Microwave Assisted Synthesis and Characterization of 1,3,4-Oxadiazole Derivative

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Abstract

2-methylcyano-5-(5-nitro vanillin)-1,3,4-oxadiazole has been prepared expeditiously using microwave method. Condensation of cyanoacetic acid hydrazide and 5-nitrovanillin gave the corresponding hydrazone which on oxidative cyclisation with chloramine T under microwave irradiation gave the corresponding 2,5- disubstituted -1,3,4-Oxadiazole.The product obtained is pure having yield 92%. The synthesized compound was characterized by FTIR. The study reveals that oxidative transformation under microwave irradiaton is very clean and rapid method. The reaction conditions and the work up procedures are simple and mild.

KEYWORDS: 2-methylcyano-5-(5-nitro vanillin)-1,3,4-oxadiazole, Chloramine-T.

Introduction

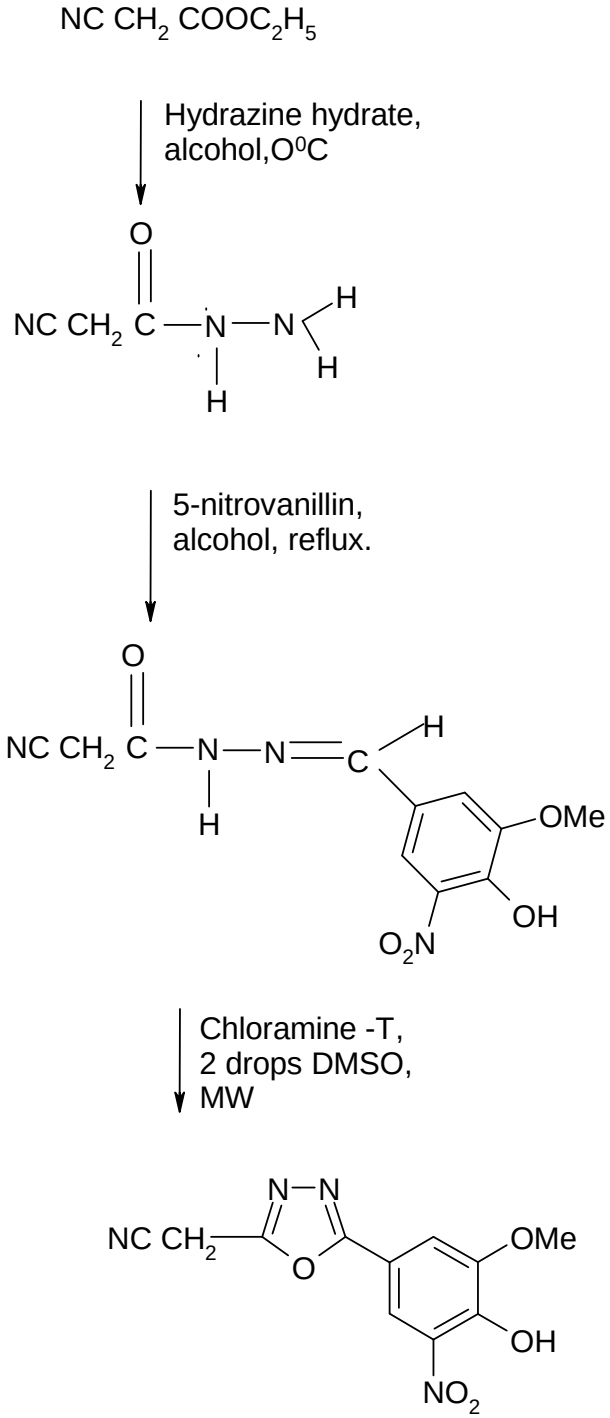
Oxadiazole derivatives belong to an important group of heterocyclic compounds and have been extensively studied in the last two decades. Among the wide variety of heterocyclic compounds 1, 3, 4 -oxadiazole derivative played a vital role in medicinal chemistry. Large number of synthetic compounds with oxadiazole nucleus studied for their anti-bacterial[1-6], anti-fungal [6-10], anti-microbial [11-18], anti-viral [19-21], anti-TB [22-23], anti-inflammatory[24-25,] and analgesic activities[26].

