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Original Article

SYNTHESIS AND BIOLOGICAL ACTIVITY OF SOME NEW THIADIAZOLE DERIVATIVE

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ABSTRACT

The synthesis of a series of 1,3,4 thiadiazole derivative from thiosemicarbazide, Benzoyl chloride and thiosemi carbazide condense with calcium Chloride guard tube, to formed [N-(5 Phenyl 1,3,4) thiadiazole-2-yl benzamide](C-1),[2-(Chloro-N(5-(Chloro phenyl)1,3,4 thiadiazole-2-yl) Benzamide] (C-2), [4-Chloro-*N*-[5-(4-chloro-phenyl)-[1,3,4] Thiadiazol-2-yl]-benzamide](C-3)and:[3-Chloro-N-[5-(3-Chloro-phenyl)-[1,3,4] Thiadiazole-2yl]benzamide] (C-4)all the new compounds have been characterized by 1 H NMR and MASS spectral data by elucidated and all newly synthesized compounds are studies for their analgesic activity.

KEYTERMS: 1, 3, 4 thiadiazole, chloro benzoic acid, Analgesic activity

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1.0 Introduction:

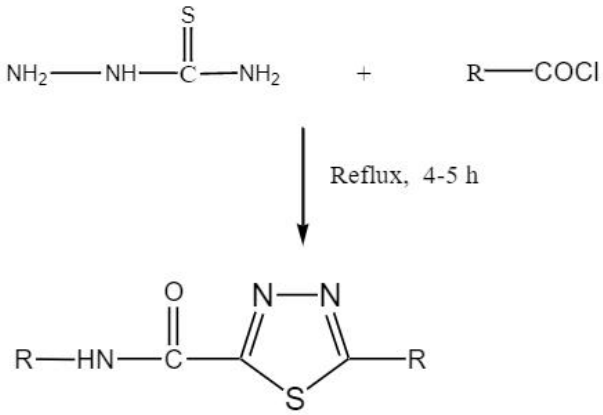
[1]The progress achieved in the in synthesis of hetrocyclic compound with biological potential is due to improvement of the methodological study of tested substance too. It is known that many 1,3,4- thiadiazole & 1,2,4- triazole derivatives. During recent years there has been intense investigation of different classes of thiadiazole compounds, many of which are known to possess intresting biological properties such as antimicrobial, anticinvulsant hyperglycemic, antituberculosis & Anti-inflammatory activities. In addition 1, 3, 4 thiadiazoles exhibit various biological activities possibly due to the presence of the –N=CS moity[2]. Synthetic route still remained the single most important route of arriving at a new biological active compounds research on Phytochemistry or any other related science; it finally bails down to the determination of the Structure and developing its synthetic route. The literature survey of Thiadiazole derivatives showed that it has diverse Biological activities. These activities prompted us to synthesize a series of 1,3,4 Thiadiazole derivatives substitution on 2,5 position containing six member ring. The newly synthesized compounds were screened for the assessment of Pharmacological activity.

2.0 Material and methods

2.1 General procedure:

1:1 (molar ratio) of aromatic acid and phosphorous penta chloride were taken in a R.B. fitted with air condenser and calcium chloride guard tube[2-4]. This mixture was heated gently to melt with vigorous shaking at around 50 C. After 30 min excess $POCl_3$ was distilled out. The residue was dried well and used for next step of the reaction. Then the Thio-semicarbazide added to the respected acid chloride and refluxed for 3-5hrs. The progress of the reaction was monitored by checking the TLC. Then excess benzene was distilled out, neutralized with aq. $NaHCO_3$ and the compound was extracted with $CHCl_3$ (25 X 4 ml). The crude was obtained by distillation of $CHCl_3$ under reduced pressure.

Scheme: 1



R=C6H5, 2-C6H4Cl, 3-C6H4Cl, 4-C6H4Cl

Compound 1: [*N*-(5-Phenyl-[1, 3, 4] Thiadiazol-2-yl)-benzamide]

Thiosemicarbazide added to the benzoyl chloride and refluxed for 3-5 hrs. The progress of the reaction was monitored by checking the TLC. Then excess benzene was distilled out, neutralized with aq. $NaHCO_3$ and the compound

was extracted with $CHCl_3$ (25 X 4 ml). The crude was obtained by distillation of $CHCl_3$ under reduced pressure.

IR(KBr)1601,1446,1312,1172,690(thiadiazole),3213(NH),1662(C=O).^{1}HNMR(CDCl3,300MHz):δ 8.76(Bs,1H),7.77(d,3H,J=7.9Hz),7.81(d,1H,J=7.9 Hz),7.62(d,1H,J=7.5Hz),7.567.42(m,H)Mass(ESI):m/z(%):281(23), 269(14), 264(18), 249(17), 248(100)

Compound 2: [2-Chloro-*N*-[5-(2-chloro-phenyl)-[1,3,4]Thiadiazol-2-yl]benzamide]

Thiosemicarbazide added to the 2- chloro benzoyl choride and refluxed for 3-5hrs. The progress of the reaction was monitored by checking the TLC. Then excess benzene was distilled out, neutralized with aq. $NaHCO_3$ and the compound was extracted with $CHCl_3$ (25 X 4 ml). The crude was obtained by distillation of $CHCl_3$ under reduced pressure.

