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SYNTHESIS OF THIADIAZOLES AND STUDY OF THEIR BIOLOGICAL ACTIVITY

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Abstract

Some 2-aldo/ketoimine derivatives of 1,3,4-thiadiazoles have been prepared from 2-amino5-(4',5'-dimethoxy2'-methylphenyl)1,3,4 - thiadiazoles and 2-amino- (5'-ethoxy4'-methoxy2'-methyl phenyl)1,3,4-thiadiazoles. Compounds were tested for their biological activity.

Introduction:--

In continuation of the growing interest in the chemistry of thiadiazoles which are reported to be biologically active (1— 4), it was worthwhile to synthesise their derivatives and to study their biological activity.

2-aldo/ ketoimines of 1,3,4- thiadiazoles have been prepared by the condensation of 2-amino5-(4',5'-dimethoxy2'-phenyl)1,3,4-thiadiazoles (l), prepared from catechol and 2-amino5-(5'-ethoxy4'-methoxy2'- methyl)1,3,4-thiadiazoles (l') prepared from Vanillin have been prepared by their condensation with aldehydes and ketones in the presence of sod. Acetate & ethanol. Their biological activity has been studied. Structure of these compounds has been elucidated on the basis of their analytical and spectral (NMR) data.

Experimental :-

The m pts were taken in the open capillary and are uncorrected. The NMR spectra were recorded in TFA on Vaman A---600 spectrometer with TMS as an external standard.

From Catechol :--

2-amino5(4',5'-diethoxy2'methylphenyl)1,3,4-thiadiazole (l) was prepared frim catechol by pathway (i) methylation using acetone and K2CO3 in DMS, (ii) Friedal Craft's formylatjonreaction. (iii) Clemnljson'sreduction (iv) methanoylation with DMS using POCl3 (v) condensation with thiisemicarbazidehydroçhloride and then cyclisation using FeCl3 & ethanol.

2-aldo/ketoamine5-(4',5'-dimethoxy2'-methylphenyl)1,3,4-thiadiazoles:--

Calculated quantity if (I) and sod. Acetate was dissolved in minimum quantity conc. HCl and to this sol of aldehyde/ketone in alcohol. Mixture was refluxed on a water bath for about an hour. Contents were removed cooled and stirred well. Matter was then allowed to stand overnight when the fine title compound (ll) separated out as a brown solid. It was recrystallized from ethanol. The analytical data of these compounds was well within the calculated limits. The NMR spectra was recorded in TFA showed additional signals due to alkyl/ phenyl groups of aldehydes and ketones (Table- ll).

From vanillin:----

2-amino5-(5'-ethoxy4'-methoxy2'-methylphenyl))1,3,4-thiadiazole(i') wss prepared by the ethylation of vanillin using fused Pot. Carbonate which was subjected to Clemnson's reduction to get ethoxymethoxytolune. This was then subjected to Vielsmeir's reaction using POCl3 & DMS to get substituted benzaldehyde. It was then condensed with thiosemicarbazide hydrochloride to have thiosemicarbazone .Thiosemicarbazone was cyclised using FeCl3 and ethanol to get 1,3,4-thiadiazoles (l').

2-aldo/keto5-(5'-ethoxy4'-methoxy2'-methylphenyl)1,3,4-thiadiazoles:--

Calculated quantity of (1') was subjected to condensation with aldehyde/ketone as discussed under heading (A) to get the aldo/ ketoimine derivatives of 1,3,4-thiadiazole. The structure wasestablished from the analytical & spectral data.

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compond	m.pt	mol.formula	% of C	% of H	% of N	% ofO/S	s.lutea	c.rubrum	s.lococcus	E.Coli
			(theo)obs	(theo)obs	(theo)obs	(theo)obs				
a	252-253	C18 H17 N3 O2 S	(64.8) 64.7	(5.1)5.2	(12.6)12.5	(9.6)9.6/(9.6)9.8	11	11	10	12
b	254-255	C19 H19 N3 O2 S	(64.9)64.2	(5.37)5.5	(11.88)9.25	(9.5)9.25/(9.05)9.15	12	10	9	NA
c	258-259	C20 21H N3 O2 S	(65.3) 65.18	(5.71)5.76	11.42)11.47	(8.7)8.75/(8.7)8.12	NA	10	9	10
d	263-264	C24 H21 N3 O2 S	(69.1) 69.24	(5.04)5.14	(10.88)10.08	(7.68)7.60/(7.68)7.66	10	NA	NA	11
e	253-254	C19 H19 N3 O2 S	(64.5) 64.4	(5.37)5.47	(11.88)11.77	(9.05)9.10/(9.05)9.11	10	11	9	11
f	254-255	C20 21H N3 O2 S	(65.28) 65.35	(5.71)5.76	(11.42)11.48	(8.8)8.6/(8.7)8.8	11	10	10	NA

Note:--- 1. N A stands for " not active".

2 It was evaluated by agar diffusion method.

(Barry A I,Gareja A, Thrap L D,AM. J. Clin.Pathol,53,149(1970)

3 conc. is 100mg/cc for s.letea&s rubrum

4 conc. is 10mg/cc for mg/cc for s. lococuss & e. coli

5 Zone of inhibition was measured after 24 hrs and 48 hours.

Compond	Additional NMR signals due to aldo/ketoimine group (group)							
a	1.3(1H, s, >N=C<) 7.2(5H,d,>N=C<)							
b	1.2(3H, s, >N=C) 8.0(5H,s,>N=C<)							
c	1.3(3H, t,>N=C<) 1.7(2H,q,>N=C<)				8.1(5H, >N=C<) 1.7(2H,q,>N=C<)			
d	7.3(10H, s, >N=C<)							
e	1.3(1H, s, >N=C<) 7.2(5H,d,>N=C<)							
f	1.2(3H, s, >N=C<) 8.0(5H,s,>N=C<)							

Discussion:---‘ The structure of compound I&l’ has already been established .In addition to the signals due to ethoxy, methoxy, methyl& phenyl groups additional signals due to protons of aldehydes and ketones in the title compounds have been observed. Due to pi electrons of N=C<moiety have also been observed. The chemical shift due to alkyl groups show down field absorption in case of alkyl groups and up field due to aryl groups of this N=C<moiety..

References:---

Andotra C S ,Langrr T C, Sharms S K, J.Indian.Chem. andSren A N Indian J Pharma Sciences,48 (6) 192-195 (1986).

Andotra C S ,Langrr T C,andSharms S K, J.Indian.Chem. Soc 66,122,123(1989)

Andotra C S, Sharma S K IndianJ. Pharma Sciences 51 (3),107-108,(1989)

Gibson M S , Tetrahedran 18,1377,(1962)

Andotra C D, Balbir SinghManhas,ActaIndicaCienciavol.XVlllc No 2, 99,(1992).