Synthesis of Some New of 3- pyrrolin-2-ones under Microwave Irradiation

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Abstract
This study is concerned with the synthesis and characterization of 2- pyrrolinones derivatives. These compounds were prepared by reacting an amine ,an aldehyde and di etheyle acetylenedicarboxylate in an ethanolic citric acid solution offered to microwave irradiation and confirmed of these compounds by using IR,NMR and Mass spectra.
Keywords: pyrroline; imines; synthesis; microwave irradiation.

1. Introduction

Microwave irradiation is a non-traditional energy source that has been widely used in organic synthesis due to significant benefits such as spectacular acceleration, higher yield under milder reaction conditions, higher purity of product by reducing unwanted side reactions and by-products, reduced solvent or reagent usage, and reduced cost.
furthermore, some reactions that do not occur or produce extremely low yields using conventional thermal heating techniques can be achieved in high yields with microwave irradiation. Microwave irradiation, which is analogous to traditional thermal heating, produces rapid intense heating, resulting in a significant reduction in reaction time, increased yield, and purity of products, as well as a green chemistry effect that is beneficial to the environment[1,2]. The simplest 2-pyrrolidinone is named 2-pyrrolidone; it is a typical component of bigger natural products and is sometimes simply referred to as pyrrolone (Fig. 1).

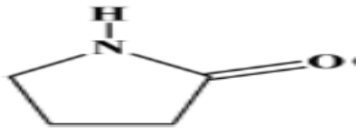


Fig. (1) structure of 2-pyrrolidinone

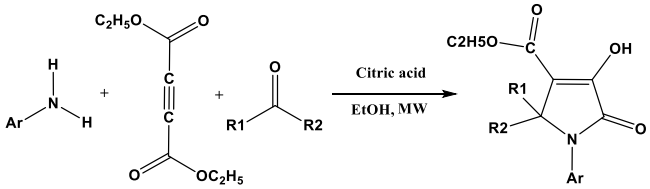
2-Pyrrolidinones are significant chemicals discovered in a variety of medicines and active natural items[3]. Many derivatives of substituted 3-pyrrolin-2-ones containing a 2-pyrrolidinone moiety have exhibited important pharmacological and biological activity, such as anti-cancer agents[4], HIV-1 integrase inhibitors[5], anti-microbial agents[6], antibacterial agents[7], and anti-inflammatory agents are all available[8] pyrrolidinone nucleus is one of the most important heterocyclic rings, with impressive pharmacological characteristics and a wide range of applications in drug development. 2-pyrrolidinone cycle is found in many natural compounds, including bilirubins, oteromycin, and staurosporine[9]. which participate in the living processes of the organisms or show various biological activities.
In this study, we devised a new process for the synthesis of substituted 3-pyrrolin-2-ones in the presence of citric acid as a green additive in a green solvent under ultrasonic irradiation, taking into account the importance of clean chemistry (Scheme1).

2. Experimental

Starting materials were obtained from Sigma-Aldrich (USA) and were used without further purification. The methods used to follow the reactions were TLC.

General synthesis of substituted 2-Pyrrolidinones by Microwave Irradiation

A solution of amine (0.01 mol), diethyl acetylenedicarboxylate (0.01 mol) and ethanol (4 ml) was magnetically stirred at room temperature were added to the mixture, aldehyde or ketone(0.01 mol) and citric acid monohydrate (0.02mol) and the content was stirred at room temperature and the content was offered to microwave irradiation . The progress of the reaction was checked by TLC (n-hexane: EtOAc, 7 : 3). After completion of the reaction, the solid product was filtered, and the pure product was obtained by recrystallization from hot ethanol.



scheme 1 synthesis of substituted 3-pyrrolin-2-ones under microwave irradation

1. Preparation of ethyl 1-(4-bromophenyl)-4-hydroxy-2-(4-methoxyphenyl)-5-oxo-2,5-dihydro-1H-pyrrole-3-carboxylate (1f)

A solution of 4-bromo aniline (0.01mol , 1.72gm) and diethyl acetylene dicar boxylate (0.01 mol,1.2 ml) in ethanol (4 ml) was magnetically stirred at room temperature were added to the mixture of 4-methoxy benzaldehyde (0.01mol, 1.21 ml) and citric acid monohydrate (0.02mol, 3.8 gm) and the content was offered to microwave irradiation for 5 min. The progress of the reaction was checked by TLC (n-hexane: EtOAc, 7: 3). After completion of the reaction, the solid product was filtered, and the pure product was obtained by recrystallization from hot ethanol.

