Synthesis, X-ray diffraction study and Antimicrobial study of 1-(4-butoxy-2-hydroxyphenyl)-3-(2,5-dimethoxyphenyl) prop-2-en-1-one

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Abstract- Chalcone moiety (1,3-diaryl-2-propen-1-ones) is the backbone of several antinuclear, cardiovascular and antispasmodic drugs. These groups of compounds constitute an important class of natural products belonging to the flavonoid family. A novel 1-(4-butoxy-2-hydroxy phenyl)-3-(2,5-dimethoxyphenyl) prop-2-en-1-one has been synthesized by chemical method. The product has been confirmed by their chemical analysis IR, ^{1}H NMR and ^{13}C NMR. To explore the structural features of the compound X-Ray diffraction (XRD) pattern has been recorded and it confirms that the title compound, $C_{21}H_{24}O_5$ belongs to monoclinic system with P 2/m space group and the crystallographic parameters are a =22.4642 (0.0756), b = 17.1823 (0.0222), c = 10.3753 (0.0324) Å and β = 92.93 (1.410) °. The final product has been screened for their antimicrobial and fungal activities against different panel of organisms.

Index Terms- Antimicrobial activities, Chalcones, Powder X-ray diffraction study Synthesis

I. INTRODUCTION

The chemistry of chalcone has been recognized as a significant field of study. An interesting feature of chalcone is that it serves as starting materials for the synthesis of various heterocyclic compounds such as pyrimidines, pyrazolines, pyrazoles, flavones, flavonols, flavanones, aurones and benzoyl coumarones as well as certain compounds like deoxybenzoins and hydantoins, which are of some therapeutic value. Natural chalcones occur mainly as petal pigments and have also been found in the heartwood, bark, leaf, fruit and root of a variety of trees and plants. Chalcone-containing plants such as *Glycyrrhiza* species have long been used as folk remedies. Chalcones and their heterocyclic analogues show various biological effects, e.g. antibacterial[1-2], antifungal[3], antituberculous[4], antitumour[5], antiinflammatory[6-7], anti diabetic activity[8-9], antileishemanial activity[10-11], antimalarial activity[12-13], antimitotic activity[14], anti spasmolytic activity[15], anti invasive activity[16-17].

In continuation of our work[18] considering the scope for further studies on chalcone derivatives, we herein report a novel chalcone derivatives, 1-(4-butoxy-2-hydroxyphenyl)-3-(3-bromophenyl) prop-2-en-1-one (Fig. 1). The synthesized compound was ascertained from spectral and physiochemical analysis. Results of IR, ^{1}H NMR and ^{13}C NMR analysis confirmed the formation of the desired product. The X-ray diffraction study further confirms the product. Antimicrobial activities of this novel chalcone derivative (1b) are also reported.

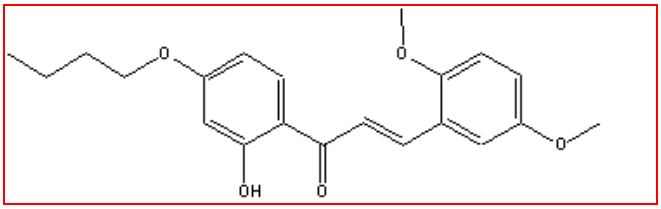


Figure 1: Chemical scheme of the title compound

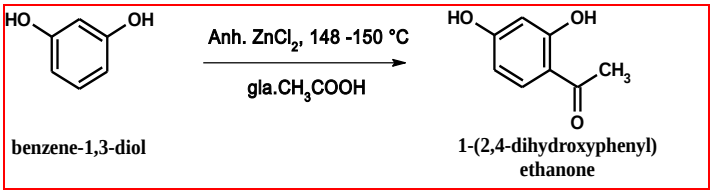
II. EXPERIMENTAL

Materials and methods

General chemicals were purchased from Merck, SD Fine and commercial source were used. All non-aqueous reactions were performed in dry glass ware.

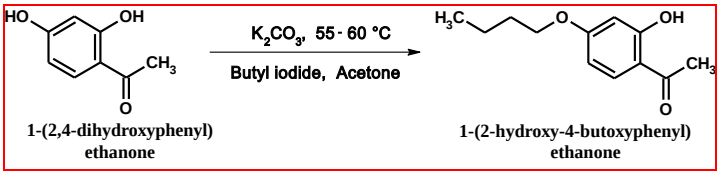
2.1 Synthesis

Step-1: Preparation of 1-(2,4-dihydroxyphenyl) ethanone (A): Anhydrous zinc chloride (0.27mole) is dissolved in glacial acetic acid (20ml) and resorcinol (0.1 mole) was added in it. The reaction mixture was boiled at 150^{o}C for 20 minutes. After completion of the reaction as indicated by TLC, contains were poured in to ice. Separated solid was filtered, washed with water, dried and crystallized from hot water. Yield: 90%, M.P: 143^{o}C (reported: 144^{0}C)., Rf. value : 0.66. [Solvent system – Toluene: Ethyl acetate (9.5:0.5)]. M.F-$C_8H_8O_3$, Elemental Analysis: C – 63.16%, H – 5.29%, O -31.55 %.



