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Eco-friendly synthesis of 1,2-dihydro-2,3-dimethyl-1-phenyl-4*H*-pyrazolo[4,3-e][1,2,4]triazin-5(6*H*)-one and 4-(2-(3,5-dimethyl-1*H*-pyrazol-4-yl)diazenyl)-1,2-dihydro-1,5-dimethyl-2-phenylpyrazol-3-one devoid of catalyst

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ABSTRACT

The target molecules 1,2-dihydro-2,3-dimethyl-1-phenyl-4H-pyrazolo[4,3-e][1,2,4]triazin-5(6H)-one and 4-(2-(3,5-dimethyl-1H-pyrazol-4-yl)diazenyl)-1,2-dihydro-1,5-dimethyl-2-phenylpyrazol-3-one were synthesized by eco friendly microwave irradiation. The chemistry of the reactions employed in the synthesis of the target compounds together with their chemical behavior, are discussed and the structures of the newly synthesized compounds were confirmed by the IR and ^{1}H-NMR and Mass spectral data.

Key Words: Pyrazoles, diazenes and Microwave irradiation**.**

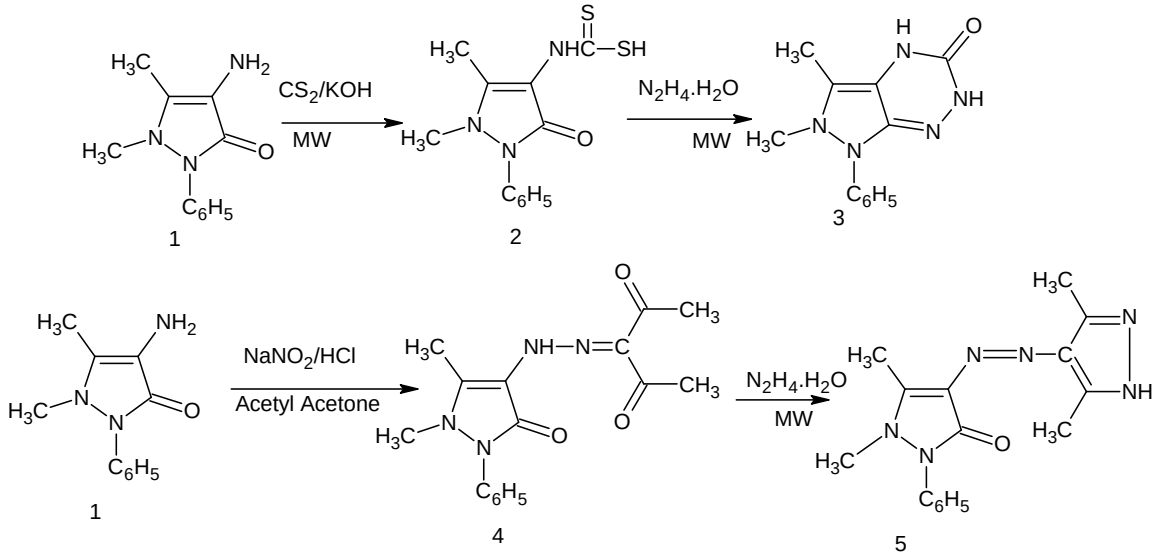
INTRODUCTION

Pyrazole and fused heterocyclic pyrazole derivatives constute an interesting class of heterocycles due to their synthetic versatility and effective biological activities [1-2]. Pyrazolo[3,4-*d*]pyrimidine derivatives have been found to possess antitumor and antileukemia activity[3-6], pyrazolo[4,3-e]- 1,2,4-triazolo[1,5-c]pyrimidine derivatives have been found to be highly potent and selective human A_3[7-10], A_2A[9] and A_2B[10] adenosine receptor antagonists.

