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Chloramine T Mediated Synthesis Of 2-Substituted-5-(2'-Thiophene) -1, 3, 4-Oxadiazole Using Microwave Irradiation

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Abstract: *In the present work, 2-methylcyano-5-(2'-thiophene)-1,3,4-oxadiazole has been prepared expeditiously by microwave irradiation.Condensation of Cyanoacetic acid hydrazide and 2-thiophenecarbaldehyde 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 is obtained in a good yield with high purity. The structure of the synthesized compound is established by FTIR and ^{1}HNMR. The study reveals that oxidative transformation under microwave irradiaton is clean and rapid. The reaction conditions and the work up procedures are mild , simple and convenient.*

Key words: *2-methylcyano-5-(2-thiophene)-1,3,4-oxadiazole, Chloramine-T.*

I. Introduction

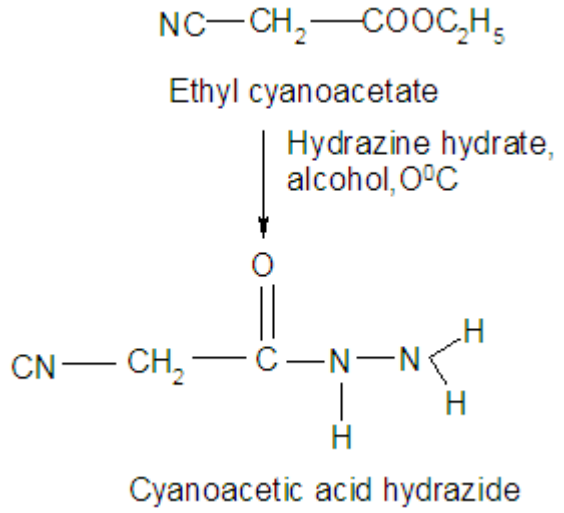
Oxadiazole derivatives belong to an important group of heterocyclic compounds and have been the subject of extensive study in the recent years. Among the wide variety of heterocyclic compounds that have been explored for developing pharmaceutically important molecules - 1,3,4-oxadiazole derivatives have played a vital role in medicinal chemistry. There are large number of synthetic compounds with oxadiazole nucleus used for anti-bacterial[1-6], anti-fungal [6-10],wide spectrum of anti-microbial [11-16], anti-viral [17-18],anti-TB [19-20],anti-inflammatory[21,-22,] and analgesic activities[22,26].

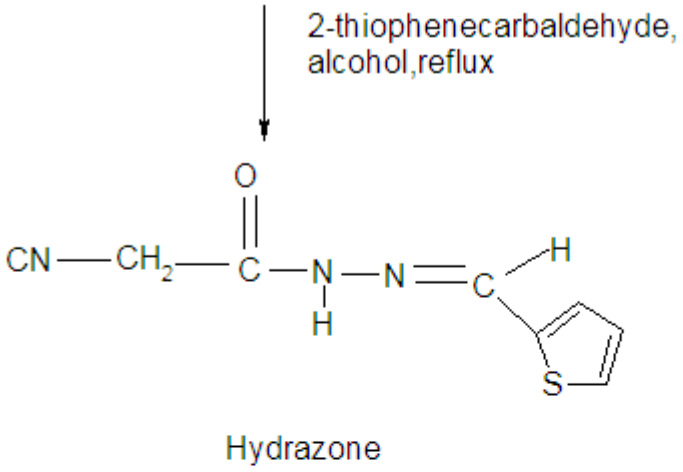
There are several methods available in the literature for the synthesis of 1,3,4-Oxadiazoles [27--29]. However, some of these methods suffer from disadvantages such as long reaction time, requirement of severe conditions [30] and using toxic oxidants[31].Chloramine-T is a very versatile oxidizing agent and is of much important in its synthetic utility[10,27].

Microwave ovens are routinely used to carry out organic reactions. The microwaves are non –ionizing radiations that transfer energy to ions in solutions and other compounds having dipole moment. Hydrocarbons such as benzene, hexane, cyclohexane etc and symmetrical molecules such as carbon tetrachloride absorb very little micro-wave energy. But chloroform, DMF, ethanol, ethylene glycol, chlorobenzene and other organic molecules with dipole moments absorb microwaves and are heated up rapidly.

