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SYNTHESIS, CHARACTERISATION AND ANTIMICROBIAL ACTIVITY OF SOME NEW CHALCONES

M. Elavarasan, M. Thamizh Thendral and S. Syed Shafi *

Department of Chemistry, Thiruvalluvar University, Serkkadu, Vellore - 632115, Tamil Nadu, India.

Keywords:

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Correspondence to Author:
S. Syed Shafi

Department of Chemistry,
Thiruvalluvar University, Serkkadu,
Vellore - 632115, Tamil Nadu, India.

E-mail: suban_shafi@yahoo.com

ABSTRACT: In this work, an attempt was made to synthesize new chalcones by Claisen - Schmidt condensation of substituted benzaldehydes with 4-aminoacetanilide in the presence of base catalyst. The synthesized chalcone derivatives was characterized by FT-IR, ^{1}H-NMR, and ^{13}C-NMR and also tested for their antimicrobial activity and compared with the standard drugs.

INTRODUCTION: Chalcones are an important class of natural products and are considered as the precursors of flavonoids and isoflavonoids. Chemically chalcones are 1, 3-diaryl-2-propen-1-ones in which two aromatic rings are joined by a three carbon bridge having a cabonyl moiety and α, β -unsaturation. Chalcones come under an aromatic ketone that forms the central core for a variety of biological compounds. Claisen - Schmidt condensation between acetophenone and benzaldehyde gives chalcones, but in this reaction instead of acetophenone, we are using acetanilide with substitution benzaldehyde gives chalcones. This reaction is catalyzed by acids and bases under homogeneous or heterogeneous condition. chalcones derivatives have received a great deal of attention due to their relatively simple structures and wide variety of pharmacological activities reported for these compounds include anti-inflammatory [1, 2] antifungal [3, 4], Antibacterial [5], anti-malarial [6] and antitumor activities [7]. For these reasons, the synthesis of chalcones and their functionalized derivatives is a primary objective. Herein we report the activity of chalcone derivatives by synthesizing a series of molecules (2a-d) and evaluating their antibacterial activity against eight microorganism strains of Gram positive and negative antifungal profile against *Staphylococcus aureus* and *Penicllium* sps. In this study, only the feature associated with "B" ring of the chalcone moiety was changed by keeping the basic skeleton intact. Three compounds found most active *in-vitro* against *Staphylococcus aureus* and *Penicllium* sps. compared to standard drug.

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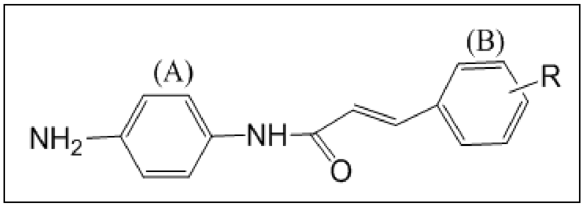


FIG. 1: SKELETON OF CHALCONE MOIETY

MATERIALS AND METHOD: Melting points were determined in open capillary tubes and are uncorrected. All the chemicals and solvents used were of laboratory Grade and solvents were purified by suitable methods FTIR Spectra were recorded using KBr disc, ^{1}HNMR and ^{13}CNMR spectra were recorded on a Brucker 400MHz NMR spectra meter using TMS as an internal standard (chemical shift in δppm) in $CDCl_3$. The Homogeneity of the products was checked by the TLC using silica gel 'G' and the eluent system was a mixture of hexane, ethyl acetate in 5:5 proportion.

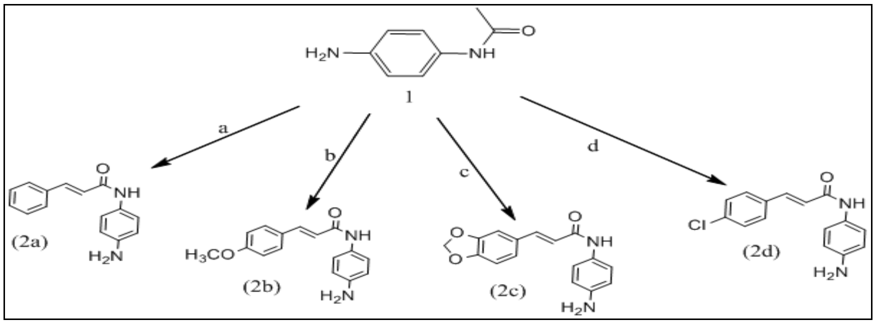
General Procedure for the Preparation of Chalcones: A solution of 4-aminoacetanilide (0.002 mol) in absolute ethanol (20 ml) is kept in constant stirring with various aromatic aldehydes in the presence of 10% NaOH (20 ml) for 4 hr. After the reaction completes, the reaction mixture was poured in cooled water and kept in freezer at overnight, the product were purified by recrystallization from suitable solvents.

