

A Novel Microwave Assisted Solvent-Free General Route to 2-Amino Imidazoles

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In an attempt to exploit the synthetic utility of microwaves in heterocyclic chemistry, 2-amino imidazoles were synthesized with various substituents at 4th and 5th positions of imidazole ring. Several aroins were also prepared by microwave irradiation using inorganic solid support and have been reacted with guanidine nitrate to give 4,5-substituted 2-amino imidazoles in very good to excellent yields.

Key Words: Aroins, 2-Amino imidazoles, Microwave irradiation, Solid support, Alumina, Zeolite.

INTRODUCTION

Imidazoles are anti-metabolites and inhibitors of histamine and are used as insecticides. They have anti-bacterial, antifungal, anti-protozoal and anthelmintic activity. Imidazole containing reagents have found useful applications in a variety of organic transformations like olefin metathesis¹, cross coupling reactions², chiral auxiliary³, etc. The literature survey revealed that very few methods are recently reported for the synthesis of substituted imidazoles⁴⁻⁶. Solvent free microwave assisted synthesis of 2,4,5-substituted imidazoles from aldehyde and 1,2-dicarbonyl compounds in the presence of ammonium acetate and alumina is reported⁷.

Solution phase microwave organic reactions have some limitations, such as the possibility of super heating of the solvents, which may result in serious explosions^{9,10}. Microwave activated dry media synthesis on solid inorganic supports is the most efficient ecofriendly technology^{11,12}. Reactions can be carried out easily at ambient pressure in open vessels by using domestic microwave ovens¹³. Moreover, the use of solid catalysts reduces the amount of toxic wastes and by product formation¹⁴. Hence, microwave assisted synthesis of benzoin, furoin and anisoin in presence of neutral alumina as solid is reported.

EXPERIMENTAL

Melting points were recorded by open capillary method and are uncorrected. Beta zeolite was obtained from Sud-Chemie India Ltd., New Delhi. The IR spectra

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were recorded on a Perkin-Elmer FTIR-1600 spectrometer; PMR (90 MHz) spectra on a Varian Perkin-Elmer R-32 spectrometer (chemical shifts ppm) with reference to TMS as internal standard. Microwave irradiation was carried out in a Samsung domestic oven (model CE 2733G) operating at 2450 MHz. The purity of the compounds was checked on pre-coated silica gel plates (Merck).

General Procedure for the Synthesis of Aroins (3a–d)

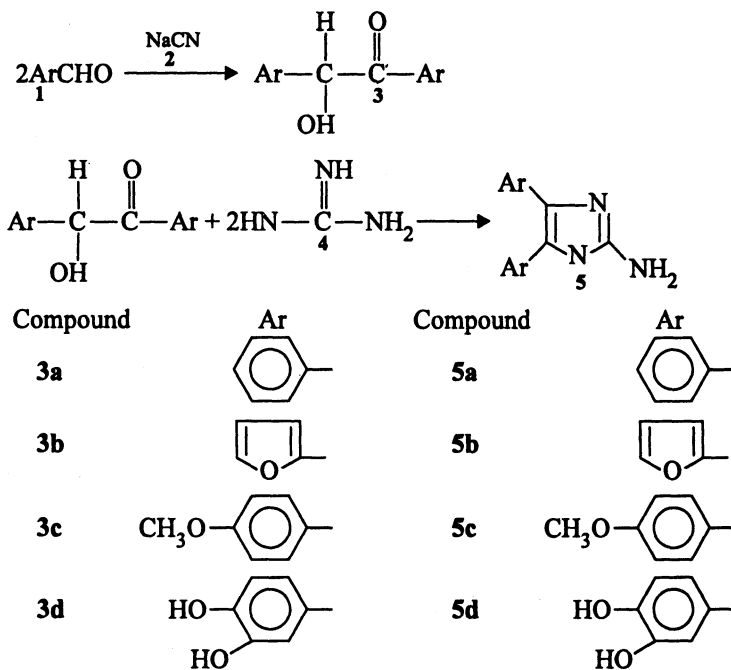
Solid Support Microwave Irradiation Technique: A mixture of aldehyde **1** (2 mmol) and sodium cyanide (**2**) (2 mmol) dissolved in ethanol (10 mL) was taken in a beaker and adsorbed over neutral alumina (1 g). The reaction mixture was air dried, kept in an alumina bath and irradiated in microwave oven for specified period of time (Table 1). On completion of reaction (monitored by TLC at an interval of every 30 s) the product was extracted into ethanol (30 mL). Solvent was recovered under reduced pressure and the product was purified by recrystallization.

