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Comparative study of synthesis of ethyl (quinolin-8-yloxy)acetate by conventional, microwave & ultrasound irradiation techniques

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ABSTRACT

Microwave and Ultrasound assisted organic synthesis has emerged as a new "lead" in organic synthesis. The technique offers simple, clean, fast, efficient, and economic for the synthesis of a large number of organic molecules. In the recent year microwave assisted organic reaction has emerged as new tool in organic synthesis. Important advantage of this technology include highly accelerated rate of the reaction, Reduction in reaction time with an improvement in the yield and quality of the product. A series of various ethyl (quinolin-8-yloxy)acetate derivatives were synthesized by the reaction of chloroethylacetate with substituted 8-hydroxy quinoline under conventional, Ultrasound irradiation and microwave irradiation conditions, purified by recrystallisation and the structure of all the compounds have been confirmed by IR, NMR and Mass spectral data.

Keywords: 8-hydroxy quinoline, microwave synthesis, ultrasound irradiation

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INTRODUCTION

The use of microwave and ultrasound irradiation in organic synthesis has become increasingly popular within the pharmaceutical and academic arenas, because it is a new enabling technology for drug discovery and development.[1,2] By taking advantage of this efficient source of energy, compound libraries for lead generation and optimization can be assembled in a fraction of the time required by classical thermal methods. Presently, thermally driven organic transformations take place by either of two ways: conventional heating or microwave accelerated heating. In the first way, reactants are slowly activated by a conventional external heat source. Heat is driven into the substance, passing first through the walls of the vessel in order to reach the solvent and reactants. This is a slow and inefficient method for transferring energy into the reacting system. In the second way, microwaves couple directly with the molecules of the entire reaction mixture, leading to a rapid rise in temperature. Since the process is not limited by the thermal conductivity of the vessel, the result is an instantaneous localized superheating of any substance that will respond to either dipole rotation or ionic conduction—the two fundamental mechanisms for transferring energy from microwaves to the substance(s) being heated.[3]

Green chemistry involves design and re-design of chemical synthesis[4] and chemical products to prevents pollution and thereby solve environmental problems. Among the challenges for chemists include discovery and development of novel and simple environmentally safe chemical processes for selective synthesis by identifying alternative reaction conditions and solvents for much improved selectivity, energy conservation and less or no toxic waste generation and inherently safer chemical products. Therefore, to address depletion of natural resources and

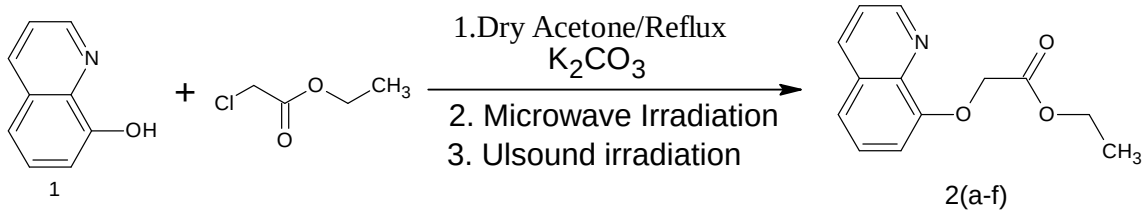
preservation of ecosystem it is just urgent to adopt so called “greener technologies” to make chemical agents for well being of human health.

Being a heterocyclic compound, 8-hydroxy quinoline finds use in research as a starting material for the synthesis of larger compounds, usually bioactive structures. Its aromaticity makes it relatively stable; although, as a heterocycle, it has reactive sites, which allow for functionalization. [5, 6]

MATERIALS AND METHODS

All raw materials used in the synthesis have been obtained from M/S Fluka AG (Bachs, Switzerland) and M/S Sigma-Aldrich chemicals and Co. Inc. (Milwoukee, WI, USA). Microwave Synthesis Reactor (Monowave 300 Anton Parr), ultrasound irradiation was carried out in Ultrasonic Bath model number XUBA3 having maximum power output of 200W and 50-60 Hertz Melting points were recorded on a Thermonik Melting point Apparatus (Campbell Electronics, Mumbai, India) and are uncorrected. IR spectra were recorded on an IR-Affinity, Shimadzu using DRS system. ^{1}H-NMR spectra have been recorded on a JEOL AL-400 FT-NMR spectrometer (400 MHz, JEOL Ltd., Tokyo, Japan), using TMS as internal standard in solvent DMSO. Mass data have been recorded on Agilent GC-MS.

