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Research Article

ULTRASOUND IRRADIATION PROMOTED SYNTHESIS OF CHALCONES, ANALOGUES, HOMOLOGUES AND RELATED FURANYL CONTAINING COMPOUNDS AND THEIR ANTIBACTERIAL ACTIVITY

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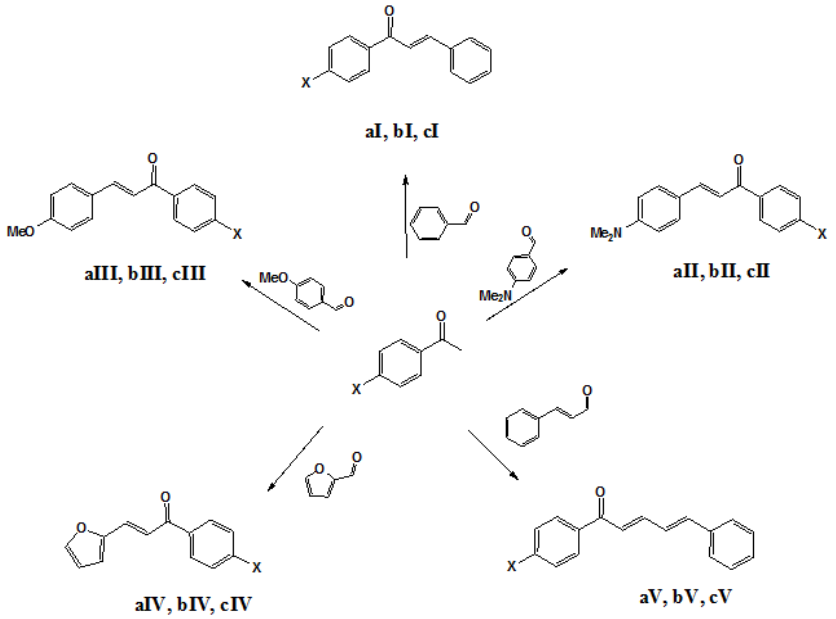
ABSTRACT

We have synthesised a series of chalcones, chalcone analogues that contain bromo- , nitro- and diethylamine substituents, homologues with an extra double bond between the two aromatic rings and related compounds with a furane B-ring, using ultrasound irradiation. Yields with NaOH in ethanol were between 20 and 99% after 1 hour. The chalcones show modest activities against *Staphylococcus aureus* and no activity against *Escherichia coli.*

Keywords: Ultrasound, Sonochemistry, Chalcones, Chalcone analogues, Chalcone homologues, *Staphylococcus aureus*, *Escherichia coli*

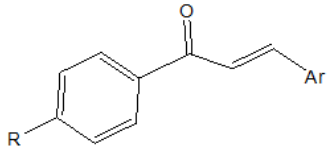
Chalcones are important chemical precursors for the synthesis of benzofuranones[1], flavanones, dihydropyrazoles[2], pyrimidines[3] and dihydrochalcones[4]. Chalcones have been demonstrated to have important biological activity against *Escherichia coli*, *Aspergillus flavus*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Salmonella typhosa*, *Aspergillus niger,* Candida *albicans*[5,6], and *Plasmodium* species[7] and have anti-inflammatory properties[8]. Chalcones are synthesised *via* the condensation of an aromatic aldehyde with an aromatic ketone. This simple condensation is usually slow and time consuming[9] and yields are often low. The condensation can be accelerated significantly with ultrasound[10,11]. Here in we have reported the first ultrasound assisted synthesis of a series of chalcones, chalcone analogues with bromo-, nitro- and diethylamine substituents, homologues with and extra double bond between the aromatic rings and related compounds with a furyal group.

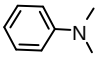
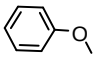
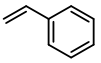
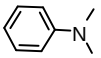
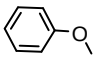
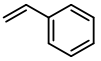
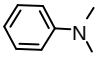
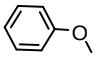
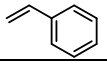
The condensation reaction was carried out using acetophenone, *p*-bromoacetophenone, and *p*-nitroacetophenone, with aromatic aldehyde as shown in Scheme 1. The reaction mixture were sonicated for 1 hour, neutralized with sulfuric acid, then cold water was added, and placed in an ice water. Sonication was performed in Bandelin electronic ultrasonic bath 35 KHz – 80/320 w. The precipitated product was filtered, washed with excess of cold water, dried at ambient temperature and recrystallized from the suitable solvent (Tables 1). The majority of the products were well recrystallized from a water-acetone. The products included 1-aryl-3-phenyl-2,propen-1-ones, 1-aryl-3-(*p*-bromophenyl)-2, propen-1-ones and 1-(*p*-nitrophenyl-3-aryl-2, propen-1-ones were obtained in good yield, the only condensation of furfural and acetophenone has failure due kinetic problem. The condensation under ultrasound irradiation provides high yield, clean and rapid synthesis in very short period of time, these are better than the reported with conventional methods[12].



