SYNERGETIC SYNTHESIS OF 2-ARLYL-[1,2,4]TRIAZOLO[5,1B][1,3,4]OXADIAZOLE-6(5H)-THIONE DERIVATIVES.

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Abstract

A series of [1,3,4] oxadiazole thiones (5) were effectively synthesized by cyclic condensation from the 0.02 mole of compounds 1-(five-phenyl-1,three,4-oxadiazol-2-yl) urea and 0.1/2 mole of thionyl chloride have been refluxed in 50mL of pyridine for 6-8 hours and then the solvent changed into vaporized. In ice-cold water, the focused product was poured. The residue received changed into filtered and recrystallized from ethanol after being rinsed with water. The compounds obtained were in good yields and characterized by spectral analyses like IR, ^{1}H-NMR and Mass.

Keywords: Aryl aldehyde, urea, thionyl chloride and pyridine

1. Introduction

The structural diversity associated with different heterocycles, such as sulfur, oxygen and nitrogen has been found to be a promising pharmaceutical option to treat the disease based on computational designing techniques. Nitrogen containing heterocycles, such as 1,3,4-oxadiazoles and 1,2,4-triazoles, got attention because they could be used to make new drugs. Because these molecules have a good metabolic profile, they are also used as pharmacophores.

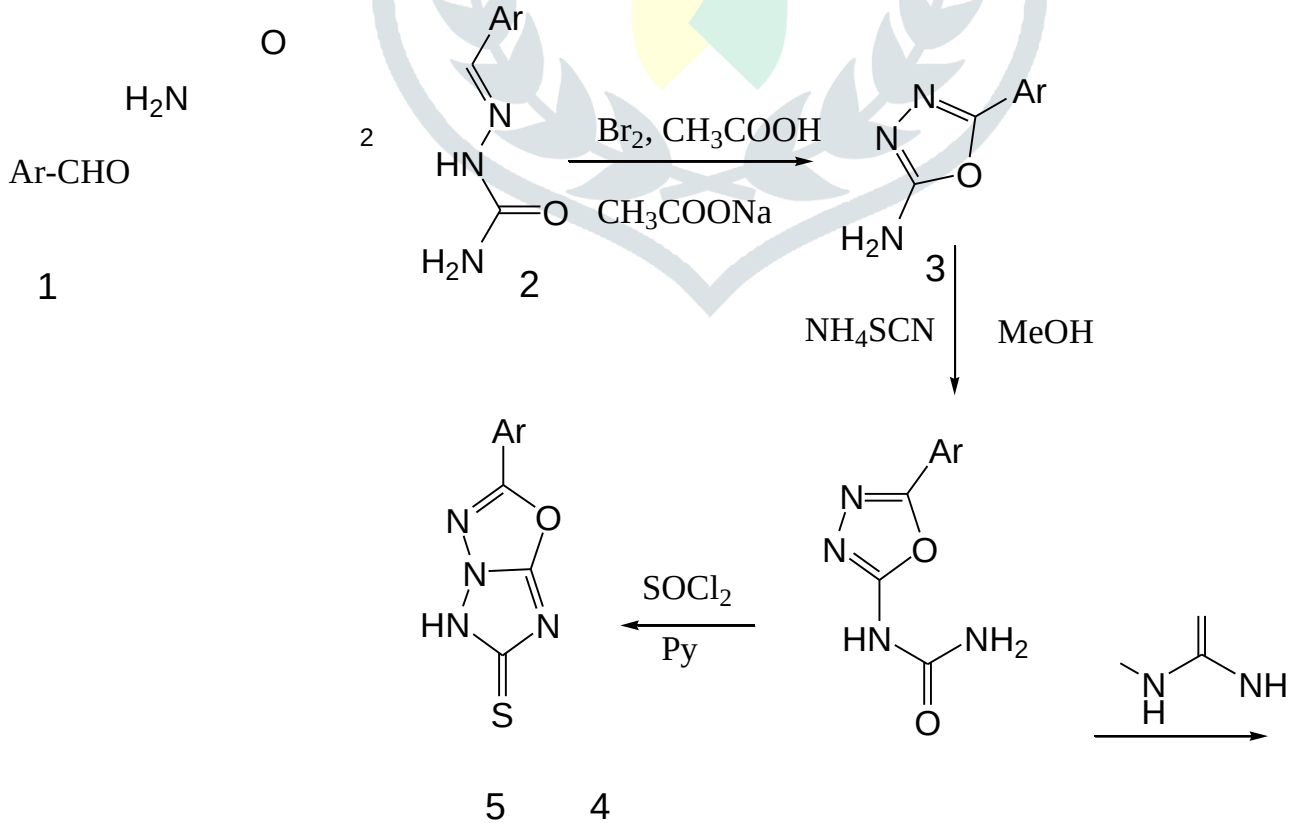
There has been a lot of interest in some of the functional scaffolds and synthetic features of [1,3,4]oxadiazole-6(5H)-thione derivatives posses good biological activities[1-3] such as antiinflammatory[4], antimycobacterial[5], anti-viral[6], anti-cancer[7] [8], antibacterial[9], antitumor[10], and antiprotozoal[11] [12]. In similar, 1,2,3-Triazoles are found to be potent antiinflammatory[13], antimicrobial agents[14], anti-viral[15] [16], anti-cancer[17-19] antibacterial[20], antifungal[21], antioxidant[22], hypoglycemic agents[23]. After thorough review on synthesis of oxadiazoles that emphasized possibilities to enhance heterocyclic synthesis through adopting alternative solvents (which includes water), catalytic transformations, and easy processing, we labored on synthesis of 1,3,4 oxadiazine thiones derivatives and the new derivatives have been suggested.

