AN EFFICIENT AND ONE SPOT SYNTHESIS OF FLUORINATED THIADIAZOLE DERIVATIVE UNDER ULTRASONIC IRRADIATION

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ABSTRACT

We have developed an efficient and one-pot synthesis of fluorinated 1,3,4-Thiadiazole by using fluorinated aromatic carboxylic with thiosemicabazide in the presence of phosphorus oxychloride as a catalyst under ultrasonic irradiation with silica-supported. The synthesis compound was characterized by ^{1}H NMR, IR, and mass spectroscopic techniques. The present approach offers the advantages such as less reaction time, simplicity of the workup procedure, low cost, and mild reaction condition.

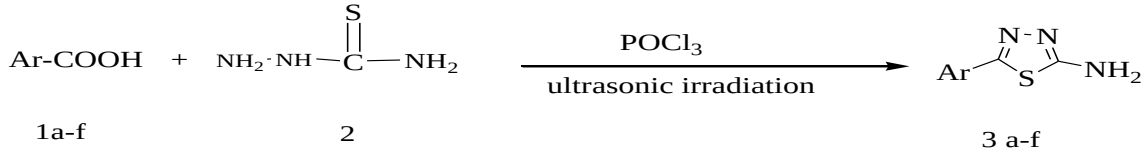
***Keywords**: One Pot, 1,3,4-Thiadazole, thiosemicarbazide, ultrasonic irradiation*

Introduction

Heterocyclic compounds containing nitrogen, and sulfur atoms played an important role in pharmaceutical sciences. Most of the known organic compounds contain heterocyclic rings in their structure. Heterocyclic moieties are found in many compounds that have biological activity that depends mainly on their molecular structure [1,[2]), Due to the importance of nitrogen-containing heterocycles in the pharmaceutical industry, medicinal chemistry, various drug development areas, and their importance in material science enough importance is given to their synthesis and characterization. Nitrogen-containing heterocyclic scaffolds have extensive therapeutic uses such as antimicrobial ([3]), Antibacterial[4], anticancer [5], anti-inflammatory[6], anti-HIV[7], anti-malarial[8]. 1,3,4-thiadiazoles derivatives are five-member with exciting isomeric forms of thiadiazoles [9].Compounds containing a 1,3,4-thiadiazole template have received momentous attention in chemical, medicinal, and pharmaceutical research as this structural scaffold is found in a variety of drugs. 1,3,4-thiadiazole and its derivatives are showing immense importance in medicinal chemistry research due to biological activity as well as producing useful intermediates in several organic preparations.

In the present day, the development of superior synthetic methodologies for industrial applications is becoming immensely significant, especially for the synthesis of organic heterocyclic scaffolds with important medicinal, pharmaceutical, and agrochemical activities.1,3,4-Thiadiazoles are heterocyclic scaffolds incorporated in many compounds presenting various pharmacological activities such as anticonvulsant [10],antiviral [11], anti-inflammatory[12],[13],anticancer[14], antibacterial [15], antimicrobial[16],[17], antiproliferative[18],[19], antioxidant[20], antitubercular[21], antitumor[22], anticancer [23].

Scheme



1a-f 2 3 a-f

Materials and Methods

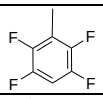
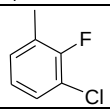
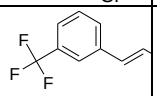
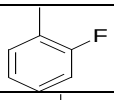
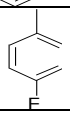
General: All solvents and reagents were purchased from Merck India Ltd and are of AR Grade and used without further purification. Melting Points were determined by the open capillary method and reported as uncorrected. The completion of reaction and purity of the synthesized compounds were checked by TLC (0.5 mm thickness) usingsilica gel-G coated Aluminum plates (Merck).

Synthesis of Fluorinated 1,3,4-thiadiazol-2-amine 3 (a-f) under ultrasonic irradiation.

The mixture offluoro substituted aromatic carboxylic acid (0.01mole), thiosemicarbazide (0.01mole), Silica oxide, and 5 ml of phosphorus oxychloride were added. The mixture was subjected to ultrasonic irradiation at 110^0C for 15for 15–20 min.The completion of the reaction was monitored 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 filter, dried, and re-crystallized from ethanol.

Results and Discussion

Table .1. Physical data of synthesized compounds 3(a-e) under ultrasonic irradiation

Entry	Compound	Ar	Reaction Time (min)	Yield (%)	M.P.(^{0}C)
1	3a		15	91	**222**
2	3b		20	88	**236**
3	3c		15	90	**155**
4	3d		20	90	165
5	3e		15	88	236

An efficient, simple, and one-pot procedure is reported for the synthesis of fluorinated 1,3,4-Thiadiazole derivative in the presence of phosphorus oxychloride under ultrasonic irradiation technique. 1,3,4-Thiadiazole derivatives are synthesized by fluorinated aromatic carboxylic acid under above of mention conditions. The formation of substituted 1,3,4-Thiadiazole derivative was confirmed by recording their IR, ^{1}H NMR, and mass spectral data. The compound 5-(3-Chloro-2-fluoro-phenyl)-[1,3,4]thiadiazol-2-ylamine **(3a).**does not show absorption band at 1702 (carbonyl stretching) broad band at 703 (C-S-C) is present. It shows absorption band at 1009, 1487, and 1607cm^{-1}is for C-F, C=C, C=N, and stretching respectively.^{1}H NMR of compound **3a**showed a broad singlet in the region of δ:7.40 which is due to de-shielded caused by the four fluorine proton, the singlet at 8.00 for the NH_2 of thiadiazole. The mass spectrum of **3a** showed a molecular ion peak at m/z 230 which is in agreement with the molecular formula $C_8H_3F_4N_3S$. in conforming to the Molecular Structure of **3b.**

Conclusions

In conclusion, we have reported an efficient and one-pot method for the synthesis of fluorinated 1,3,4-Thiadiazole by using fluorinated aromatic acid and thiosemicarbazide in of presence phosphorus oxychloride under ultrasonic irradiation. This method offers several advantages, including the low cost, high yields, clean reactions, and short reaction time for the synthesis of one-pot synthesis of 1,3,4-thiadiazole. These derivatives have been given a key to more modifications in pharmacophore replacements.

Data Availability

5-(3-Chloro-2-fluoro-phenyl)-[1,3,4]thiadiazol-2-ylamine (3a)

Yield 84 %, m.p.151◦C; IR spectrum cm^{-1}: 703 (C-S-C stretching), 3385 (**N**H_2stretching.); 1487(C=C Ar stretching), 1607 (C=N stretching),1009 (C-F stretching),; ^{1}H NMR spectrum, δ, ppm : 7.40 (dd, J=7.96, 8.4, 1H) , 7.52(1H, d, J=7.96, 1H), 8.00(s,2H), 8.16(d, J=8.4, 1H). (MS: *m/z*: 230 (M+H)

5-(2,3,5,6-Tetrafluoro-phenyl)-[1,3,4]thiadiazol-2-ylamine (3b)

Yield 82 %, m.p. 222 ◦C; IR spectrum, ν, cm^{-1}: 793 (C-S-C stretching), 3313 (**N**H_2 stretching.); 1413 (C=C Ar stretching), 1595 (C=N stretching),1030 (C-F stretching) ,; ^{1}H NMR spectrum, δ, ppm ::8.02 (s, 1H), 8.01 (s,1H). (MS: *m/z*: 250 $(M+H)^+$.

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Conflicts of Interest

Authors do not have any conflict of interest with any person, institution, or agency

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