RESEARCH PAPER | Chemistry | Volume : 4 | Issue : 11 | November 2014 | ISSN - 2249-555X

Synthesis and Anti-Inflammatory Active Sulpha/Substituted 1, 2-Diazoles

KEYWORDS: synthesis, anti-inflammatory activity, sulphonamide 1,3-diketone, 4-Fluoro acid hydrazide

Rachana
Department of Chemistry Hindu College, Moradabad,(UP) India

Lalit Gupta
Department of Chemistry Hindu College, Moradabad,(UP) India

C.S. Gupta
Department of Chemistry Hindu College, Moradabad,(UP) India

C.P. singh
Department of Chemistry Sahu Jain College, Najibabad,(UP) India

Sumit Bhatt
Department of Chemistry Sahu Jain College, Najibabad,(UP) India

ABSTRACT *A Novel compound namely N1-(4-Fluoro) 3, 5 dimethyl-4-(N-4-sulfamoyl-azo)-1, 2-diazoles has been synthesised by two step processes. Synthesis of N1-4- sulphamoylphenylhydrazono-3, 5-dimethyl propane-1, 3-dione and sulphonamide, which interacting with 4-Fluoro benzoic acid hydrazide to form final compound. The newely synthesised compound N1-(4-Fluorobenzoyl)-3, 5-dimethyl 4-(N1-4-sulfamoyl phenyl azo) 1,2-diazoles was screened for anti-inflammatory activity.*

INTRODUCTION

A heterocyclic compound is one which possesses cyclic structures with at least one hetro atom in the ring. Nitrogen, oxygen and sulphur are the most common hetero atoms. Heterocyclic compounds are very widely distributed in nature and essential to the life in various ways. Vitamin C exists in the form of five membered (furan) or six member (Pyron) rings containing one oxygen atom. Most member of Vitamin B group possess heterocyclic ring containing nitrogen. One example is vitamin B6 (Pyridoxime), which derivative of pyridine essential in amino acid metabolism.

1, 2-diazole is a heterocyclic compound having varied biological activity and still of great scientific interest now a days. They are widely found in bioorganic and medicinal chemistry with application in drug discovery2.

Nitrogen based heterocyclic compounds are very important in the field of medicinal chemistry. The present diazoles were prepared because of its good biological activity. Compounds including a

1, 2-diazole nucleus and N-substituted derivatives are known to possess various biological activity1.

Among these types of molecules have been shown to have various important biological activity such as antibacterial, antifungal, antiviral, diuretic, antituberculostatic, anti-HIV, antihistaminic anticancer, anticonvulsant, anti-inflammatory and analgesic properties3-7.

Sulpha/substituted 1, 2-diazoles may serve as the alternative sources for the development of new antiinflamatory agents due to their biological activity. Sulpha/substituted 1, 2-diazoles used for the treatment of anti-inflammatory in different systems of medicine have shown diuretic activity when tested on animal models. On the basis of the use of diuretics, but no previous pharmacological study was carried out to test anti-inflammatory the activity of sulpha/substituted 1, 2-diazoles. The main aim of the present investigation was to evaluate the claimed anti-inflammatory activity of sulpha/substituted 1, 2-diazoles.

MATERIAL AND METHOD

The 1.3-diketones, sulphanilamide, 4-Fluoro benzoic acid hydrazide and all reference compound were purchased from Aldrich Chemicals, Ethanol, sodium acetate, glacial acetic acid and all other reagents were purchased from S.D. Chem. TLC was performed on pre-coated plastic sheets of silica gel G/UV- 254 of 0.2 mm thickness (Macherey-Nagel, Germany).