Various methods of synthesis of 1,3,4-oxadiazoles [27] are available in the literature. However, these methods suffer from disadvantages such as long reaction time, severe reaction conditions [28] and use of toxic oxidants[29]. Chloramine-T is a very versatile oxidizing agent and is of much important in its synthetic utility[27].

In present work we report the microwave assisted synthesis of 2,5- disubstituted -1,3,4-oxadiazole in presence of Chloramine T as a oxidizing agent.

Microwave technique has certain advantages like (i) small amount of solvent is needed (ii) the reaction can be carried out in shorter time and (iii) the product yields are improved.

The reaction sequence leading to the formation of the title compound is outlined in the Scheme



2-methylcyano-5-(5-nitrovanillin)-1,3,4-oxadiazole

EXPERIMENTAL:-

Synthesis 2-methylcyano-5-(5-nitro vanillin)-1,3,4-oxadiazole

To the ethyl cyanoacetate in alcohol , hydrazine hydrate was added dropwise in molar ratio 1:1 with stirring at O^0C. The hydrazide obtained on condensation with 5-nitrovanillin yielded the corresponding hydrazone which on oxidative cyclisation with Chloramine T under microwave irradiation yielded the corresponding 2,5- disubstituted -1,3,4-Oxadiazole .

(i)**Synthesis of cyanoacetic acid hydrazide** [30]

To the solution of ethyl cyanoacetate in alcohol, hydrazine hydrate in molar ratio of 1:1 was added dropwise with constant stirring in ice bath. The white product obtained was purified in ethanol and the product was confirmed by M.P.

(ii)**Synthesis of hydrazone from Cyanoacetic acid hydrazide (2)**

Cyanoacetic acid hydrazide and 5-nitrovanillin in molar ratio of 1:1 were refluxed in alcohol with constant stirring for 2 h. Coloured solid product was obtained. The product obtained was separated by filtration. Residue was washed with alcohol to get desired product .

FTIR spectrum of the compound was recorded using FTIR spectrophotometer (Perkin Elmer) and data obtained is presented in Table 1.

Table(1) : FTIR data of the hydrazone

COMPOUND	COLOUR	M.P. (^OC)	%YIELD	I.R.ν cm^{-1}					
				C≡N	C=N	C=O	N-H	NO_2	O-H
2	yellow	210	90	2283	1612	1666	3093	1542	3190

(III) Synthesis of 2-methylcyano-5-(5-nitrovanillin)-1,3,4-oxadiazole (3):

To the mixture of hydrazone and Chloramine T in molar ratio of 1:1, 2 drops of DMSO was added ,the clear liquid obtained was heated in microwave for 10 sec. Alcohol was then added to the reaction mixture which gave coloured product. Finally product obtained was separated by filtration. Residue obtained was washed first with alcohol and then by ether to get pure compound.

The FTIR spectrum of compound obtained is recorded and data is presented in Table 2.

Table(2) : FTIR data of 2-methylcyano-5-(5-nitrovanillin)-1,3,4-oxadiazole

COMPOUND	%YIELD	I.R. ν cm^{-1}					
		C≡N	C=N	N-N	NO_2	C-O-C	O-H
3	92	2218	1613	1060	1546	1252 and 1157	3304

1H NMR (δ ppm,DMSO-d_6): 7.1-7.9 (m,Ar-CH,2H), 3.75 (s,OCH_3,3H) , 2.9 (s ,CH_2,2H), and 11.20(s,OH,H).

The formation of 1,3,4-oxadiazole derivative was confirmed by the absence of peak due to amide carbonyl group and presence of peak at 1159 and 1258cm^{-1} gave the evidence for the ring closure further peak 1531 cm^{-1} is due to NO_2 group .

RESULT AND DISCUSSIONS:-

The IR spectra of the hydrazone showed peak at 1703 cm^{-1} due to carbonyl of amide group and at 1617cm^{-1} due to C=N group. The formation of 1,3,4-oxadiazole derivative

was confirmed by the absence of peak due to amide carbonyl group and presence of peak at 1159 cm^{-1} and 1258cm^{-1} gave the evidence for the ring closure, further peak at 1531 cm^{-1} is due to NO_2 group. The ^1H NMR analysis of the final compound showed signals corresponding to the multiplicities for different types of protons and is consistent with the assigned structure.The oxidative transformation under microwave irradiaton is very clean and rapid. The reaction conditions and the work up procedures are easy, simple and very mild.

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