Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2012, 4(1):779-782

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis, characterization and anti-inflammatory activity *of some 1, 3,4 - oxadiazole derivatives*

Arvind Kumar Singh*, R. Parthsarthy and M. Lohani

**National Institute of Medical Sciences, Jaipur, Rajasthan, India*
Kamla Nehru Institute of Management and Technology, Faculty of Pharmacy, Sultanpur, U.P.

ABSTRACT

2,5 Di-substituted 1,3,4-oxadiazole derivatives was synthesized by the reaction between benzoylchloride and various chlolro, nitro-benzoylchloride and semicarbazide to synthesized (C_1-C_7) compounds. These compounds were tested for their anti-inflammatory activity determined by rat paw oedema method. All the synthesized compounds have been characterized by ^{1}H NMR, IR and Mass spectral data. The compounds were purified by column chromatography. All synthesized derivatives were determined by the carrageenan induced rat paw oedema model for Anti-inflammatory activity. The entire compound gives good response for anti-inflammatory activity for this activity indomethacine was used as standard drug and compared to new synthesized drugs. Some New Synthesized drugs have to shown better activities for anti-inflammatory.

Keywords: 1, 3, 4-Oxadiazoles, Anti-inflammatory.

INTRODUCTION

1, 3, 4-Oxadiazole are heterocyclic compounds containing one oxygen & two nitrogen atom in a five member ring. 1,3,4-oxadiazole derivatives have to placed a major role in the pharmaceutical chemistry .The number of so many synthetic compounds with oxadiazole nucleus used for antibacterial [1-5] ,antifungal[6-9] ,analgesic and anti-inflammatory activities [10-13].Derivatives of 1,3,4-oxadiazole with suitable substitution at 2,5 – position have been already reported to possible biological activities . 1,3,4-oxadiazole derivatives act as anticonvulsant & diuretics[14]. These observations and our interest in the pharmaceutical chemistry of heterocyclic compounds promoted us. We have synthesized different derivatives of, 1, 3, 4-oxadiazole with different substituent at 2 & 5-position. These derivatives have been also screened for their anti-inflammatory activity. Mostly five member aromatic system having three heteroatom's at symmetrical position have been studied because of their physiological properties.[15-16] it is also well established that various derivatives of 1,3,4-oxadiazole exhibit broad spectrum of pharmacological properties such as antibacterial and antifungal activities.[17-18],1,3,4-oxadiazole showed antibacterial properties similar to those of well known sulphonamide drugs.[19]

EXPERIMENTAL SECTION

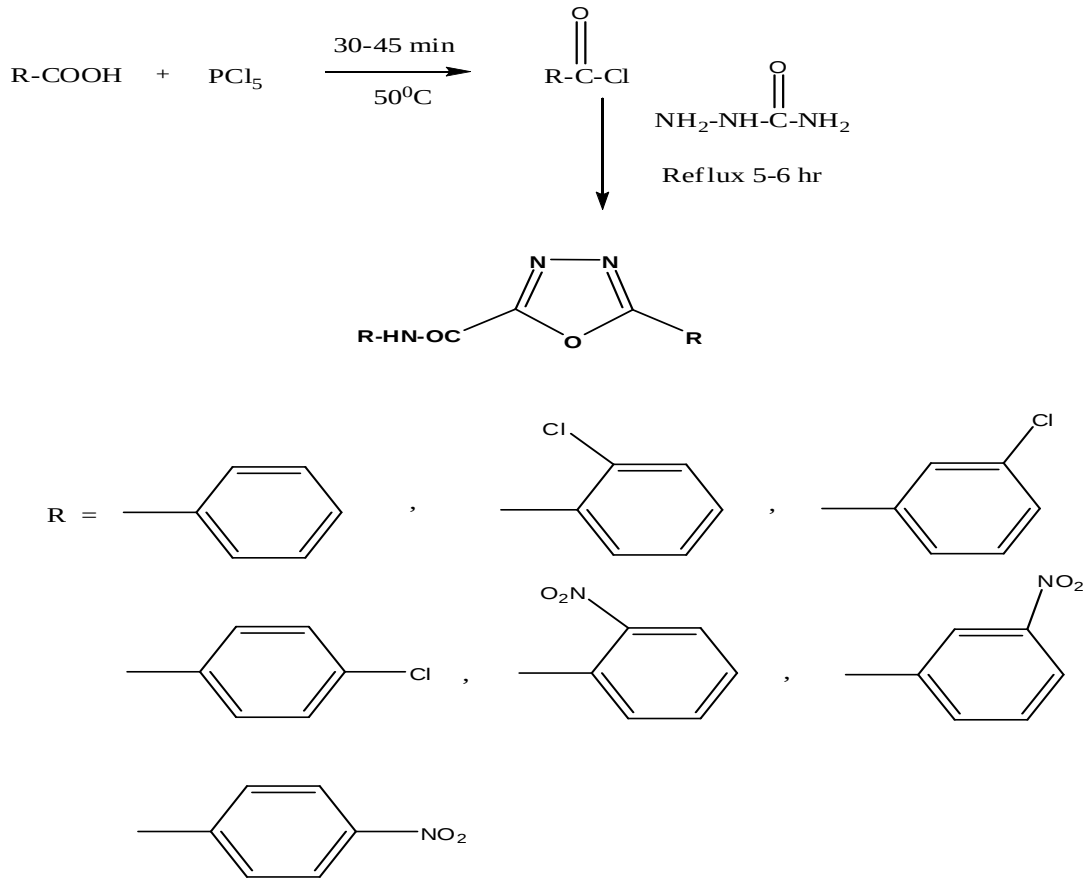
All chemicals were supplied by (Merck & S.D.fine chemicals Lucknow India). Melting point (m.p) was determined by open capillary tube method. Purification of the compounds was checked by column chromatography & silica gel-G (60-120mess) & silica gel GF_{254} (4:1) for preparation of the TLC plates and used the solvent system 5% ethyl acetate in pet. Ether & spots were seen under iodine vapours & UV light chamber. IR spectra were obtained on a Perkin-Elmer 1720 FT-IR-Spectrometer (KBr-sol^n/pellets). ^{1}HNMR spectra were noted an Brucker Ac-400 MHz spectrometer using TMS as internal standard in DMSO/$CDCl_3$ & mass spectra (m/z %) recorded by VG ZAB-HS (FAB) instrument.