Reaction of 0.02 mole of compounds 1-(5-phenyl-1,3,4-oxadiazol-2-yl)urea and 0.025 mole of thionyl chloride were refluxed in 50mL of pyridine for 6-8 hours and then the solvent was vaporized. In ice-cold water, the concentrated product was poured. The residue obtained was filtered, and recrystallized from ethanol after being rinsed with water.

2. Experimental Section

All of the chemicals and regents had been commercially available and of studies grade. For sample spotting in skinny layer chromatography AL silica gel 60F254 (E. Merck- Germany) TLC plates were used. new derivatives had been synthesized and characterized on the idea of elemental analysis and spectroscopic techniques which include IR, 1H-NMR and Mass. IR spectra have been recorded using Perkin – Elmer 1000 tool in KBr pellets. 1H NMR spectra were recorded in DMSO – d6 using TMS as inner widespread using 300 MHz spectrometer.

2.1 Scheme:



1-Arylidenesemicarbazide (2)

Aromatic aldehyde (0.05 mole) and semicarbazide (0.05 mole) were dissolved in 60 mL of warm ethanol and 100 mL of warm water, respectively. Both solutions were progressively combined with constant stirring. After cooling, the product was separated, filtered, dried, and recrystallized with 75 percent ethanol.

5-Aryl-1,3,4-oxadiazol-2-amine(3)

Arylidenesemicarbazide (0.01 mole) and sodium acetate (0.02 mole) were dissolved in 30-40 mL glacial acetic acid in a round bottom flask, then slowly added bromine (0.7 mL in 5 mL glacial acetic acid) while swirling magnetically. The solution was poured over crushed ice after half an hour of stirring, to get the solid product. The obtained solid product was filtered, separated, and recrystallized from ethanol.

1-(5-phenyl-1,3,4-oxadiazol-2-yl)urea(4)

Ammonium thiocyanate (0.05 mole) was prepared as an aqueous solution in 5 mL water and diluted to 20 mL. The solution was heated to 90 degrees Celsius. Drop wise additions of **5-Aryl**1,3,4-oxadiazol-2-amine (0.05 mole) were made with moderate stirring. After that, the mixture was reduced to a thick yellow mass by boiling it. The resulting substance was then quickly mixed with crushed ice. The solid product obtained was filtered, dried, and recrystallized using an ethanol-water [1:2] mixture.

2-Arlyl-[1,2,4]triazolo[5,1-b][1,3,4]oxadiazole-6(5H)-thione(5)

0.02 mole of compounds 1-(5-phenyl-1,3,4-oxadiazol-2-yl)urea and 0.025 mole of thionyl chloride were refluxed in 50 mL of pyridine for 6-8 hours and then the solvent was vaporized. In ice-cold water, the concentrated product was poured. The residue obtained was filtered, and recrystallized from ethanol after being rinsed with water.

