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Synthesis of Arylfuran Propenones and Study of their Mosquito-Larvicidal and Antibacterial Properties

Chemistry

KEYWORDS : Chalcones, Arylfuryl chalcones, Antibacterial activity and Mosquito-larvicidal activity.

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ABSTRACT

A series of novel arylfuranpropenones (chalcones) (4a-p), are synthesized by treating different arylfurfurals (2) with 2,3,4-trichloroacetophenone (3) in the presence of aqueous alkali and ethanol as solvent. The novel arylfuraylpropenones (4a-p) were characterized by FT-IR, 1H-NMR, 13C-NMR, Mass spectra and elemental analyses and were screened for their mosquito-larvicidal and antibacterial activities in which a few of them exhibit moderate activities. Among all the novel derivatives, the compounds (4k) and (4p) may be considered as a potential antibacterial agents as well as mosquito-larvicidal agents.

Introduction

The advances in literature and in technology in recent years have helped to synthesize wide variety of 1,3-diaryl propen-1-ones or 1,3-diphenyl-2-propen-1-ones, commonly known as chalcones or propenones. Chalcones are α, β - unsaturated ketones containing the reactive keto ethylenic group (–CO–CH=CH–). The presence of α, β- unsaturated carbonyl system in makes them biologically active. Hence, they serve as one of the major midway moiety for different heterocyclic modifications and are unique model molecules possessing wide range of biological activities viz., antibacterial [Nielsen *et al.,*2004, 2005; Mehta *et al.,* 1978], antifungal [Bhakuni *et al.,*1984; Wood *et al.,* 1999; Lopez *et al.,* 2001; Boeck *et al*., 2005; Eloshly *et al.,* 2001], antiviral [Cheenpracha *et al.,* 2005; Yayli *et al.,* 2005], anti-inflammatory [Robinson *et al.,* 2005; Nowakowska, 2007], antitumor [Rao *et al.,* 2004] , antioxidant [Simmonds *et al.,*1990], tyrosinase inhibitors [Saydam *et al.,*2003], cytotoxic [Cabrera *et al.,* 2007] and anticancer [Modzelewska *et al.,* 2006; Onyilagna *et al.,* 1997], anaesthetic [Hishmat *et al*., 1996], analgesic, ulcerogenic [Zhao *et al*., 2005], antiplatelet [Liu *et al*., 2001], antiulcerative [Franceso *et al*., 2007], antimalarial [Nielson *et al*., 1995], antifilarial [Awasti *et al*., 2009], anticonvulsant [Kaushik *et al*., 2010], antituberculosis [Sivakumar *et al*., 2007], analgesic [Viana *et al*., 2003], anti-HIV [Tiwari *et al*., 2000], larvicidal [Begum *et al*., 2010], insect antifeedent [Khatib *et al*., 2005], insecticidal [Mudaliar *et al*., 1995] properties and also well known for exhibiting non- linear optical (NLO) properties with excellent blue light transmittance and good crystallizability [Harrison *et al*., 2006]. Addition to all the above facts the heterocyclic compounds containing substituted arylfuran moiety too exhibit diverse biological activities such as antimalarial, and antiviral, antifungal, antibacterial, anticancer activities [Holla *et al*., 1999, 2000; Bhat *et al*., 2004] and so on.

Prompted by the enormous significance of propenones and their derivatives due to their biological activities a plan was drawn to synthesize different arylfuranpropenones and to study their antibacterial property and larvicidal activity in mosquito, since the development of new antibacterial and mosquito-larvicidal agents are always in great demand because the available agents have unsatisfactory status with lots of side effects.

2. *Pharmacology*

The synthesized compounds **(4a-p)** were evaluated for antibacterial properties and larvicidal activity in mosquito.

2.1 *Antibacterial activity*

All the synthesized compounds were evaluated for their antibacterial properties by Disc diffusion method [Bauer *et al*., 1966; Vardar Unlu *et al*., 2003]. The microorganisms used in study of antibacterial properties were collected from Institute of Microbial Technology (IMTECH), Chandigarh, India. Two Gram positive bacteria namely; *Staphylococcus aureus* MTCC-7443 and *Bacillus subtilis* MTCC-441; two Gram negative bacteria namely *Escherichia coli* MTCC-725, *Aeromons hydrophila* MTCC-1739 were used.

The bacterial strains were inoculated on Nutrient Agar (NA) and incubated for 24h at 37°C. Sterile empty discs (6mm diameter) (Himedia Laboratories Pvt. Ltd. Mumbai). The test compounds were dissolved in 5ml of DMSO taken as the solvent. From the stock solution 100µl of respective compound in the selected concentration (500µg/disc) was loaded on the disc individually and aseptically, dried and were used for screening the antibacterial assay.

Sterile discs were saturated with 100µl of the test solution, dried under laminar air flow and placed on the Nutrient Agar (NA) plate for bacteria, which was inoculated with a lawn of the test microorganisms. Plates were incubated at 37°C, for 18 to 24h for bacteria. The compounds that produced distinct circular zones of inhibition around the discs and the diameters of clear zones were determined and used as an indication of antibacterial activity. Ampicillin, an antiobiotic drug at a dose of 10µg/disc was used as the reference standard.

2.2 *Larvicidal activity in Mosquito*

All the synthesized compounds were tested for their mosquito-larvicidal activity using Malaria Vector *Anopheles stephensi* as per the standard WHO guidelines [WHO, 1981]. In 500ml beakers containing 250ml of water and 25 numbers of late III or early IV instar mosquito larvae for various concentrations of the extracts. A negative control was kept with each set of experiment and mortality was recorded after 24h of exposure. Malathion, commercial insecticide (Hindustan Insecticides Ltd, New Delhi, India) was used as the reference standard. Experiments were performed in triplicates for each sample. Median lethal concentration (LC_{50}) with 95% confidence limit was calculated using Abbott's formula and Log probit analysis [Raymond *et al*., 1993] and results are expressed as mg/ml. Relative potency was determined for comparison with the reference standard using

the formula.