General procedure for synthesis of compounds (c_1 to c_7):-
(1:1 molar ratio) Aromatic, phosphorus pentachloride and benzene were taken in RBF, fitted with air condenser & calcium chloride guard tube. The 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 reaction. Then added semicarbazide to the respected acid chloride & reflux for 5 hrs. These programs of the reaction were monitored by checking the TLC. The excess benzene was distilled out neutralizing with aq. $NaHCO_3$ & the compound was extracted with chloroform. The crude was obtained by distillation of chloroform under reduce pressure.

Anti-inflammatory activity[20]:
Anti-inflammatory activities of all synthesized derivatives were determined by the carrageenean induced rat paw oedema model. We taken albino rats (100-200 gm) in different groups divided as control, test and standard and six animals were in each groups. Overnight fasted animals were used and during that period only tap water was given. Generally , Indomethacine was used as standard drug , both test and standard drugs was suspended in 1% carboxy methyl cellulose (CMC) and administered orally through gastric gavage needle and in control group 1% CMC is administered . After one hour of the compound administration we induced the carrageenean (1%) by the sub planner surface of the right hind paws of animals . Initial paw volume and after paw volume was measured 3 hour and 6 hour after the administration of carrageenan . Percent paw oedema inhibition is calculated.

RESULTS AND DISCUSSION

SCHEME: 1



After the experiment it have concluded that the compounds which synthesized in the project having good yield value. The synthesize oxadiazole compounds identified and characterize by IR, ^{1}H NMR and MASS spectra. After it the Pharmacological activity was done. The entire compound gives good response for Anti- inflammatory activity:[3-Chloro-N-[5-(3-Chloro-phenyl)-[1,3,4] oxadiazole-2yl]benzamide **(C_4),**and [4-Nitro-N-[5-(4-Nitro-phenyl)-[1,3,4] oxadiazole-2yl] benzamide **(C_7)**. Substitution of 2-chloro-benzoic acid, at 2,5- position anti-inflammatory activity greater **(c_2)** than 3-chloro substituted compound **(c_3)**and 4-cloro-benzoic acid compound**(c_4)** substituted at 2,5 position anti-inflammatory activity greater than 2-chloro-substituted compound**(c_2).** While

Substitution of 4-nitro-compounds **(c_7)** at 2,5-position greater than other 2-nitro and 3-nitro substituted compounds **(c_5&c_6).**

Compound 1: [*N*-(5-Phenyl-[1, 3, 4] oxadiazol-2-yl)-benzamide]
IR(KBr,cm-1) : 3214(NH) ,1664(C=O) , 1070(N-N) ,1232(C-O-C) ; ^{1}HNMR(DMSO-ds,400 M hz),8.72(s,1H, J=7.6hz) , 7.72 (d,3H, J=7.9hz), 7.82(d,1H, J=7.9hz),7.62(d,1H,J=7.6hz,MASS (ESI):m/z(%),266(23),262(14) ,260(100), 249 (17), 248(100). analytical calculated for $C_{15}H_{11}N_3O_2$ C=67.90,H=4.23,N=15.86,O=12.12 found=C=67.92,H=4.15,N=15.84,O=12.07.