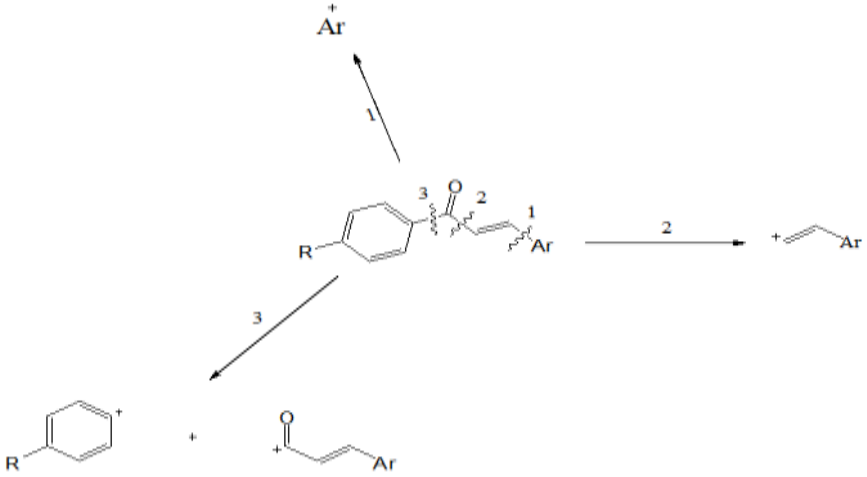
Scheme 1: Compounds synthesised.

Table 1: Yield, properties and antibacterial properties of compounds



No.	R	Ar	Yield %	Mating point	Crystallization solvent	Staphylococcus aureus (+ev)	Echerichia coli (-ev)
aI	H		55.40	55-57	Methanol	+6	-
aII	H		74.23	107-108	Ethanol	-	-
aIII	H		66.41	76-78	Ethanol	-	-
aIV	H		Not observed				
aV	H		71.88	84-86	Ethanol	+3	-
bI	Br		19.81	91-92	Acetone-H_2O	-	-
bII	Br		98.76	142-143	Acetone-H_2O	+3	-
bIII	Br		89.85	147-149	Acetone-H2O	-	-
bIV	Br		90.75	66-68	Acetone-H_2O	+6	-
bV	Br		96.13	153-154	Acetone-H_2O	-	-
cI	NO_2		41.08	94-95	Acetone-H_2O	+6	-
cII	NO_2		64.32	207-208	Acetone-H_2O	-	-
cIII	NO_2		73.74	166-168	Acetone-H_2O	-	-
cIV	NO_2		97.81	119-121	Acetone-H_2O	-	-
cV	NO_2		95.04	173-174	Acetone-H_2O	-	-

The products were characterised with ^{1}H-NMR, IR, Mass Spectrometry and UV-Vis spectroscopy. IR spectra were recorded on a Burker tensor 27 spectrometer with ZnSi cell. NMR spectra were measured on Bruker spectrometer (600 MHz) using TMS as internal standard and $CDCl_3$ as solvent. Mass spectra were determined on a GC-MS Shimadzu spectrometer. The high stereo selectivity of the reaction, giving exclusively *trans* alkenes, was proved with ^{1}H NMR (J = 15 Hz for all compounds). IR indicated the presence of the enone group. The mass spectroscopy results provide the exact mass of target chalcones, in addition to useful fragments observed in all the synthetic compounds, this fragments results through pathways 2 and 3 as shown in Scheme 2. The UV-Vis spectra has showed two λ_{max} at around 227 nm and 300nm due to π-π* and n-π* respectively.



Scheme 2: General fragmentation pathways of the prepared compounds observed by EI-MS

The antibacterial activity of synthetic compounds was measured using the cup-plate agar diffusion method. No activity against *Echerichia coli* (-ev) was observed whereas compounds aI, aV, bII, bIV, cI, aII, shown low to modest activities against *Staphylococcus aureus* (-ev).

The report represented high yield, clean and rapid ultrasound promoted synthesis of a series of chalcones, chalcone analogues, homologues and related compounds with a furyal group and their antibacterial activity.