Spectral Data

2-(4-chlorophenyl)-[1,2,4]triazolo[5,1-b][1,3,4]oxadiazole-6(5H)-thione(5a)

Pale yellow solid compound; Yield: 60%; M.P. 210 °C; IR (cm−1) KBr: 3434.62 (NH), 1599.95 (C=C), 742.19 (C-Cl); 1H-NMR (DMSO-d6); 11.2 (s, NH, 1H), 7.4-7.8 (m, 4H, Ar-H); MS (m/z) 268 (M+).

2-(2-chlorophenyl)-[1,2,4]triazolo[5,1-b][1,3,4]oxadiazole-6(5H)-thione(5b)

Pale yellow solid compound; Yield: 60%; M.P. 210 °C; IR (cm−1) KBr: 3434.62 (NH), 1599.95 (C=C), 742.19 (C-Cl); 1H-NMR (DMSO-d6); 11.2 (s, NH, 1H), 7.4-7.8 (m, 4H, Ar-H); MS (m/z) 268 (M+).

2-phenyl-[1,2,4]triazolo[5,1-b][1,3,4]oxadiazole-6(5H)-thione(5c)

Orange colour powder compound; Yield 65%; M.P.: 205°C; IR (cm−1) KBr: 3388.75 (NH), 1620.40 (C=C), 3115.11 (C-H); 1H-NMR (DMSO-d6); 11.4 (s, 1H, NH), 7.6-7.8 (m, 5-H, ArH); MS (m/z) 234 (M+).

3. Results and Discussion

The synthesis of 1,3,4 oxadiazine thiones was described as outlined in the scheme. Aryl[1,2,4]triazolo[5,1-b][1,3,4]oxadiazole-6(5H)-thione synthesized from starting material Aromatic aldehyde (0.05 mole) and semicarbazide (0.05 mole) were dissolved in 60 mL of warm ethanol and 100 mL of warm water, respectively which forms Arylidenesemicarbazide (2). Compound 2 reacts with sodium acetate (0.02 mole) were dissolved in 30-40 mL glacial acetic acid in a round bottom flask, then slowly added bromine forms compound (3). Ammonium thiocyanate (0.05 mole) was prepared as an aqueous solution in 5 mL water and diluted to 20 mL. The solution was heated to 90 degrees Celsius. Drop wise additions of **5-Aryl-**1,3,4-oxadiazol-2-amine (0.05 mole) were made with moderate stirring. After 0.02 mole of compounds 1-(5-phenyl-1,3,4oxadiazol-2-yl)urea and0.025 mole of thionyl chloride were refluxed in 50 mL of pyridine for 68 hours and then the solvent was vaporized. In ice-cold water, the concentrated product was poured. The residue obtained was filtered, and recrystallized from ethanol after being rinsed with water. The reaction mixture was homogenised by refluxing it for the required amount of time. The remaining solvent was allowed to evaporate, and the resulting crude product was refined by column chromatography on silica gel eluted with EtOAc-n-hexane (2:8), yielding pure 1,8naphthyridine derivatives after crystallisation with hot ethanol. The structure of the compound **5a** was confirmed by IR, ^{1}H NMR and mass spectra. In IR spectrum of **5a**, the (NH) absorption bands appeared at 3434.62,, cm^{-1}. The ^{1}HNMR spectrum of the compound **5a** showed signals in the range of 11.2 for (s, NH, 1H), 7.4-7.8 (m, 4H, Ar-H) for aromatic ring. The mass spectrum of the same compound 3a showed molecular ion peak at m/z 268 (M+). Further, the structure of other derivatives **5b** and 5c was characterized in similar manner as 5a.

4. Conclusion

An unconventional synthetic strategy was employed to synthesize all of the targeted 1,3,4 oxadiazole derivatives as part of our ongoing research and development of a greener, more flexible, and efficient method for the synthesis of heterocyclic molecules. Over traditional approaches, the above method offers significant advantages, such as greater selectivity, simplicity, catalyst-free reaction, and pollution-free settings. 1HNMR, IR, and mass spectrum data were used to evaluate all of the derivatives.

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