

SYNTHESIS AND CHARACTERIZATION OF SOME CHALCONES CONTAINING SUBSTITUTED BENZYLOXY PHENYL RING SYSTEM BY MICROWAVE IRRADIATION

Jyoti Prajapati and Dr. Shiv Singh Dulawat*

Department of Chemistry, Pacific Academy of Higher Education and Research University,
Udaipur-313001 (Raj.) India.

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***Corresponding Author**

Dr. Shiv Singh Dulawat

Department of Chemistry,
Pacific Academy of Higher
Education and Research
University, Udaipur-313001
(Raj.) India.

ABSTRACT

A convenient microwave induced synthesis of chalcone derivatives are obtained by the reaction of substituted acetophenone with benzaldehyde containing substituted benzyloxy phenyl ring system using NaOH/EtOH. The synthesized compounds were characterized by their IR, ^1H NMR, mass spectral data and elemental analysis. The method has several advantages in comparison with conventional synthesis including clean reaction procedure, easy workup and short reaction time giving excellent yields of product.

KEYWORDS: Chalcones, benzyloxy phenyl ring, microwave irradiation.

INTRODUCTION

The use of microwaves in organic synthesis (Microwave Induced Organic Reaction Enhancement (MORE))^[1-2] has increased dramatically in the last years, receiving widespread acceptance and becoming an indispensable tool. In organic synthesis^[3-5] microwave technology has become a powerful tool, since by employing this technique it is generally possible to prepare organic compounds very fast, with better yields and high purity compared to other more conventional methods. Chalcones^[6-8] having an α , β -unsaturated carbonyl compounds have been popular substrates for the generation of various heterocyclic compounds of therapeutic importance. The presence of enone functionality in chalcone moiety is the key factor for its biological activity as antiinflammatory,^[9-10] anticancer,^[9] antibacterial,^[10] antineoplastic,^[11] antimalarial,^[12] antileishmanial^[13] and diuretic activities. Further the importance of chalcones and analogous compounds in pharmaceutical and

biological field is well known. In the present communication we report the reaction of different acetophenone derivatives with benzaldehyde to form chalcones (B I) to (B-V). The structures of the various synthesized compounds were assigned on the basis of their elemental and spectral (IR, ^1H NMR and MASS) data.

MATERIALS AND METHODS

Experimental Section

Melting points were determined in an open capillary tube and are uncorrected. Thin layer chromatography of synthesized compounds was performed on silica gel-G plates using benzene-ethyl acetate (9:1) solvent system and iodine as visualizing agent. The IR spectra of synthesized compound were recorded on DIGILAB FTS-14 or Perkin- Elmer 157P spectrophotometer in KBr (ν_{max} in cm^{-1}). ^1H NMR was recorded on CDCl_3 on a Varian CFT-20 or Bruker DRX-300 (300 MHz) spectrometer using TMS as internal standard (chemical shifts in δ , ppm). MS was recorded on Jeol SX-102 spectrometer. All compounds gave satisfactory elemental analysis and spectral data. All the reactions were carried out in a domestic microwave oven. (Kenstar, output energy 1200W, frequency 2450 MHz, model no. MO9706).

(I) General procedure for the synthesis of 4-(p-Chlorobenzoyloxy)-3-methoxybenzaldehyde (A)

Equimolar amount (0.01mol) 4-Hydroxy-3-methoxybenzaldehyde(a) and 4-chlorobenzyl chloride(b) dissolved in DMF (8ml) & heated at $55-60^\circ\text{C}$ and then added K_2CO_3 (0.02 mol) and reflux for 6-7 hrs, after that add water so the product was precipitated. The product was filtered, washed with water and recrystallised from EtOH.