Spectroscopic data

1,3-diphenyl-(2E)-propen-1-one [aI]: V_{max}: 1661 (C=O),; δ_H (600 MHz, $CDCl_3$, Me_4Si)7.44 (3H, m, ph), 7.53 (2H, t, J = 7.4 H_z), 7.56 (1H, d, J = 15.7 H_z), 7.60 (1H, t, J = 7.4 H_z), 7.66 (2H, dd, J = 4.3 & 7.7 H_z), 7.84 (1H, d, J = 15.7 H_z), 8.04 (2H, d, J = 7.1 Hz, H-) ppm; M/z (%): 208 (M^+ - 84); λ_{max} (Methanol 227, 308).

3-(*p*-N,N dimethylaminophenyl)-1-phenyl-(2E)-propen-1-one [aII]: V_{max}: 1647 (C=O),; δ_H (600 MHz, $CDCl_3$, Me_4Si) 3.05 (6H, s, NMe_2), 6.71 (2H, d, J = 8.9H_z), 7.36 (1H, d, J =15.5 H_z), 7.51 (2H, t, J = 7.7 H_z), 7.56 (3H, m, ph), 7.82 (1H, d, J = 15.5 H_z), 8.03 (2H, d, J = 8.3 H_z) ppm; M/z (%): 251 (M^+ - 100) ; λ_{max} (Methanol 265, 420).

3-(*p*-methoxyphenyl)-1-phenyl-(2E)-propen-1-one [aIII]: V_{max}: 1657 (C=O); δ_H (600 MHz, $CDCl_3$, Me_4Si) 3.85 (3H, s, OMe), 6.95 (2H, d, J = 8.7 H_z), 7.51 (1H, d, J = 15.6 H_z), 7.52 (2H, t, J = 7.7 H_z), 7.56 (1H, t, J = 7.4 H_z), 7.57 (2H, d, J = 8.6 H_z), 7.80 (1H, d, J = 15.6 H_z), 8.03 (2H, d, J = 8.08 H_z); M/z (%): 238 (M^+ - 100)); λ_{max} (Methanol 228, 311).

1,5-diphenyl-(2E,4E)-pentadiene-1-one [aV]: V_{max}: 1653 (C=O); δ_H (600 MHz, $CDCl_3$, Me_4Si) 6.93 (1H, dd, J = 1.6 Hz), 6.96 (1H, d, J = 15.6 H_z), 7.01 (1H, d, J = 14.9 H_z), 7.24 (1H, d, J = 7.3 H_z), 7.29 (2H, d, J = 7.65 H_z), 7.42 (4H, m, ph), 7.49 (1H, t, J = 7.4 H_z), 7.53 (1H, dd, J = 14.9, 7.9 H_z), 7.90 (2H, d, J = 8.04 Hz); M/z (%): 234 (M^+ - 100); λ_{max} (Methanol 227, 309).

3-(*p*-bromophenyl)-1-phenyl-(2E)-propen-1-one [bI]: V_{max}:1673 (C=O); δ_H (600 MHz, $CDCl_3$, Me_4Si) 7.43 (3H, m, ph), 7.50 (1H, d, J=15.7 H_z), 7.65 (4H, m, ph), 7.83 (1H, d, J=15.7 H_z), 7.90 (2H, d, J= 8.6 H_z); M/z (%): 268, 288 (M^+ - 58, 56); λ_{max} (Methanol 227, 311).

1-(*p*-bromophenyl)-3-(*p*-N,N dimethylaminophenyl)-(2E)-propen-1-one [bII]: V_{max}: 1663 (C=O); δ_H (600 MHz, CDCl3, Me_4Si) 3.06 (6H, s, NMe_2), 6.70 (2H, d, J= 8.8 H_z), 7.28 (1H, d, J=15.4 H_z), 7.55 (2H, d, J = 8.8 H_z), 7.63 (2H,d, J= 8.5 H_z), 7.81 (1H, d, J=15.4 H_z), 7.88 (2H, d, J= 8.5 H_z); M/z (%): 329, 331 (M^+ - 100,98); λ_{max} (Methanol 274.5, 426).

1-(*p*-bromophenyl)-3-(*o*-methoxyphenyl)-(2E)-propen-1-one [bIII]: V_{max}: 1655 (C=O); δ_H (600 MHz, $CDCl_3$, Me_4Si) 3.85 (3H, s, OMe), 6.93 (2H, d, J= 8.7 H_z), 7.35 (1H, d, J = 15.6 H_z), 7.59 (2H, d, J = 8.7 H_z), 7.61 (2H,d, J = 8.9 H_z), 7.79 (1H, d, J = 15.5 H_z), 7.87 (2H, d, J = 8.5 H_z); M/z (%): 316, 318 (M^+ - 53, 52)); λ_{max} (Methanol 230, 270, 341).

