Antimicrobial and Antileishmanial Studies of Novel (2*E*)-3-(2-Chloro-6-methyl/methoxyquinolin-3-yl)-1-(Aryl)prop-2-en-1-ones

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Thirty eight heterocyclic chalcones were synthesized by condensing formylquinolines with diverse methyl arylketones. The target compounds were characterized by spectroscopic techniques (NMR, IR, MS) and elemental analysis. The X-ray crystallographic study of (2*E*)-3-(2-chloro-6-methylquinolin-3-yl)-1-(2,3-dihydro-1,4-benzodioxin-6-yl)prop-2-en-1-one (1p) was also performed for the structure confirmation. The title compounds were screened for anti-microbial and antileishmanial activities. The compounds 1c—e, 1g, 1j—m, 1p, 1r—s, 2g, 2j—p, and 2r—s were found potentially active antileishmanial agents, while 1f—i, 1l, 1o—p, 2f—i, 2l, and 2o—p showed remarkable antibacterial activity. Only compounds 1g and 2g—h exhibited significant antifungal activity.

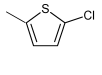
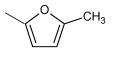
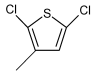
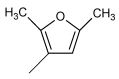
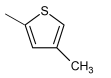
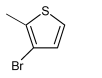
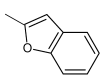
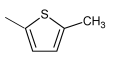
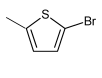
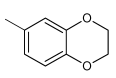
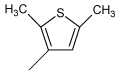
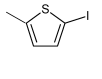
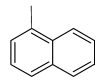
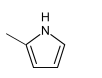
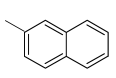
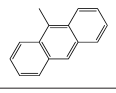
Key words chalcone; antimicrobial activity; antileishmanial activity; formylquinoline; arylketone

Chalcones are α,β-unsaturated ketones which constitute an important group of natural products that serve as precursors for the synthesis of various heterocyclic compounds like pyrimidines, imidazoles,[1)] pyrazoles,[2)] 2-pyrazolines[3,4)] and flavonoids.[5,6)] Chalcones, either natural or synthetic, are known to exhibit various biological activities such as anti-inflammatory,[7,8)] antifungal,[9—12)] antioxidant,[13—16)] antimalarial,[17—20)] antituberculosis,[21)] analgesic,[22)] anti-human immunodeficiency virus (HIV)[23)] and antitumor activities.[23—25)] Some of them act as anticancer,[26)] antiviral[27)] and anti-AIDS agents.[28)] Quinoline-based chalcones have been reported to possess antimalarial activity.[29)] Chalcones as well as some quinoline derivatives have already been recognized for their antimicrobial[30,31)] and antileishmanial activities.[32—34)] In the present study, the quinoline nucleus and chalcone functionality have been incorporated in a single molecule (**1a**—**s**, **2a**—**s**) and deliberated their antimicrobial and antileishmanial activities with variation of substituents at different positions in the Ar ring.

The two precursors, 2-chloro-6-methyl-3-formylquinoline and 2-chloro-6-methoxy-3-formylquinoline, were prepared by reported method.[35)] Synthesis of the title compounds (**1a**—**s**, **2a**—**s**), was based on Claisen–Schmidt condensation.[36,37)] For this purpose, the prepared formyl quinolines were condensed with commercially available methyl arylketones (Table 1), in the presence of sodium hydroxide. The *E*-configuration was confirmed by X-ray structure of (**1p**) and two more chalcones (**1k**, **1m**) which were already reported.[38)] Spectral data (IR, ^{1}H-NMR and MS) of all the newly synthesized chalcones were in full agreement with the proposed structures. Configuration of the double bond (**1a**—**s**, **2a**—**s**) was confirmed by coupling constant in ^{1}H-NMR.

