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SYNTHESIS OF TRIAZOLOTHIADIAZOLE DERIVATIVES

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ABSTRACT
6-(substituted phenyl)-3-phenyl[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole are nucleus for developing numerous biologically active heterocycle. Cyclization with acids gives five six membered heterocycle derivatives. In this article we report the synthesis of a series of 1,2 4-triazolo-1,3,4-thiadiazoles starting from benzohydrazide obtaining potassium salts which is stir at RT for 16 hrs. to form 1,2,4-triazole which is heat in microwave with substituted acids using phosphorous oxychloride as cyclizing agent.

KEYWORDS: *Triazolothiadiazole, Heterocycle, Microwave, IR, NMR, GCMS*

1. INTRODUCTION

Triazolothiadiazole heterocyclic containing triazolothiadiazole nucleus having immense pharmacological activities. The triazolothiadiazole moiety present in compounds are obtaining for new products which possess most important pharmacological actions. Triazolothiadiazole consist of important class of biologically active drug molecules which has attracted attention of researchers due to their wide range of pharmacological properties. These compounds are being synthesized as drugs by many researchers in order to combine diseases with minimal toxicity and maximal effects. These active compounds provided therapeutic path to develop effective biologically active triazolothiadiazole. [1, 2, 3]

2. MATERIALS AND METHODS

All solvents are of analytical grade and reagents purchased from sigma-aldrich. ^{1}H NMR spectra recorded on Bruker AVANCE III™ 500 spectrometer in DMSO as solvent, using TMS as an internal standard and chemical shifts expressed as ppm. GCMS spectra were determined on Shimadzu GCMS real time analysis while IR spectra done by Bruker IR Solution 8400s. The reaction progress was monitored by TLC pre-coated silica gel G plates.

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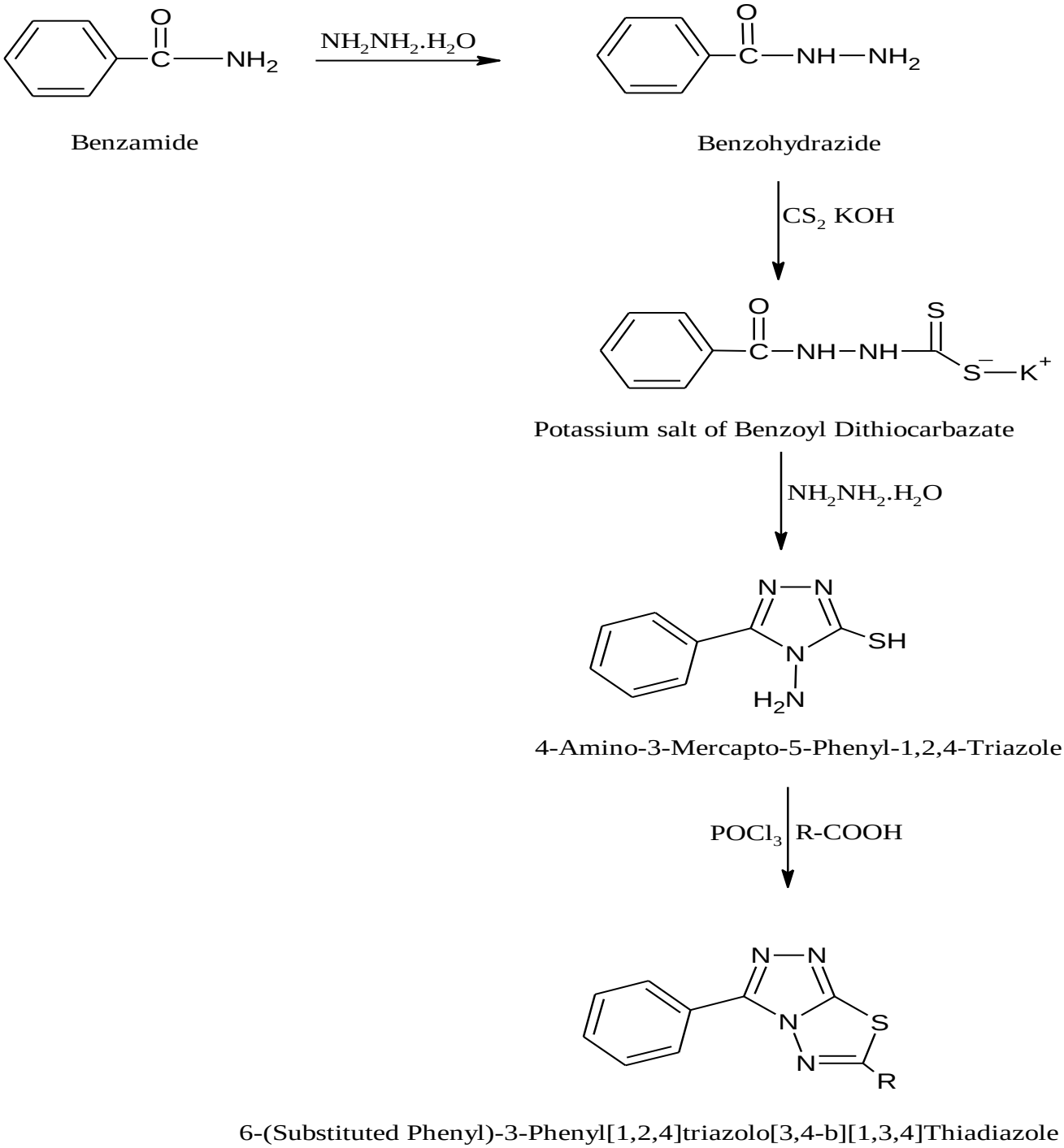
General schemes for synthesis of 6-(substituted phenyl)-3-phenyl[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole