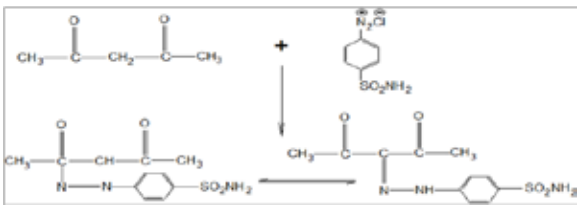
General: Melting points of the N1-(4-Fluorobenzoyl) 3, 5 dimethyl-4(N-4-sulfamoylphenylazo)-1, 2-diazole was determined using an open-ended capillary tube method and are uncorrected. The purity of the synthesized compound was checked by TLC. A FT-IR spectrum was recorded on a Perkin-Elmer1605 series FT-IR in a KBr Disc, 1H NMR spectra was recorded at 300 MHz on a Burker FT-NMRspectrophotometer using TMS as internal standard.

Step-1; Synthesis of N1-4-sulphamoylphenyl hydrazono-3,5-dimethyl propane-1,3-dione: An ice cooled solution of 3,5-dimethyl propane–1,3-dione (0.03 mole) in ethanol containing sodium acetate (6 grams) a diazotized solution of sulphonamide (0.05 mole) were gradually added with stirring and cooling. The reaction mixture was further strirring for 20 minutes, the coloured hydrazono compounds precipitated by addition of ice cold water. It was filtered off, washed with water, dried and recrystallised from ethanol/acetic acid [Fig.1]. On analysis, it was found to be N1-4-sulphamoylphenyl hydrazono-3,5-dimethyl propane-1,3-dione [Fig. 1].

Volume : 4 | Issue : 11 | November 2014 | ISSN - 2249-555X

Synthesis of novel N1-4-fluorobenzoyl, 5-dimethyl-4(N-4-sulfamoylphenylazo)-1,2-diazole

Fig.1: Synthesis of N1-4-sulphamoylphenyl hydrazono-3, 5-dimethyl propane-1,3-dione



N1-4-sulphamoylphenyl hydrazono 3, 5-dimethyl propane-1,3-dione: A yellow crystalline poeder. Mp 198-2000C, Yield 82.34%, molecular formula C16H15O4N3S (348.76): C, 55.10; H, 4.34; O, 18.35; N, 12.04; S, 10.17. Found: 54.92; 4.56; O, 18.17; N, 12.48; S, 9.87, IR (KBr) in cm-1 1440 (C-C),1560 (C=C of aromatic ring), 1260 (C-N), 1680 (C=O), 3087 (NH), 3275 (SO2NH2). 1HNMR (CDCl3) δ in ppm, 2.81 (s, 3H CH3), 6.75-7.68 (m, 9H, Ar-H), 6.92 (s, 2H NH2), 10.43 (s, 1H NH).

Step-II; Synthesis of N1-(4-Fluorobenzoyl, 3,5-dimethyl-4(N-4-sulfamoyl phenylazo)-1,2-diazole:

A solution of N1-4-sulphamoylphenyl-hydrazono 3,5-dimethyl propane-1,3-dione (0.02 mole) in glacial acetic acid was added to 4-Fluoro benzoic acid hydrazide (0.05 mole refluxed on water bath for 4 hours and left overnight. On cooling, shining recrystallised crystals, separated out which was collected by filtration, washed well with water, dried and recrystallised from glacial acetic acid to give N1-(4-Fluoro benzoyl)3,5 dimethyl-4(N-4-sulfamoylphenylazo)-1,2-diazole

[Fig. 2].

