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DESIGN, MICROWAVE ASSISTED SYNTHESIS AND CHARACTERIZATION OF OXADIAZOLES

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ABSTRACT

A series of 1,3,4-oxadiazole derivatives have been synthesized by microwave irradiation method. Microwave assisted organic synthesis is a simple, easy, efficient, economical and eco-friendly for the synthesis of a number of molecules. The main advantages of the microwave assisted reactions are rapid and improved yields and quality of the product. The various carboxylic acid components have been made use in the cyclocondensation reaction with semicarbazide by conventional and microwave irradiation methods in the presence of concentrated sulphuric acid. The products obtained from microwave synthesis have been purified and characterized by their physical and analytical data.

KEYWORDS: Oxadiazole, Microwave synthesis, Ecofriendly, Semicarbazide.

INTRODUCTION

In the recent year microwave assisted organic reaction has emerged as new tool in organic synthesis. The reactions are very fast and are completed within short times and purity enhanced as compared with conventional heating methods.[1] Literature survey reveals that among the heterocyclic compounds, 1,3,4-oxadiazole is an important moiety for development of new drugs. Several of their derivatives are reported to exhibit a variety of biological and pharmacological activities, viz., antibacterial[2], anti-inflammatory[3], antitubercular[4], antidiabetic[5], anticancer[6], antioxidant[7] and anticonvulsant.[8] Hence, this field has-ever-growing importance resulting in the development scores of oxadiazoles. The various carboxylic acid components have been made use in the cyclocondensation reaction with

semicarbazide by conventional and microwave irradiation methods in the presence of concentrated sulphuric acid. In conventional method the reaction mixture was heated on reflux for 2- hours on a water bath. The synthesis of oxadiazoles was subjected to the microwave irradiation at 180 W for 3-6 min, with a pulse rate of 30 sec, each in a domestic Samsung microwave oven. The products are obtained by microwave methods are in quantitative yields and excellent purities. The product obtained in each of such reactions was purified and characterized as 2-amino-5-substituted 1,3,4-oxadiazole.

MATERIALS AND METHODS

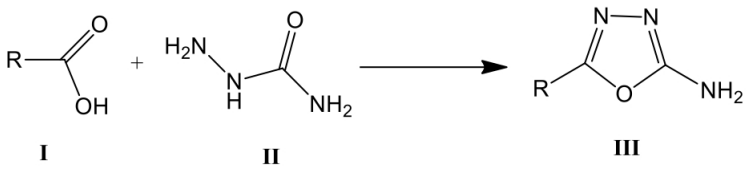
Experimental procedures are given as general methods. A domestic Samsung microwave oven was used for microwave irradiation synthesis. All melting points were determined in open capillaries using Toshnwal melting point apparatus. Infra-red spectra of the compounds were recorded in KBr pellet using Bruker FTIR spectrometer.

Experimental Work

Synthesis of 2-amino-5-substituted-1,3,4-oxadiazole derivatives

Plan of Work and Scheme-I

It is planned to synthesize a new series of 2-amno-5-substituted 1,3,4-oxadiazoles containing different alkyl/aryl/substituted aryl groups at C-5 position. The various carboxylic acid components have been made use in the cyclocondensation reaction with semicarbazide by conventional and microwave irradiation methods. The synthesis of the title compounds has been effected as outlined in **Scheme-I**.



I **II** **III**

Scheme-I

General Procedure

Conventional Method (Method-A)

Appropriate aliphatic or aromatic carboxylic acid (0.05 M) and semicarbazide hydrochloride (0.05 M) were taken into a RB flask and dissolved in alcohol (25 mL) by shaking. To this, concentrated sulphuric acid (10 drops) was added while shaking and the reaction mixture was heated under reflux for 2-3 hrs, on a hot water bath. After completion of the reaction

(monitored by TLC) alcohol was removed to a possible extent by distillation and the residue was cooled and triturated with crushed ice. The product was filtered, washed with small portion of cold water and dried. It was purified by recrystallization from hot alcohol.

Microwave Irradiation Method (Method-B)

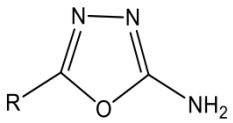
Appropriate aliphatic or aromatic carboxylic acid (0.05 M) and semicarbazide (0.05 M) were taken into a beaker and dissolved in minor quantity of dimethylformamide (10 mL). To this solution concentrated sulphuric acid (10 drops) was added while stirring. A funnel was hanged in the beaker and covered with a watch glass. The reaction mixture was subjected to the microwave irradiation at 180 W for 3-6 min, with a pulse rate of 30 sec, each in a domestic Samsung microwave oven. The solvent was removed by distillation and residue was cooled and triturated with crushed ice. The resultant product was filtered, washed with small portions of cold water and dried. It was purified by recrystallization from hot alcohol.

The product obtained in each of such reactions was purified and characterized as 2-amino-5-substituted 1,3,4-oxadiazole. Physical and analytical data of new 1,3,4-oxadiazoles are presented in **Table-1.**

Spectral characterization data of IIIb

IR (KBr, Cm^{-1}) υ: N-H Stretching = 3342, Aromatic stretching=3014, N=O Stretching=1562, C-N Stretching=1438, C-O-C Stretching=1204.

Table1. Physical and analytical data of 2-amino-5-substituted-1,3,4-oxadiazole derivatives



III

S. No	Compound Code	R	Molecular formula	molecular weight	Method-A (% yield)	Method-B (% yield)	m.p (°C)
1	IIIa	C_6H_5	$C_8H_7N_3O$	161	59	70	112-115
2	IIIb	C_6H_4-4NO_2	$C_8H_6N_4O_3$	206	67	86	232-235
3	IIIc	C_6H_4-4Cl	$C_8H_6N_3O_6$	195	63	78	192-200
4	IIId	C_6H_4CH=CH	$C_{10}H_9N_3O$	187	52	73	110-120
5	IIIe	C_6H_4-4NH_2	$C_8H_8N_4O$	176	68	89	240-245
6	IIIf	C_6H_4-2OH	$C_8H_7N_3O_2$	177	59	74	128-130

RESULTS AND DISCUSSION

A series of 2-amino-5-substituted 1,3,4-oxadiazole compounds have been synthesized by a rapid microwave irradiation method. The newly synthesized compounds have been purified either by recrystallization from suitable solvents or by the column chromatography techniques. The synthesized compounds have been characterized the with the help of their analytical and spectral data. The MWI method has a significant increase in yields with a shorter reaction times have been recorded in the solvent MWI method. All the synthesized drugs have given appreciable yield with reduced reaction times.

CONCLUSIONS

From the above result, it would be concluded that the microwave assisted method is very convenient method due to enhanced reaction rates, higher yields, improved purity, ease of work up after the reaction and eco-friendly reaction conditions compared to the conventional methods. Microwave irradiated synthesis of 1,3,4-oxadiazoles was carried out to get higher yield with less reaction time period as compared to conventional method.

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