SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME 2,5-DISUBSTITUTED 1,3,4-OXADIAZOLES

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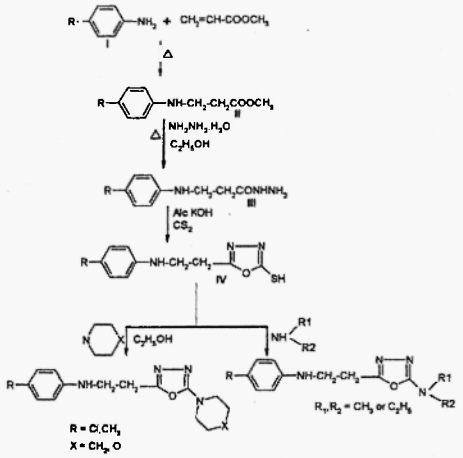
Abstract: 4-Chloro aniline is condensed with methyl acrylate in presence of acetic acid to yield methyl-β-(4-chloro methyl aniline)-propionate, which was futher treated with hydrazine hydrate in presence of ethanol to obtain β -alanine-N-(4-chloro methyl-phenyl) hydrazide, on cyclization with ethanolic potassium hydroxide and carbon disulphide gives 2-mercapto-5-(4-chloro methyl-anilino ethyl)-1,3,4-oxadiazole (1-4). These oxadiazoles on refluxing with Morpholine / Piperidine / Dimethylamine / Diethylamine gave 2,5-disubstituted derivatives. Antimicrobial activity of these compounds was studied (5).

Key words: Oxadiazole , Propionate

Introduction

Substituted 1,3,4-oxadiazoles are of considerable pharmaceutical and therapeutic interest (6), which is documented by steadily increasing number of publications and patents. For these reasons the chemistry of 1,3,4,-Oxadizoles has been the subject to many investigators (7).

During the present investigation 4-chloro aniline is condensed with methyl acrylate in presence of acetic acid to get methyl-β-(4-chloro/ methyl aniline)-propionate (**II**), Treatment of II with hydrazine hydrate in presence of ethanol gave β-alanine-N-(4-chloro / methyl-phenyl) hydrazide (**III**) which on cyclization with ethanolic potassium hydroxide and carbon disulphide gives 2-mercapto-5-(4-chloro/ methyl-anilino ethyl)-1,3,4-oxadiazole(**IV**).The compound IV treated with Morpholine / Piperidine / Dimethylamine / Diethylamine gave title compounds (Scheme-1). The structure of all the new compounds were established by spectral and analytical data.



Scheme-1

Materials and Methods

All the chemicals required for the present study were obtained from SD Fine Chemicals, Mumbai.

Melting points were determined by open capillary tube method and are uncorrected. TLC was run on silica gel-G plates using benzene: acetone (8:2) as irritants; the spots were located by exposure to iodine vapors as visualizing agent. The NMR of the compounds were recorded on Bruker VXRO-300 (300 MHz) spectrometer with TMS as internal standard (chemical shifts in δ ppm) and IR spectra were recorded on Bomem Michelson spectrophotometer by using KBr pellet technique spectral data were in accord with assigned structure.

Synthesis of A_1-A_8

2-Mercapto-5-(4-chloro/methyl-anilinoethyl)-1,3,4-oxadiazoles (IV) was refluxed with equimolar quantities of various substituted aromatic secondary amines (morpholine/piperidine/diethylamino/ dimethylamino) in presence of alcohol for 8 hrs. Then ethanol was removed under reduced pressure and kept over night. The solution was poured onto the crushed ice with stirring neutralized with dilute acetic acid. The separated white solid was filtered, washed with cold water, dried and recrystalized from ethanol. (A_1-A_8) Physical data of synthesis compound is included in table-1.

Spectral Data

The compound A_2 exhibits characteristic IR bands in the region 3350-3150(NH); 3120-2850(Aryl/Alkyl); 1240-1300(C-O) and 1450-1490(C-N) cm^{-1} respectively.

The NMR Spectrum shows a singlet at 1.6 δ (6H, 2-CH_2); 0-2.2 (3H, 1-CH_3); triplet 2.5 (2H 1-CH_2); and 3.5 (2H, 1-CH_2); singlet 3.8 δ (4H, 2-CH_2); doublet 6.5-7.0(4H, Aryl).

Biological Activity

Synthesised Compounds were tested for antibacterial activity (Chloramphenicol and ampicillin as Standard) by following cup plate diffusion method against *staphylococcus aureus* (Gram +ve) and *Escherichia coli* (Gram –ve) bacteria.

Compounds showed considerable activity against all species tested at 100 µgm /disc and 200 µgm/disc, the chloro substituted compounds showed promising activity remaining compound showed mild to moderate activity. The compounds A_2 have prominent antimicrobial activity against E.coli and S.aureus (Table-2).

Table-1: Physical data of synthesis compounds

Compound	R	R_1	m. p. ^{0}C	Yield %
A_1	$-CH_3$		165 – 168	45
A_2	$-CH_3$		151 – 153	55
A_3	$-CH_3$		105 – 107	52
A_4	$-CH_3$		94 – 97	46
A_5	-Cl		170 – 172	60
A_6	-Cl		160 – 162	51
A_7	-Cl		102 – 104	49
A_8	-Cl		95 - 97	52

All Compounds gave correct elemental data.

Table-2: Antibacterial screening results of compound A_1 to A_8
Inhibition zone (in mm)

Compound	*S. aureus*		*E. coli*	
	100 µ gm	200 µ gm	100 µ gm	200 µ gm
A_1	07	08	07	08
A_2	14	19	16	22
A_3	07	07	06	07
A_4	07	06	07	08
A_5	06	07	08	09
A_6	09	10	10	11
A_7	07	08	07	08
A_8	09	09	09	08
Chloramphinicol	16	22	18	30
Ampicillin	18	26	21	32

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References

1. Lietuvos T.S.R. Aukstuju Mokyklu Mokslo Darbai, *Chem. Ir. Chem Tech.* **3**, 69 (1963).
2. R. Baltrusis and I. Mariosius Khim Geterotsikl soedn, *Chem. Abstr.* **72**, 111413t (1970).
3. Z. F. Solomko, M. S. Malinovskii and V. T. Braichemko, *Khim fourm Zh.* **5**, 11 (1971).
4. M.B. Talwar, R. Desai Shobha, S. Somannavar and S. C Bennur, *Indian J. of Heterocyclic Chemistry.* **5**, 215 (1996) .
5. M. C. Hosur, M. B. Talawar, U. V. Laddi , R. S. Bennur and S.C. Bennur, *Indian J. of Heterocylic Chem.* **3**, 237 (1994).
6. M. P. Hutt, E. F. Elslager and L. M. werbet, *J Heterocyclic Chem.* **7** (1970), 511.
7. Chang Hoon Lee, Hyun In cho and Kee Jung Lee, *Bull Korean Chem. Soc.* **22**, 1153 (2001).
8. U. V. Laddi, R. S. Desai, Y. S. Somannaver, R. S. Bennur and S. C. Bennur, *Indian Drugs.*, **34**, 666 (1997).

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