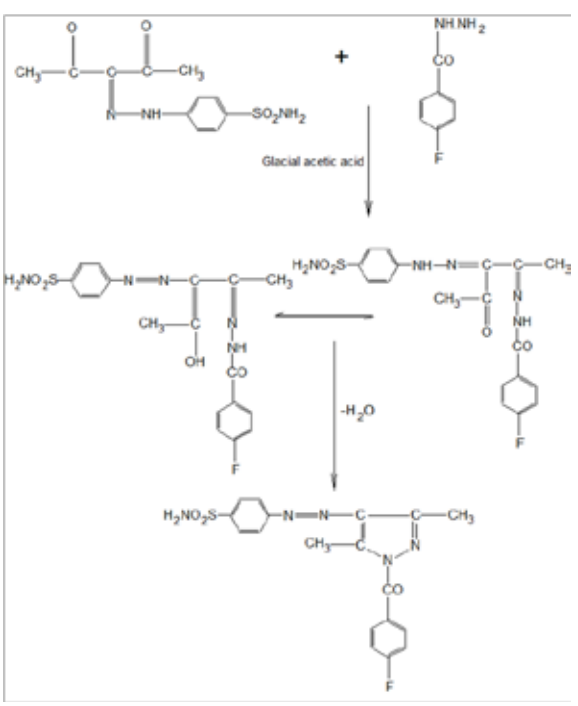


Fig.2: Synthesis of N1-(4-Fluorobenzoyl N1-3,5-dimethyl-4(N-4-sulphamoylphenylazo)-1,2-diazole

N1(4-Fluorobenzoyl)-3,5-dimethyl-4(N-sulfamoylphenylazo)-1,2-diazole: A yellow crystalline powder, mp 226-228 0C, Yield 72.13%. Molecular formula C23H20O3N5F5, anal. Calcd for C23H20O3N6S (463.90: C, 59.55; H, 4.34; O, 10.35; N, 18.12; S, 18.12; S, 7.64. Found: C, 58.97; H,

4.64; O, 10.29; N, 18.37; S, 7.73. IR (KBr) in cm-1 740 (C-C), 1240 (C-N), 1535 (C=C of aromaticring), 1585 (C=N), 1460 (N=N), 3055 (aromatic C-H), 3135 (NH), 1707 (C=O), 3082 (NH2). 1HNMR (CDCl3) δ in ppm, 2.79 (s, 3H CH3), 6.65-7.58 (m, 13, Ar-H), 7.10 (m, 4H NH2).

Animals: Adult's male Wistar albino rats, each in the weight range of 180-200 gm were used for this experiment. They were procured from National Vertinary Research centre, Bareilly, India. The animals were randomly allocated to six treatment groups of six animals each and kept in polypropylene cages and housed under standard conditions of temperature, humidity, dark light cycle (12h-12h) and diet.

Anti-inflammatory activity8, 13: The activity of the newly synthesized compounds compared to indomethacin as a reference compound was measured before and 4h after carrogeenan injection. Percent of the oedema inhibition was calculated as regards saline control group and potency was calculated as regards the percentage of the change of indometacin and tested compounds , as depicted in Table 1. All the tested compounds showed a reasonable inhibition of oedema size ranging between a 12.5%, for compound 25.4% for compound (b) 28% for compound, 32.7% for compound sulphonamide 1,2-diazole (c), 44.4% for compound sulphapyrimidine 1,2-diazole (d) and 29.9% for indomethacin. In activity relationship point of view, the anti-inflammatory activity of the pyrimidine was found to be the promising one. But sulphonamide also showed good anti-inflammatory activity (32.7%).

Table 1: Anti-inflammatory effect of sulpha/substituted-1,2-diazoles

Compound	Dose (mg/kg)	Oedema		Oedema (%) (X=SE)	Oedema inhibition (%)	Potency
		Zero min (basal)	4 h oedema (cm) (% increase)			
Control	1 mL saline	0.23±0.006	0.46±0.01	109.1±6.3	--	--
a $C_{14}H_{13}NCl$	70	0.20±0.002	0.37±0.01	81.3±4.8	-25.48	0.9
b $C_{14}H_{13}NF$	70	0.22±0.002	0.38±0.03	78.3±4.1	-28	0.9
c $C_{13}H_{11}N_3O_2$	70	0.21±0.003	0.41±0.2	94.8±5.3	-13.1	0.4
d $C_{19}H_{14}N_2O_2S$	70	0.22±0.002	0.37±0.02	73.1±4.4	-32.7	1.1
e $C_{23}H_{18}N_4O_2S$	70	0.20±0.00	0.32±0.001	60.7±4.9	-44.4	1.5
f $C_{23}H_{19}N_5O_2S$	70	0.20±0.00	0.32±0.004	60.7±4.9	-44.4	1.5
Indomethacin	35	0.26±0.003	0.39±0.03	76.5±3.6	-29.9	1

CONCLUSION

The Present Study reveals that, synthesised compoundN1(4-Fluorobenzoyl)-3,5-dimethyl 4-sulfamoylphenylazo)-1,2-diazole possess significant at 100 and 200 mg/kg but the effect declined at higher dose.