Compound 2: [2-Chloro-*N*-[5-(2-chloro-phenyl)-[1,3,4]oxadiazol-2-yl]benzamide]
IR(KBr,cm-1): 3270(NH),1670(C=O) ,1072(N-N)1240(C-O-C),776(C-Cl) ;1HNMR (DMSO-ds,400mhz) ,7.96(d,1H,J=7.5) ,7.78(d,1H,J=7.4) ,7.72(d,2H,J=8.87),7-7.8(m,3H,J=8.2) ; MASS(CSM),m/z (%) ,analytical calculated for $C_{15}H_9N_3O_2Cl_2$; C=49.60, H=2.96, N=23.48.found C=49.62,H=2'86,N=23.44.

Compound 3: [4-Chloro-*N*-[5-(4-chloro-phenyl)-[1,3,4] oxadiazol-2-yl]-benzamide]
IR(KBr , cm-1)P: 3272(NH) , 1668(C=O), 1076(N-N) ,1242(C-O-C) ,778(C-Cl); 1HNMR (DMSO-ds,400mhz) ,7.76(d,2H,J=7.3hz), 7.68(d,1H,J=7.2hz),7.73(d,2H,J=8.2 hz) ,7.78(m,3H,J=8.32hz); MASS(C-SI),m/z(%) analytical calculated for C15H9N3O2Cl2 , C=48.98,H=2.83,N=23.48, found, C=47.96,H=2.81,H=23.32

Compound 4:[3-Chloro-N-[5-(3-Chloro-phenyl)-[1,3,4] oxadiazole-2yl]benzamide
IR(KBr ,cm-1): 3268(NH), 1668(C=O) ,1072(N-N),1242(C-O-C), 725(C-Cl); 1HNMR(DMSO,ds,400mhz) ,7.72-7.75(d,2H,J=8.4hz),7.78(m,3H,J=8.32hz). MASS(CSM);M\Z%-Anal calculator for C15H9N3O2Cl2, C=48.41,H=2.79, N=23.25,Found C=47.98,H=2.76 N=23.16.

Table 1 : Physical properties of compounds (C_1 to C_7)

Compounds	Yield (%)	Rf	MP(°C)	Mol. Formula	Mol.Wt.
C_1	72%	0.715	212	$C_{15}H_{11}N_3O_2$	265.2
C_2	66%	0.692	214	o-$C_{15}H_9N_3O_2Cl_2$	334.16
C_3	79%	0.678	213	m-$C_{15}H_9N_3O_2Cl_2$	334.16
C_4	82%	0.682	211	p-$C_{15}H_9N_3O_2Cl_2$	334.16
C_5	80%	0.721	273	o-$C_{15}H_9N_5O_6$	355.26
C_6	73%	0.761	266	m-$C_{15}H_9N_5O_6$	355.26
C_7	78%	0.672	271	p-$C_{15}H_9N_5O_6$	355.26

Table: 2 Anti-inflammatory activities of compounds C_1 TO C_7)

Columns	Dose Mg/kg	Inhibition of paw oedema after 3 hrs(%)1	Inhibition of paw oedema after 6 hrs(%)2
C-1	30	3.28+_ 0.28	58.24
C-2	30	2.48+_0.23	56.48
C-3	30	3.46+_0.22	51.16
C-4	30	1.62+_0.27	70.98
C-5	30	3.26+_0.241	59.48
C-6	30	3.22+_0.281	53.98
C-7	30	1.52+_0.271	69.54
Control	_	0 .36 +_0.28	_
Indomethacine	40	1.78+_0.340	66.44

1- Dose for 1-7: 30mg/kg b.wt
2- Dose for indomethacine 40mg/kg b.wt
mean±SEM,n+6

Compound 5: [2-Nitro-N-[5-(2-Nitro-phenyl)-[1,3,4] oxadiazole-2yl]benzamide
IR(KBr Cm-1) :- 3272(NH), 1670(C=O), 1078(N-N), 1260(C-O-C), 780(C-Cl) H1NMR (DMS+ds400M H2):- 7.70(d,1H,J=7.25Hz), 7.78(d,1H,J=7.4Hz), 7.78(d,2H,J=8.1Hz), 7.25(m,3H,J=8.21Hz) Mass(CSM) (M/Z(%)— Anal calculator for C14H9N5O6 C=48.97, H= 2-93, N=30.48, formed C=48.27, N=2.90, N=30.42

