Synthesis of some nitrogen heterocycles under microwave irradiation in solventless system

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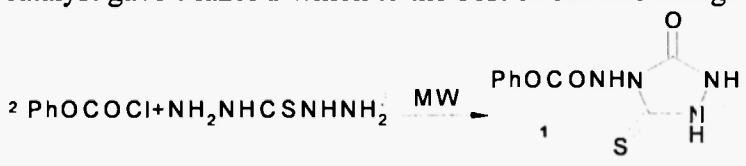
A Superior and fast method of synthesis of some nitrogen heterocycles under microwave irradiation in solventless system is described.

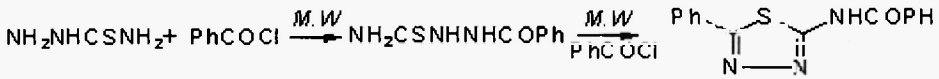
Because of the increasing importance of 1,2,4-triazoles[1] 1,3,4-thiadiazoles[2] and 1,2,4-triazines[3] in the chemical literature , we felt that an approach to the synthesis of these heterocyclic systems simpler, faster and in more eco-freindly condition than those hitherto described would be a great value.
Up until now the above compounds have been prepared in two step condensation and cyclization reaction in solvents under classical heating.
There has been considerable attention in the creation and development of ever green and solventless method in organic methodology[4] dictated by stringent environment protection laws[5]. Organic solvents are not only expensive but are often flammable, toxic and environmentally hazardous.
Microwave irradiation in organic synthesis is a useful technique nowadays[6].Dery media using microwave thermolysis have attracted much attention because it omits the use of hazardous and relatively expensive organic solvents and the reaction can be conducted in open vessels[7].
Solvent-free organic reactions or dry media techniques under microwave irradiation are one of the main topics of research in our laboratory[8].We have recently reported the synthesis of heterocyclic systems under microwave irradiation in solventless system[9].In view of current trust on solventless system , there is merit in developing a truly solvent-free condition for synthesis of heterocyclic systems.Herein we wish to report our results for the synthesis of some useful basic heterocyclic system which are interesting from the biological point of view as well as being used as precursor for synthesis of fused bicyclic heterocycles.
1,2,4-Triazoles have attracted much attention as pharmacological target[1].These compounds can be prepared by various methods[10].One pot reaction of phenyl chloroformat with thiohydrocarbazide under microwave irradiation without solvent and catalyst gave triazol **1** which to the best of our knowledge has not yet been reported.



Scheme 1

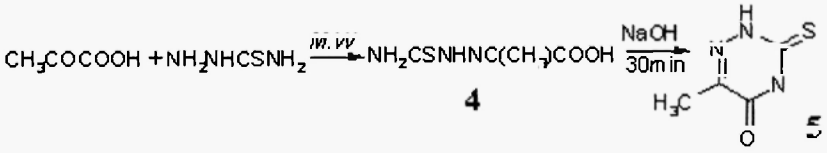
Thiadiazoles are important group of heterocyclic compounds that hold a special place among pharmaceutically important natural and synthetic materials[2].
2-Benzimido-5-phenyl-1, 3, 4-thiadiazole[11]**3** was obtained by one pot reaction of benzoyl chloride and thiosemicarbazide under microwave irradiation in solventless system.

It is notworthy to mention that upon exposure to microwave for only 30 sec the intermediate **2**can be isolated which is condensed and cyclized in the reaction with more benzoyl chloride to afford **3**.



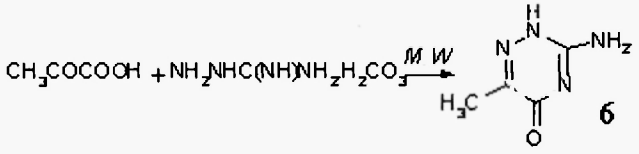
2 **3** Scheme 2

Thiosemicarbazone of pyruvic acid **4**,was obtained from the reaction of thiosemicarbazide and pyruvic acid under microwave irradiation for 2 min .We could not cyclize **4** to the corresponding 1,2,4-triazine[12] **5** under microwave irradiation. However **4** can be cyclized to **5** by refluxing in NaOH for 30 min.



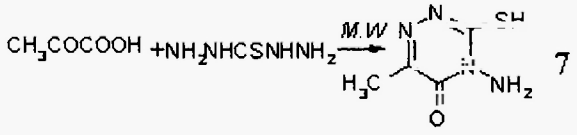
4 **5** Scheme 3

6-Methyl-3-amino-1, 2, 4-triazin-5-one[13] **6** was synthesized in a one pot reaction of aminoguanidinium hydrogen carbonat with pyruvic acid under microwave irradiation in slventless system in 3 min.



6 Scheme 4

One pot reaction of pyruvic acid and thiocarbohydrazide under microwave irradiation gave 4-amio-6-methyl-1, 2, 4-triazin-5-one[14]**7**.



7 Scheme 5

In conclusion,these procedures for the synthesis of above heterocycles have some advantages over the existing methods and will make a useful and important addition to the present methods.The main advantages of this new method are mild reaction condition,reduced reaction times, high yields and lack of expensive and hazardous solvents.

Experimental

The melting points were obtained using an Electrotermal IA 9100 Digital Melting Point. The IR spectra recorded on a 4300 Shimadzu spectrometer.^{1}HNMR spectra were recorded on a 500 MHZ spectrometer using TMS as internal standard.

General procedure

Two reactants (equivalent mole,in the case of products 1 and 3,two moles of phenyl chloroformate and benzoyl chloride) were mixed in a beaker thoroughly using a spatula. The beaker is placed in a microwave oven for the specified time. The crude was then crystallized from appropriate solvent.

Selected data for 1
Irradiation time 9min (900W), m.p 215^{0}C from methanol, yield 65%.
IR:(KBr disk)3340,3300,3200,175o,1590,1490,1275cm^{-1}.
^{1}HNMR:δ(d_6DMSO):7.17(s,1H,NH),7.33(,5H,Ph),9.88(s,1H,NH),10.4(s,1H,NH).
MS, m/e,M^+: 158(100),94(98),66(34), 252(34) 39(29).

Selected data for 3
Irradiation time 3min (360W), mp 220^{0}C from ethanol, yield 85%.
^{1}HNMR: δ(d_6-DMSO),7.55(m,5H,Ph),7.67(m ,1H,aromatic),7.98(m,2H,aromatic), 8.12(m,2H,aromatic),3.19(s,1H,NH).

Selected data for 5
Irradiation time 2min (900W), mp 180^{0}C from water (Lit[12] mp=181-3^{0}C), yield 90%.

Selected data for 6
Irradiation time, 3min (900W), mp>300^{0}C from water (Lit[13] mp>300^{0}C), yield 83%.
^{1}HNMR :δ(d_6-DMSO),1.9(s,3H,CH_3),3.7(s,2H,NH_2),6.5(s,1H,NH).

Selected data for 7
Irradiation time 5min (900W), mp 180^{0}C from water (Lit[14] mp =181-3^{0}C), Yield 90%.

Acknowledgments
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Caution
Although we did not have any accident,using of microwave oven in an efficient hood is highly recommended.

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