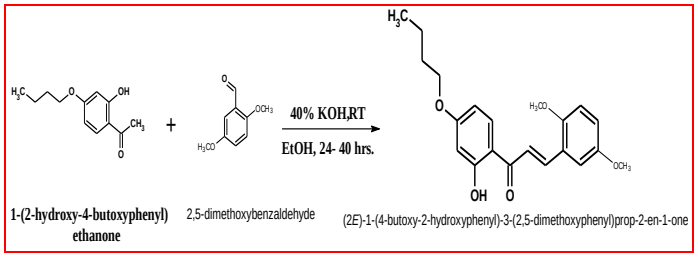
Step-2: Preparation of 2-hydroxy-4-butoxy acetophenone (B):
acetophenone (0.1 mole), anhydrous potassium carbonate (0.4 mole) and butyl iodide (0.1 mole) in dry acetone (150 ml) were refluxed for 48 hours. Acetone was removed by distillation, later on residue was poured into ice water and dilute cold HCl and 6-7

pH of mixture was adjusted by addition of dilute HCl. Solid separated was collected, washed with water, dried and crystallized from petroleum ether as colorless needles. Yield: 80%, M.P: 44°C, Rf. value: 0.56. [Solvent system – Toluene: Ethyl acetate (9.5:0.5)]., M.F-, $C_{12}H_{16}O_3$ Elemental Analysis: – 69.20%, H – 7.73%, O- 23.07%.



Step-3: Preparation of 1-(4-butoxy-2-hydroxyphenyl)-3-(2,5-dimethoxyphenyl) prop-2-en-1-one. (1b):

2-hydroxy-4-butoxy acetophenone (0.01 mole) and 2, 5-dimethoxy benzaldehyde (0.01 mole) were dissolved in ethanol (40 ml) and a solution of potassium hydroxide (40%, 40 ml) was added in it. The reaction mixture was stirred at room temperature for 24 hours. After completion of the reaction as indicated by TLC, contents were poured in to crushed ice and acidified with diluted HCl. The solid separated was washed with water, filtered, dried and crystallized from methanol as yellow needles. Yield: 93%, m.p.:110°C, Rf. value: 0.55. [Solvent system – Toluene: Ethyl acetate (9.5:0.5)]. M.F-$C_{21}H_{26}O_5$, Elemental Analysis: C – 70.74%, H – 6.81 %.



2.2 Characterizations

Thin layer chromatography (TLC) was performed on pre-coated plates, silica gel 60-F254 (Merck 1.16834, layer thickness 0.25 mm) using toluene / methanol mixtures (8:2) as developing system. The detection of the products on TLC was carried out in iodine vapor.

Melting points were determined on a POLMON INSTRUMENTS MODEL: MP- 96, Range: 25°C TO 350°C, Resolution: 0.1°C fitted with a microscope.

Fourier Transform Infra Red (FTIR) spectroscopy (Model: Perkin Elmer 100) of the frequency range of 400–4000 cm^{-1}.

^{1}H-NMR and ^{13}C-NMR spectra were recorded with a Fourier transform instrument at 400 MHz (Bruker AVANCE 400). All deuteried solvents used for the preparation of the samples were chloroform ($CDCl_3$), methanol (CD_3OD) and dimethyl sulfoxid (DMSO-*d*6). Samples were dissolved in Acetonitrile/ dichloromethane (85:15).

Powder diffraction patterns of the title compound has been collected with a SIEMENS D 5000 diffractometer using CuKα1 radiation (λ = 1.5406 Å)

III. RESULTS AND DISCUSSION

3.1 Spectroscopic evaluation of 1-(4-butoxy-2-hydroxy phenyl)-3-(2,5-dimethoxyphenyl) prop-2-en-1-one (1b):

IR(cm^{-1}): 2964 (C-H str. (asym)alkyl), 2882 (C-H str. (sym) alkyl), 1465 (C-H def (asym) alkyl), 1012 (C-H def(sym) alkyl), 3063 (C-H str.arom.), 1583. (C=C str. arom.), 1097 (C-H i.p.def arom.), 822 (C-H o.o.p.def.arom.), 3243 (OH str. phenol), 1273 (C-O-C (sym)ether), 1049 (C-O-C (asym) ether), 971.2 (CH=CH def.chalcone), 3009 (CH=CH str. chalcone), 1635 (C=C str. chalcone).

^{1}H NMR ($CDCl_3$) δppm: 3.79(s, 3H, OCH_3), 3.84(s, 3H, OCH_3), 0.89-0.93 (trip, 3H ,OCH_2-CH_2-CH_2 CH_3), 1.36-1.45 (2H ,-OCH_2-CH_2-CH_2CH_3), 1.66-1.71) (quintet , 2H, -OCH_2-CH_2-CH_2-CH_3), 4.02-4.05 (triplet , 2H, -OCH_2-CH_2-), 6.43 (s, 1H), 6.53(d, 1H, J=7.2Hz), 7.03 (s, 1H,), 7.57(s, 1H,), 7.94(d, 1H, J=15.6Hz, chalcone), 7.96(d, 8.32(d, 1H, J=15.6Hz, chalcone), 1H, J=7.6Hz), 8.23 (s, 1H), 13.51(s, OH). **MS**: m/z 356.