N- (4-Aminophenyl) cinnamamide, (2a): Orange -yellow powder, Yield 60%, m.p. 159 ºC; TLC (Hexane: Ethylacetate, 5:5). IR: (KBr, cm^{-1}) 3294 (N-H), 3185 (Aromatic C-H stretch), 2875 (C-H stretch), 1749 (NH-C=O), 1603 (CH=CH of carbonyl conjugated double bond), 1519 (C=C of aromatic ring). ^{1}HNMR (400 MHz, $CDCl_3$) δ/ppm: 8.71 (s, 1H, N-H), 8.32-8.34 (t, 2H, - CO-CH=CH), 7.99-7.97 (d, 1H, = CH-Ar), 7.49-7.47 (d, 2H, Ar-H), 7.84-7.81 (d, 2H, Ar-H). ^{13}CNMR (400 MHz, $CDCl_3$) δ/ppm: δ 168.57 (-NH- C=0), δ 135.94 (=C-Ar), δ 120.86; 121.69; 128.90; (Aromatic C), 135.29 (Carbonyl-C=).

(E)- N- (4-Aminophenyl)- 3- (4-methoxyphenyl) acrylamide (2b): Orange-yellow powder, Yield 80%, m.p. 145 ºC; TLC (Hexane: Ethylacetate, (5:5). IR: (KBr, cm^{-1}) 3238 (N-H), 3058 (Ar CH stretch), 2846 (C-H stretch), 1658 (NH-C=O), 1540 (C=C of aromatic ring), 1310 (C–N). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ppm: 8.44 (ss, 1H, N- H), 7.51-7.52 (d, 1H, -CO-CH=), 7.25 (d, 1H, =CH-Ar), 6.95 (d, 2H, Ar-H), 7.16-7.17 (d, 2H, Ar-H), 3.86 (s, 2H, (NH_2)), 2.16(s, O-CH_3) ^{13}CNMR (400 MHz, $CDCl_3$) δ/ppm: δ 162.38 (-NH-C=0), δ 135.94 (=C-Ar), δ 130.58; 129.30, 121.89; 121.58; 120.90 (Aromatic C), 114.30 (Carbonyl-C=), δ 55.40 (-O-CH_3).

(E)-N- (4-Aminophenyl)-3-(benzo[d][1, 3]dioxol-5-yl) acrylamide (2c): Yellow powder, Yield 62%, m.p. 130 ºC; TLC (Hexane: Ethylacetate, 2:8). IR: (KBr, cm^{-1}) 3449 (N-H), 3221 (Ar C-H stretch), 3048 and 2901 (C-H stretch), 1657 (NH-C=O), 1593 (CH=CH of –Carbonyl-CH=CH-), 1540 (C=C of aromatic ring). ^{1}HNMR (400 MHz, $CDCl_3$) δ/ppm: 8.33 (ss, 1H, N-H), 6.86-6.88 (d, 1H, -CO-CH=), 7.08-7.51 (m, 7H, Ar-H), 6.03(s, 2H, O-CH_2-O). ^{13}CNMR (400 MHz, $CDCl_3$) δ/ ppm: δ 168.41 (-NH-C=0), δ 148.58 (=C-Ar), δ 106.92; 108.37; 120.81; 121.67; 121.93; 125.83; 131.31; 135.95 (Aromatic C), 120.01 (Carbonyl-C=).

(E)- N- (4- Aminophenyl)- 3- (4- chlorophenyl) acrylamide (2d): Light yellow powder, Yield 67%, m.p. 148 ºC; TLC (Hexane: Ethylacetate, 5:5). IR: (KBr, cm^{-1}) 3294 (N-H), 3186 (Ar C-H stretch), 3121 and 3061 (C-H stretch), 1661 (NH-C=O), 1568 (CH=CH of –Carbonyl-CH=CH-), 1542 (C=C of aromatic ring).^{1}HNMR (400 MHz, $CDCl_3$) δ/ppm: 10.01(s, 1H, OC-NH), 8.65 (d, 1H,-CO-CH=), 7.92-7.93(d, 2H, Ar-H), 7.57-7.63 (m, 4H, Ar-H), 2.05(s, 2H, NH_2).