3.0 Reaction Scheme



R= -H, -OH, -diCH$_3$, -NH$_2$, -CN, -CHO

4.0 Experimental

Method 1: Conventional Method

4.1 Synthesis of ethyl (quinolin-8-yloxy)acetate

A mixture of 8-hydroxyquinoline (0.01M, 1.45gm), ethylchloroacetate (0.01M, 1.22gm) and anhydrous K_2CO_3 (0.005M, 0.69gm) in dry acetone was refluxed on water bath for 18 hours. Reaction was monitored by TLC. The mixture was then filtered and solvent was removed under reduced pressure. The resulting solid was recrystallized from ethanol. The characterization data is given on table 2

Method 2: Microwave Irradiation Method

4.2 Synthesis of ethyl (quinolin-8-yloxy)acetate

A mixture of 8-hydroxyquinoline (0.01M, 1.45gm), ethylchloroacetate (0.01M, 1.22gm) and anhydrous K2CO3 (0.005M, 0.69gm) was mixed thoroughly and taken in 10ml vial, content of the vial was irradiated under microwave irradiation for 8 minutes at 200^0 C. Reaction was monitored by TLC. Solid product thus formed was purified by recrystallisation. The characterization data is given on table 2

Method 3: Ultrasound Irradiation

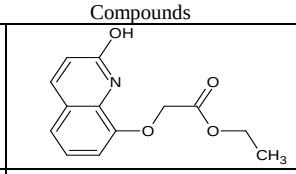
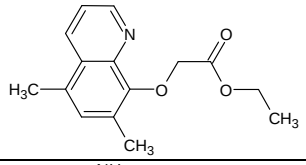
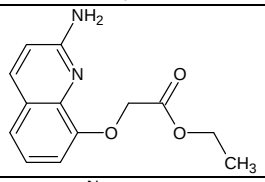
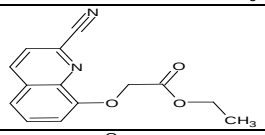
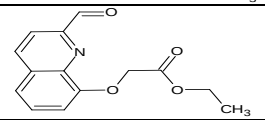
4.3 Synthesis of ethyl (quinolin-8-yloxy)acetate

A mixture of 8-hydroxyquinoline (0.01M, 1.45gm), ethylchloroacetate (0.01M, 1.22gm) and anhydrous K2CO3 (0.005M, 0.69gm) were taken in 100ml round bottom flask, Content of the flask was subjected to ultrasound irradiation for 10 minutes. After completion of reaction the content was poured into crushed ice, resulting solid thus obtained was separated through filtration, formation of product was confirmed by spectroscopic techniques .The characterization data is given on table 2

5.0 Table 1: Comparative data of synthesized compounds

Comps	-R	MP[^{0}C]	Conventional Method		Microwave Irradiation Method		Ultrasound Irradiation Method	
			Time (min.)	Yield (%)	Time (min.)	Yield (%)	Time (min.)	Yield (%)
2a	-H	95	720	62	4	92	10	79
2b	-OH	105	736	39	6	90	10	75
2c	-diCH_3	97	748	70	10	82	10	82
2d	-NH_2	102	720	55	5	79	10	77
2e	-CN	99	750	58	6	76	10	76
2f	-CHO	100	735	65	4	80	10	78

5.1 Table 2: Characterisation data of synthesized compounds

Compounds		^{1}H NMR (δ ppm)	IR (cm^{-1})	MS
2a		2.30 (t, 3H), 3.18 (q, 2H), 4.13 (s, 2H), 8.3(s,1H), 7.18-8.26 (m, 6H, Ar-H)	1732(-COO), 3320 (-OH)	247[M^+] ($C_{13}H_{13}NO_4^+$)
2b		2.40 (t, 3H), 3.27 (q, 2H), 4.25 (s, 2H), 2.30 (t, 3H), 2.47 (t, 3H), 7.10-8.30 (m, 6H, Ar-H)	1728(-COO), 2865 (-CH_3)	259[M^+] ($C_{15}H_{17}NO_3^+$)
2c		2.26 (t, 3H), 3.28 (q, 2H), 4.45 (s, 2H), 5.30 (s, 2H) 7.15-8.36 (m, 6H, Ar-H)	1730(-COO), 3350 (-NH)	246[M^+] ($C_{13}H_{14}N_2O_3^+$)
2d		2.10 (t, 3H), 3.60 (q, 2H), 4.56 (s, 2H), 7.11-8.36 (m, 6H, Ar-H)	1740(-COO), 690 (-CN)	256[M^+] ($C_{14}H_{12}N_2O_3^+$)
2e		2.30 (t, 3H), 3.18 (q, 2H), 4.13 (s, 2H), 9.35 (s, 1H), 7.18-8.26 (m, 6H, Ar-H)	1743(-COO), 699 (C-S)	259[M^+] ($C_{14}H_{13}NO_4^+$)

RESULTS AND DISCUSSION

The acceleration of synthesize compounds **2(a-f)** by microwave and ultrasound irradiation method to shorten the reaction time and elimination and minimization of side product formation is already finding acceptance in pharmaceutical industry (combinatorial chemistry) and synthesis by microwave and ultrasound irradiation method may pave the way towards the greener and more sustainable approach to chemical synthesis. In synthesis process it was found that the use of MW or ultrasound irradiation leads to a low reaction time and higher yield.

CONCLUSION

We have successfully synthesized variety of these heterocyclic compounds by using various greener techniques, such as Microwave and ultrasound irradiation. Synthesis of ethyl (quinolin-8-yloxy)acetate derivatives was carried out in good yields for the under microwave and ultrasound irradiation. The present procedure is carried out in a shorter reaction time and good yield and easier workup. Though the time taken by the microwave synthesis may be lesser than the ultrasound synthesis, the compounds obtained by the microwave is highest of the three methods utilized for the synthesis of the ethyl (quinolin-8-yloxy)acetate derivatives.

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