SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME 3,6,8-TRIARYL-1,2,4-TRIAZOLO [3,4-b][1,3,4]OXADIAZEPINES

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ABSTRACT

A number of 3,6,8-triaryl-1,2,4-triazolo [3,4-b][1,3,4]oxadiazepines **2** have been synthesized by cyclocondensation of 4-amino-5-aryl-3-mercapto-1,2,4-triazoles **1** with diaroylmethane (scheme1).Their antimicrobial activity has been screened against E.coli, B. subtilis and S.aureus.

KEY WORDS: 4-amino-5-mercapto-1,2,4-triazole, substituted-1,2,4-triazolo[3,4-b] [1,3,4] oxadiazepines, bactericidal activity.

1. INTRODUCTION

Triazole nucleus is well documented for their diverse biological activities like fungicial [1,2], bactericidal [3,4], herbicidal [2], anticancer [5] and others [6]. Oxadiazepine nucleus is also known for their diverse biological activities like bactericidal [7]. In view of these facts, it is worthwhile to unite these two biolabile nuclei together to see the additive effect in their biocidal properties. With this objective , we synthesized the title compounds **2a-f.**

The required 4- amino- 3-mercapto-1,2,4-triazoles **1** were prepared essentially by the condensation of mercapto oxadiazoles [7] with hydrazine hydrate. The required mercapto oxadiazoles were prepared by cyclisation of 3-acyldithiocarbozate ester. Cyclocondensation of **1** with diaroylmethane in alcoholic KOH furnished the title compounds **2a-f,** scheme 1. The structural assignments of the synthesized compounds were based on elemental analyses, IR, ^{1}HNMR and mass spectral data.

ANTIMICROBIAL ACTIVITY

The bactericidal activity of the synthesized compounds **2a-f** have been assayed against gram positive and gram negative bacteria *E. coli*, *B. subtilis* and *S. aureus* by using cup plate agar diffusion method [8]. Bacteria were cultured in nutrient agar medium which was prepared by dissolving peptone 5.0 g, beef extract 3.0 g ,sodium chloride 3.0 g, bacto agar 20 g in 1000 mL distilled water at 80^0 C and pH of the medium was adjusted to 7.2-7.3 before sterilizing the medium at 1.5 kg cm^{-1} for 20 minutes.The solution of the synthesized compounds were made in DMSO at 100 µg/mL concentration and Whatmann filter paper no.1 discs (5 mm in diameter) were used. Filter paper discs containing the synthesized compounds were placed at 37^0 C for 24 hours. The bacteria were precultured overnight in nutrient broth at 37±1 ^{0}C for 24 hours.After incubation period, the zone of inhibitions were measured in mm. Known antibiotics like

norfloxacin and ciprofloxacin were used for comparison at same concentration. The results are recorded in table 2.

EXPERIMENTAL SECTIONS

Melting points were taken in open capillaries and are uncorrected IR spectra *v* max in cm^{-1} were recorded, on PE 781 spectrophotometer using KBr disc and ^{1}HNMR spectra, in DMSO-d6 on a varion EM 390 CW spectrophotometer at 90 MHz using TMS as internal reference (chemical shift in δ ppm). The purity of the compounds were checked by TLC.

3,6,8-Triphenyl-1,2,4-triazolo[3,4,-b][1,3,4]oxadiazipines 2a

A mixture of 4-amino-3-mercapto-5-phenyl-1,2,4-triazole 1.9 g (0.01M), dibenzoyl methane 2.24 g (0.01 M), and KOH 0.6 g (0.012 M) in methanol was refluxed for 6 hrs.During refluxing H_2S gas was evolved. When evolution of H_2S gas seized (which is confirmed by lead acetate moistened filter paper test), the reaction solution was filtered and poured into cold water.The desired compound was precipitated out, which was filtred, washed with water, dried and recrystallized from aq. Ethanol M.P. 155^0 C, yield 60 %; IR (KBr) ν in cm^{-1} 3010 (C-H, Aromatic), 1620 (C=N, endo). ^{1}H NMR; δ 6.9-7.7 (m, 16H, ArH and –CH=C<), MS m/z 364. The other compounds were also prepared similarly and are recorded in Table-1.

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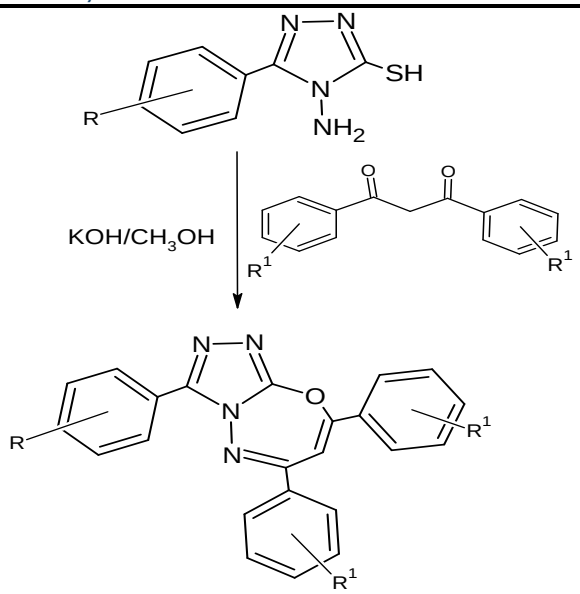

SCHEME I

Table-1: Physical Data of Compounds **2a-f.**

Comp.	R	R'	M.P.	yield (%)	Molecular Formula	Analysis % found (calcd.) C	H	N
2a	H	H	155	60	$C_{23}H_{16}N_4O$	75.95 (75.82)	4.51 (4.40)	15.28 (15.38)
2b	H	4-CH_3	177	55	$C_{25}H_{20}N_4O$	76.43 (76.53)	15.18 (15.10)	14.20 (14.28)
2c	4- Cl	H	185	57	$C_{23}H_{15}N_4OCl$	69.38 (69.26)	3.85 (3.76)	14.28 (14.20)
2d	4-Cl	4-CH_3	170	60	$C_{25}H_{19}N_4OCl$	70.44 (70.34)	4.54 (4.45)	13.02 (13.13)
2e	4-OCH_3	H	167	62	$C_{24}H_{18}N_4O_2$	73.22 (73.10)	4.72 (4.57)	14.24 (14.31)
2f	4-OCH_3	4-CH_3	182	65	$C_{26}H_{22}N_4O_2$	74.02 (73.93)	5.18 (5.21)	13.15 (13.27)

Table-2 Bactericidal Activity of compounds **2a-f**

Compound No.	*E. coli*	*B. subtilis*	*S. aureus*
2a	19	18	17
2b	19	19	18
2c	21	22	22
2d	21	20	15
2e	21	18	16
2f	20	18	18
Norfloxacin	28	27	27
Ciprofloxacin	27	26	25