Antileishmanial Activity According to the results obtained, it is evident that unsubstituted thiophenyl derivatives

Table 1. Aryl Moiety (Ar) of Aromatic Ketones (**a**—**s**)

Ketones	Ar	Ketones	Ar	Ketones	Ar
a		**g**		**m**	
b		**h**		**n**	
c		**i**		**o**	
d		**j**		**p**	
e		**k**		**q**	
f		**l**		**r**	
				s	

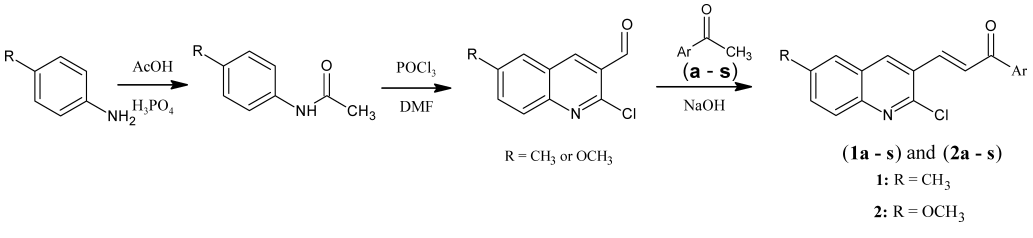


Chart 1

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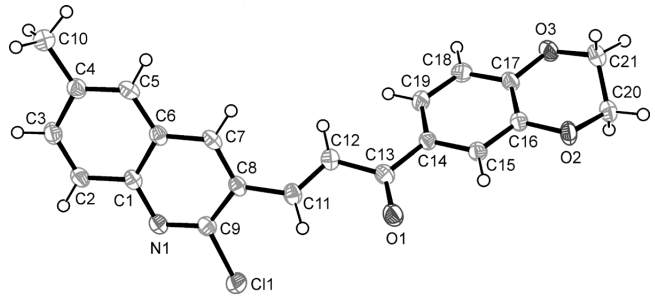

Fig. 1. ORTEP-3 Diagram of Compound **1p** with the Numbering Scheme

Displacement ellipsoids are drawn at the 50% probability level, H atoms are represented by circles of arbitrary radii.

(**1a**, **2a**) are almost equally active (IC_{50}=0.58±0.02 μg/ml for **1a** and IC_{50}=0.59±0.01 μg/ml for **2a**), comparable to the standard, amphotericin B (IC_{50}=0.56±0.20 μg/ml) while the activity enhances considerably by the substitution of methyl and halo groups at position 5 of thiophenyl ring (**1d**, **2d**, **1g**, **2g**, **1j**, **2j**, **1k**, **2k**; Table 2). Among the compounds, derivatized at position 5, chloro analogues (**1g**, **2g**) are the most active. However, incorporation of these functionalities at position 3 of thiophenyl ring (**1b**, **2b**, **1f**, **2f**, **1i**, **2i**) instead of position 5, deactivates the compounds except of bromo derivative (**1i**) perhaps due to electronic and steric reasons. Incorporation of methyl group at position 4 (**1c**) in category **1** increases the activity than its analogue **1b**, derivatized at position 3 (IC_{50}=0.75±0.05 μg/ml for **1b** and IC_{50}=0.27±0.02 μg/ml for **1c**), while no prominent difference in activities is observed by the same change in category **2** (**2b**, **2c** respectively, Table 2). Similarly, the replacement of two methyl groups at position 2 and 5 of thiophenyl ring (**1e**, **2e**) by two chloro groups (**1h**, **2h**), significantly decreases the activity (by about 5 times) in category **1**; reverse is observed in case of category **2**. In case of furanyl derivatives, incorporation of a second methyl group at position 2 considerably decreases the activity (**1n**) than of the mono substituted one (**1m**) in category **1**, whereas in category **2** no marked difference is observed whether one (**2m**) or two (**2n**) methyl groups are present on the furanyl ring. For the rest of the compounds, no systematic change in anti-leishmanial activities is observed (Table 2).

Antibacterial Activity Compounds **2h**, and **2o**—**p**, from substituted heteroaryl derivatives have shown promising antibacterial activities (almost equivalent to standard) against all the three bacterial strains *i.e.*, *Escherichia coli*, *Micrococcus luteus* and *Staphylococcus aureus*. Among the two series of compounds, unsubstituted thiophenyl derivatives (**1a**, **2a**) exhibited almost equivalent antibacterial activities to that of the standard (Table 3). Activity decreases considerably by the substitution of methyl and halo groups at position 5 of thiophenyl ring (**1d**, **2d**, **1g**, **2g**, **1j**, **2j**, **1k**, **2k**; Table 3). Incorporation of chlorine at position 5 of thiophenyl ring (**1g**, **2g**) enhanced the activity to a considerable extent; it is further increased by the incorporation of another chlorine atom at position 2 (**1h**, **2h**). However, incorporation of same groups at positions 3 and 4 (**1b**, **1c**, **1f**, **1i**, **2b**, **2c**, **2f**, **2i**) exhibited no difference in activity except of bromo derivatives. In case of furanyl derivatives, incorporation of a second methyl group at position 2 (**1n**, **2n**) considerably decreases the activity than of the mono substituted one (**1m**, **2m**). In general, activity enhances by the substitution of aromatic rings with electron withdrawing groups and is suppressed by the incorporation of electron donating methyl groups. No systematic change has been observed in antibacterial activities for the rest of the compounds (Table 3).