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)-3)-22. Preparation of ethoxycarbonyl)-4-hydroxy-2-(4-methoxyphenyl)-5-oxo-2,5-dihydro-1H-pyrrol-1-yl) benzoic acid(1g)

A solution of 2-amino benzoic acid (0.01 mol , 1.37 gm) and diethyl acetylene dicarboxylate (0.01 mol ,1.2 ml) in ethanol (4 ml) was magnetically stirred at room temperature , were added to the mixture of 4-methoxy benazaldehyde (0.01 mol, 1.21 ml) and citric acid monohydrate (0.02 mol, 3.8 gm) and the content was offered to microwave irradiation for 10 min .The progress of the reaction was checked by TLC (n-hexane : EtOAc, 7: 3). After completion of the reaction, the solid product was filtered, and the pure product was obtained by recrystallization from hot ethanol.

3. Preparation of ethyl 1-(4-(3-(ethoxycarbonyl)-4-hydroxy-2-(4-hydroxyphenyl)-5-oxo-2,5-dihydro-1H-pyrrol-1-yl) phenyl)-4-hydroxy-2-(4-methoxyphenyl)-5-oxo-2,5-dihydro-1H-pyrrole-3-carboxylate(1h)

A solution of p-phenylene di amine (0.01mole,1.08 gm) and diethyl acetylene dicarboxylate (0.02mol 2.4 ml) in ethanol (4 ml) was magnetically stirred at room temperature were added to the mixture of 4-methoxy benazaldehyde (0.02 mol, 2.42 ml) and citric acid monohydrate (0.04 mol, 7.6 gm) and the content was offered to microwave irradiation for 10 min. The progress of the reaction was checked by TLC (n-hexane: EtOAc, 7: 3). After completion of the reaction, the solid product was filtered, and the pure product was obtained by recrystallization from hot ethanol.

4. Preparation of ethyl 1-(4-(3-(ethoxycarbonyl)-4-hydroxy-2-((E)-2-hydroxyprop-1-en-1-yl)-2-methyl-5-oxo-2,5-dihydro-1H-pyrrol-1-yl) phenyl)-4-hydroxy-2-((Z)-2-hydroxyprop-1-en-1-yl)-2-methyl-5-oxo-2,5-dihydro-1H-pyrrole-3-carboxylate(1i)

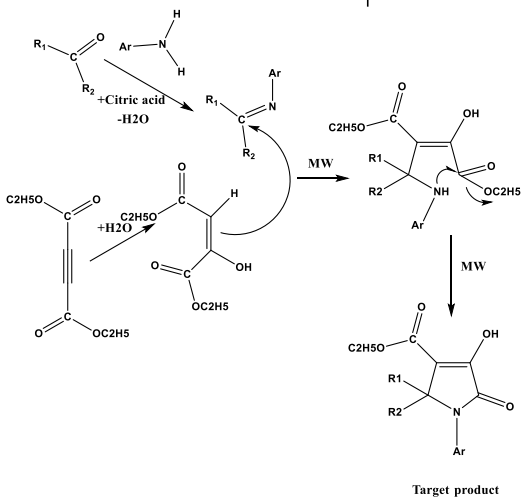
A solution of p-phenylene diamine (0.01 mol , 1. 08 gm) a diethyl acetylene dicarboxylate (0.02mol,2.4 ml) in ethanol (4 ml) was magnetically stirred at room temperature were added to the mixture of acetylacetone (0.02mol ,4 ml) and citric acid monohydrate (0.04 mol, 7.6 gm) and the content was offered to microwave irradiation for 7 min .The progress of the reaction was checked by TLC (n-hexane : EtOAc, 7: 3). After completion of the reaction, the solid product was filtered, and the pure product was obtained by recrystallization from hot ethanol.

