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Optimizations of Reaction Parameters of Microwave Enhanced Synthesis of 4,4´-Dihydroxychalcone

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Different reaction parameters of microwave enhanced synthesis of 4,4´-dihydroxychalcone have been optimized. The variations in reaction time as well as in yield of resulting compound under different set of reaction conditions have also been examined. The structure of 4,4´-hydroxychalcone has been established on the basis of its spectral data.

Key Words: Optimization, Microwave irradiation, Chalcone.

INTRODUCTION

Benzylideneacetophenones constitute a class of naturally occurring pigments which are often referred to as chalcone. The term was first coined by Kostanecki[1] who did pioneering work in the synthesis of benzylideneacetophenone and its derivatives by the Claisen-Schmidt condensation of acetophenone with benzaldehyde in the presence of aqueous alkali or sodium ethoxide, resulting in the formation of α,β-unsaturated ketone[2]. Chalcones find use as intermediates in the synthesis of biologically active molecules such as pyrazolines[3], thiophene[4], cumarines[5], isoxazolines[6], benzothiazepines[7], pyrimidinones[8], pyrazoles[9]. The chalcones and their analogues exhibit various biological activities like antibacterial[10], larvicidal[11], antimalarial[12], anticancer[13] and antimycobacterial[14], *etc*.

In past few decades microwave-induced organic reaction enhancement (MORE) chemistry[15] gained popularity as a non-conventional technique for rapid organic synthesis[16]. It is an efficient, facile, environmental friendly approach with grater selectivity, enhanced reaction rate and significant increase in yield of product. Keeping all in view a simple, facile, eco-friendly and non-conventional approach has been followed for synthesis of 4,4´-dihydroxychalcone using house hold microwave oven. Optimizations of different reaction conditions were also explored to keep other parameters constant to get better yield of resulting compound.

EXPERIMENTAL

UV spectrum was taken by using Perkin-Elmer Lambda 15 UV/Vis spectrometer. IR spectrum of the compound was recorded on a Schimatzu 8201 PC spectrometer (4000-400 cm^{-1}) by using KBr palates and absorption bands are reported in cm^{-1}. The $^1H_1$ NMR spectrum was recorded on Bruker DRX-300 (300 MHz FT NMR)

spectrometer in deutreted methanol using TMS as internal standard and chemical shift are expressed in δ (ppm) values. The FAB mass spectrum was recorded on a Jeol S X 102 mass spectrometer using argon/xenon (6 KV, 100 mA) as the FAB gas. All reactions were monitored by thin layer chromatography carried out on 0.2 mm silica gel G plats using suitable solvent system. The purity of the compound was ascertained by thin layer chromatography as well as preparative TLC using suitable solvent system. Samsung G2739N microwave oven (20 L capacity, 2450 MHz, 1500 W) has been used in synthesis of compound. All the chemicals used were obtained from E-merck/Glaxo Ltd., Mumbai. The reagents and solvents such as chloroform, acetone and ethanol used were of LR and AR grade.

Synthesis of 4,4´-dihydroxychalcone: The microwave induced condensation of 4-hydroxyacetophenone (0.01 mol) with 4-hydroxy benzaldehyde (0.01 mol) has been carried out by using ethanol as energy transfer medium in the presence of different condensing agents in the specially designed conical flask fitted with calcium chloride guard tube to absorb solvent vapours. The progress of the reaction was monitored by silica gel thin layer plates using chloroform:acetone (8:2) solvent system as well as by the appearance of coloured product during reaction. The resultant mixture was cooled, neutralized with ice chilled dilute HCl (5 %), stirred, when precipitate of crude substituted chalcone obtained which was filtered, washed thoroughly with ice cold distilled water, till free from acid. Different sets of reaction conditions were experimented to get optimize conditions for better results shown in Tables 1-3. All above reactions were carried out in presence of ethanol (solution phase) but some set of reactions also proceeded in presence of solid phase *i.e.* in presence of various absorbents which are mentioned in Table-4.