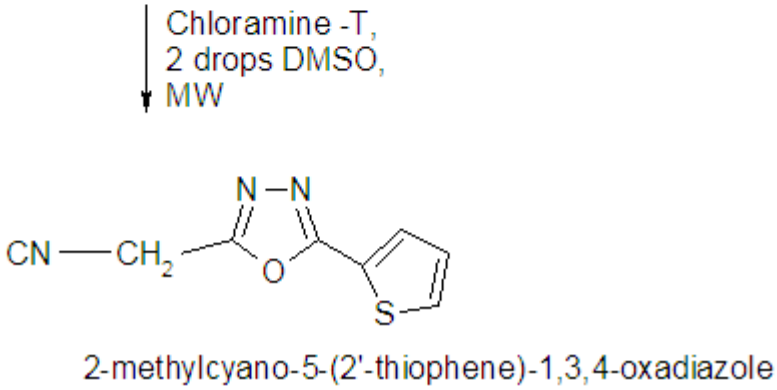
The advantage of using microwave oven for organic reactions are (i) small amount of solvent is needed, (ii) the reaction can be carried out in shorter reaction time and (iii) the yields are improved. We report herein a efficient method for the synthesis of 2,5- disubstituted -1,3,4-Oxadiazole using Chloramine- T under microwave irradiation.

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





Hydrazone



2-methylcyano-5-(2'-thiophene)-1,3,4-oxadiazole

II. Experimental

The uncorrected M.P. of the synthesized compounds were recorded in an open capillary tubes**.** FTIR spectra were recorded on BRUKER (model 3000), 1H NMR spectra were recorded on Varian, Mercury plus, 300MHz NMR spectrometer .For recording NMR spectra DMSO was used as a solvent and TMS was used as an internal standard.

1.1 General procedure for synthesis of 2-methylcyano-5-(2'-thiophene)-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 to give the corresponding hydrazide. The hydrazide on condensation with 2-thiophenecarbaldehyde yielded the corresponding hydrazone which on oxidative cyclisation with ChloramineT under microwave irradiation yielded the corresponding 2,5- disubstituted -1,3,4-Oxadiazole .

1.1.1. Synthesis of cyanoacetic acid hydrazide[32](1):-To the 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 recrystallised in ethanol and the product was confirmed by M.P.

1.1.2. Synthesis of hyrazone from Cyanoacetic acid hydrazide (2):- Cyanoacetic acid hydrazide and 2-thiophenecarbaldehyde in molar ratio of 1:1 were refluxed in alcohol with stirring for 2 hours, when solid product separates. The product obtained was filtered and washed several times with alcohol to yield the corresponding hydrazone. Yield, spectral data is listed in Table(1).

Table (1) Physical and spectral data for the compounds 2

COMPOUND	%YIELD	I.R. cm^{-1}		
		C≡N	C=N	C=O
2	90	2222	1599.91	1660.62

1.1.3. Synthesis of 2-methylcyano-5-(2'-thiophene)-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 under

microwave irradiation for 12 secs, followed by addition of alcohol to give solid product, which was filtered .The product was recrystallised using DMF: alcohol (75:25).
Yield: 89%.
IR(ν cm^{-1}KBr):- 1616 (C=N), 1010 (N-N), 1163 and 1262 (C-O-C).
1H NMR (δ ppm,DMSO-d_6): 7.1-7.4 (m,Ar-CH,3H) , 2.228(s ,-CH_2, 2H).

III. Result And Discussions:

The IR spectra of the hydrazones showed peak at1660.62 cm^{-1} due to carbonyl of amide group and at 1599.91cm^{-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 1163cm^{-1} and 1262 cm^{-1} gave the evidence for the ring closure. The oxidative transformation under microwave irradiaton is very clean and rapid. The reaction conditions and the work up procedures are mild, simple and convenient.

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