5. Preparation of diethyl 1,1'-(1,4-phenylene) bis(2-benzoyl-4-hydroxy-5-oxo-2-phenyl-2,5-dihydro-1H-pyrrole-3-carboxylate) (1j)

A solution of p-phenylene diamine (0.01mol,1.08 ml) and diethyl acetylene dicarboxylate (0.02mol,2. 4 ml) in ethanol (4 ml) was magnetically stirred at room temperature were added to the mixture of benzil (0.02mol, 4.2 gm) and citric acid monohydrate (0.04mol, 7.6 gm) and the content was offered to microwave irradiation for 10 min .The progress of the reaction was checked by TLC (n-hexane : EtOAc, 7: 3). After completion of the reaction, the solid product was filtered and the pure product was obtained by recrystallization from hot ethanol.

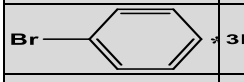
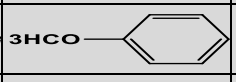
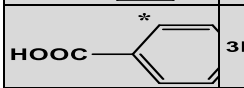
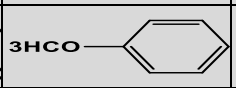
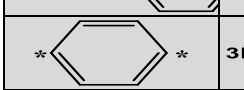
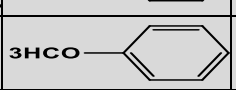
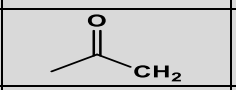
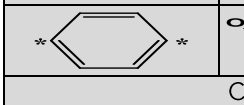
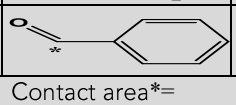
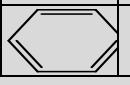
3. Result and Discussion

Our research was focused on the verification of pyrrolidinones synthesis via a convenient and easy method. The effect of ultrasound irradiation in accelerating the reactions attracted our attention. Ultrasound irradiation has been established as a significant technique in synthetic organic chemistry, where it has been applied as an efficient energy and heating source for organic reactions. To achieve suitable conditions for the synthesis of substituted 3-pyrrolin-2-ones, various reaction conditions were investigated for the reaction of aniline, diethyl acetylenedicarboxylate, 4-chlorobenzaldehyde and citric acid as a green additive in ethanol solvent as a model reaction. We first optimized the reaction conditions, such as the effects of solvents, additive amount and ultrasound irradiation power.



Scheme 2 proposed mechanistic path for the synthesis of substituted 3-pyrrolin-2-ones

Table 1: Structue of R1, R2 and Ar that contact with target product

Ar	R2	R1	Com.
		H	1f
		H	1g
		H	1h
		CH3	1i
			1j

Contact area*=

Analysis of Infrared Spectra

IR spectra of compound 1(f-j) in KBr disk show bands correspond to the stretching vibration of the aromatic C-H, aliphatic C-H, carbonyl amide group, carboxyle group , ethoxy group and OH group.(Aromatic C-H) 3075-3153; (C-H aliphatic)

2962-2985 Cm-1 ; (C=O) 1670-1725 Cm-1;(OH carboxyle) 3063-3072 Cm-1 ;CH3-O) 10221-1074 Cm-1 ; (OH) 3063-3498 Cm-1 .

ANALYSIS OF 1H-NMR SPECTRA

The 1H-NMR spectrum of 1(f-j) shows a trplet signal at δ1.06-2.92 ppm, a quartet signal at δ2.57-2.75 ppm for methylene group,a multiplet signal at δ 6.47-7.97 ppm for aromatic protons, a singlet signal at δ9.06-9.87 ppm for (OH) group , finally a singlet signal at δ9.55-11.33 ppm for carboxylic group.

ANALYSIS OF 13C NMR SPECTRA

The 13C NMR spectrum of 1(f-j) showed signals at δ14.49-43.17ppm for (CH3) signal at δ 55.36-72.60 ppm for (CH2). A multiplet for aromatic carbons at δ 109.99-151.95 ppm, a singlet of carbonyl group at 175.02-175.60ppm, asinal at δ191.77-195.28ppm for (COOH).

4. Conclusion

In this study five compounds from 2-Pyrrolidinones have been synthesized using of amine, diethyl acetylenedicarboxylate and aldehyde or ketone and citric acid monohydrate as acatalyst this method gave an excellent result with high yield and the duration of the reaction was shorter.

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