Results and Discussion

3.1 *Chemistry*

The different arylfurfurals(2) were prepared by a single step diazotization reaction (Scheme 1) [Akasi et al., 1949, 1951; Rondestvedt 1976]. The general synthetic strategy employed to prepare the novel arylfuranpropenones was based on Claisen–Schmidt condensation reaction. A series of propenones were prepared by condensing substituted arylfurfurals (2) with 2,3,4-trichloroacetophenone (3) in presence of 20% Sodium hydroxide solution and ethanol a solvent at room temperature (Scheme 2). The structures of the newly synthesized arylfuranpropenones (4a-p) were confirmed on the basis of spectral and elemental analyses. The schemes and characterization data of the synthesized compounds are tabulated in Scheme 1, Scheme 2 and Table 1.

3.2 Pharmocological Screening

3.2.1 *Antibacterial activity:*

Among the novel tested compounds **(4a-p)**, the following compounds, **(4b), (4g), (4h), (4j), (4n),** and **(4p)** showed broad spectrum antibacterial activity against Gram positive and Gram negative bacteria, but with different sensitivity **(Figure 1)**, **(Table 2)**. Considering the tested compounds which gave the values > 12 mm are effective, following interpretations are drawn: Compounds **(4g)** and **(4h)** are sensitive only against Gram positive bacteria. **(4j)** is sensitive against only one of the Gram positive bacteria, i.e., *B. Subtilis*. **(4k)** is effective against only Gram positive bacteria, of which *B. subtilis is more sensitive than S. aureus.* **(4n)** also showed effective against only Gram positive bacteria, where, *S. aureus* is more sensitive than *B. subtilis.* **(4p)** is more effective against both Gram positive bacteria almost with the similar sensitivity.

The reference standard, **Ampicillin** was highly sensitive against Gram positive and Gram negative bacterial species. However, tested compounds cannot directly be compared with the reference standard for their efficacy since it depends on therapeutic index, which varies for different bioactive compounds depending upon the ratio between lethal dose and therapeutic dose.

3.2.2 Larvicidal activity in Mosquito

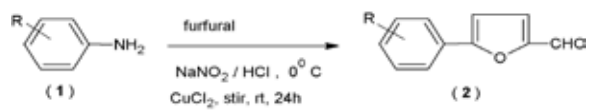
Anopheles stephensi is a malarial vector, breeds mostly in stagnant water known to be the root cause of urban and domestic malaria. Insects have the tendency of developing resistance to insecticidal/ mosquito-larvicidal agents due to continual exposure. Therefore, there is always demand for new agents possessing the mosquito-larvicidal property to control the disease vectors. In the present study, all the compounds showed mosquito larvicidal activity but with different potentiality, IC_{50} values ranging from (21.7 to 86.6 mg/mL) **(Figure 2)**, **(Table 3)**. Among the tested compounds (**4a-p**), the compound **(4p)** (IC_{50} 21.7 mg/mL) was found to be highly effective followed by **(4k)** ((IC_{50} 25.7 mg/mL) and **(4j)** (IC_{50} 29.8 mg/mL) against mosquito (*A. stephensi*) larvae. Compounds, namely **(4f)** (IC_{50} 47.5 mg/mL) and (**3i) (**IC_{50} 49.3 mg/mL) showed moderate activity. The compounds, **(4p)** and **(4k)** carrying dinitro groups **(4p)**, chloro and nitro groups **(4k)** which are electron withdrawing in nature may have the contributions in their relatively higher activity. Heterocyclic compounds with electron donating and electron withdrawing groups have been reported to possess larvicidal activity [Begum Naznin *et al*. 2011; Gulzar *et al*., 2013]. Thus, our observation is in parallel with the previous research reports. Relative potency indicates that novel arylfuran propenones tested in the present study are not as effective as that of Malathion, a commonly used insecticide particularly to control the mosquito larvae. However, among the novel derivatives, (**4p)** and (**4k)** may be considered as mosquito-larvicidal agents after subjected to further studies for their half-life in the environment (persistence) and health hazards to non-target organisms.

4. Experimental section

The chemicals used in the work were obtained from Sigma Aldrich (India), Alfaaesar (U. K.), Apollo Scientific (U. K.) and Merck (India). Melting points of arylfuranpropenones **(4a-p)** were determined in open capillary tubes and are uncorrected. The purity of synthesized compounds was confirmed by TLC. The FT-IR spectra (cm^{-1}) were recorded on a **Shimadzu-FTIR 577** Infrared spectrophotometer in KBr pellets. The ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a **Brucker AMX-400(400 MHz)** spectrometer using $CdCl_3$-*d* as solvent and TMS as the internal standard. The Mass spectra of the chalcones were recorded on **Perkin-Elmer 018444 –Y, Triple Quadrupole LC/ MS** Spectrometer. The elemental analysis was carried out on an **Elementar Vario EL III** analyzer.

4. 1. General Procedure for the Preparation of arylfurfurals (2)

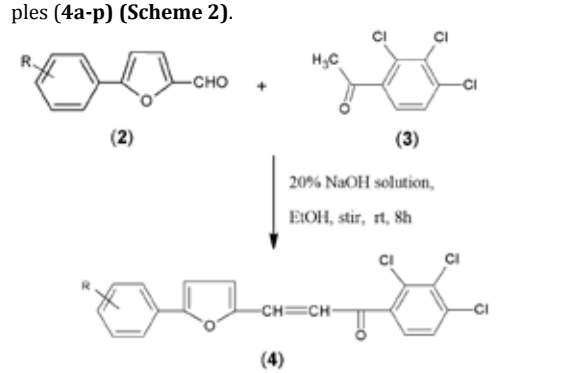
The syntheses of arylfurfurals (5[1]-aryl-furan-2-aldehydes) [Holla *et al*., 1998] (**2**) were done according to the procedure well described in the literature. The arylation to furfural was done according to Meerwein reaction using copper as catalyst. The different substituted aromatic primary amines (**1**) were treated with nitrous acid ($NaNO_2$ in water) in the presence of hydrochloric acid at 0°C to yield diazonium salts. Furan-2-aldehyde was added to the diazonium salts in drops, followed by $CuCl_2$ at temperature 0-5°C. With the completion of addition of the reagents, the reaction mixture is stirred at room temperature for 24h. The purity of the compounds was checked by TLC. The precipitate obtained was dried; yield and melting points were noted and recrystallized from ethanol **(Scheme 1)**.