Table 2. Antileishmanial Activity of the Series **1a**—**s** and **2a**—**s** (IC_{50})

Compounds	IC_{50} (μg/ml)	Compounds	IC_{50} (μg/ml)
1a	0.58±0.02	**2a**	0.59±0.01
1b	0.75±0.05	**2b**	0.82±1.25
1c	0.27±0.02	**2c**	0.84±0.35
1d	0.34±0.06	**2d**	0.61±0.05
1e	0.16±0.19	**2e**	0.93±0.08
1f	0.78±0.07	**2f**	0.68±0.56
1g	0.23±0.50	**2g**	0.23±0.50
1h	0.81±0.45	**2h**	0.69±0.06
1i	0.57±0.01	**2i**	0.79±0.78
1j	0.42±0.62	**2j**	0.32±0.62
1k	0.31±0.03	**2k**	0.41±0.03
1l	0.33±0.06	**2l**	0.33±0.06
1m	0.37±0.10	**2m**	0.27±0.10
1n	0.84±0.58	**2n**	0.29±0.03
1o	0.87±1.25	**2o**	0.22±0.19
1p	0.26±0.08	**2p**	0.46±0.08
1q	0.91±1.69	**2q**	0.57±0.02
1r	0.21±0.04	**2r**	0.31±0.04
1s	0.29±0.03	**2s**	0.39±0.03
Standard drug MIC (μg/ml±S.D.) (Amphotericin B)	0.56±0.20	Standard drug MIC (μg/ml±S.D.) (Amphotericin B)	0.56±0.20

Antifungal Activity Among the compounds under investigation, un-substituted thiophenyl derivatives (**1a**, **2a**) are found almost equivalent in their antifungal activities to the standard. In general, activity decreases in the compounds having substitution at position 2, 3 and 5 by the incorporation of electron donating methyl groups at aromatic rings while it enhances by the substitution of electron withdrawing groups. Among the electron withdrawing groups, activity increases with the electronegativity of the substituent. However, such substitutions at position 4 (**1c**, **2c**) displayed no marked difference in the activities. No systematic change has been observed in antibacterial activities for the rest of the compounds (Table 3).

Conclusion

Amongst the compounds tested for antibacterial study, **1f**—**i**, **1l**, **1o**—**p**, **2f**—**i**, **2l**, and **2o**—**p** showed remarkable antibacterial activity. Especially, compounds **1h**, **1l**, **1o**—**p**, **2h**—**i**, and **2o**—**p** showed significant activity against *E. coli* and **1h**—**i**, **2h**—**i** and **2o** against *M. luteus* while **1h**—**i**, **1p**, **2g**, **2h**—**i**, **2l** and **2p** were found most active against *S. aureus*. Compunds **1g**, and **2g**—**h** displayed more antifungal activity, against all the fungi, than the standard flucanazole. As far as antileishmanial activity is concerned, the compounds **1c**—**e**, **1g**, **1j**—**m**, **1p**, **1r**—**s**, **2g**, **2j**—**p**, and **2r**—**s** exhibited marvelous antileishmanial activity, while others showed moderate activity.

