



A Novel and Environmentally Benign synthesis of Imidazolidinone derivatives

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Received on 4th February and finalized on 19th February 2013.

ABSTRACT

A fast and highly efficient method for the synthesis of imidazolidinone derivatives by cycloaddition of glycine on Schiff's base catalyzed by recyclable indium (III) chloride under microwave irradiation was developed. Microwave assisted reactions have resulted in better yields of the desired products when compared with yield obtained under conventional conditions. Reaction proceeded smoothly and quantitatively at ambient temperature.

Keywords: Imidazolidinone, Cycloaddition, Schiff's base, Microwave.

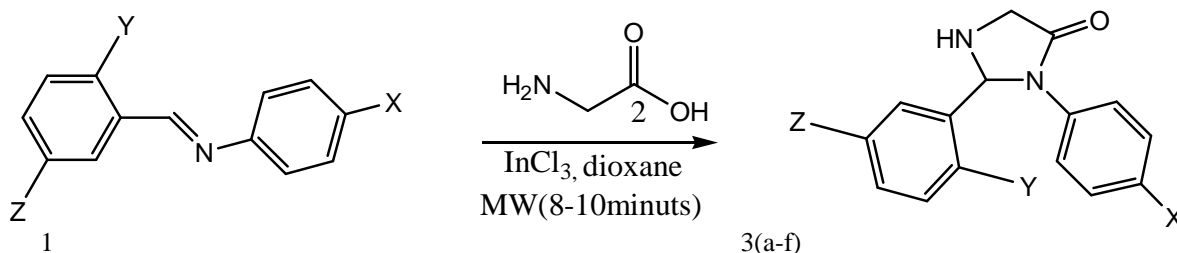
INTRODUCTION

The importance of heterocyclic compounds has long been recognized in the field of synthetic organic chemistry. Among them more attentions is given especially to sulphur and nitrogen containing heterocyclic compounds as they possess a broad spectrum of biological activity and are used in various fields of pharmacy. Imidazolidinone have attracted much attention of synthetic chemists as they have been reported to demonstrate a wide range of pharmacological activities which include antifungal[1,2], anti-bacterial[3,4], anti-tumor[5], anti-cancer[6,7], anti-inflammatory[8] and calcium-channel-blocker[8]. In view of pharmacological importance mentioned above imidazolidinone appear as an attractive scaffold for synthesis of drug like library. Microwave irradiation is well known to promote the synthesis of a variety of organic compounds, where chemical reactions are accelerated because of selective absorption of microwave by polar molecule[13]. As part of our programme towards the non traditional approach to the experimental set up of organic reactions, the concept of "Microwave induced Organic Reaction Enhancement" (MORE) chemistry has been utilized for rapid, sustainable and efficient synthesis. Microwave assisted organic synthesis[14-18] has attracted attention in recent years because of its association with enhanced reaction rates, high yields, improved purity, ease of work up after the reaction and eco-friendly reaction conditions compared to the conventional methods

We report here an efficient method for the synthesis of imidazolidinone involving microwave activation as non-conventional energy source and InCl_3 as heterogeneous Lewis acid catalyst (Scheme1) as part of our program to develop new, simple, selective, eco-friendly methodologies for the synthesis of biodynamic heterocyclic compounds[9-12].

MATERIALS AND METHODS

All chemicals use were reagent grade and were used as received without further purification, ^1H NMR spectra were recorded on a Bruker Avance DPX-400FT spectrometer (1400MHz) using TMS as an internal reference and CDCl_3 as solvent . Mass spectra were recorded on a JEOL SX-102 (FAB) mass spectrometer at 70ev. Melting points were determined by open glass capillary method and are uncorrected. **General Procedure for Synthesis of Imidazolidinone:** Schiff's base were synthesized by usual procedure. Then to a mixture of synthesized Schiff's base (0.01 mol) and glycine (0.01 mol) in 20 ml of dioxane was added indium chloride (0.004 mol) and the reaction mixture was irradiated by microwaves for 2 minutes and mixed outside the oven and again irradiated for 2 min. This mixing and irradiation cycles at regular intervals of 2 minutes continued for the required time of (8-10min). The progress of the reaction was monitored by TLC. The product obtained was dried and purified through column chromatography (70:30 (v/v); ethylacetate : hexane)



Scheme 1: Microwave assisted synthesis of imidazolidinone derivatives using InCl_3 as catalyst