(II) General procedure for the synthesis of 1-(p-chlorophenyl)-3-[4'-(p-chlorobenzoyloxy)-3'-methoxyphenyl]-propenone (B-I)

(a')- Conventional (Classical) Method

Equimolar amounts (0.01mol) of substituted acetophenone and synthesized benzaldehyde (4-(p-Chlorobenzoyloxy)-3-methoxybenzaldehyde) was dissolved in ethanol (100mL) and was gradually added a solution of sodium hydroxide (40% 10 mL) and the reaction was (monitored by TLC) allowed to proceed with stirring for a period of 5 to 7 hrs at room temperature. The reaction mixture was decomposed by ice cold 2 N HCl (40mL). The separated cloured product was filtered, washed with water (3X50 mL) dried and recrystallised with appropriate solvent to afford analytical samples.

(b')- Microwave Induced Solution Phase Method

To a solution of substituted acetophenone (0.01 mol) and synthesized benzaldehyde (4-(p-Chlorobenzoyloxy)-3-methoxybenzaldehyde) (0.01mol) in ethanol (18-20mL) was taken in a 100 mL Borosil flask fitted with a funnel as a loose top. Sodium hydroxide solution (40% 10 mL) was added and the reaction mixture was subjected to microwave irradiation at 25% microwave power (300W) for 5-6 minutes with short interval of 30sec⁻¹ min. to avoid the excessive evaporation of solvent. After the completion of the reaction (monitored by TLC), the reaction mixture was cooled and acidified with ice cold 2 N HCl (35mL). The separated product was filtered, washed with water, dried and recrystallised from ethanol to afford analytical samples.

(c')- Microwave Induced Solid Phase Method (Al₂O₃)

Equimolar amounts (0.01mol) of substituted acetophenone and synthesized benzaldehyde (4-(p-Chlorobenzoyloxy)-3-methoxybenzaldehyde) was dissolved in ethanol (12-15mL) in a 100 mL Borosil flask. The solution was adsorbed in basic alumina (4gm) with constant stirring. Adsorbed material was mixed properly, dried in air and placed inside the microwave oven for 5-7 min. at medium power level (600W). After the completion of the reaction (TLC) the mixture was cooled at room temperature and the reaction mixture was extracted with ethanol (3X15 mL). Removal of the solvent under reduced pressure yielded the product which on recrystallisation with EtOH.

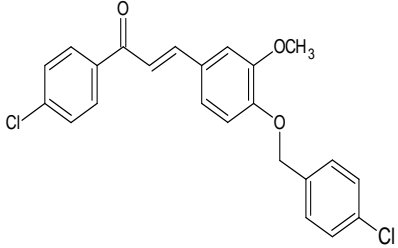
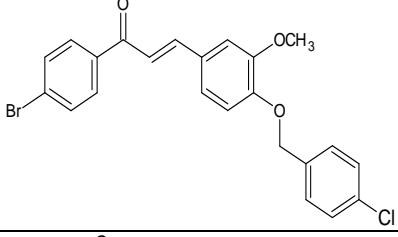
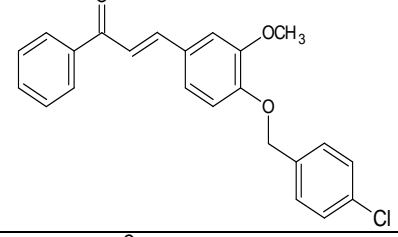
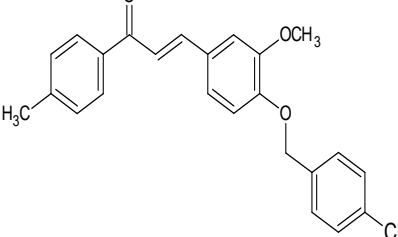
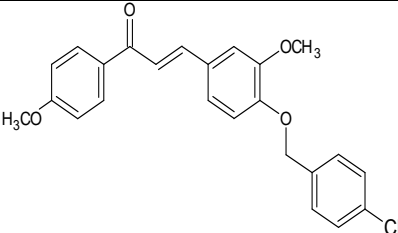
Physical characterization of synthesized compounds (B-I) to (B-V).