Experimental

General Melting points were obtained on Gallenkamp melting point apparatus and were uncorrected. IR spectra were recorded in KBr pellets on Perkin Elmer infrared spectrophotometer. ^{1}H-NMR spectra were recorded in $CDCl_3$ on Brücker/XWIN NMR (400 MHz) and tetramethylsilane (TMS)

Table 3. Antimicrobial Activity of Compounds (**1a**—**s**, **2a**—**s**)

Compound	Antibacterial activity zone of inhibition in mm			Antifungal activity zone of inhibition in mm		
	E. coli	*M. luteus*	*S. aureus*	*A. flaves*	*A. niger*	*C. lunata*
1a	21	31	34	10	11	12
1b	16	23	25	8	10	11
1c	14	27	31	7	9	8
1d	13	22	26	4	10	9
1e	11	20	22	3	8	5
1f	30	28	30	20	15	11
1g	32	30	38	18	17	15
1h	36	35	39	13	15	10
1i	28	34	40	16	17	12
1j	20	22	31	10	9	10
1k	15	21	19	7	9	11
1l	36	33	37	10	11	14
1m	16	27	31	12	13	10
1n	11	17	15	3	5	6
1o	36	30	31	8	16	11
1p	37	30	39	11	12	15
1q	11	25	35	10	15	13
1r	15	17	25	11	10	11
1s	10	15	11	10	12	10
2a	22	32	35	11	12	13
2b	20	28	29	7	6	5
2c	16	23	37	10	11	9
2d	14	27	30	8	8	10
2e	12	22	24	4	7	6
2f	31	30	33	22	17	10
2g	33	32	39	20	21	18
2h	38	35	41	25	22	20
2i	37	34	40	12	14	11
2j	21	20	30	9	6	11
2k	14	18	12	6	8	10
2l	30	36	41	16	16	13
2m	18	30	32	10	10	11
2n	13	19	12	2	3	8
2o	37	34	33	11	17	18
2p	38	32	41	12	13	16
2q	12	27	37	13	16	14
2r	25	30	35	10	11	11
2s	17	20	13	11	13	12
Standarad	39	36	43	17	18	16
DMF	+ve	+ve	+ve	+ve	+ve	+ve

+ve indicates microbial growth. Control: DMF (0.01% solution in distilled water). Standard for antibacterial: Chloramphenicol (1.00 mmol/ml). Standard for antifungal: Flucanazole (1.00 mmol/ml).

was used as internal standard (chemical shifts, δ in ppm). Mass spectra were recorded on a Jeol MSRoute instrument. Phosphoryl chloride, aromatic ketones, *p*-anisidine, *p*-toluidine and *N*,*N*-dimethylformamide (Aldrich and Alpha Aesar) were used as received. Elemental analyses were performed by C.S.I.C., Madrid, Spain and were within ±0.4% of predicted values for all compounds.

General Procedure for the Synthesis of Chalcones 1a—s and 2a—s The two precursors, 6-methyl/methoxy-substituted 2-chloro-3-formylquinolines, were synthesized according to the literature procedure. A mixture of formylquinoline (10 mmol) and an aromatic ketone (10 mmol) in methanol (50 ml) was stirred at room temperature, followed by dropwise addition of aq. NaOH (4 ml, 10%). The stirring was continued for 2 h and the reaction mixture was then kept at 0 °C (24 h). Subsequently, it was poured onto ice-cold water (200 ml). The precipitates were collected by filtration, washed with cold water followed by cold MeOH. The resulting chalcones were recrystallised from $CHCl_3$.

(2*E*)-3-(2-Chloro-6-methylquinolin-3-yl)-1-thien-3-ylprop-2-en-1-one 1a 72% yield. Pale yellow solid. mp 183—185 °C. IR (KBr) cm^{-1}: 1648 (C=O), 1592 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.54 (3H, s, Me), 7.39 (1H, dd, H_4', J=2.8 Hz), 7.44 (1H, d, H_α, J=15.7 Hz), 7.6 (1H, d, H_7, J=8.6 Hz), 7.62 (1H, s, H_5), 7.70 (1H, d, H_5', J=4.7 Hz), 7.91 (1H, d, H_8, J=8.5 Hz), 8.18 (1H, d, H_β, J=15.8 Hz), 8.20 (1H, dd, H_2', J=2.2 Hz), 8.36 (1H, s, H_4). MS (*m*/*z*): 313 (M^+, 7.9%), 278 (M^+-Cl, 100%). *Anal.* Calcd for $C_{17}H_{12}NOClS$: C, 65.07; H, 3.85; N, 4.46. Found: C, 65.02; H, 3.75; N, 4.41.