Scheme 1

4.2. General procedure for the preparation of arylfuranpropenones(4a-p).

A mixture of arylfurfural (0.01 mol) **(2)** and 2,3,4-trichloroacetophenone (0.01 mol) **(3)** (CAS no.13608-87-2) were stirred in ethanol (30 ml) in the presence of aqueous NaOH (20%, 20ml) for 8h at room temperature. The reaction mixture was poured into crushed ice and acidified with HCl. The solid separated was filtered and recrystallized from ethanol to afford analytical samples (**4a-p) (Scheme 2)**.



R= 4-Cl; 2-Cl; 3-Cl; 2,4-Cl_2; 3,4-Cl_2; 2,5-Cl_2; 3,5-Cl_2; 2,4,5-Cl_3; 3-Cl-4-F; 2-Cl-4-NO_2; 2-Cl-5-NO_2; 2-NO_2-4-Cl, 4-Br, 4-NO_2; 2-NO_2, 2,4-$(NO_2)_2$

Scheme 2

Table 1.
Characterization data of arylfuranpropenones (4a-p)

Compound	R	m.p. (°C) (Yield %)	Mol. Formula (Mol. wt)	% Composition, found (Cald) C	H	N
4a	4-Cl	86-88 (79)	$C_{19}H_{10}Cl_4O_2$ (412.09)	55.35 (55.38)	2.47 (2.45)	-

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4b	2-Cl	148-150 (78)	$C_{19}H_{10}Cl_4O_2$ (412.09)	55.35 (55.38)	2.47 (2.45)	-
4c	3-Cl	132-134 (75)	$C_{19}H_{10}Cl_4O_2$ (412.09)	55.35 (55.38)	2.47 (2.45)	-
4d	2,4-Cl_2	162-164 (69)	$C_{19}H_9Cl_5O_2$ (446.54)	51.08 (51.10)	2.06 (2.03)	-
4e	3,4-Cl_2	110-112 (72)	$C_{19}H_9Cl_5O_2$ (446.54)	51.08 (51.10)	2.05 (2.03)	-
4f	2,5-Cl_2	178-180 (81)	$C_{19}H_9Cl_5O_2$ (446.54)	51.09 (51.10)	2.05 (2.03)	-
4g	3,5-Cl_2	116-118 (78)	$C_{19}H_9Cl_5O_2$ (446.54)	51.07 (51.10)	2.05 (2.03)	-
4h	2,4,5-Cl_3	192-194 (72)	$C_{19}H_8Cl_6O_2$ (480.98)	47.42 (47.45)	1.70 (1.68)	-
4i	3-Cl-4-F	110-112 (68)	$C_{19}H_9Cl_4FO_2$ (430.84)	53.08 (53.06)	2.10 (2.11)	-
4j	2-Cl-4-NO_2	88-90 (65)	$C_{19}H_9Cl_4NO_4$ (457.09)	49.95 (49.93)	1.99 (1.98)	3.03 (3.06)
4k	2-Cl-5-NO_2	120-122 (63)	$C_{19}H_9Cl_4NO_4$ (457.09)	49.95 (49.93)	2.00 (1.98)	3.05 (3.06)
4l	2-NO_2-4-Cl	98-100 (60)	$C_{19}H_9Cl_4NO_4$ (457.09)	49.95 (49.93)	1.99 (1.98)	3.03 (3.06)
4m	4- Br	92-94 (81)	$C_{19}H_{10}BrCl_3O_2$ (456.55)	49.96 (49.98)	2.24 (2.21)	-
4n	4-NO_2	232-234 (63)	$C_{19}H_{10}Cl_3NO_4$ (422.65)	53.98 (53.99)	2.40 (2.38)	3.29 (3.31)
4o	2-NO_2	138-140 (60)	$C_{19}H_{10}Cl_3NO_4$ (422.65)	54.01 (53.99)	2.39 (2.38)	3.30 (3.31)
4p	2,4-$(NO_2)_2$	124-126 (62)	$C_{19}H_9Cl_3N_2O_6$ (467.65)	48.82 (48.80)	1.93 (1.94)	5.98 (5.99)

Table 2. Antibacterial Activity
Antibacterial Activity (Zone of Inhibition Test) of arylfuranpropenones (4a-p) and Ampicillin (Reference Standard)

Tested Samples (500 µg/disc)	Diameter of inhibition zone (mm±SD)[A]			
	Bacterial strains			
	Gram positive		Gram negative	
	B. subtilis	S. aureus	E. coli	A. hydrophila
4a	8.65±0.68	9.82±0.49	7.95±0.76	0
4b	9.71 ±0.67	9.59±0.63	11.86±0.55	10.67±0.57
4c	7.78±0.46	8.44±0.61	0	0
4d	0	7.62±0.73	9.26±0.65	8.95±0.87
4e	9.50±0.37	0	7.72±0.43	0
4f	7.89 ±0.91	8.13±0.65	0	7.14±1.08
4g	8.98 ±0.91	8.21±0.65	13.22±0.70	12.94±1.08
4h	10.50±0.72	8.79±0.79	13.24±0.59	14.23±0.62
4i	7.76±0.68	0	7.82±0.76	8.23±0.57
4j	14.78±0.46	10.93±0.61	7.33±0.58	8.45±0.71
4k	16.50±0.72	14.82±0.79	0	8.24±0.59
4l	7.82±0.87	0	9.04±0.63	10.66±0.59
4m	9.50±0.72	8.28±0.79	0	0
4n	12.71 ±0.87	14.59±0.73	10.36±0.65	8.65±0.87
4o	0	0	9.79±0.59	9.03±0.62
4p	17.31 ±0.69	16.73±0.35	10.69±0.41	8.43±0.28
[B]Ampicillin	28.92±0.79	25.48±0.83	21.31±0.67	23.68±0.74

[A]Mean values (n = 3)
[B] Reference standard (10 µg/disc) used as reference standard.
'0' Zone of inhibition < 6 mm indicating no sensitivity.