Comp. No.	Molecular formula	M.W.	M.P. (°C)	Elemental analysis Calculated/ Found			
				% C	% H	% Cl	% O
(B-I)	C ₂₃ H ₁₈ Cl ₂ O ₃	413.29 (412.51)	160	66.84	4.39	17.16	11.61
				65.92	4.50	17.35	11.05
(B-II)	C ₂₃ H ₁₈ BrClO ₃	457.74 (455.89)	183	60.35	3.96	7.75	10.49
				60.23	3.66	7.63	10.45
(B-III)	C ₂₃ H ₁₉ ClO ₃	378.85 (376.27)	148	72.92	5.05	9.36	12.67
				71.98	5.00	9.45	12.50
(B-IV)	C ₂₄ H ₂₁ ClO ₃	392.87 (390.97)	152	73.37	5.39	9.02	12.22
				73.10	5.43	8.91	12.20
(B-V)	C ₂₄ H ₂₁ ClO ₄	408.87 (407.54)	142	70.50	5.18	8.67	15.65
				70.35	5.10	8.27	15.58

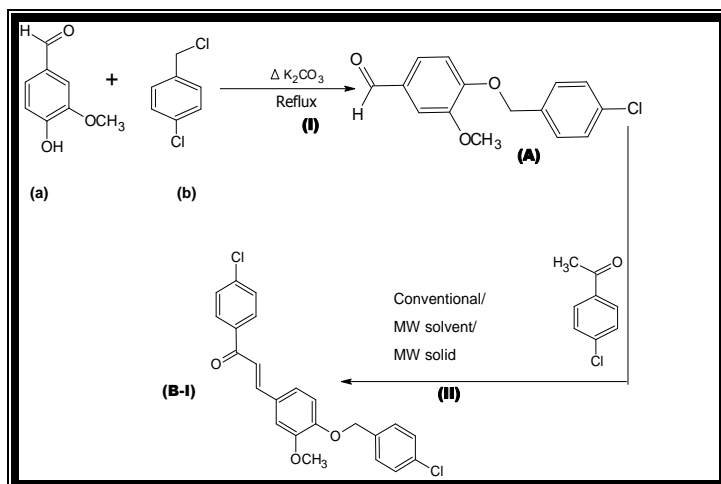
Experimental data of synthesized compounds (B-I) to (B-V).

Comp. No.	Reaction Time			% Yield		
	Classical Method (Hrs)	MW Methods (Min)		Classical Method	MW Methods	
	(a)	(b)	(c)	(a)	(b)	(c)
(B-I)	6	5-6	6-7	65	90	74
(B-II)	7	4-6	5-6	58	91	78
(B-III)	6.5	4-5	4-7	61	89	76
(B-IV)	5.5	4-6	5-6	69	88	75
(B-V)	6	4-5	4-6	70	90	80

Molecular formula & Structure of synthesized compounds (B-I) to (B-V).

No.	Actophenone Derivatives	Substitute in Actophenone Derivative	Molecular Formula of Synthesized Chalcones (B-I) to (B-V)	Structure of Synthesized Chalcones (B-I) to (B-V)
1	C ₈ H ₇ ClO	Cl	C ₂₃ H ₁₈ Cl ₂ O ₃	
2	C ₈ H ₇ BrO	Br	C ₂₃ H ₁₈ BrClO ₃	
3	C ₈ H ₈ O	H	C ₂₃ H ₁₉ ClO ₃	
4	C ₉ H ₁₀ O	CH ₃	C ₂₄ H ₂₁ ClO ₃	
5	C ₉ H ₁₀ O ₂	OCH ₃	C ₂₄ H ₂₁ ClO ₄	

REACTION SCHEME



SPECTRAL ANALYSIS OF SYNTHESIZED COMPOUNDS

(A):- 4-(p-Chlorobenzyloxy)-3-methoxybenzaldehyde

IR ν max (KBr) cm^{-1} : 2925 (-CHO), 1239 (Ar-O), 1066 (-OCH₃), 655 (monosubstituted benzene), ¹H NMR (CDCl₃, δ ppm): δ 9.83 (s, 1H, CHO), 5.14 (s, 2H, OCH₂) 6.95-8.01 (m, 7H, Ar-H) 3.92 (s, 3H, -OCH₃). MS (m/z): 276[M⁺].

