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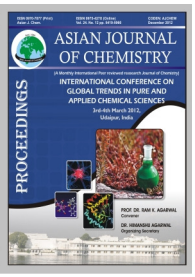

Microwave Assisted High Speed Chemistry, A New Technology for Pharmaceutical Industry†

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Green technologies are required essentially to protect our environment from pollution. Microwave-induced organic reaction enhancement techniques are potentially valuable as they reduce the need for organic solvents and also increase 'atom economy' by improving product selectivity and chemical yield. This method displays both economic and environmental advantages. High yields are achieved even on a gram scale, while reaction times are considerably shortened. Ceric ammonium nitrate has been found to be an efficient catalyst for the solid phase green synthesis of amide derivatives of substituted carboxylic acid with urea in excellent yields under microwave irradiation conditions. Present paper reveals the method of synthesis of some amide derivatives using ceric ammonium nitrate as catalyst and their pharmaceutical application.

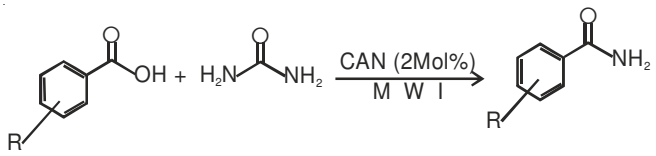
Key Words: Microwave-induced organic reaction enhancement, Atom economy, Ceric ammonium nitrate, Microwave irradiation, Amide derivatives.

INTRODUCTION

Microwave-induced organic reaction enhancement techniques are safe since all the reactions are conducted in open systems to avoid any chance of explosions that have been observed in sealed systems. Microwave-assisted rapid organic reactions constitute an emerging technology that could make industrially important organic synthesis more eco-friendly than conventional reactions[1]. Ceric ammonium nitrate provides both an inexpensive and non-toxic green solution to the synthesis of many amide derivatives of pharmaceutical uses[2]. Microwave may be considered as more efficient source of heating than conventional systems[3,4]. The reactions in solid phase occur more efficiently and more selectivity compared to reactions carried out in solvents. Reactions are simple to handle, reduce pollution, comparatively cheaper to operate and are especially important in pharmaceutical industry. Among the lanthanide reagents, cerium(IV) ammonium nitrate is one of the most important catalyst in organic synthesis[5].

EXPERIMENTAL

The reaction of benzoic acid with urea in the presence of ceric ammonium nitrate (2 mol %) under microwave irradiation gave the corresponding product in 90 % yield.



A mixture of carboxylic acid (1 m mol) and urea (2 m mol) was ground well and mixed with ceric ammonium nitrate (2 mol %). The mixture was irradiated at 160 W for 1 min. On completion of the reaction, the reaction mixture was cooled to room temperature and extracted with ethyl acetate. The extract was washed with a solution of 2M HCl, 5 % $NaHCO_3$ and finally with water. The organic layer was dried over anhydrous $MgSO_4$. The obtained product was purified by simple washing with hexane (Table-1).

RESULTS AND DISCUSSION

The reactions under microwave irradiation were usually completed within 3-5 min, which otherwise require 12 h or more of normal heating[6]. Solvent free organic synthesis and transformations are industrially useful and largely green. The term pollution is used to describe the introduction of harmful substances into the environment as a result of domestic, agricultural or industrial activities. Pollution in any form is harmful to human life and unless checked in time may threaten our survival. The green part of the method is operational

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TABLE-2
PHARMACEUTICAL APPLICATIONS OF AMIDE DERIVATIVES

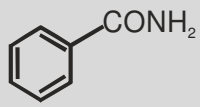
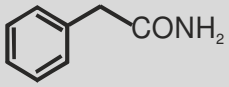
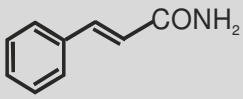
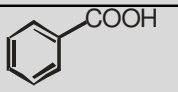
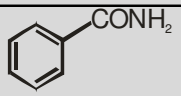
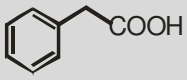
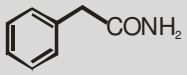
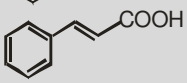
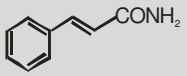
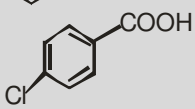
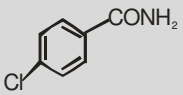
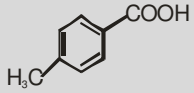
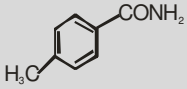
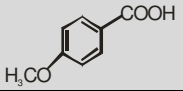
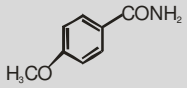
S. No.	Amides	Derivatives	Pharmaceutical Applications
1.		(a) 4-[(methyl sulfonyl) amino] benzamides	Antiarrhythmic
		(b) *N*-(2-hydroxy-4-substituted phenyl) benzamides	Antimicrobial
		(c) Benzimidazolyl benzamide	
		(d) (2-oxochromen-3-yl) benzamides	Antiinflammatory and Analgesic
		(e) N-(4-methyl-2-oxo-2H-chromen-7-yl) benzamides	
		(f) *N*-(β-diethylaminoethyl) benzamide	Tuberculostatic
		(g) *N*-methyl benzamide	Antagonist
		(h) 3,5-disubstituted benzamide	
		(i) 2,2' Dithio (2-hydroxy phenyl) Benzamide (DNBH)	Antibacterial
		(j) Disulfide benzamides	Anti-HIV
		(k) 3-[(2,4-dioxothia zolidin-5-yl) methyl] benzamide	Antidiabetic
		(l) Substituted methylene amide	Cardiovascular disorders
		(m) Benzamide riboside	Antitumor
		(n) Acylaminosalicylic acid amide	Pesticide
2.		(a) 1,3-oxazolidin-3-yl) phenyl acetamide	Antitumor
		(b) Gem-difluoro derivative of phenylacetamide	Antiinflammatory and antirheumatic
		(c) N-substituted phenylacetamide	Antineuropathic Antirheumatiod arthritis & Antiinflammatory
		(d) *N,N*-Diethyl Phenyl acetamide	Insect repellent on foetus and reproduction in rats
		(e) *N*-phenyl phenylacetamide	Anti HIV
		(f) *N*-Substituted Phenylacetamide	Antimicrobial
3.		(a) *p*-Arylthio cinnamide	Antagonist and antiinflammatory
		(b) *N*-(Phenylalkyl) cinnamide	Antagonist
		(c) Piperidinylindoline cinnamide	
		(d) Aminocycloalkyl Cinnamide	Arrhythmia, Analgesics & Anesthetics

TABLE-1
CAN PROMOTED MORE SYNTHESIS OF AMIDE DERIVATIVES

S. No.	Carboxylic acid	Time (s)	Product	Yield (%)
1.		60		90
2.		180		88
3.		90		86
4.		120		86
5.		150		77
6.		180		78

simplicity, faster reaction rates, high conversions and cleaner reaction profile, non-toxic, inexpensive and environmentally friendly. This method is no time one pot synthesis and is a boon for developing pharmaceutical industry in India. The *N*-substituted benzamide derivatives have been reviewed for antibacterial, antinflammatory, analgesic and antiulcer actions[7]. Pharmaceutical compositions of amide derivatives are used as, therapeutic agents for hypertension, angina, pectoris, asthma, renal and peripheral circulatory disturbances and inhibitors of vasospasm (Table-2).

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