1-(*p*-bromophenyl)-3-(*o*-furyl)-(2E)-propen-1-one [bIV]: V_{max}: 1655 (C=O); δ_H (600 MHz, $CDCl_3$, Me_4Si) f- 6.54 (1H, dd, J = 3.4 &1.8 H_z), 6.76 (1H, d, J = 3.4 H_z), 7.41 (1H, d, J= 15.3 H_z), 7.55 (1H,d, J= 1. 5 H_z), 7.60 (1H, d, J =15.2 H_z), 7.65 (2H, d, J = 8.5 H_z), 7.90 (2H, d, J = 8.6 H_z); M/z (%): 276, 278 (M^+ - 58, 58) ; λ_{max} (Methanol 227, 313).

1-(*p*-bromophenyl)-5-phenyl-(2E,4E)-pentadiene-1-one [bV]: V_{max}: 1648 (C=O); δ_H (600 MHz, $CDCl_3$, Me_4Si) 7.02 (2H, m, C=C), 7.06 (1H, d, J = 15.0 Hz), 7.35 (1H, t, J = 7.3 Hz), 7.39 (2H, t, J = 7.6 Hz), 7.52 (2H, d, J = 8.6 Hz), 7.61 (1H, not resolved), 7.64 (2H, d, J = 8.6 Hz), 7.86 (2H, d, J = 8.5 Hz); M/z (%): 312, 314 (M^+ - 65, 63); λ_{max} (Methanol 279, 350).

3-(*p*-nitrophenyl)-1-phenyl-(2E)-propen-1-one [cI]: V_{max}: 1662 (C=O); δ_H (600 MHz, $CDCl_3$, Me_4Si) 7.44 (3H, m, ph), 7.45 (1H, d, J = 15.7 Hz), 7.66 (2H, dd, J = 5.5 & 2.0 Hz), 7.85 (1H, d, J = 15.7 Hz), 8.13 (2H, d, J = 8.8 Hz), 8.35 (2H, d, J = 8.8 Hz); M/z (%): 253 (M^+ - 64); λ_{max} (Methanol 267, 314).

1-(*p*-nitrophenyl)-3-(*p*-N,N dimethylaminophenyl)-(2E)-propen-1-one [cII]: V_{max}: 1646 (C=O); δ_H (600 MHz, $CDCl_3$, Me_4Si) 2.99 (6H, s, NMe_2), 6.68 (2H, d, J = 8.9 Hz), 7.24 (1H, d, J = 15.4 Hz), 7.54 (2H, d, J = 8.9 Hz), 7.80 (1H, d, J = 15.4 Hz), 8.10 (2H, d, J = 8.8 Hz), 8.32 (2H, d, J = 8.8 Hz); M/z (%): 296 (M^+ - 100); λ_{max} (Methanol 269, 345, 440).

1-(*p*-nitrophenyl)-3-(*o*-hydroxyllphenyl)- (2E)-propen-1-one [cIII]: V_{max}: 1656 (C=O); δ_H (600 MHz, $CDCl_3$, Me_4Si) 3.89 (3H, s, OMe), 6.98 (2H, d, J = 8.8 Hz), 7.37 (1H, d, J = 15.6 Hz), 7.64 (2H, d, J = 8.7 Hz), 7.83 (1H, d, J = 15.6 Hz), 8.14 (2H, d, J = 8.8 Hz), 8.35 (2H, d, J = 8.8 Hz); M/z (%): 283 (M^+ - 100); λ_{max} (Methanol 263, 351).

1-(*p*-nitrophenyl)-3-(*o*-furyl)-(2E)-propen-1-one [cIV]: V_{max}: δ_H (600 MHz, $CDCl_3$, Me_4Si) 6.54 (1H, dd, J = 3.4 & 1.8 Hz), 6.79 (1H, d, J = 3.4 Hz), 7.40 (1H, d, J = 15.3 Hz), 7.56 (1H, d, J = 8.9 Hz), 7.63 (1H, d, J = 15.3 Hz), 8.14 (2H, d, J = 8.9 Hz), 8.34 (2H, d, J = 8.9 Hz); M/z (%): 243 (M^+ - 48); λ_{max} (Methanol 269, 352).

1-(*p*-nitrophenyl)-5-phenyl-(2E,4E)-pentadiene-1-one [cV]: V_{max}: 1654 (C=O); δ_H (600 MHz, $CDCl_3$, Me_4Si) 7.06 (3H, m, C=C), 7.38 (3H, m, ph), 7.51 (2H, d, J = 8.0 Hz), 7.64 (1H, dd, J = 15.0, 8.7 Hz), 8.09 (2H, d, J = 8.8 Hz), 8.34 (2H, d, J = 8.9 Hz); M/z (%): 297 (M^+ - 100); λ_{max} (Methanol 270, 345).

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