JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

An efficient one-pot synthesis of fluorinated 1,3,4-thiadiazole derivative by under microwave irradiation and ultrasonic irradiation.

[1]Satish B. Kamble, [2]Narendra P. Surse, [3]Sarthak V. Khedekar, [4]Amit L. Shinde [5]Ram Khalapure.

[1]Department Of Chemistry, J.E.S. College Jalna-431203 India, [2]Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad, Maharashtra 431004, India
[3]Department Of Physics, J.E.S. College Jalna-431203, India [4]Department Of Physics, J.E.S. College Jalna-431203 India
[5]Department Of Chemistry, L.B.S. Sr. College Partur-431501, India

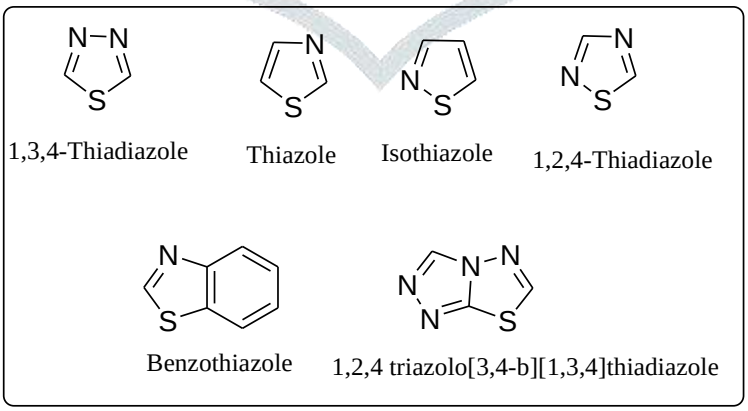
Abstract: An efficient and one-pot synthesis is developed for the fluorinated 1, 3, and 4-thiadiazole derivatives by conventional and modern techniques such as microwave irradiation. The reaction of a fluoro-substituted aromatic carboxylic acid with thiosemicarbazide was carried out in the presence of phosphorus oxychloride under microwave irradiation and ultrasonic irradiation. The compounds were synthesised, and 1H NMR, IR, and mass spectroscopy methods were used to characterize them.

Keywords: One pot, 1, 3, 4-thiadiazole, thiosemicarbazide, microwave irradiation, and ultrasonic irradiation.

INTRODUCTION

1,3,4-thiadiazoles is important and well-known heterocyclic compounds containing nitrogen and sulfur that exhibit a wide variety of biological activities [1,2] .1,3,4] thiadiazole compounds, many of which are known to possess interesting biological properties such antimicrobial [3], antibacterial [4], anticancer [5], antiviral [6], anti-inflammatory[7], anti-oxidant [8] and, antifungal [9,10]. It exhibits the diagnostic section exhibits a complete investigation of the isomeric form and the anticancer activity of bio caster 1,3,4-thiadiazoles due to therapeutic potential [11]

It has been observed that the heterocyclic compounds containing Sulfur and Nitrogen demonstrated outstanding chemical behaviors and a broad spectrum of versatile biological activities. 1,3,4-Thiadiazole, Thiazole, Isothiazole,1,2,4-Thiadiazole, Benzothiazole, 1,2,4 triazole [3,4-b][1,3,4] thiadiazole are some example of Sulfur and Nitrogen-Containing Heterocyclic Compound.



Scheme

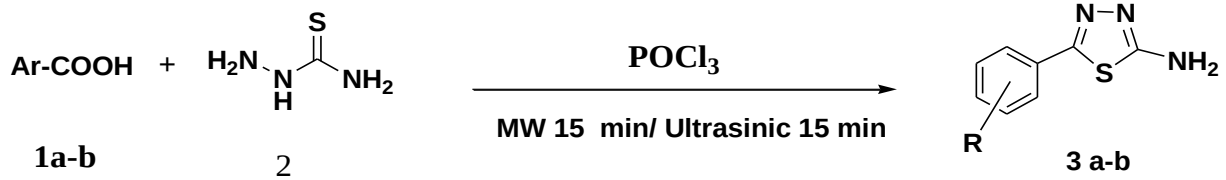


Table 1. Physical data of synthesized compounds 3(a-j) using ultrasonic irradiation method and ultrasonic Condition.