Scheme 1: Synthetic pathway for the compund (R1-R4; Ra1-Ra2)

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2.1 Microwave Synthesis of benzohydrazide (R1)

5gm (0.04M) of benzamide, 2.4mL (0.05M) of hydrazine hydrate were placed in RBF. Reaction mixture was irradiated for 15 min. in microwave oven at 280 watt. The reaction was monitored using TLC. After completion of reaction the reaction mixture was brought to R.T and the precipitated product was filtered. Melting point was determined.

White coloured solid; MF= $C_7H_8N_2O$; MW= 136 gm/mol; MP= 110-112^{0}C; Mobile Phase = Chloroform: ethanol (8:2)

2.2 Microwave Synthesis of potassium benzoyl dithiocarbazate (R2)

To a stir suspension of 1.9gm (0.035M) of potassium hydroxide in 5mL of ethanol, added 4.32gm (0.03M) of benzohydrazide in portion taking care that earlier portion dissolved completely. Later, dropping funnel was clamped over the flask and 2.1 mL (0.035M) of carbon disulfide solution was added with in a period of 2-3 min. in reaction mixture. As the addition of carbon disulfide, yellowish white solid separate out from the solution and finally whole solution thicken up. To this 30ml ethanol was further added and stirred for 16hrs. at R.T. The RM was filtered, the salt prepared was obtained in nearly quantitative yield and was employed without further purification.

2.3 Microwave Synthesis of 4-amino-3-mercapto-5-phenyl-1,2,4-triazole (R3)

6.6gm (0.03M) of suspension of potassium salt in 5mL of ethanol, 2mL (0.04M) of hydrazine hydrate was irradiated for 10 min. in microwave oven at 210 watt. The colour of the RM changes to green with evaluation of H_2S gas, and homogeneous solution resulted. Cold water was added and the solution was slowly acidified with conc. HCl. The precipitated solid was filtered. Melting point was determined.

White coloured solid; MF= $C_8H_8N_4S$; MW= 192 gm/mol; MP= 192-194^{0}C; Mobile Phase = Chloroform: ethanol (8:2)

2.4 Microwave Synthesis of 6-(substituted phenyl)-3-phenyl [1,2,4]triazolo[3,4-b] [1,3,4]thiadiazole (R4)

A mixture of (0.007M) 4-amino-3-mercapto-5-phenyl-1,2,4-triazole and (0.007M) appropriate substituted aromatic acid in (0.2ml) phosphorous oxychloride was irradiated in microwave oven for 5-8 min. at 210 watt. The reaction was monitored using TLC. After completion of reaction the reaction mixture was cooled to RT and gradually poured onto crushed ice. The separated solid was filtered, washed with water. Melting point was determined.

2.5 Microwave synthesis of 6-(2-chloro phenyl)-3-phenyl[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (Ra1)

White coloured solid; MF = $C_{15}H_9ClN_4S$; MW = 312gm/mol; MP = 120-122^{0}C; Percentage Yield = 1.70gm; 80.23%; Mobile Phase = Chloroform: ethanol (8:2); R*f* value = 0.65; ^{1}H NMR (Ar-H:7.5-7.6); FTIR (C=C Ar 1681, C=N Str 1610, C-Cl 742, C-S-C Str 709); GCMS (m/z= 314, 250, 236, 202, 177, 101, 90, 63).

2.6 Microwave synthesis of 6-(4-nitro phenyl)-3-phenyl[1,2,4]triazolo[3,4-b] [1,3,4]thiadiazole (Ra2)

Pale yellow coloured solid; MF = $C_{15}H_9N_5O_2S$; MW = 325 gm/mol; MP = 167-169^{0}C; Percentage Yield = 2.12gm; 83.33%; Mobile Phase = Chlororfom: ethanol (8:2); R*f* value = 0.59; ^{1}H NMR (Ar-H: 8.1-8.3); FTIR (C=C Ar 1688, C=N Str 1610, C-NO_2 Str 1538, C-S-C Str 714); GCMS (m/z= 325, 261, 247, 152, 137, 101, 90, 76).

3. RESULT AND DISCUSSION

In the present work, a mixture of 1,2,4-triazole and substitued aromatic acid in phosphorous oxychloride was irradiated in microwave oven for 5-8 min. at 210 watt to obtained 6-(substituted phenyl)-3-phenyl [1,2,4]triazolo[3,4-b] [1,3,4]thiadiazole (R4). Further the reaction progress of synthesized compounds was monitored by TLC pre-coated silica gel G plates. Structure of all the synthesized compounds was confirmed by their spectral data interpretation.

4. CONCLUSION

We perform synthesis of a library of synthetic small molecules and identification of triazolo-thiadiazole derivative. The target triazolothiadiazole derivatives synthesized by microwave irradiation as time required for completion of reaction was too less as compare to conventional heating whereas compound synthesized by microwave irradiation was more pure as compare to compounds synthesized by conventional synthesis.

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