(2*E*)-3-(2-Chloro-6-methylquinolin-3-yl)-1-(3-methylthien-2-yl)prop-2-en-1-one 1b 53% yield. Pale yellow solid. mp 172—173 °C. IR (KBr) cm^{-1}: 1654 (C=O), 1594 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.45—2.66 (s, Me×2), 7.02 (1H, d, H_4', J=4.9 Hz), 7.40 (1H, d, H_α, J=15.4 Hz), 7.49 (1H, d, H_5', J=4.9 Hz), 7.58 (1H, dd, H_7, J=8.6 Hz), 7.64 (1H, s, H_5), 7.90 (1H, d, H_8, J=8.6 Hz), 8.18 (1H, d, H_β, J=15.4 Hz), 8.35 (1H, s, H_4). MS (*m*/*z*): 327 (M^+, 25.8%), 292 (M^+-Cl, 100%). *Anal.* Calcd for $C_{18}H_{14}NOClS$: C, 65.95; H, 4.30; N, 4.27. Found: C, 65.89; H, 4.29; N, 4.25.

(2*E*)-3-(2-Chloro-6-methylquinolin-3-yl)-1-(4-methylthien-2-yl)prop-2-en-1-one 1c 45% yield. White solid. mp 150 °C. IR (KBr) cm^{-1}: 1656 (C=O), 1593 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.25—2.48 (s, Me×2), 7.18 (1H, s, H_5'), 7.31 (1H, s, H_4'), 7.44 (1H, d, H_α, J=15.5 Hz), 7.48 (1H, dd, H_7, J=8.6 Hz), 7.51 (1H, s, H_5), 7.83 (1H, d, H_8, J=8.5 Hz), 8.21 (1H, d, H_β, J=15.6 Hz), 8.41 (1H, s, H_4). MS (*m*/*z*): 328 (M^+, 11.4%), 125 ($M^+-C_{12}H_9NCl$, 100%). *Anal.* Calcd for $C_{18}H_{14}NOClS$: C, 65.95; H, 4.30; N, 4.27. Found: C, 65.87; H, 4.24; N, 4.26.

(2*E*)-3-(2-Chloro-6-methylquinolin-3-yl)-1-(5-methylthien-2-yl)prop-2-en-1-one 1d 44% yield. Bright yellow solid. mp 198 °C. IR (KBr) cm^{-1}: 1652 (C=O), 1596 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.54—2.57 (s, Me×2), 6.87 (1H, d, H_4', J=3.6 Hz), 7.42 (1H, d, H_α, J=15.6 Hz), 7.58 (1H, dd, H_7, J=8.6 Hz), 7.62 (1H, s, H_5), 7.71 (1H, d, H_3', J=3.8 Hz), 7.90 (1H, d, H_8, J=8.6 Hz), 8.18 (1H, d, H_β, J=15.6 Hz), 8.35 (1H, s, H_4). MS (*m*/*z*): 327 (M^+, 12.1%), 292 (M^+-Cl, 100%). *Anal.* Calcd for $C_{18}H_{14}NOClS$: C, 65.95; H, 4.30; N, 4.27. Found: C, 65.89; H, 4.27; N, 4.22.

(2*E*)-3-(2-Chloro-6-methylquinolin-3-yl)-1-(2,5-dimethylthien-3-yl)prop-2-en-1-one 1e 67% yield. Pale yellw solid. mp 128—130 °C; IR (KBr) cm^{-1}: 1648 (C=O), 1585 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.44—2.72 (s, Me×3), 7.10 (1H, s, H_4'), 7.33 (1H, d, H_α, J=15.7 Hz), 7.58 (1H, dd, H_7, J=8.6 Hz), 7.62 (1H, s, H_5), 7.90 (1H, d, H_8, J=8.6 Hz), 8.08 (1H, d, H_β, J=15.7 Hz), 8.33 (1H, s, H_4). MS (*m*/*z*): 341 (M^+, 48.2%), 306 (M^+-Cl, 100%). *Anal.* Calcd for $C_{19}H_{16}NOClS$: C, 66.75; H, 4.72; N, 4.10. Found: C, 66.61; H, 4.63; N, 4.05.