Compound	X	Y	Z
3a	OH	Cl	Br
3b	OH	Cl	OCH_3
3c	OH	Cl	NO_2
3d	OH	Cl	H
3e	OH	Cl	Cl
3f	OH	Cl	OH

RESULTS AND DISCUSSION

Schiff's base (1a-f) required for the synthesis of (3a-f) were synthesized by using procedure described in the literature. Glycine on cycloaddition with (1a-f) gave (3a-f) in which nucleophilic addition of NH_2 group of glycine on electrophilic carbon of Schiff's base. Followed by nucleophilic substitution on carboxylic group yielded (3a-f). The Lewis acid InCl_3 facilitates nucleophilic addition as well as substitution by activating amine and carboxylic acid due to coordination of lone pair of electron with metal. ^1H NMR signal at δ 2.5, confirms that the proton is linked directly to more electronegative atom and peak at δ 4.55 confirmed that the carbon containing protons is linked to atoms other than carbon, The common signals which appears at, δ 8.6 and 6.4 - 7.3 in all compounds were assigned to methylene and aromatic protons respectively. Presence of sulphur and nitrogen's was confirmed by mass spectrometry. All data were fully consistent with assigned molecular structure. Yield of synthesized compounds was excellent (65-85%) and there was considerable reduction in reaction time (table 1).

Table 1: Time and yield of the synthesized compounds

Compound	Time	Microwaves	Yield
3a	10min	MW	85%
3b	9min	MW	75%
3c	8min	MW	70%
3d	9min	MW	65%
3e	10min	MW	75%
3f	9min	MW	85%

3a, 2-(5-Bromo-2-hydroxyphenyl)-3-(4-chlorophenyl)imidazolidin-4-one.

¹HNMR (400MHz, CDCl₃) : δ 2.0 (m, 1H, NH), 3.49 (d, 2H,CH₂), 5.0 (s, 1H, OH), 6.01(d, 2H, CH₂), 6.06- 7.32 (m, 7H, Ar-H)

3b, 3-(4-Chlorophenyl)-2-(2-hydroxy-5-methoxyphenyl)imidazolidin-4-one.

¹HNMR (400MHz, CDCl₃) : δ 2.0 (m, 1H, NH), 3.49 (d, 2H,CH₂), 3.73 (s, 3H, OCH₃), 5.0 (s,1H, OH), 6.01(d, 2H, CH₂), 6.40- 7.32 (m, 7H, Ar-H).

3c, 3-(4-Chlorophenyl)-2-(2-hydroxy-5-nitrophenyl)imidazolidin-4-one.

¹HNMR (400MHz, CDCl₃) : δ 2.0 (m, 1H, NH), 3.49 (d, 2H,CH₂), 5.0 (s,1H, OH), 6.01(d, 2H, CH₂), 6.82- 7.32 (m, 7H, Ar-H)

3d, 3-(4-Chloro-phenyl)-2-(2-hydroxy-phenyl)-imidazolidin-4-one.

¹HNMR (400MHz, CDCl₃) : δ 2.0 (m, 1H, NH), 3.49 (d, 2H,CH₂), 5.0 (s,1H, OH), 6.01(d, 2H, CH₂), 6.61-7.32 (m, 8H, 7Ar-H)

3e, 2-(5-Chloro-2-hydroxy-phenyl)-3-(4-chloro-phenyl)-imidazolidin-4-one

¹HNMR (400MHz, CDCl₃) : δ 2.0 (m, 1H, NH), 3.49 (d, 2H, CH₂), 5.0 (s,1H, OH), 6.01(d, 2H, CH₂), 6.55-7.32 (m, 7H, 7Ar-H)

3f, 3-(4-Chloro-phenyl)-2-(2, 5-dihydroxy-phenyl)-imidazolidin-4-one

¹HNMR (400MHz, CDCl₃) : δ 2.0 (m, 1H, NH), 3.49 (d, 2H, CH₂), 5.0 (s,1H, OH), 6.01(d, 2H, CH₂), 6.36-7.32 (m, 7H, 7Ar-H)

APPLICATIONS

This Micro wave assisted reaction proceeded smoothly and quantitatively at ambient temperature with good yield.

CONCLUSIONS

From the above mentioned results it is concluded that microwave assisted synthesis has proved to be fast and highly efficient method for the synthesis of imidazolidinone derivatives by cycloaddition of glycine on Schiff's base catalyzed by recyclable indium (III) chloride under microwave irradiation. It has resulted in better yields of the desired products when compared with yield obtained under conventional conditions.

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