(B-I):- 1-(p-chlorophenyl)-3-[4'-(p-chlorobenzyloxy)-3'-methoxyphenyl]-propenone

IR ν max(KBr) cm^{-1} :- 1662 (C=O), 1580 (C=C), 1260 (Ar-O), 1055 (-OCH₃), 3055 (Ar-H), 696, 731 (monosubstituted benzene). ¹H NMR (CDCl₃, δ ppm): 5.17[s, 2H, OCH₂], 3.76 [s, 3H, OCH₃], 6.93 [d, J=7.95 Hz, 1H, =CH_a], 7.79 [d, J=15.54 Hz, 1H, =CH_b], 6.90-8.03 [m, 11H, ArH]. MS (m/z): 413 [M]⁺, 399 [C₂₃H₂₀Cl₂O₂]⁺, 315 [C₁₈H₁₇ClO₃]⁺, 262 [C₁₅H₁₅ClO₂]⁺, 201 [C₁₄H₁₈O]⁺, 142 [C₇H₇ClO]⁺, 140 [C₈H₉Cl]⁺, 138 [C₈H₁₀O₂]⁺, 112 [C₆H₅Cl]⁺.

(B-II):- 1-(p-bromophenyl)-3-[4'-(p-chlorobenzyloxy)-3'-methoxyphenyl]-propenone

IR ν max (KBr) cm^{-1} :- 1645 (C=O), 1590 (C=C), 1254 (Ar-O), 1045 (-OCH₃), 3060 (Ar-H), 693, 1080 (monosubstituted benzene). ¹H NMR (CDCl₃, δ ppm): 5.21 [s, 2H, OCH₂], 3.78 [s, 3H, OCH₃], 6.95 [d, J=7.92 Hz, 1H, =CH_a], 7.64 [d, J=15.52 Hz, 1H, =CH_b], 6.83-8.09 [m, 11H, Ar-H]. MS (m/z): 457 [M]⁺, 443 [C₂₃H₂₀ClBrO₂]⁺, 315 [C₁₈H₁₇ClO₃]⁺, 262 [C₁₅H₁₅ClO₂]⁺, 201 [C₁₄H₁₈O]⁺, 185 [C₈H₉Br]⁺, 142 [C₇H₇ClO]⁺, 138 [C₈H₁₀O₂]⁺, 112 [C₆H₅Cl]⁺.

(B-III):- 1-phenyl-3-[4'-(p-chlorobenzyloxy)-3'-methoxyphenyl]-propenone

IR ν max (KBr) cm^{-1} : 1654 (C=O), 1595 (C=C), 1285 (Ar-O), 1040 (-OCH₃), 3059 (Ar-H), 698, 702 (monosubstituted benzene). ¹H NMR (CDCl₃, δ ppm): 5.22 [s, 2H, OCH₂], 3.75 [s,

3H, OCH₃], 6.90 [d, J=7.96 Hz, 1H, =CH_α], 7.83 [d, J=15.55 Hz, 1H, =CH_β], 6.91-8.13 [m, 12H, Ar-H]. MS (m/z): 378 [M]⁺, 364 [C₂₃H₂₁ClO₂]⁺, 315 [C₁₈H₁₇ClO₃]⁺, 262 [C₁₅H₁₅ClO₂]⁺, 201 [C₁₄H₁₈O]⁺, 142 [C₇H₇ClO]⁺, 138 [C₈H₁₀O₂]⁺, 112 [C₆H₅Cl]⁺, 106 [C₈H₁₀]⁺.