(2*E*)-3-(2-Chloro-6-methylquinolin-3-yl)-1-(3-chlorothien-2-yl)prop-2-en-1-one 1f 74% yield. Bright yellow solid. mp 184—186 °C. IR (KBr) cm^{-1}: 1650 (C=O), 1592 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.53 (3H, s, Me), 7.07 (1H, d, H_4', J=5.2 Hz), 7.50 (1H, d, H_5', J=5.2 Hz), 7.59 (1H, dd, H_7, J=8.5 Hz), 7.64 (1H, s, H_5), 7.82 (1H, d, H_α, J=15.6 Hz), 7.90 (1H, d, H_8, J=8.6 Hz), 8.22 (1H, d, H_β, J=15.5 Hz), 8.37 (1H, s, H_4). MS (*m*/*z*): 347 (M^+, 4.2%), 312 (M^+-Cl, 100%). *Anal.* Calcd for $C_{17}H_{11}NOCl_2S$: C, 58.63; H, 3.18; N, 4.02. Found: C, 58.54; H, 3.16; N, 3.99.

(2*E*)-3-(2-Chloro-6-methylquinolin-3-yl)-1-(5-chlorothien-2-yl)prop-2-en-1-one 1g 89% yield. Bright yellow solid. mp 180 °C. IR (KBr) cm^{-1}: 1656 (C=O), 1598 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.54 (3H, s, Me), 7.03 (1H, d, H_4', J=4.0 Hz), 7.39 (1H, d, H_α, J=15.6 Hz), 7.60 (1H, dd, H_7, J=8.6 Hz), 7.63 (1H, s, H_5), 7.68 (1H, d, H_3', J=4.0 Hz), 7.91 (1H, d, H_8, J=8.5 Hz), 8.21 (1H, d, H_β, J=15.6 Hz), 8.36 (1H, s, H_4). MS (*m*/*z*): 347 (M^+, 6.9%), 312 (M^+-Cl, 100%). *Anal.* Calcd for $C_{17}H_{11}NOCl_2S$: C, 58.63; H, 3.18; N, 4.02. Found: C, 58.57; H, 3.13; N, 3.99.

(2*E*)-3-(2-Chloro-6-methylquinolin-3-yl)-1-(2,5-dichlorothien-3-yl)prop-2-en-1-one 1h 53% yield. Pale yellow solid. mp 128 °C. IR (KBr) cm^{-1}: 1664 (C=O), 1595 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.53 (3H, s, Me), 7.15 (1H, s, H_4'), 7.46 (1H, d, H_α, J=15.7 Hz), 7.60 (1H, dd, H_7, J=8.6 Hz), 7.63 (1H, s, H_5), 7.90 (1H, d, H_8, J=8.6 Hz), 8.14 (1H, d, H_β, J=15.7 Hz), 8.34 (1H, s, H_4). MS (*m*/*z*): 383 (M^+, 5.7%), 346 (M^+-Cl, 100%). *Anal.* Calcd for $C_{17}H_{10}NOCl_3S$: C, 53.35; H, 2.63; N, 3.66. Found: C, 53.22; H, 2.58; N, 3.62.

(2*E*)-1-(3-Bromothien-2-yl)-3-(2-chloro-6-methylquinolin-3-yl)prop-2-en-1-one 1i 64% yield. Bright yellow solid. mp 189—191 °C; IR (KBr) cm^{-1}: 1650 (C=O), 1591 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.54 (3H, s, Me), 7.16 (1H, d, H_4', J=5.16 Hz), 7.58 (1H, d, H_5', J=5.1 Hz), 7.59 (1H, dd, H_7, J=8.6 Hz), 7.65 (1H, s, H_5), 7.83 (1H, d, H_α, J=15.5 Hz), 7.91 (1H, d, H_8, J=8.6 Hz), 8.22 (1H, d, H_β, J=15.5 Hz), 8.38 (1H, s, H_4). MS (*m*/*z*): 393 (M^+, 5.1%), 356 (M^+-Cl, 100%). *Anal.* Calcd for $C_{17}H_{11}NOClSBr$: C, 51.99; H, 2.82; N, 3.57. Found: C, 51.96; H, 2.79; N, 3.58.