Table 3. *Larvicidal activity in Mosquito*
Larvicidal activity of arylfuranpropenones (4a-p) against A. stephensi – a malaria vector and Malathion (Reference Standard)

Tested compounds	LC50 (mg/mL)	95% CI	LC90 mg/mL)	95% CI	*Relative potency
4a	76.8	60.54 – 92.81	115.2	97.14 – 133.27	0.11
4b	79.2	62.23 – 96.04	120.98	103.36 – 138.58	0.11
4c	61.3	46.07 - 76.53	90.45	75.24 – 105.66	0.14
4d	72.8	55.44 – 89.58	113.57	96.08 – 131.04	0.12
4e	81.6	63.58 – 99.66	115.05	96.01 – 134.12	0.11
4f	47.5	34.91 – 60.13	70.3	55.63 – 84.97	0.18
4g	86.6	71.37 – 101.23	135.9	118.98 – 152.83	0.10
4h	70.5	56.22 – 84.76	105.04	88.7 – 121.32	0.12
4i	49.3	38.28 – 60.32	71.45	57.66 – 85.24	0.17
4j	29.8	22.62 – 36.97	45.05	32.36 – 57.69	0.29
4k	25.7	19.16 – 32.23	37.78	24.17 – 51.39	0.34
4l	62.2	48.62 – 75.79	99.52	84.43 – 114.61	0.14
4m	62.5	48.48 – 76.54	93.12	76.49 – 109.73	0.14
4n	58.7	45.62 – 71.08	87.49	70.48 – 104.52	0.15
4o	77.5	61.46 – 93.56	124.77	106.13 – 143.39	0.11
4p	21.7	14.72 – 28.69	32.11	20.72 – 43.45	0.40
[a]Malathion	8.7	6.66 – 10.79	12.01	8.39 – 15.69	1

CI – Confidence Interval
***Relative potency - LC_{50} standard / LC_{50} tested substance**
[a]Malathion – Reference standard

Figure 1. Antibacterial activity of arylfuranpropenones (4a–p) and Ampicillin (Reference Standard)

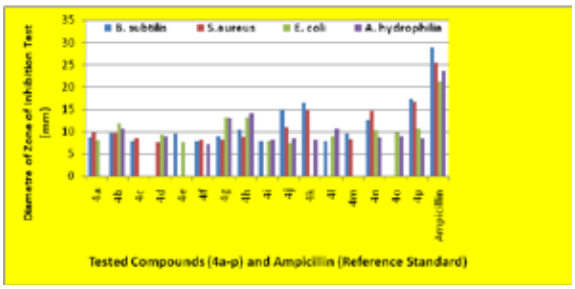
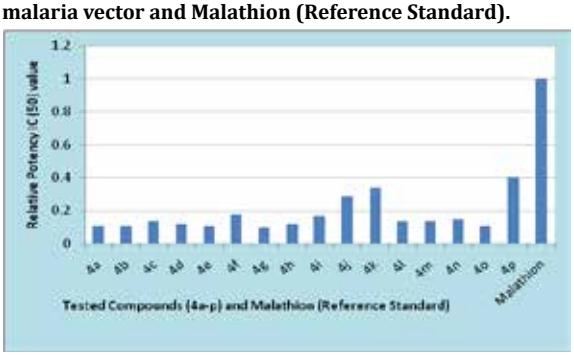


Figure 2. Relative potency of Larvicidal activity of arylfuranpropenones (4a-p) against Anopheles stephensi - a malaria vector and Malathion (Reference Standard).



4.3 The Analyses of the samples (4a-p):
The IR, ^{1}H- NMR, ^{13}C-NMR, mass spectral data and elemental analyses of synthesized furanyl propenones are mentioned below:

4.3.1. (2*E*)-3-[5-(4-chlorophenyl)furan-2-yl]-1-(2,3,4-trichlorophenyl)prop-2-en-1-one (4a):
IR (KBr, cm^{-1}): 3020 (Ar-H), 1669 (-C=O) 1579, 1516 and 1443 (C=C), 792, 767, 748 and 698 (Ar-Cl). ^{1}H-NMR ($CDCl_3$-*d*, δ, ppm): 6.83 (1H, d, *J*=3.6 Hz, furan ring), 6.94 (1H, d, *J*=3.6 Hz, furan ring), 7.03 (1H, d, *J*=16 Hz, =CH-Ar), 7.19 (1H, d, *J*=16 Hz, =CH-Ar), 7.26 (1H,d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.43 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.75 (2H, d, *J*=8.8 Hz, 4-chlorophenyl), 8.18 (2H, d, *J*=8.8 Hz, 4-chlorophenyl). ^{13}C-NMR: 191.22 (-C=O), 153.43 and 151.79 (-CH=CH-), 110.69, 119.23, 120.79, 123.93 (4-C atoms of furan ring), 123.84 and 124.45 (4 C-atoms of 4-chlorophenyl), 126.95, 128.43, 131.29, 134.96, 136.16, 139.18, 145.29 and 147.13 correspond to aryl C-atoms. LC-MS, [M$^+$], (m/z): 413.09/415.09/417.09; Anal. Cald for $C_{19}H_{10}Cl_4O_2$: C, 55.38; H, 2.45; Found: C, 55.35; H, 2.47. m. p. 86-88°C; Yield: 79%

4.3.2. (2*E*)-3-[5-(2-chlorophenyl)furan-2-yl]-1-(2,3,4-trichlorophenyl)prop-2-en-1-one (4b):
IR (KBr, cm^{-1}): 3064 (Ar-H), 1660 (-C=O) 1514, 1477 and 1431 (C=C), 792, 763, 741 and 699 (Ar-Cl). ^{1}H-NMR ($CDCl_3$-*d*, δ, ppm): δ 6.77 (1H, d, *J*=3.6 Hz, furan ring), 6.81 (1H, d, *J*=3.6 Hz, furan ring), 7.01(1H, d, *J*=15.6 Hz, =CH-Ar), 7.21 (1H, d, *J*=15.6 Hz, =CH-Ar), 7.26 (1H, d, *J*=7.8 Hz, 2,3,4-trichlorophenyl), 7.43 (1H, d, *J*=7.8 Hz, 2,3,4-trichlorophenyl), 7.57 (1H, d, 2-chlorophenyl), 7.71 (1H, d, 2-chlorophenyl), 7.31 and 7.54 (2t, 2H, 2-chlorophenyl). ^{13}C-NMR: 191.31 (-C=O), 150.59 and 155.61 (-CH=CH-), 109.30, 119.71, 122.59 and 122.87 (4-C atoms of furan ring), 124.52, 126.92, 128.61, 128.75, 130.21, 131.12, 131.38, 131.91, 132.90, 135.03, 135.96 and 139.47 correspond to aryl C-atoms. LC-MS, [M$^+$], (m/z): 412. 9/414.9/416.9; Anal. Cald for $C_{19}H_{10}Cl_4O_2$: C, 55.38; H, 2.45. Found: C, 55.35; H, 2.47. m.p. 148-150°C; Yield: 78%