^{13} C NMR ($CDCl_3$) δppm: 165.89 (C-1,C-OH),114.18(C-2 & C-16), 192.35(C-3, C= O), 121.33(C-4, CH=CH, chalcone), 123.77(C-5, CH=CH, chalcone),118.93(C-6),108.17(C-7),166.30 (C-8), 101.70 (C-9), 68.27 (C-10,-OCH_2-CH_2-), 30.94(C-11,OCH_2-CH_2-CH_2-CH_3), 19.19 (C-12, -OCH_2-CH_2-CH_2CH_3), 14.08 (C-13,OCH_2-CH_2-CH_2 CH_3), 5 5.15(C-14, OCH_3), 56.59(C-15, OCH_3), 133.07(C-17), 153.26(C-18), 138.07(C-19,20), 153.72(C-21).

3.2 Powder X-ray diffraction study

Powder X-ray diffraction has routinely been used as a non-destructive fingerprinting technique in laboratory and industry for several decades. Every solid crystalline compound gives its own unique X-ray diffraction pattern consisting of a set of Bragg peaks. The diffraction pattern for a compound can be considered analogous to a fingerprint, or barcode, with the peak positions determined by the unit cell symmetry and lattice parameters. When we collect XRD data, we can use these fingerprints to identify not only what phases are present in our sample but also index the pattern to obtain information about the unit cell size and shape. Powder diffraction patterns of the title compound has been collected with a SIEMENS D 5000 diffractometer using CuKα1 radiation (λ = 1.5406 Å) as shown in Fig 2.

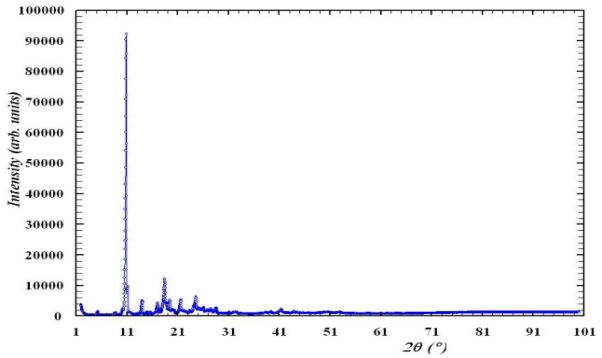


Figure 2: Powder diffraction patterns for the title compound

The experimental 2θ range was 2–99° with a step size of 0.01° and a counting time of 60 s per step. The program of graphic tool for powder diffraction named WinPLOTR package[19] was used to determine the observed diffraction peak positions of the title compound. Analytical indexing of the powder pattern and determination of the space group were performed using CRYSFIRE 2002[20], which is designed to launch the most common indexing programs.

Table 1: Crystallographic data for $C_{21}H_{26}O_5$

Unit-cell parameters with standard deviation	a	22.4642 (0.0756) Å
	b	17.1823 (0.0222) Å
	c	10.3753(0.0324) Å
	α	90.00 (0.000) °
	β	92.93 (1.410) °
	γ	90.00(0.000) °
Volume	3999.525 $Å^3$	
Crystal family	Monoclinic	
Space group	P 2/m	

3.3 Antimicrobial activities

Synthesized title compound has been screened for their antimicrobial activity against different panel of organisms, i.e., E.coli, P.aeruginosa, S.aureus, S.pyogenes and antifungal strains C. albicans., using Gentamycin and K. Nystatin as reference standards respectively. The Serial dilution technique was followed by micro method as per NCCLS-1992 manual[21]. The observed Minimum Inhibitory Concentrations (MIC) values, for bacterial and fungal strains of the title compound are presented in Table 2a and Table 2b respectively.

Table 2a: Minimal Inhibition Concentrations of Bacterial Strains (MIC) in µg/ml

	S.aureus MTCC 96	*S. pyogenus* MTCC 443	*E. coli* MTCC 442	*P. aeruginosa* MTCC 441
Std. Drug Gentamycin	0.05	1.0	0.25	0.5
Present study	6.25	25	100	250

Table 2b: Minimal Inhibition Concentrations of Fungal Strain (MIC) in µg/ml

	C. albicans MTCC 227
Std. Drug K .Nystatin	1000
Present study	500

IV CONCLUSION

A novel chalcone derivative, 1-(4-butoxy-2-hydroxyphenyl)-3-(3-bromophenyl) prop-2-en-1-one has been synthesized by chemical method. The product has been confirmed by their chemical analysis, IR, 1H NMR and 13C NMR and further confirms by powder X-ray diffraction study. The antimicrobial activities of the novel chalcone derivative have been investigated and their responses against specific bacteria are good.

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