(B-IV):- 1-(p-methylphenyl)-3-[4'-(p-chlorobenzyloxy)-3'-methoxyphenyl]-propenone

IR ν max (KBr) cm⁻¹: 1670 (C=O), 1592 (C=C), 1273 (Ar-O), 1036 (-OCH₃), 3053 (Ar-H), 746,689 (monosubstituted benzene). ¹H NMR (CDCl₃, δppm): 5.20 [s, 2H, OCH₂], 2.30 [s, 3H, CH₃], 3.78 [s, 3H, OCH₃], 6.94 [d, J=7.93 Hz, 1H, =CH_α], 7.80 [d, J=15.58 Hz, 1H, =CH_β], 6.88-8.03 [m, 11H, Ar-H]. MS (m/z): 392 [M]⁺, 378 [C₂₄H₂₃ClO₂]⁺, 315 [C₁₈H₁₇ClO₃]⁺, 262 [C₁₅H₁₅ClO₂]⁺, 201 [C₁₄H₁₈O]⁺, 142 [C₇H₇ClO]⁺, 138 [C₈H₁₀O₂]⁺, 120 [C₉H₁₂]⁺, 112 [C₆H₅Cl]⁺.

(B-V):- 1-(p-methoxyphenyl)-3-[4'-(p-chlorobenzyloxy)-3'-methoxyphenyl]-propenone

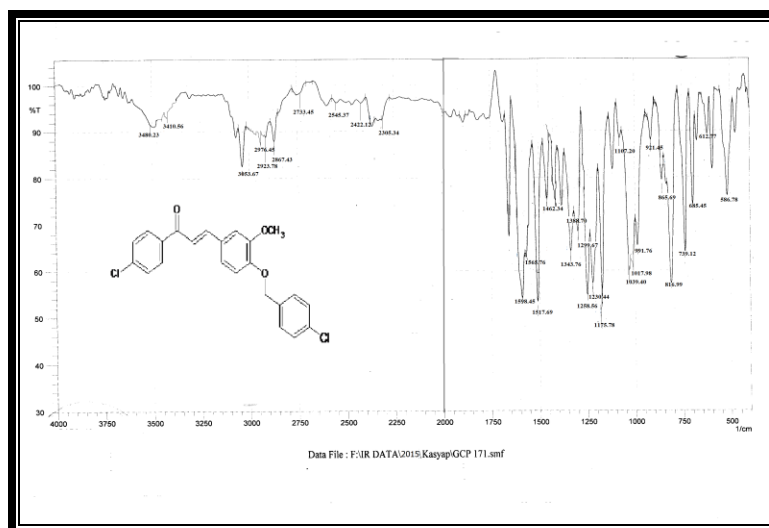
IR ν max (KBr) cm⁻¹: 1658 (C=O), 1589 (C=C), 1232 (Ar-O), 1032 (-OCH₃), 3070 (Ar-H), 742,676 (monosubstituted benzene). ¹H NMR (CDCl₃, δppm): 5.20 [s, 2H, OCH₂], 3.84 [s, 3H, OCH₃], 3.94 [s, 3H, OCH₃], 6.84 [d, J=7.94 Hz, 1H, =CH_α], 7.91 [d, J=15.57 Hz, 1H, =CH_β], 6.93-8.08 [m, 11H, Ar-H]. MS (m/z): 408 [M]⁺, 394 [C₂₄H₂₃ClO₂]⁺, 315 [C₁₈H₁₇ClO₃]⁺, 262 [C₁₅H₁₅ClO₂]⁺, 201 [C₁₄H₁₈O]⁺, 142 [C₇H₇ClO]⁺, 138 [C₈H₁₀O₂]⁺, 136 [C₉H₁₂O]⁺, 112 [C₆H₅Cl]⁺.