Microwave (MW) irradiation has been widely exploited in the last decades to carry out a striking number of organic syntheses, benefiting from the dielectric heating in terms of reduced reaction times and increased yields, especially when coupled with solvent-free techniques. Generally three types of solvent-free procedures can be coupled with dielectric heating provided by a microwave source: reactions among neat reagents, reactions among supported reagents on mineral solid supports and phase transfer catalysis reactions. The neat reagents procedure is doubtlessly the most pursued one due, above all, to its easy work-up and negligible use of solvents for purification/separation stages. One of the most fertile applications in this field, also known as Microwave Assisted Organic Syntheses (MAOS) technique, is heterocyclic chemistry, as reported in a recent review[11]. In particular, the synthetic pathways of pyrazole derivatives represent an interesting topic since these compounds have numerous applications in the pharmaceutical and agrochemical industry[123].

In view of this we under took synthesis of 1,2-dihydro-2,3-dimethyl-1-phenyl-4*H*-pyrazolo[4,3-e][1,2,4]triazin-5(6*H*)-one and 4-(2-(3,5-dimethyl-1*H*-pyrazol-4-yl)diazenyl)-1,2-dihydro-1,5-dimethyl-2-phenylpyrazol-3-one by microwave irradiation.

Scheme



1 2 3 1 4 5

MATERIALS AND METHODS

Chemicals and solvents were reagent grade and used without further purification. Melting points were determined on a capillary melting point apparatus and are uncorrected. The ^{1}H NMR spectra were recorded in the indicated solvent on a Varian 500 MHz and 200 MHz spectrometer with TMS as internal standard. All chemical shifts (δ) were reported in ppm from internal TMS. Mass spectra were measured on a a Jeol JMS D-300 spectrometer. Infrared spectra were recorded in KBr on Brucher-IFS-66 FTIR spectrophotometer. The homogeneity of the compounds was checked using precoated TLC plates (E.Merk Kieselgel 60 F_{254}).

1-Phenyl-1,2-dihydro-4*H*-pyrazolo[4,3-*e*][1,2,4] triazine-5 (6*H*)-thione (3)
(0.01mole) of potassium hydroxide, compound **(1)** and carbondisulfide were irradiated in microwave oven for 1 min and cooled. Then 1ml of hydrazine hydrate was added and kept in microwave oven for about 30 sec. The solid product was filtered, washed with ethanol.

IR: 3448 cm^{-1} (-NH), 1717 cm^{-1} (C=O), 1636 cm^{-1} (C=N).
^{1}H-NMR in DMSO-d_6 : δ = 2.21(s, 3H), 2.72 (s, 3H), 7.55 to 7.75 (m, 5H), 8.95 (brs, 1H), 9.22 (brs, 1H).
Mass: m/z 242.8 (M+).

4-(2-(3,5-dimethyl-1*H*-pyrazol-4-yl)diazenyl)-1,2-dihydro-1,5-dimethyl-2-phenylpyrazol-3-one (5)
A mixture of compound **(4)** (0.01mole) and hydrazine hydrate (0.02mole) was heated under reflux in ethanol (25ml) for (10-12hrs), cooled and orange solid product was obtained.

IR : 3412 cm^{-1}, (-NH) 1722 cm^{-1}, (C=O), 1558 cm^{-1}, (C-N).
^{1}H-NMR in DMSO-d_6 : δ =2.08(S, 3H), 2.20(S, 3H), 2.38(S, 3H), 2.78(S, 3H), 7.40-7.61 (m, 5H), 13.01(brs, 1H).
Mass: m/z 312.8 (M+H).

CONCLUSION

We have developed an efficient protocol synthesis of 1,2-dihydro-2,3-dimethyl-1-phenyl-4*H*-pyrazolo[4,3-e][1,2,4]triazin-5(6*H*)-one and 4-(2-(3,5-dimethyl-1*H*-pyrazol-4-yl) diazenyl)-1,2-dihydro-1,5-dimethyl-2-phenyl pyrazol-3-one. We also report that the process adopted in this process follows operational simplicity, cleaner reaction, easer work-up and are environmentally co-friendly reactions compared to other methods.

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