TABLE-1
COMPARISON BETWEEN CLASSICAL AND MICROWAVE PROCEDURES

Compound	Classical conditions		Microwave conditions		m.p.
	Time (min)	Yield (%)	Time (min)	Yield (%)	
3a	30	90	10	98	137
3b	40	37.5	10	75	136
3c	90	23	10	80	106
3d	90	35	10	78	128
5a	120	65	15	85	110
5b	150	60	20	85	172
5c	150	58	20	80	155
5d	165	62	20	82	150

Typical Procedure for the Synthesis of 2-amino 4,5-biphenyl imidazole **5a** (Scheme-1)

To a mixture of benzoin (1.05 g, 0.005 mol) and guanidine nitrate (0.61 g, 0.005 mol), beta zeolite 200 mg was added and triturated in a glass mortar and irradiated in microwave oven for 15 min. The reaction was monitored by TLC (ethylacetate : Chloroform 3 : 1). The product was extracted into a mixture of chloroform and ethanol (50 mL) and filtered. The catalyst was washed with mixed solvent (3 times, 10 mL each). The filtrate and combined washings were then concentrated under reduced pressure. The residue obtained was recrystallized from ethanol.



Scheme-1

Classical synthesis

To a mixture of benzoin (1.05 g) and guanidine nitrate (0.61 g), ethylene glycol (15 mL) was added and shaken. The suspension was refluxed in an oil bath for 2 h. The solution was then poured on to 30 g of crushed ice with stirring and set aside for 1 h. A pale yellow precipitate that settled was filtered and dried.

RESULTS AND DISCUSSION

Synthesis of diaryl hydroxyl ketones (aroin)s generally involves high reaction time and the product is isolated in very low yield. These disadvantages have been overcome by the microwave irradiation technique and better results in terms of yield and reaction time were observed. The enhancement in rate of reaction may be due to the fact that alumina acts as catalyst.

The spectral data for **3a–d** are in accordance with the structures. Synthesis of 2-amino imidazoles by classical method is also the first report of its kind. This involves heating at higher temperature in a conventional oil bath increasing the risk of accidents. The reaction can be easily carried out in a domestic microwave oven reducing the reaction time and the product is obtained in a better yield. Zeolites are molecular sieves which are employed as catalysts for the clean and economical process for the production of organic compounds^{15–18}. The spectral data are as follows:

5a: 4,5-biphenyl-2-amino imidazole; IR: 710, 1260, 1350, 1650, 3500; PMR: 3.8, 5.5.

5b: 4,5-difuryl-2-amino imidazole; IR: 1250, 1350, 1650, 3600; PMR: 3.8, 5.5.

5c: 4,5-di(4-methoxy phenyl)-2-amino imidazole; IR: 1350, 1380, 1650, 3030; PMR: 3.8, 5.5, 6.87, 7.17.

IR data is discussed for **3c** as representative case. It gave peaks at 3030 for aromatic compounds, 3500 for primary amines, 1350 for secondary amines, 1250 for cyclic, C—O stretching. PMR: chemical shift at 3.73 for CH₃—O (peak area 2), 3.8 for NH₂ (2 protons), 5.5 for NH (1 proton), 6.87 for *p*-substituted benzene.

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