			Microwave Irradiation		Ultrasonic Irradiation		
Entry	Compound	Ar	Reaction Time (min)	Yield (%)	Reaction Time (h)	Yield (%)	M.P.(^{0}C)
1	3a	2-F	15	94	15	93	165
2	3b	4-F	15	95	15	92	235

Experimental: General: All the chemicals and reagents used were of analytical grade and the completion of the reaction and purity of the synthesized compounds was checked by TLC (0.5 mm thickness) using silica gel-G coated Aluminium plates (Merck). Melting points of the compounds were determined in the open capillary tube by digital Melting Point Apparatus and were uncorrected.

Synthesis of 5-phenyl substituted 1, 3,4-thiadiazol-2-amine 3(a-b) under the microwave.

The mixture of substituted aromatic carboxylic acid (0.005mole), thiosemicarbazide (0.005mole), and 1 ml of phosphorus oxychloride were added. The mixture was irradiated under microwave irradiation at 120^{0}C for 15 min. The completion of the reaction was checked by TLC. After completion of the reaction, the RBF was removed from the oven. The reaction mixture was poured onto crushed ice dropwise with continuous stirring, neutralized by saturated KOH. Then filtered, dried, and recrystallized from methanol.

General procedure for one spot Synthesis of 5-phenyl substituted 1,3,4-thiadiazol-2-amine.

The mixture of substituted aromatic carboxylic acid (0. 005 moles), thiosemicarbazide (0.005 mole), and 1ml of phosphorus oxychloride were added. The mixture was irradiated under Ultrasonic irradiation at 110 ^{0}C for 15 min. The completion of the reaction was checked by TLC. After completion of the reaction, the RBF was removed from the oven. The reaction mixture was poured onto crushed ice dropwise with continuous stirring, neutralized by saturated KOH. Then filtered, dried, and recrystallized from methanol.

Spectral data of compound

5-(2-fluorophenyl)-1,3,4-thiadiazol-2-amine (3a)

Yield 93 %, m.p.165 °C; IR spectrum cm^{-1}: 710 (C-S-C stretching), 3345 (**N**H_2 stretching.); 1455 (C=C Ar stretching), 1623 (C=N stretching), 987 (C-F stretching) ,; ^{1}H NMR spectrum, δ, ppm : 6.30 (s,2H, NH_2), 8.12 (dd, J=7.80, 8.4, 1H) , 8.27 (1H, d, J=7.80, 1H), 8.52 (d, J=8.32, 1H), 8.71 (d, J=8.32, 1H). (MS: *m/z*: 196 $(M+H)^+$.

5-(4-fluorophenyl)-1,3,4-thiadiazol-2-amine (3b)

Yield 92 % m.p.235 °C; IR spectrum, ν, cm^{-1}: 610 (C-S-C stretching), 3310 (NH_2 stretching.) ; 1427 (C=C Ar stretching), 1503 (C=N stretching),1072 (C-F stretching) ,; ^{1}H NMR spectrum, δ, ppm :: 6.43 (s,2H, NH_2), 7.48 (d, J=8.92, 2H), 8.92 (d, J=8.92, 2H), (MS: *m/z*: 196 (M +H)

RESULT AND DISCUSSION

An efficient method is pronounced for the synthesis of the 1,3,4-thiadiazole derivative using the one-pot reaction of fluorinated aromatic carboxylic acid and thiosemicarbazide in the presence of phosphorus oxychloride as a catalyst under microwave irradiation and ultrasonic irradiation. The structural elucidation of synthesized compound 3a is based on its IR, ^{1}H NMR, and mass spectral studies. The IR absorption band around 710 cm^{-1} could be attributed to the –C–S–C functional group IR band observed at 3345 is due to NH_2 Group. IR spectrum of **3a** exhibits absorption bands at 1455, 1623, 987 cm^{-1} indicating the presence of C=C, C=N, C-F groups respectively. ^{1}H NMR spectrum peaks due to NH_2 protons appeared at δ:6.30. Peaks for three aromatic protons appeared between 7.12-8.71. Further, the LC mass spectrum showed a molecular ion peak at m/z 195 which is in conform the molecular Structure of **3a.**

ACKNOWLEDGMENT

We are thankful to SAIF Punjab University, Chandigarh for providing the spectral data.

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