4.3.3. (2*E*)-3-[5-(3-chlorophenyl) furan-2-yl]-1-(2,3,4-trichlorophenyl)prop-2-en-1-one (4c):
IR (KBr, cm^{-1}): 3078 (Ar-H), 1656 (-C=O) 1510, 1458 and 1433 (C=C), 815, 792, 775 and 684(Ar-Cl). ^{1}H-NMR ($CDCl_3$-*d*, δ, ppm): δ 6.79 (1H, d, *J*=3.6 Hz, furan ring), 6.82 (1H, d, *J*=3.6 Hz, furan ring), 7.02 (1H, d, *J*=16 Hz, =CH-Ar), 7.23 (1H, d, *J*=16 Hz, =CH-Ar), 7.36 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.49 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.80 (1H, d, 2,3,4-dichlorophenyl), 7.31-7.71 (4H, m, 3-chlorophenyl).^{13}C-NMR: 191.36 (-C=O), 150.70 and 155.66 (-CH=CH-), 109.34, 119.73, 122.62 and 122.90 (4-C atoms of furan ring), 124.53, 126.93, 128.65, 128.79, 130.23, 131.15, 131.40, 131.94, 132.91, 135.05, 135.05 and 139.98 coresspond to aryl C-atoms. LC-MS, [M$^+$], (m/z): 412. 9/414.9; Anal. Cald for $C_{19}H_{10}Cl_4O_2$: C, 55.38; H, 2.45. Found: C, 55.35; H, 2.47. m. p. 132-134°C; Yield: 75%

4.3.4. (2*E*)-3-[5-(2,4-dichlorophenyl)furan-2-yl]-1-(2,3,4-trichlorophenyl)prop-2-en-1-one (4d):
IR (KBr, cm^{-1}): 3066 (Ar-H), 1660 (-C=O) 1543, 1508 and 1452 (C=C), 819, 792, 744, 713 and 688 (Ar-Cl). ^{1}H-NMR ($CDCl_3$-*d*, δ, ppm): δ 6.85 (1H, d, *J*=3.6 Hz, furan ring), 7.24 (1H, d, *J*=3.6 Hz, furan ring), 7.02 (1H, d, *J*=16 Hz, =CH-Ar), 7.23 (1H, d, *J*=16 Hz, =CH-Ar), 7.29 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.85 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.33 and 7.35 (2H, dd, *J*=2.4 Hz, 2,4-dichlorophenyl). 7.49 (1H, s, 2,4-dichlorophenyl). ^{13}C-NMR: 191.38 (-C=O), 152.43 and 150.22 (-CH=CH-), 114.21, 119.46, 123.42, 126.66 (4-C atoms of furan ring), 126.97, 127.57, 128.67, 129.08, 130.79, 131.40, 131.46, 131.84, 132.92, 134.63, 136.05 and 139.39 correspond to aryl C-atoms. LC-MS, [M$^+$], (m/z): 447.3/449.1; Anal. Cald for $C_{19}H_9Cl_5O_2$: C, 51.10; H, 2.03. Found: C, 51.08; H, 2.06. m. p. 162-164°C; Yield: 69%

4.3.5. (2*E*)-3-[5-(3,4-dichlorophenyl)furan-2-yl]-1-(2,3,4-trichlorophenyl)prop-2-en-1-one (4e):
IR (KBr, cm^{-1}): 3034 (Ar-H), 1654 (-C=O) 1587, 1560 and 1458(C=C), 819, 788, 690 and 618 Ar-Cl). ^{1}H-NMR ($CDCl_3$-*d*, δ, ppm): 6.79 (1H, d, *J*=3.6 Hz, furan ring), 6.82 (1H, d, *J*=3.6 Hz, furan ring), 7.02 (1H, d, *J*=15.6 Hz, =CH-Ar), 7.23(1H, d, *J*=15.6 Hz, =CH-Ar), 7.48 (1H, d, *J*=6.4 Hz, 2,3,4-trichlorophenyl), 7.50 (1H, d, *J*=6.4 Hz, 2,3,4-trichlorophenyl), 7.30 (1H, d, *J*=8 Hz 3,4-dichlorophenyl), 7.53 (1H, d, *J*=2.4 Hz, 3,4-dichlorophenyl). 7.80 (1H, d, *J*=2.4 Hz, 3,4-dichlorophenyl). 7.56 (1H, d, *J*=2 Hz, meta coupling 3,4-dichlorophenyl). ^{13}C-NMR: 191.32 (-C=O), 154.68 and 150.92 (-CH=CH-), 109.60, 119.64, 123.15 and 123.60 (4-C atoms of furan ring), 126.18, 126.94, 128.67, 129.38, 130.99, 131.42, 131.75, 132.95, 132.75 133.39, 136.05 and 139.43 coresspond to aryl C-atoms. LC-MS, [M$^+$], (m/z): 447.2/449.1; Anal. Cald for $C_{19}H_9Cl_5O_2$: C, 51.10; H, 2.03. Found: C, 51.08; H, 2.05. m. p. 110-112°C; Yield: 72%.

4.3.6. (2*E*)-3-[5-(2,5-dichlorophenyl)furan-2-yl]-1-(2,3,4-trichlorophenyl)prop-2-en-1-one (4f):
IR (KBr, cm^{-1}): 3020 (Ar-H), 1660 (-C=O) 1597, 1546 and 1465(C=C), 812, 796, 744, 692 and 654 (Ar-Cl). ^{1}H-NMR ($CDCl_3$-*d*, δ, ppm): δ 6.86 (1H, d, *J*=3.6 Hz, furan ring), 7.29 (1H, d, *J*=3.6 Hz, furan ring), 7.04 (1H, d, *J*=15.6 Hz, =CH-Ar), 7.23 (1H, d, *J*=15.6 Hz, =CH-Ar), 7.39 (1H, d, *J*=8.4 Hz, 2,3,4-trichlorophenyl), 7.50 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.23 (1H, d, *J*=6 Hz, 2,5-dichlorophenyl), 7.31 (1H, d, *J*=6 Hz, 2,5-dichlorophenyl), 7.88 (1H, d, *J*=7.8 Hz, 2,5-dichlorophenyl); ^{13}C-NMR: 191.43 (-C=O), 151.94 and 150.48 (-CH=CH-), 114.76, 119.29, 123.74 and 126.94 (4 C- atoms of furan ring), 127.95, 128.68, 129.01, 129.14, 129.30, 131.43, 131.78, 132.13, 132.96 133.24, 136.09 and 139.34 correspond to aryl C-atoms. LC-MS, [M$^+$], (m/z): 447.9; Anal. Cald for $C_{19}H_9Cl_5O_2$: C, 51.10; H, 2.03. Found: C, 51.09; H, 2.05. m. p. 178-180°C; Yield: 81%.