SCHEME - 1: SYNTHESIS OF CHALCONE DERIVATIVES (2a-d)

a) BENZALDEHYDE, NaOH/EtOH b) ANISALDEHYDE c) PIPERANAL d) CHLOROBENZALDEHYDE

Compound	R	M. P. (ºC)	Yield (%)	Mol. formula	Mol. weight	Recrystal
2a	H	158-159	60	$C_{15}H_{14}N_2O$	238.12	1
2b	O-CH_3	144-145	80	$C_{16}H_{16}N_2O_2$	268.09	1
2c	O-CH_2-O	130-132	62	$C_{16}H_{14}N_2O_3$	282.53	1
2d	4-Cl	148-149	67	$C_{15}H_{13}N_2OCl$	274.64	1

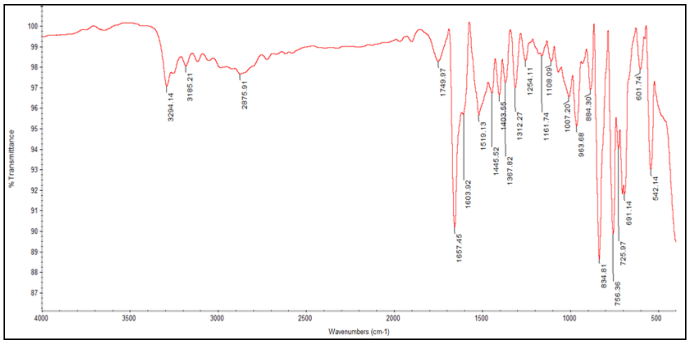


FIG. 2: COMPOUND - 2A IR

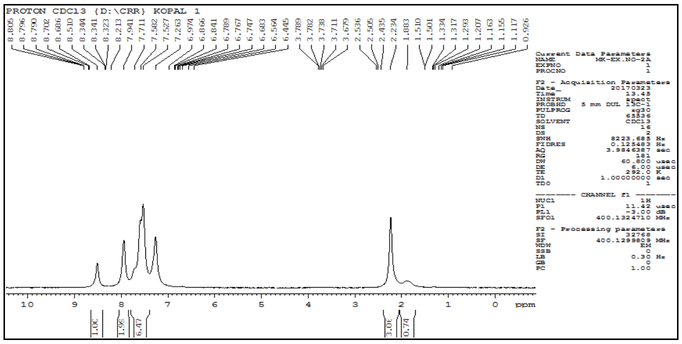


FIG. 3: 2a 1H NMR

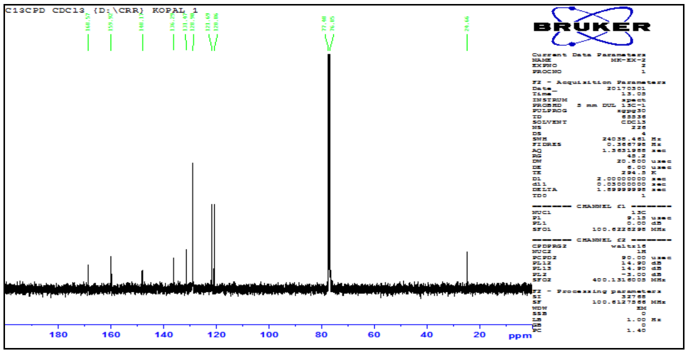


FIG. 4: 2a ^{13}C NMR

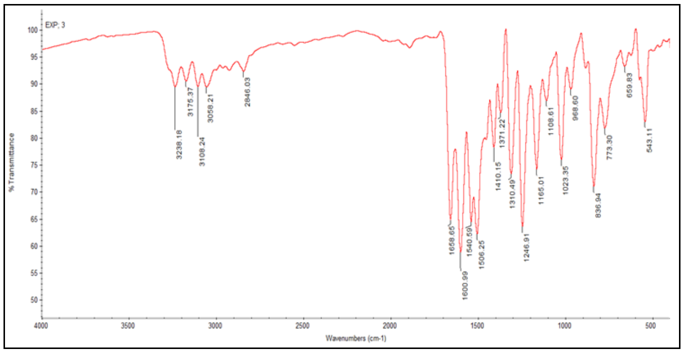


FIG. 5: 2b IR

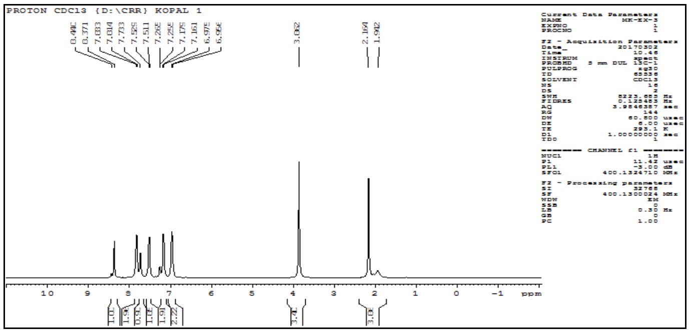


FIG. 6: 2b ^{1}HNMR

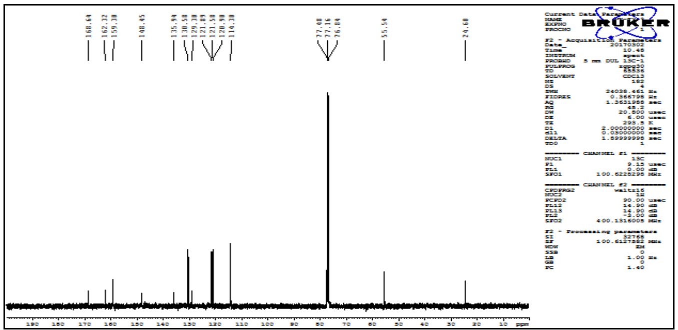


FIG. 7: 2b ^{13}C NMR

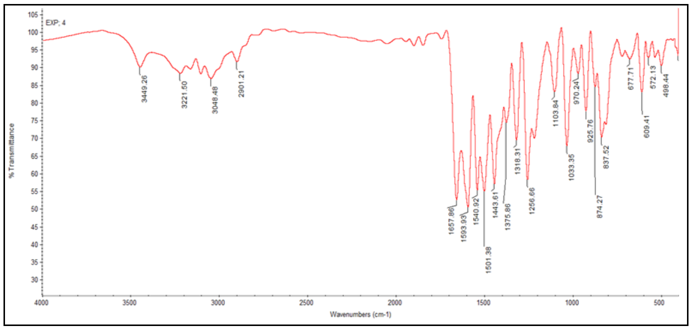


FIG. 8: 2c IR

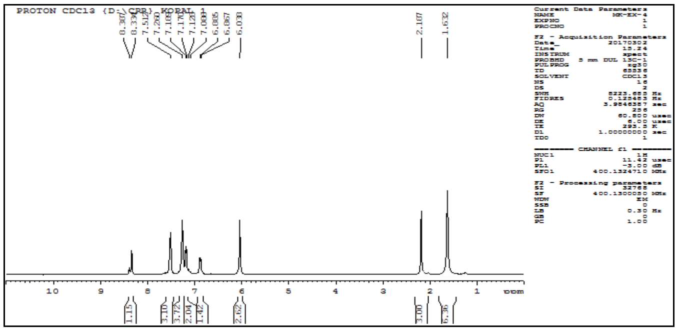


FIG. 9: 2c ^{1}H NMR

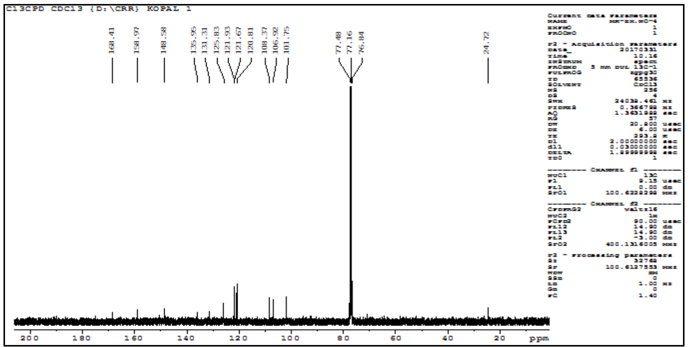


FIG. 10: 2c ^{13}C NMR

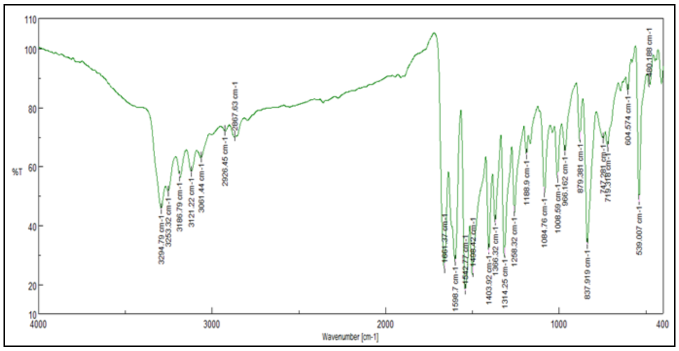


FIG. 11: 2d IR

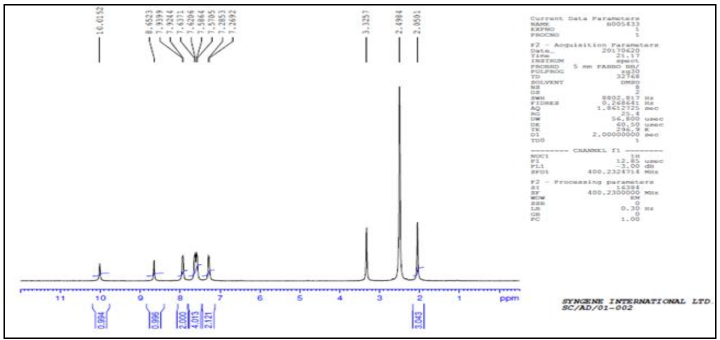


FIG. 12: 2d ^{1}H NMR

RESULTS AND DISCUSSION: In this reaction synthesis of chalcones carried out by the reaction of 4-aminoacetanilide and different aromatic aldehyde with 10% NaOH in absolute ethanol and the products were purified by recrystallization from suitable solvents. The synthesized product has been fully characterized by IR, ^{1}H-NMR and ^{13}C-NMR spectroscopy