of Some 5-Thioxo-1,3,4-Oxadiazolo-[3,2–a]-*s*-Triazine-7-Ones.

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N′-(5-Aryl-1,3,4-oxadiazol-2-yl)-N^3-(4-chlorophenyl) ureas on cyclo-condensation with carbon disulphide gave 2-aryl-6-(4-chlorophenyl)-5-thioxo-1,3,4-oxadiazolo-[3,2–a]-s-triazine-7-ones. These compounds were evaluated for antibacterial and antifungal activity.

INTRODUCTION

A wide variety of substituted oxadiazoles[1,2] have been reported to possess promising antibacterial activity, while some *s*-substituted triazines exhibit a variety of pharmacological activities. In view of these observations it was considered of great interest to synthesize some fused ring compounds like 5-thioxo-1,3,4-oxadiazolo-[3,2–a]-*s*-triazine. In this paper we are reporting the synthesis of some tri-substituted aryl derivatives of 5-thioxo-1,3,4-oxadiazolo-[3,2-a]-s-triazine-7-ones and their biological activity. 2-(2′,4′-Dialkoxy-5′-alkylphenyl)-6-(4-chlorophenyl)-5-thioxo-1,3,4-oxadiazolo [3,2-a]-s-triazine-7-ones were synthesized by the condensation of corresponding ureas (IV) with carbon disulphide. The required ureas were prepared by 2-amino-5-aryl-1, 3, 4-oxadiazole (II) with ethyl chloroformate followed by treatment with 4-chloro aniline. 2-Amino-5-aryl-1,3,4-oxadiazoles (II) were prepared by oxidative cyclization of the substituted aryl aldehyde semicarbazones (I) by the method of Gibson[6]. The structures of the compounds were established on the basis of analytical and spectral data (IR and ^{1}H NMR).

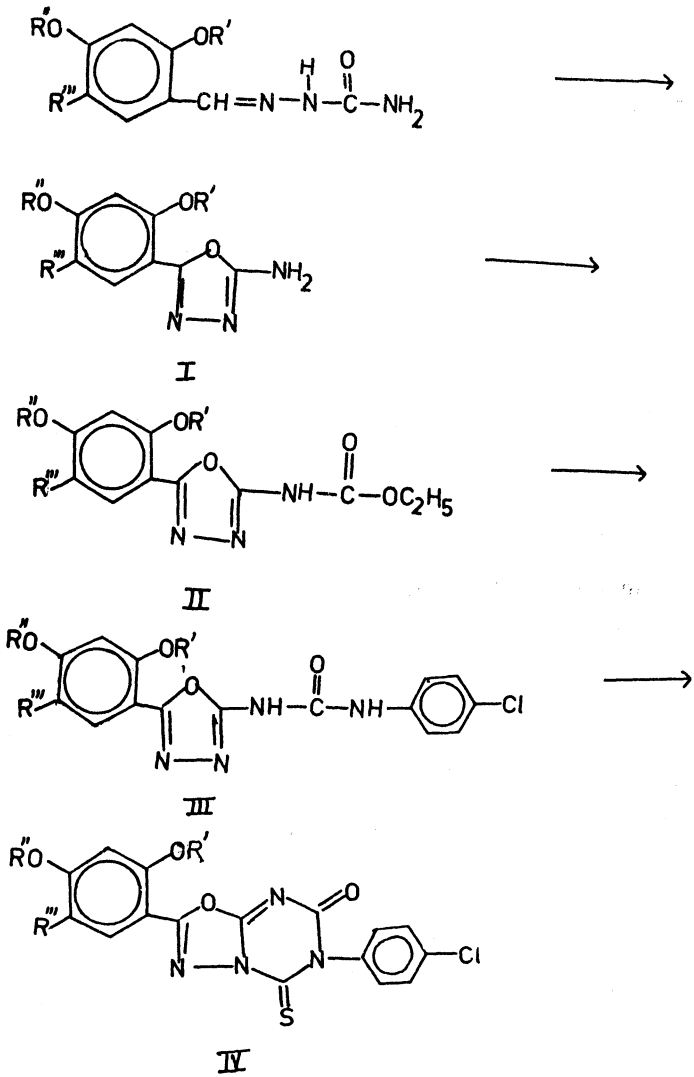
EXPERIMENTAL

2,4-Dialkoxy-5-alkylbenzaldehyde were converted into corresponding semicarbazones which were cyclized by oxidative cyclization with bromine in glacial acetic acid in presence of anhydrous sodium acetate gave 2-amino-5-aryl-1,3,4-oxadiazoles.

Ethyl N-[5-(2′,4′-dialkoxy-5′-alkylphenyl)-1,3,4-oxadiazole-2-yl] carbamate (II)

2-Amino-5-(2′,4′-dialkoxy-5′-alkylphenyl)-1,3,4-oxadiazole (0.04 mol) in pyridine (160 ml) were added to ethyl chloroformate (0.044 mol) and

triethylamine (10 ml) and the mixture was refluxed for 1–2 hrs, poured into dil. HCl (50%) and the carbamates thus formed were recrystallized from ethanol.



N′-[5-(2′,4′-dialkoxy-5′-alkylphenyl)-1,3,4-oxadiazole-2-yl]-N^3-(4-chlorophenyl) urea (III)

An equimolar mixture of II and 4-chloroaniline in ethanol was refluxed for 20–22 hrs; after the removal of ethanol, the residue was washed with water and recrystallized from ethanol. The IR spectra were recorded in KBr and exhibited

the following peaks: ν_{max}^{KBr} cm^{-1}: 3500–3400 (N–H stretching vibration), 1660–1700 (>C=O stretching vibration), 1655–1630 (N–H bending vibration), 1630–1580 (>C=N stretching vibration), 1280–1210 (–C–O–C– asymmetrical stretching vibration), 1075–1030 (–C–O–C– symmetrical stretching vibration), 800–600 (C–Cl stretching vibration).