TABLE-1
OPTIMIZATION OF MICROWAVE POWER TO KEEP REACTION TIME CONSTANT

MW power (Watt)	Condensing agent	Reaction time (s)	Yield (%)
*750	KOH (12 N, 8 mL)	90	82
600	KOH (12 N, 8 mL)	90	72
50	KOH (12 N, 8 mL)	90	65
300	KOH (12 N, 8 mL)	90	55
180	KOH (12 N, 8 mL)	90	50

*Optimum microwave power to get maximum yield of 4,4´-dihydroxychalcone.

TABLE-2
OPTIMIZATION OF REACTION TIME TO KEEP MICROWAVE POWER CONSTANT

MW power (Watt)	Condensing agent	Reaction time (s)	Yield (%)
750	KOH (12 N, 8 mL)	105	Viscous mass
*750	KOH (12 N, 8 mL)	90	82
750	KOH (12 N, 8 mL)	60	70
750	KOH (12 N, 8 mL)	45	48
750	KOH (12 N, 8 mL)	30	25

*Optimum reaction time to get maximum yield of 4,4´-dihydroxychalcone.

TABLE-3
OPTIMIZATION OF CONDENSING AGENT TO KEEP
MICROWAVE POWER AND REACTION TIME CONSTANT

Condensing agent	MW powder (Watt)	Reaction time (s)	Yield (%)
*KOH (12 N, 8 mL)	750	90	82
NaOH (12 N, 8 mL)	750	90	75
$NaOCH_3$ (12 N, 8 mL)	750	90	70
Borax (12 N, 8 mL)	750	90	No reaction
Anhyd.$AlCl_3$ (12 N, 8 mL)	750	90	25

*Optimum condensing agent to get maximum yield of 4,4´-dihydroxychalcone.

TABLE-4
OPTIMIZATION OF ABSORBENT TO KEEP OTHER PARAMETERS CONSTANT

Absorbent	MW power (Watt)	Reaction time (s)	Yield (%)
Basic Al_2O_3	750	90	90
*Neutral Al_2O_3	750	90	98
Silica gel	750	90	35
Bentenite	750	90	68

*Optimum absorbent to get maximum yield of 4,4´-dihydroxychalcone.

RESULTS AND DISCUSSION

Lemon yellow coloured 4,4´-dihydroxychalcone synthesized by rapid and efficient microwave assisted method showed characteristic colour reactions of chalcones. It gave reddish orange colour with conc. H_2SO_4 and intense yellow colour with Ac_2O-conc. H_2SO_4 reagents. From Table-1, it is evident that microwave assisted synthesis of 4,4´-dihydroxychalcone proceeded quickly with very good yield at 750 watt microwave power. Optimum reaction time was found to be 90 s at which high yield of product obtained (Table-2). Among all the condensing agents KOH gave most favourable yield of product (Table-3). The effect of absorbent on yield of product has also been studied (Table-4). It is observed that the presence of solid absorbent increases the yield of product significantly as compare to solution phase. Neutral alumina enhanced yield of product notably.

The resulting compound was characterized by UV, IR, ^{1}H NMR and mass spectra. The presence of characteristic IR peak of ketovinyl group (-CO-CH=CH-) at 1642 cm^{-1} and broad peak at 3215 cm^{-1} due to hydroxy groups support the chalcone skeleton with in resulting molecule. ^{1}H NMR spectrum showed a pair of doublet corresponding to vinylic H_α and H_β at 7.56 and 8.00 ppm, respectively. Strong mass peak [M^+] and [M-1] peak showed in mass spectrum of compound.

4,4´-Dihydroxychalcone: Lemon yellow powder; m.p. 130 ºC; UV (MeOH) λ_{max}: 223, 345 nm; IR (KBr, cm^{-1}) ν_{max}: 3215 (-OH), 3035.1 (aromatic -CH stretching), 2000-1800 (aromatic summation bands), 1642 (-CO-CH=CH-) 1348 (in plane -OH bending), 1222 (-C-OH stretching), 1168 (phenyl-C- stretching), 612 (-OH out of plane bending); ^{1}H NMR (CD_3OD, 300 MHz) δ: 7.56 (d, 1H, H_α), 8.00 (d, 1H, H_β); FAB-MS at m/z 240 [M^+], 239 [M^+-1], 212, 147, 121, 119, 107, 77.

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