RESULT AND DISCUSSION

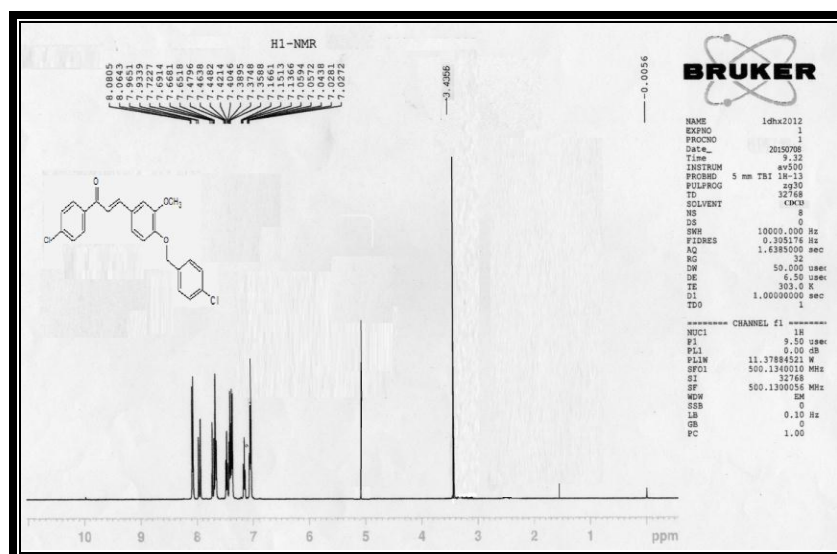
Reported synthesis of chalcone derivatives by the condensation of synthesized 4-(p-Chlorobenzyloxy)-3-methoxybenzaldehyde with substituted acetophenone using NaOH/ethanol to yield novel chalcone containing benzyloxy phenyl ring system under microwave irradiation (Scheme I & II). Microwave irradiation has been used to accelerate organic reactions because of high heating efficiency, providing remarkable rate enhancement, dramatic reduction in reaction times with improvement in yield and quality of products. Reactions that require hours or even days by conventional heating can often be accomplished in second or minutes by microwave heating.^[14] this technique has several advantages including clean reaction procedure, no need of catalyst, short reaction time and high yields of product. The obtained derivatives were characterized using spectroscopic technique, their IR spectra, the characteristic transmittance in the region of 3039-3073 cm⁻¹ are observed due to aromatic alkanes. The IR frequency of carbonyl group shifted -C=O band to lower frequency region 1645-1670 cm⁻¹, supporting the presence of α,β-unsaturated carbonyl group in all the compounds. Medium to intense absorption peaks in the range 1601-1577 cm⁻¹ are observed

which are due to benzene ring vibrations. The position and number of these transmittance values depend upon the substituting group with aromatic ring. The out of plane C-H deformation vibrations for monosubstituted benzene fall in the range $800\text{--}600\text{ cm}^{-1}$. Characteristic absorptions in the region $1285\text{--}1232\text{ cm}^{-1}$ is found due to Ar-O group in compound. The mass spectra of all compounds were recorded & major peak is selected for the mass fragmentation. The PMR Spectra exhibited protons as two doublets around δ 7.7-7.9 and δ 7.6-8.0 respectively. The aromatic proton of the ring was seen in the region δ 6.83-8.09.

IR SPECTRUM OF 1-(p-CHLOROPHENYL)-3-[4'-(p-CHLOROBENZYLOXY)-3'-METHOXYPHENYL]-PROPENONE (B-I)



NMR SPECTRAL STUDIES OF 1-(p-CHLOROPHENYL)-3-[4'-(p-CHLOROBENZYLOXY)-3'-METHOXYPHENYL]-PROPENONE (B-I)



CONCLUSION

In summary we reported the synthesis of novel chalcone derivatives **(B-I)** to **(B-V)** containing benzyloxy phenyl ring system. Microwave induced solution phase/solid phase methods found to be excellent and convenient reaction route in terms of simple reaction procedure, quick reaction time giving percent yield of product as compared to conventional method.

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