2-(2',4'-dialkoxy-5'-alkylphenyl)-6-(4-chlorophenyl)-5-thioxo-1, 3, 4-oxadiazolo [3, 2–a]-s-triazie-7-one (IV):

A mixture of III (0.01 mol), ethanol (40 ml) and carbon disulphide (1.52 g, 0.02 mol) was refluxed for 6–7 hrs, concentrated to a small volume, poured into ice-cold water, acidified with dil. HCl and the precipitated product IV was obtained. It was recrystallized from ethanol. The IR spectra were recorded in KBr and exhibited the following peaks: ν_{max}^{KBr} cm^{-1}; 1600 (>C=O stretching vibration), 1280–1060 (–C–O–C– asymmetrical stretching vibration), 800–600 (C–Cl stretching vibration). Their ^1H NMR spectra were recorded in $CDCl_3$ which showed the following signals: δ 0.8–1.2 (t, $-CH_2-CH_3$), 1.2–6.65 (t, $-OCH_2-CH_3$ and m, saturated $-CH-CH_2-$ gps), 2.2–2.73 (t or q, Ar–CH_2–), 3.64–3.73 (s, $-OCH_3$), 4.05–4.10 (q, $-OCH_2-CH_3$), 7.0–7.8 (m, 6H, Ar–*H*). The melting points and elemental data of these compounds are reported in Table 1.

Antibacterial and antifungal screening

The bactericidal and fungicidal activities were evaluated against *Candida albicans, Aspergillus niger, Staphylococcus aureus, Escherichicia coli, Sarcina lutea* and *Salmonella typhi.* All the compounds were dissolved in DMF in 1 mg/ml concentration. Nutrient agar petri plates were used for bacterial microorganisms and Sabround's agar for fungal micro-organisms. These plates ware flooded with overnight grown micro-organisms and filter paper discs soaked in the compound solution were placed in the respective plates. The activities of these compounds were recorded by measuring the zone of inhibition around every disc. The standard drug gramoneg was used which shows 30 mm of inhibition. the results are reported in Table 1.

The above mentioned compounds have no significant activity against antifungal activity. But these compounds are active against antibacterial activity and hence need further investigation.

ACKNOWLEDGEMENT

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TABLE 1

Comp. No.	R′	R″	R‴	Mol. formula	m. pt. (°C)	Elemental Analysis % Found (required)			Biological activity		
						C	H	N	*S. lutea*	*S. typhe*	*S. aureus*
IVa	CH_3	CH_3	C_2H_5	$C_{20}H_{17}N_4O_4SCl$	181–182	53.96 (53.99)	3.86 (3.82)	12.60 (12.59)	15 mm	N.A.	17 mm
IVb	C_2H_5	C_2H_5	C_2H_5	$C_{22}H_{21}N_4O_4SCl$	190–191	55.89 (55.87)	4.46 (4.44)	11.87 (11.85)	15 mm	14 mm	16 mm
IVc	CH_3	C_2H_5	C_2H_5	$C_{21}H_{19}N_4O_4SCl$	175–177	54.92 (54.96)	4.16 (4.14)	12.19 (12.21)	14 mm	N.A.	17 mm
IVd	C_2H_5	CH_3	C_2H_5	$C_{21}H_{19}N_4O_4SCl$	186–188	54.94 (54.96)	4.16 (4.14)	12.19 (12.21)	N.A.	N.A.	N.A.
IVe	CH_3	CH_3	C_3H_7	$C_{21}H_{19}N_4O_4SCl$	175–176	54.93 (56.96)	4.18 (4.14)	12.23 (12.19)	15 mm	17 mm	18 mm
IVf	C_2H_5	C_2H_5	C_3H_7	$C_{23}H_{23}N_4O_4SCl$	194–196	56.75 (56.73)	4.74 (4.72)	11.53 (11.51)	14 mm	17 mm	17 mm
IVg	CH_3	C_2H_5	C_3H_7	$C_{22}H_{21}N_4O_4SCl$	183–184	55.88 (55.89)	4.42 (4.44)	11.87 (11.85)	16 mm	N.A.	14 mm
IVh	C_2H_5	CH_3	C_3H_7	$C_{22}H_{21}N_4O_4SCl$	171–172	55.85 (55.89)	4.40 (4.44)	11.84 (11.85)	17 mm	16 mm	N.A.
IVi	CH_3	CH_3	C_4H_9	$C_{22}H_{21}N_4O_4SCl$	197–198	55.86 (55.89)	4.40 (4.44)	11.84 (11.85)	15 mm	16 mm	16 mm
IVj	C_2H_5	C_2H_5	C_4H_9	$C_{24}H_{25}N_4O_4SCl$	188–190	57.56 (57.54)	4.96 (4.99)	11.20 (11.18)	17 mm	18 mm	15 mm
IVk	CH_3	C_2H_5	C_4H_9	$C_{23}H_{23}N_4O_4SCl$	178–179	56.75 (56.73)	4.74 (4.72)	11.52 (11.51)	17 mm	N.A.	N.A.
IVl	C_2H_5	CH_3	C_4H_9	$C_{23}H_{23}N_4O_4SCl$	168–170	56.77 (56.73)	4.75 (4.72)	11.52 (11.51)	N.A.	16 mm	N.A.

N.A.—Not active

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