Compound 6: [3-Nitro-N-[5-(3-Nitro-phenyl)-[1,3,4] oxadiazole-2yl]benzamide
IR(KBrCm-1):- 3271(NH), 1668(C=O), 1070(N-H), 1265(C-O-C), 786(C-Cl) H1NMR (DMS+ds400M H2):- 7.71(d, 1H, J=7.24Hz), 7.77(d, 1H, J=7.3Hz), 7.73(d, 1H, J=8.3Hz), 7.22(m, 1H, J=8.21Hz), Mass,(CSM) M/Z(%)—Anal calculator for C14H9N5O6 C=48.92, H=2.44, N=30.47, found C=48.46, H=2.90, N=30.45

Compound 7: [4-Nitro-N-[5-(4-Nitro-phenyl)-[1,3,4] oxadiazole-2yl]benzamide
IR(KBr Cm-1) :- 3272(NH), 1665(C=O), 1078(N-N), 1260(C-O-C), 783(C-Cl) H1NMR (DMS+ds400M H2):- 7.70(d,1H,J=7.23H2), 7.2(d,1H,J=7.2H2), 7.74(d,1H,J=8.4H2), 7.26(m,1H,J=8.20H2), Mass,(CSM) M/Z(%)—Anal calculator for C14H9N5O6 C=48.98, H=292, H=30.46, formed C=48.92, H=2.48, N=30.36

Acknowledgement
I am heart fully thankful to extent my profound gratitude to Dr. R.PATH SARTHY kamla Nehru institute of management of technology sultanpur(up) for his kind support through my phd Work.Now I take the opportunity to express my sincere to my Brother Mr. Subrata Jana (the award of PhD) from Bengal Engineering & science university, Howrah india.

REFERENCES

[1].Sahin G, Palaska E, Ekizoglu M & Ozalp M, *Farmaco*,57(7),**2002**,539.
[2].Dhiman A M, Wadodkar K N & Purohit S D,*Indian J Chem*, 40B **2001**,539.
[3].Hiremath S P, Sonar V N, Sekhar K R, Purohit M G,*Indian J Chem*, 28B, **1989**, 626.
[4].Mashooq A Bhat, Khan S A & Siddiqui N, *Indian J Heterocyclic Chem*,14,**2005**,271.
[5].Priya V Frank & Balakrishna Kalluraya, *Indian J Chem*, 44B,**2005**,1456.
[6].Hansong Chen, Zhengming Li & Yufeng Han,*J Agric Food Chem*,48, **2000**, 5312
[7].Xia-Juan Zou, Lu-Hua Lai, Gui-Yu Jin & Zu-Xing Zhang,*J Agric Food Chem*, 50, **2002**, 3757.
[8].Saad H, *Indian J Chem*, 35B, **1996**,980.
[9].Shetgiri N P, Nayak B K, *Indian J Chem*, 44B, **2005**, 1267.
[10].Ram V J,*Indian J Chem*, 35B, **1988**, 980.
[11].Misra U, Hikari A,Saxena A K, Gurtu S& Shankar K, *Eur J Med Chem*, 31, **1996**, 629.
[12].Omar F A, Mahfouz N M & Rahman M A, *Eur J Med Chem*,31, **1996**, 819.
[13].Mohd Amir & Shikha Kumar, *Indian J Heterocyclic Chem*, 14, **2003**, 51.
[14].Thomas J, Ger, Pat 2403, 357/1974(1974 *Chem.Abstr*. 81, 1361536).
[15].Hetznein A and MOCKEL K, *Adv.Hetrocycle chem*. **1996**, 7,183
[16].Sandstorm *j,Adv. Hetrocycle chem*. **1968**,9,165.
[17].Hosam saad, *Indian j,chem*., **1996**,35B,980.
[18].Hui xp,chu,CH,zangzu,wangQ,AND ZhangQ,*Indian j,chem*.,**2002**,41B,2176.
[19].H.Golgolab.I.Lalezari,L,Hosseini,Gohari,j,Hetrocycle.chema10,(**1973**),387-390(chem. Abstr)79(**1973**,921597).
[20].C.A.Winter E.A.Risely ND G.N.Nuss, *Proc,soc.exp.Biol:*111(**1962**) 554-564.