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Microwave Assisted Synthesis and Thermal Behavior Study of a Compound Containing 1, 3, 4 - Oxadiazole Rings

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Abstract: ***1, 3 - bis [5 - (3 - methoxy - 4 - hydroxyphenyl) - 1, 3, 4 - oxadiazol - 2 - yl]propane was synthesized in two steps. In the first step, glutaric acid dihydrazide was condensed with vanillin (aldehyde) to yield the corresponding dihydrazone. The dihydrazone on oxidative cyclisation gave the corresponding bis - 1, 3, 4 - oxadiazole. Chloramine - T was employed as a reagent for oxidative cyclising. The oxidative cyclisation step was carried under microwave irradiation. The synthesized compound was characterized by FTIR and NMR spectroscopy. Further thermogravimetric analysis was done to study the thermal stability of the synthesized product. The study reveals that oxidative transformation under microwave irradiation is very clean, rapid and the reaction conditions and the work up procedures are simple and mild.***

Keywords: bis - 1, 3, 4 - oxadiazole, chloramine - T, dihydrazone, microwave irradiation

1. Introduction

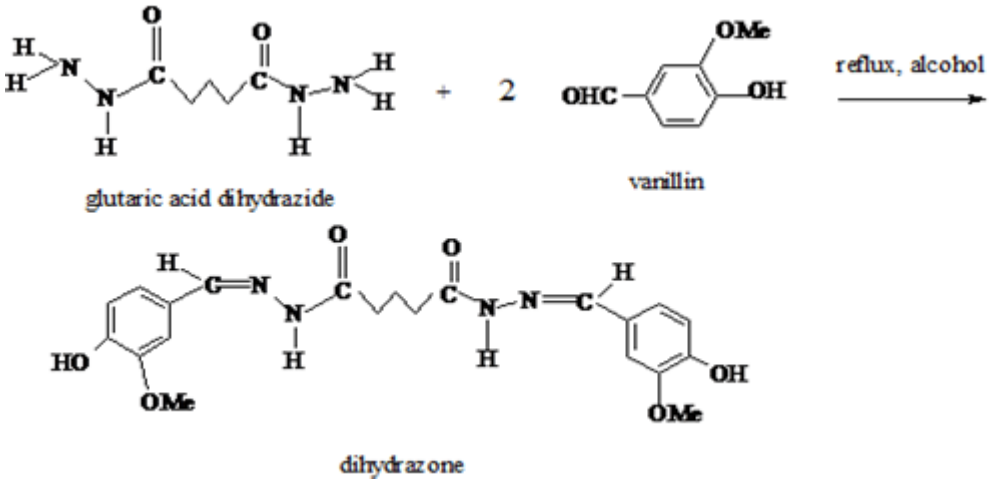
In the recent years, 1, 3, 4 - oxadiazole derivatives has attracted attention of chemist due to its varied pharmacological activities, which results due to 1, 3, 4 - oxadiazole moiety itself and various substituent attached on C - 2 and C - 5 position of the ring. The compounds of 1, 3, 4 - oxadiazoles with substituent like 6 - bromonaphthyl [1], 3, 4, 5 - trimethoxy phenyl [2], 2 - adamantyl [3, 4], amino [5], substituted amino [6], mercapto [7, 8], substituted mercapto [9], biphenyl [10] etc have been reported. Also derivatives of 1, 3, 4 - oxadiazole with other heterocyclic unit like coumarinyl [11], naphthyridinyl [12], indolyl [13], pyridyl [14], thienyl [15] etc. have been reported. Further bis - (5 - substituted) - 1, 3, 4 - oxadiazoles [16, 17] have also been synthesized. Compounds with substituted 1, 3, 4 - oxadiazoles are studied for biological activities like anti - microbial [18], anti - inflammatory [19], anticonvulscent [20], analgesic [21], antitumor [22] etc. In most of research papers authors tried to establish the structural relationship of various substituent with the biological activities that accompanies the substituent.

Recent publications are enriched with synthesis of bis - heterocyclic compounds and their pharmacological profile [23, 24]. Amongst the bis - heterocyclic compounds, synthesis of bis - 1, 3, 4 - oxadiazole moiety with various substituents at C - 5 position of the rings and their biological activities are reported [25, 26].

We report synthesis of bis - 1, 3, 4 - oxadiazoles with three - (CH_2) - groups in linkage between the two 1, 3, 4 - oxadiazle rings attached at C - 2 position and a substituent on C - 5 position of both the rings. In this work, glutaric acid dihydrazide was condensed with vanillin (aldehyde) to yield the corresponding dihydrazone. The dihydrazone on oxidative cyclisation gave the corresponding bis - 1, 3, 4 - oxadiazole. The oxidative cyclisation was carried out using chloramine - T as an oxidative cyclising reagent under microwave irradiation. Microwave technique has certain advantages: (i) amount of solvent employed is reduced considerably (ii) the reaction time is reduced and (iii) the product yields are improved. The oxidative cyclisation reaction was carried out using two to three drops of DMSO as reaction medium. The structure of the newly synthesized compound was established using FTIR and ^{1}H NMR. The thermogravimetric analysis was carried out to study the thermal stability of the synthesized compound.