data. The IR spectrum of the synthesized chalcones was recorded and it gives an absorption band near 1700 - 1650 cm^{-1} representing the presence of -C=O group. The absorption band at 1650 - 1580 cm^{-1} confirms the aromatic –C=C- group. The ^{1}H NMR and ^{13}C NMR of synthesized chalcones give ^{1}H NMR (400 MHz, CDCl$_3$) δ/ppm: 6.70-6.38 (d, 1H, -CO-CH=), 7.99-7.97 (d, 1H, =CH-Ar) and ^{13}C NMR (400 MHz, CDCl$_3$) δ/ppm: δ 166.13 (-NH-C=0), δ 138.48 (=C-Ar), 128.13 (Carbonyl-C=) confirms formation of chalcones.

Pharmacological Results:

Antibacterial Activity: Nutrient Agar (NA) plates were seeded with 8 h broth culture of different bacteria. Sterile paper disc (6 mm in diameter) impregnated with 50 µl of different concentrations of samples were allowed to dry before being placed onto the seeded top layer of the agar plates. Each of the discs was gently placed at equidistance on top of the agar layer to give better contact with agar. The plates were then incubated at 37 °C for 24 h. gentamycin (10 µg) was used as positive controls and DMSO / chloroform as negative control. The antibacterial activity was evaluated by measuring the diameter of inhibition zone. Solvent and growth controls were kept, the zones of inhibition and minimum inhibitory concentrations (MIC) noted. Results of these studies are compared with the standard.