IR(KBr)1602,1445,1315,1171,691(thiadiazole),3212(NH),1663(C=O).^{1}HNMR(DMSO-ds,400MHz):7.96(d,1H,J=7.5),7.8(d,1H,J=7.4),7.7(d,2H,J=8.8),7.6-7.5(m,3H),7.4(m. 2H) Mass (CPS):m/z(%) calculated 350.222, found 350.245

Compound 3: [4-Chloro-*N*-[5-(4-chloro-phenyl)-[1,3,4] Thiadiazol-2-yl]-benzamide]

Thiosemicarbazide added to the 4- chloro benzoyl choride and refluxed for 3-6hrs. The progress of the reaction was monitored by checking the TLC. Then excess benzene was distilled out, neutralized with aq. $NaHCO_3$ and the compound was extracted with $CHCl_3$ (25 X 4 ml). The crude was obtained by distillation of $CHCl_3$ under reduced pressure..

IR(KBr)1602,1445,1315,1171,691(thiadiazole),3212(NH),1663(C=O).^{1}HNMR (DMSO-ds, 400 MHz):6.56(S, 1H), 7.74(d, 1H, J=7.3 Hz), 7.5(d, 1H, J=8.24 Hz), 7.63(m, 3H), 7.7(d, 1H, J=4.4 Hz), 7.9(d, 1H, J=8.6Hz), 8.1(d, 1H, J=4.8Hz) Mass(LCMS2): Intensity(CPS): calculated 350.222 , found 350.125

Compound 4: [3-Chloro-N-[5-(3-Chloro-phenyl)-[1,3,4] Thiadiazole-2yl]benzamide

Thiosemicarbazide added to the 3- chloro benzoyl choride and refluxed for 3-5hrs. The progress of the reaction was monitored by checking the TLC. Then excess benzene was distilled out, neutralized with aq. $NaHCO_3$ and the compound was extracted with $CHCl_3$ (25 X 4 ml). The crude was obtained by distillation of C Cl_3 under reduced pressure.

IR(KBr)1602,1445,1315,1171,691(thiadiazole),3212(NH),1663(C=O).^{1}H^{1}HNMR(DMSOds,400Hz):7.86(d,1H,J=7.2),7.62(d,1H,J=7.2),7.52(d,2H,J=8.2),7.57.6(m,3H),7.41(m,2H),7.39(d,1H,J=7.2). Mass(LCMS2): Intensity(CPS):m/z calculated 350.222 found 349.912

2.2 Purification of the compounds:

The compounds were purified by column chromatography using silica gel (60-120 mess) and 5% EtOAc in pet petroleum ether. The actual fraction was collected by regular checking of TLC. Finally the compounds were further purified by preparative TLC

Table 1: SOME PHYSICAL PROPERTIES OF THE COMPOUNDS

compound	m.p (^{0}c)	Yied (%)	solubiliy	Rf value	odour	Mwt	colour
c-1	82	62	$CHCl_3$	0.715	aromatic	281.0	Yellowish colour
c-2	85	58	$CHCl_3$	0.691	aromatic	350.2	Yellowish colour
c-3	86	59	$CHCl_3$	0.672	aromatic	350.1	Yellowish colour
c-4	85	61	$CHCl_3$	0.712	aromatic	349.9	Yellowish colour

2.3 Analgesic activity:

Each colony standard bred albino mice 22-35gm were used to evaluate analgesic activity.it was determind as described by the method based on acetic acid induced writhing response in mice for this experiment 42 mice and they were divided into 7 groups containing 6 animals each[5-6]. All the animals receive 0.6%^{v} of 10ml/kg body weight of acetic acid intraperitonially and number of writhing was recorded after 10 min upto next 15 min. the same groups animals were used next day for evaluating analgesic activity.Group-1recieve 0.5ml tween -80(0.1%and served control group 2 receive 100mg/kg body weight of salicylic acid (aspirin) orally and served asthe remaining 5 groups recived varies test compounds at a dose of 100mg/kg body weight orally in the form of suspension in 0.1/ tween after 1hr.

Table: 2

Sl. No	Compound	Mean no of writhing ±SEM	% protection
1	Control	42.15± 3.16	-
2	Asprin	10.00±0.22	80.00
3	C-1	15.30±1.97	63.65
4	C-2	15.30±1.97	57.64
5	C-3	18.24 ±.69	56.76
6	C-4	16.34±68	57.53

Seven animals in each group, value are mean ±SEM P<0.05, P<0.01, P<0.001 when compared to control.

3.0 Result &conclusion: After the experiment it is concluded that the compounds which are synthesized in the project having good yield value. The synthesize Thiadiazole compounds identified and characterise by ^{1}H NMR a spectra. After it the Pharmacological

activity was done. The entire compound gives good response for analgesic activity.

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