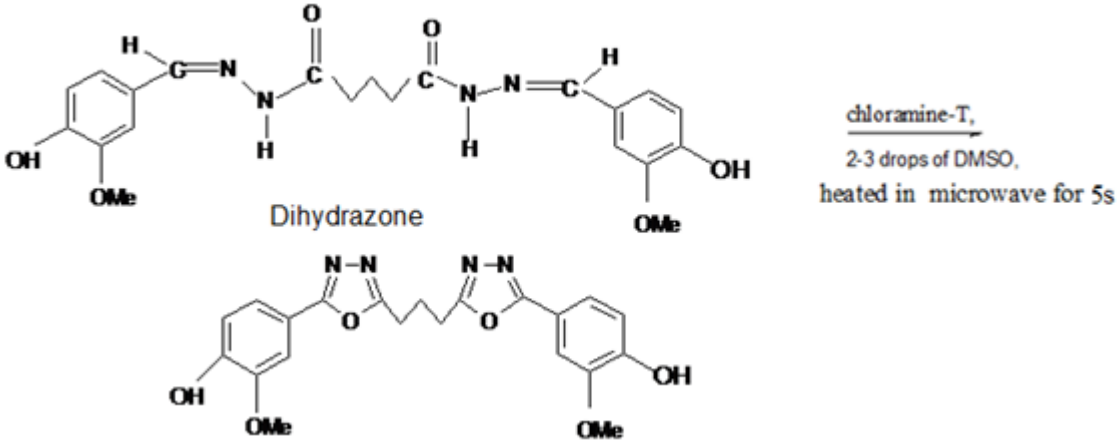
Synthesis of 1, 3 - bis [5 - (3 - methoxy - 4 - hydroxyphenyl) - 1, 3, 4 - oxadiazol - 2 - yl] propane:
The synthesis is carried out in two stages:

a) Synthesis of bis (3 - methoxy - 4 - hydroxybenzaldehyde) glutaroyldihydrazone:
To the alcoholic solution of glutaric acid dihydrazide (0.01 mol), vanillin (0.02 mol) was added and mixture was refluxed in alcohol with continuous stirring for 1½ h. The corresponding hydrazone obtained was separated, washed several times by alcohol. [27]



Yield = 90%, **M. P.** = 158°C
IR (ν cm⁻¹KBr): 1602 (C=N), 1640 (C=O), 3194 (N - H) & 3401 (O - H)

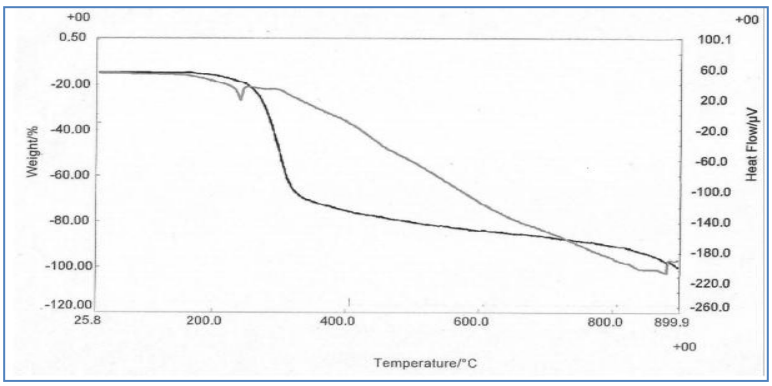
b) Synthesis of 1, 3 - bis [5 - (3 - methoxy - 4 - hydroxyphenyl) - 1, 3, 4 - oxadiazol - 2 - yl]propane: C4
To a mixture of bis (3 - methoxy - 4 - hydroxybenzaldehyde) glutaroyldihydrazone (0.006 mol) and chloramine - T (0.012 mol), 2 - 3 drops of DMSO were added. Addition of DMSO brought both reactants in liquid phase. The reaction mixture was heated in a microwave for 5s. The reaction mixture was cooled followed by addition of alcohol. The product obtained was separated by filtration was washed several times with alcohol and recrystallised.



1, 3 - bis [5 - (3 - methoxy - 4 - hydroxyphenyl) - 1, 3, 4 - oxadiazol - 2 - yl]propane
Yield= 90 % **M. P.** =209°C;
IR (ν cm⁻¹KBr): 1624 (C=N), 1056 (N - N), 1266 and 1146 (C - O - C);

^{1}H nmr (δ ppm, DMSO - $d_{6,}$): 1.87 (p, 2H, ring - C - CH_2 - , J=6.0), 2.24 & 2.65 (t, 4H, 2 x ring - CH_2 - , J=6.1), 3.79 (s, 6H, 2x –OCH_3), 7.68 - 7.90 (m, 6H, Ar - CH, J=8.5).

The TG/DTA analysis:



The TG/DTA curves indicate that the compound is thermally stable up to 250^0C. The DTA peak shows an endothermic peak at 225^0C due to decomposition of the compound and the second endothermic peak at 890^0C due to pyrolysis of the compound.

2. Conclusion

The oxidative cyclisation of bis (3 - methoxy - 4 - hydroxybenzaldehyde) glutaroyldihydrazone to 1, 3 - bis [5 - (3 - methoxy - 4 - hydroxyphenyl) - 1, 3, 4 - oxadiazol - 2 - yl] propane under microwave irradiation using chloramines - T as a cyclising agent is rapid, clean and energy saving.

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