4.3.7. (2*E*)-3-[5-(3,5-dichlorophenyl)furan-2-yl]-1-(2,3,4-trichlorophenyl)prop-2-en-1-one (4g):
IR (KBr, cm^{-1}): 3065 (Ar CH), 1665 (-C=O), 1594, 1541 and 1469 (C=C), 814, 798, 751, 701 and 661 (Ar-Cl). ^{1}H-NMR ($CDCl_3$-*d*, δ, ppm): δ 6.84 (1H, d, *J*=3.6 Hz, furan ring), 7.19 (1H, d, *J*=3.6 Hz, furan ring), 7.02 (1H, d, *J*=15.6 Hz, =CH-Ar), 7.23 (1H, d, *J*=15.6 Hz, =CH-Ar), 7.35 (1H, d, *J*=8.4 Hz, 2,3,4-trichlorophenyl), 7.43 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.27 (1H, s, 3,5-dichlorophenyl), 7.31 (1H, s, 3,5-dichlorophenyl), 7.42

(1H, s, 3,5-dichlorophenyl); ^{13}C-NMR: 191.38 (-C=O), 150.94 and 150.46(-CH=CH-), 114.72, 119.21, 123.54 and 126.94 (4 C- atoms of furan ring), 127.87, 128.63, 129.31, 129.54, 129.70, 131.45, 131.88, 132.23, 133.06 133.26, 136.19 and 139.44 correspond to aryl C-atoms. LC-MS, [M$^+$], (m/z): 447.9; Anal. Cald for $C_{19}H_9Cl_5O_2$: C, 51.10; H, 2.03. Found: C, 51.07; H, 2.05. m. p. 116-118^{o}C; Yield: 78%.

4.3.8. (2*E*)-1-(2,3,4-trichlorophenyl)-3-[5-(2,4,5-trichlorophenyl)furan-2-yl] prop-2-en-1-one (4h):
IR (KBr, cm^{-1}): 3055 (Ar-H), 1675 (-C=O), 1584, 1561 and 1479 (C=C), 859, 816, 802, 787, 748 and 686(Ar-Cl). ^{1}H-NMR ($CDCl_3$-*d*, δ, ppm): δ 6.85 (1H, d, *J*=3.6 Hz, furan ring), 7.28 (1H, d, *J*=3.6 Hz, furan ring), 7.04 (1H, d, *J*=16 Hz, =CH-Ar), 7.24 (1H, d, *J*=16 Hz, =CH-Ar), 7.30 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.50 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.57(1H, s, 2,4,5-trichlorophenyl), 7.98 (1H, s, 2,4,5-trichlorophenyl); ^{13}C-NMR: 191.37 (-C=O), 151.10 and 150.65 (-CH=CH-), 114.87, 119.23, 123.94 and 126.94 (4 C- atoms of furan ring), 127.73, 128.69, 129.05, 129.17, 131.42, 131.60, 131.85, 132.24, 132.70, 134.57, 136.14 and 139.27 correspond to aryl C-atoms. LC-MS, [M$^+$], (m/z): 481.9/483.9/485.9; Anal. Cald for $C_{19}H_8Cl_6O_2$: C, 47.45; H, 1.68. Found: C, 47.42; H, 1.70. m .p. 192-194^{o}C; Yield: 72%

4.3.9. (2*E*)-3-[5-(3-chloro-4-fluorophenyl)furan-2-yl]-1-(2,3,4-trichlorophenyl)prop-2-en-1-one (4i):
IR (KBr, cm^{-1}): 3024 (Ar-H), 1664 (-C=O) 1577, 1556 and 1468 (C=C), 1033 (Ar-F), 832, 798, 765 and 692 (Ar-Cl). ^{1}H-NMR ($CDCl_3$-*d*, δ, ppm): 6.79 (1H, d, *J*=3.6 Hz, furan ring), 6.82 (1H, d, *J*=3.6 Hz, furan ring), 7.01 (1H, d, *J*=15.6 Hz, =CH-Ar), 7.21 (1H, d, *J*=15.66 Hz, =CH-Ar), 7.42 (1H, d, *J*=6.4 Hz, 2,3,4-trichlorophenyl), 7.46 (1H, d, *J*=6.4 Hz, 2,3,4-trichlorophenyl), 7.32 (1H, d, *J*=8 Hz 3-chloro-4-flurophenyl), 7.56- 7.72 (2H, m, 3-chloro-4-flurophenyl). 7.56 (1H, d, *J*=2 Hz, meta coupling 3-chloro-4-flurophenyl). ^{13}C-NMR: 192.22 (-C=O), 153.78 and 151.82 (-CH=CH-), 110.20, 120.34, 124.25 and 124.80 (4 C-atoms of furan ring), 126.38, 127.14, 128.77, 129.48, 131.09, 131.52, 131.85, 132.97, 133.05 133.59, 136.45 and 139.73 coresspond to aryl C-atoms. LC-MS, [M$^+$], (m/z): 431.8/433.8; Anal. Cald for $C_{19}H_9Cl_4FO_2$: C, 53.06; H, 2.11. Found: C, 53.08; H, 2.10. m. p. 110-112^{o}C; Yield: 68%