Antifungal Activity: All the synthesized compounds were also screened for their in vitro antifungal activity against Mucor, *Aspergillus niger* and *Penicillium* strains. The zone of inhibition was measured in millimeters. Antifungal activities of all compounds were screened by the turbidometry method [8, 9]. Activity of extract was compared with standard antibiotics fluconazole fungi. DMSO was used as solvent. All compounds are active against Mucor, *A. niger* and Penicillium.

Results of Antibacterial Activity:

Plates: Inhibition zone of compounds K1, K2, K3 on *Staphylococcus aureus* and *Klebsiella pneumoniae* at 50 µg/mL.

Standard = Ciprofloxacin A – Compound K1, B – Compound K2, C – Compound K3

FIG. 13: INHIBITION ZONE OF COMPOUNDS K1, K2, K3 ON *STAPHYLOCOCCUS AUREUS* AND *KLEBSIELLA PNEUMONIAE*

S. no.	Microorganisms	Control (Solvent)	A	B	C	Ciprofloxacin
1	*Staphylococcus aureus*	-	6 mm	5 mm	10 mm	12 mm
2	*Klebsiella pneumonia*	-	4 mm	8 mm	7 mm	20 mm

Results of Antifungal Activity:

Plates: Inhibition zone of compounds K1, K2, K3 on *Penicllium* sps and *Mucor* sps at 50µg/mL.

Standard = Amphotericin-B
A – Compound K1; B – Compound K2
C – Compound K3

FIG. 14: INHIBITION ZONE OF COMPOUNDS K1, K2, K3 ON *PENICLLIUM* SPS AND *MUCOR* SPS

S. no.	Microorganisms	Control (Solvent)	D	E	F	Amphotericin-B
1	*Penicllium* sps	DMSO	7 mm	18 mm	10 mm	12 mm
2	*Mucor* sps	DMSO	7 mm	11 mm	8 mm	15 mm

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CONFLICTS OF INTEREST: Nil

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