ACKNOWLEDGMENT

The authors express their sincere thank to Principal, Hindu College, Mooradabad and Sahu Jain (P.G.), College, Najibabad for providing lab facilities and also thank to CDRI Lucknow, IIT, Roorkee for Providing IR, NMR spectral data and pharmacological data.

Volume : 4 | Issue : 11 | November 2014 | ISSN - 2249-555X

REFERENCE

Achson a, an introduction to the chemistry of heterocyclic compounds 3rd edition, Wiley interscience, India 2000. | 2. G. capan, N. Ulusoy, N. Ergenc, M. Krtaz, New 6-phenylimidazo [2, 1-b]thiazole derivatives: Synthesis and antifungal activity. Monatsh. Chem. 1999, 130, 1399 | 3. R.U. Roy, R. desai, K.R. Desai, "synthesis and Antimicrobial Activity of 1, 2, 4-Thiazoles, | E-Journal of Chemistry, 2005, 2(6), 1. | 4. M.G. Vigorita, R. Ottana, F. Monforte, R. maccari, A. Trovato, M. T. Monforte, M.F. | Taviano, Synthesis and anti-inflammatory, analgesic activity of 3,3-(1,2-ethandiyl)-bis[2- aryl-4-thiazolidinone] chiral compounds. Part 10. | 5. C.V. Kavitha, S. basappa, S. Nanjunda, K. Mantelingu, S. Doreswamy, M. A. Sridhar, J.S. | Prasad, K.S. Rangappa, Synthesis of new bioactive venlafaxine analogs: Novel thiazolidin- | 4-ones as antimicrobilas. Bioorg. Med. Chem. 2006, 14, 2290. | 6. R. Ottana, R. Maccari, M.L. Bareca, G.Bruno, A. Rotondo, A. Rossi, G. Chiricosta, R. Di Paola, L. Sautebin, S. Cuzzocrea, M.G. Vigorita, 5-Arylidene-2-imino-4-thiazolidinones: Design and synthesis of novel anti-inflammatory agents. Bioorg. Med. Chem. 2005, 13, | 4243. | 7. G. kucukguzel, A. Kocatepe, E. De Clercq, F. Sahin, M. Gulluce, Synthesis and biological activity of 4-thiazolidinones, thiosemicarbazides derived from diflunisal hydrazide. Eur. J. med. Chem. 2006, 41, 353. | 8. Radwan, M.A.A., Rageb E.A. Saby, N.M. El-Shenaway, S.M., Potential anti- inflammatory and analgesic agents, Bioorganic and medicianal chemistry 2007, 15, 3832- | 3841. | 9. Singh N, Bhatia, S.K., Kumar A, Thiazolyl/ formazanyl-1, 2-diazoles as potent anti- inflammatory agent, European Jour. Of medicinal Chem., 2008, 43, 2597-2609. | 10. S. Jain, R. nagwanshi, M. Bakhru and S. Bageria, Antimicrobial Activity of Heteroarylchalcones and their Products, Journal of Indian Chemical Society, 2011, 88, 1571-1570 | 11. T. Giresh, G. Mohiddin, Z. Khan and R.R. Kumble, Synthesis of 1,3,4-Thiazole appended to Coumarins as antimicrobial agent, Journal of Indian Chemical Society, 2011, 88, 1459-1463 | 12. P. Samadhiya, Ritu Sharma, S.K. Srivastava and S.D. Sharma, Synthesis and biological evaluation of Some 2-amino-5-Nitrothiazole derivative, Journal of Indian Chemical Society, 2013, 90, 231-238 | 13. R.J. Deshmukh and S.P. Deshmukh, Synthesis and antimicrobial activity of 3 aryl-thiadiazole derivative, Journal of Indian Chemical Society, 2013, 90, 1027-1031 |