4.3.10. (2*E*)-3-[5-(2-chloro-4-nitrophenyl)furan-2-yl]-1-(2,3,4-trichlorophenyl) prop-2-en-1-one (4j):
IR (KBr, cm^{-1}): 3055 (Ar-H), 1663 (-C=O) 1570, 1526 and 1497(C=C), 1514 and 1388 (NO_2 asymmetric & symmetric stretch) 855, 825, 796 and 748 (Ar-Cl). ^{1}H-NMR ($CDCl_3$-*d*, δ, ppm): 6.79 (1H, d, *J*=3.6 Hz, furan ring), 6.84 (1H, d, *J*=3.6 Hz, furan ring), 6.99 (1H, d, *J*=16 Hz, =CH-Ar), 7.24 (1H, d, *J*=16 Hz, =CH-Ar), 7.32 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.49 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.61 (1H, s, 2-chloro-4-nitrophenyl), 7.67 (1H, d, *J*=3.2 Hz, 2-chloro-4-nitrophenyl), 7.71 (H, d, *J*=3.2 Hz, 2-chloro-4-nitrophenyl). ^{13}C-NMR: 191.21(-C=O), 150.27 and 151.99 (-CH=CH-), 113.11, 118.88, 121.65 and 124.15 (4 C- atoms of furan ring), 124.65, 127.19, 128.87, 130.19, 131.71, 132.45, 133.01, 135.54, 136.35 and 139.37 correspond to aryl C-atoms. LC-MS, [M$^+$], (m/z): 458.09/460; Anal. Cald for $C_{19}H_9Cl_4NO_4$: C, 49.93; H, 1.98; N, 3.06. Found: C, 49.95; H, 1.99; N, 3.03. m. p. 88-90^{o}C; Yield: 65%

4.3.11. (2*E*)-3-[5-(2-chloro-5-nitrophenyl)furan-2-yl]-1-(2,3,4-trichlorophenyl) prop-2-en-1-one (4k):
IR (KBr, cm^{-1}): 3028 (Ar-H), 1665 (-C=O) 1595, 1543 and 1467 (C=C), 1512 and 1386 (NO_2 asymmetric & symmetric stretch), 819, 795, 765 and 698 (Ar-Cl). ^{1}H-NMR ($CDCl_3$-*d*, δ, ppm): δ 6.88 (1H, d, *J*=3.6 Hz, furan ring), 7.20 (1H, d, *J*=3.6 Hz, furan ring), 7.02 (1H, d, *J*=15.6 Hz, =CH-Ar), 7.22 (1H, d, *J*=15.6 Hz, =CH-Ar), 7.35 (1H, d, *J*=8.4 Hz, 2,3,4-trichlorophenyl), 7.48 (1H, d, *J*=8 Hz, 2, 3, 4-trichlorophenyl), 7.23 (1H, d, *J*=6 Hz, 2-chloro-5-nitroophenyl), 7.29 (1H, d, *J*=6 Hz, 2-chloro-5-nitroophenyl), 7.72 (1H, d, *J*=7.8 Hz, 2,5-dichlorophenyl); ^{13}C-NMR: 191.34 (-C=O), 151.92 and 150.58 (-CH=CH-), 114.86, 119.19, 123.84 and 126.98 (4 C- atoms of furan ring), 128.05, 128.88, 129.11, 129.24, 129.51, 131.63, 131.88, 132.23, 133.06 133.34, 136.19 and 139.44 correspond to aryl C-atoms. LC-MS, [M$^+$], (m/z): 458.09/460; Anal. Cald for $C_{19}H_9Cl_4NO_4$: C, 49.93; H, 1.98; N, 3.06. Found: C, 49.95; H, 1.99; N, 3.03. m. p. 120-122^{o}C; Yield: 63%

4.3.12. (2*E*)-3-[5-(4-chloro-2-nitrophenyl) furan-2-yl]-1-(2,3,4-trichlorophenyl) prop-2-en-1-one (4l):
IR (KBr, cm^{-1}): 3065 (Ar-H), 1660 (-C=O) 1573, 1522 and 1499 (C=C), 1512 and 1386 (NO_2 asymmetric & symmetric stretch) 850, 827, 796 and 765 (Ar-Cl). ^{1}H-NMR ($CDCl_3$-*d*, δ, ppm): 6.77 (1H, d, *J*=3.6 Hz, furan ring), 6.81 (1H, d, *J*=3.6 Hz, furan ring), 6.97 (1H, d, *J*=16Hz, =CH-Ar), 7.22 (1H, d, *J*=16Hz, =CH-Ar), 7.30 (1H,d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.49 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.60 (1H, d, *J*=2.4 Hz, 4-chloro-2-nitrophenyl), 7.72 (1H, d, *J*=3.2 Hz, 4-chloro-2-nitrophenyl), 7.73 (1H, d, *J*=3.2 Hz, 4-chloro-2-nitrophenyl). ^{13}C-NMR: 191.11(-C=O), 150.07 and 151.89 (-CH=CH-), 113.01, 118.82, 121.45 and 124.05 (4 C- atoms of furan ring), 126.31, 126.75, 127.09, 128.67, 129.99, 131.19, 131.51, 132.25, 132.98, 135.24, 136.25 and 139.17 correspond to aryl C-atoms. LC-MS, [M$^+$], (m/z): 458.09/459.9; Anal. Cald for $C_{19}H_9Cl_4NO_4$: C, 49.93; H, 1.98; N 3.06. Found: C, 49.95; H, 1.99; N, 3.03. m. p. 98-100^{o}C; Yield: 60%

4.3. 13. (2*E*)-3-[5-(4-bromophenyl)furan-2-yl]-1-(2,3,4-trichlorophenyl)prop-2-en-1-one (4m):
IR (KBr, cm^{-1}): 3048 (Ar-H), 1665 (-C=O) 1573, 1519 and 1498 (C=C), 821, 798 and 776 (Ar-Cl), 661(Ar-Br). ^{1}H-NMR ($CDCl_3$-*d*, δ, ppm): 6.85 (1H, d, *J*=3.6 Hz, furan ring), 6.96 (1H, d, *J*=3.6 Hz, furan ring), 7.05 (1H, d, *J*=16 Hz, =CH-Ar), 7.21 (1H, d, *J*=16 Hz, =CH-Ar), 7.27 (1H,d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.42 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.65 (2H, d, *J*=8.8 Hz, 4-bromophenyl), 7.70 (2H, d, *J*=8.8 Hz, 4-bromophenyl). ^{13}C-NMR: 190.98 (-C=O), 152.83 and 150.89 (-CH=CH-), 110.59, 118.93, 120.49 and 123.63 (4 C- atoms of furan ring), 124.04 and 124.65 (4 C- atoms of 4-bromophenyl), 126.98, 128.53, 131.19, 135.06, 136.16, 139.21, 144.89 and 146.93 correspond to aryl C-atoms. LC-MS, [M$^+$], (m/z): 457.5/459.5; Anal. Cald for $C_{19}H_{10}BrCl_3O_2$: C, 49.98; H, 2.21; Found: C, 49.96; H, 2.24. m. p. 92-94^{o}C; Yield: 81%

4.3.14. (2*E*)-3-[5-(4-nitrophenyl)furan-2-yl]-1-(2,3,4-trichlorophenyl) prop-2-en-1-one (4n):
IR (KBr, cm^{-1}): 3052 (Ar-H), 1658(-C=O) 1583, 1512 and 1489 (C=C), 1510 and 1382 (NO_2 asymmetric & symmetric stretch) 850, 806, 748 and 688 (Ar-Cl). ^{1}H-NMR ($CDCl_3$-*d*, δ, ppm): 6.87 (1H, d, *J*=3.6 Hz, furan ring), 6.99 (1H, d, *J*=3.6 Hz, furan ring), 7.08 (1H, d, *J*=16 Hz, =CH-Ar), 7.24 (1H, d, *J*=16 Hz, =CH-Ar), 7.31 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.51 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.87 (2H, d, *J*=8.8 Hz, 4-nitrophenyl), 8.29 (2H, d, *J*=8.8 Hz, 4-nitrophenyl). ^{13}C-NMR: 191.18 (-C=O), 154.43 and 151.99 (-CH=CH-), 111.69, 119.46, 121.38 and 124.03 (4- C atoms of furan ring), 124.54 and 124.95 (4 C-atoms of nitrophenyl), 127.05, 128.73, 131.49, 135.02, 136.26, 139.28, 145.49 and 147.43 correspond to aryl C-atoms. LC-MS, [M$^+$], (m/z): 421.9/424; Anal. Cald for $C_{19}H_{10}Cl_3NO_4$: C, 53.99; H, 2.38; N, 3.31. Found: C, 53.98; H, 2.40; N, 3.29. m. p. 232-234^{o}C; Yield: 63%

4.3.15. (2*E*)-3-[5-(2-nitrophenyl)furan-2-yl]-1-(2,3,4-trichlorophenyl)prop-2-en-1-one (4o):
IR (KBr, cm^{-1}): 3067 (Ar-H), 1669 (-C=O) 1514, 1525 and 1412(NO_2 asymmetric & symmetric stretch), 1487 and 1451(C=C), 847, 802, 758 and 690 (Ar-Cl). ^{1}H-NMR ($CDCl_3$-*d*, δ, ppm): δ 6.77 (1H, d, *J*=3.6 Hz, furan ring), 6.81 (1H, d, *J*=3.6 Hz, furan ring), 6.97 (1H, d, *J*=15.6 Hz, =CH-Ar), 7.22 (1H, d, *J*=15.6 Hz, =CH-Ar), 7.28 (1H, d, *J*=7.8 Hz, 2,3,4-trichlorophenyl), 7.48 (1H, d, *J*=7.8 Hz, 2,3,4-trichlorophenyl), 7.51(1H, d, *J*=1.6Hz, 2-nitrophenyl), 7.60-7.78 (3H, m, 2-nitrophenyl). ^{13}C-NMR: 191.18 (-C=O), 151.28 and 154.64 (-CH=CH-), 112.62, 118.92, 123.06 and 123.72 (4- C atoms of furan ring), 124.12, 127.08, 128.64, 129.15, 129.51, 131.46, 131.51, 132.08, 132.93, 136.14, 139.25, and 147.78 correspond to aryl C-atoms. LC-MS, [M$^+$], (m/z): 423.6; Anal. Cald for $C_{19}H_{10}Cl_3NO_4$: C, 53.99; H, 2.38; N, 3.31. Found: C, 54.01; H, 2.39; N, 3.30. m. p. 138-140^{o}C; Yield: 60%

4.3.16. (2*E*)-3-[5-(2, 4-dinitrophenyl)furan-2-yl]-1-(2,3,4-

trichlorophenyl)prop-2-en-1-one (4p):
IR (KBr, cm^{-1}): 3042 (Ar-H), 1681 (-C=O) 1545 and 1462 (NO_2 asymmetric & symmetric stretch) 1553, 1528 and 1482 (C=C), 838, 799 and 761 (Ar-Cl). ^{1}H-NMR ($CDCl_3$-*d*, δ, ppm): δ 6.79 (1H, d, *J*=3.6 Hz, furan ring), 6.84 (1H, d, *J*=3.6 Hz, furan ring), 7.03 (1H, d, *J*=15.6 Hz, =CH-Ar), 7.21 (1H, d, *J*=15.6 Hz, =CH-Ar), 7.29 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.81 (1H, d, *J*=8 Hz, 2,3,4-trichlorophenyl), 7.6 (1H, s, 2,4-dinitrophenyl), 7.35 and 7.38 (2H, dd, *J*=2.4 Hz, 2,4-dinitrophenyl). ^{13}C-NMR: 192.48 (-C=O), 153.47 and 151.24 (-CH=CH-), 115.23, 119.86, 123.82 and 125.96 (4 C- atoms of furan ring), 126.87, 127.77, 128.87, 129.68, 130.89, 131.60, 131.96, 132.24, 133.52, 134.73, 136.25 and 139.49 coresspond to aryl C-atoms. LC-MS, [M^+], (m/z): 466.6/468.6; Anal. Cald for $C_{19}H_9Cl_3N_2O_6$: C, 48.80; H, 1.94; N, 5.99. Found: C, 48.82; H, 1.93; N, 5.98. m. p. 122-126°C; Yield: 62%

5. Conclusion
Among all the novel arylfuranpropenones **(4a-p)**, the compounds, **(4k)** and **(4p)** may be recommended as drug candidates for diseases caused by ***B. subtilis*** and ***S. aureus***, which are found to be highly sensitive compared to the other novel tested compounds. The compounds, **(4p)** and **(4k)** can also be considered as potential agents to control malaria spread by A***. stephensi***. Hence they may be considered as mosquito-larvicidal agents after subjected to further studies for their half-life in the environment (persistence) and health hazards to non-target organisms.

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