(2*E*)-1-(5-Bromothien-2-yl)-3-(2-chloro-6-methylquinolin-3-yl)prop-2-en-1-one 1j 55% yield. Pale brown solid. mp 160—161 °C. IR (KBr) cm^{-1}: 1653 (C=O), 1588 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.54 (3H, s, Me), 7.10 (1H, d, H_4', J=4.0 Hz), 7.17 (1H, d, H_3', J=4.0 Hz), 7.38 (1H, d, H_α, J=15.6 Hz), 7.60 (1H, dd, H_7, J=8.5 Hz), 7.63 (1H, s, H_5), 7.91 (1H, d, H_8, J=8.3 Hz), 8.21 (1H, d, H_β, J=15.6 Hz), 8.36 (1H, s, H_4). MS (*m*/*z*): 393 (M^+, 10.9%), 358 (M^+-Cl, 100%). *Anal.* Calcd for $C_{17}H_{11}NOClSBr$: C, 51.99; H, 2.82; N, 3.57. Found: C, 51.98; H, 2.77; N, 3.56.

(2*E*)-3-(2-Chloro-6-methylquinolin-3-yl)-1-(5-iodothien-2-yl)prop-2-en-1-one 1k 87% yield. Pale yellow solid. mp 178 °C. IR (KBr) cm^{-1}: 1648 (C=O), 1596 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.54 (3H, s, Me), 7.36 (1H, d, H_4', J=3.9 Hz), 7.37 (1H, d, H_α, J=15.5 Hz), 7.50 (1H, d, H_3', J=3.9 Hz), 7.59 (1H, dd, H_7, J=8.7 Hz), 7.62 (1H, s, H_5), 7.90 (1H, d, H_8, J=8.5 Hz), 8.20 (1H, d, H_β, J=15.6 Hz), 8.35 (1H, s, H_4). MS (*m*/*z*): 439 (M^+, 12.6%), 404 (M^+-Cl, 100%). *Anal.* Calcd for $C_{17}H_{11}NOClSI$: C, 46.44; H, 2.52; N, 3.19. Found: C, 46.41; H, 2.45; N, 3.17.

(2*E*)-3-(2-Chloro-6-methylquinolin-3-yl)-1-(1*H*-pyrrol-2-yl)prop-2-en-1-one 1l 70% yield. Bright yellow solid. mp 214 °C. IR (KBr) cm^{-1}: 1654 (C=O), 1594 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.47 (3H, s, Me), 6.24 (1H, dd, H_4', J=3.5 Hz), 6.70 (1H, d, H_3', J=3.5 Hz), 7.05 (1H, d, H_5', J=4.2 Hz), 7.41 (1H, d, H_α, J=15.6 Hz), 7.57 (1H, dd, H_7, J=8.6 Hz), 7.63 (1H, s, H_5), 7.91 (1H, d, H_8, J=8.6 Hz), 8.18 (1H, d, H_β, J=15.7 Hz), 8.35 (s, 1H, H_4). MS (*m*/*z*): 295 (M^+, 8.5%), 260 (M^+-Cl, 100%). *Anal.* Calcd for $C_{17}H_{13}N_2OCl$: C, 68.81; H, 4.42; N, 9.44. Found: C, 68.72; H, 4.36; N, 9.40.

(2*E*)-3-(2-Chloro-6-methylquinolin-3-yl)-1-(5-methyl-2-furyl)prop-2-en-1-one 1m 95% yield. Deep yellow solid. mp 158 °C. IR (KBr) cm^{-1}: 1664 (C=O), 1594 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.45—2.54 (s, Me×2), 6.24 (1H, dd, H_4', J=3.4 Hz), 7.29 (1H, d, H_3', J=3.5 Hz), 7.45 (1H, d, H_α, J=15.7 Hz), 7.58 (1H, dd, H_7, J=8.6 Hz), 7.63 (1H, s, H_5), 7.90 (1H, d, H_8, J=8.6 Hz), 8.22 (1H, d, H_β, J=15.8 Hz), 8.38 (1H, s, H_4). MS (*m*/*z*): 311 (M^+, 8.3%), 276 (M^+-Cl, 100%). *Anal.* Calcd for $C_{18}H_{14}NO_2Cl$: C, 69.34; H, 4.53; N, 4.49. Found: C, 69.32; H, 4.47; N, 4.48.

(2*E*)-3-(2-Chloro-6-methylquinolin-3-yl)-1-(2,5-dimethyl-3-furyl)prop-2-en-1-one 1n 92% yield. Deep yellow solid. mp 145—147 °C; IR (KBr) cm^{-1}: 1648 (C=O), 1596 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.29—2.62 (s, Me×3), 6.34 (1H, s, H_4'), 7.22 (1H, d, H_α, J=15.9 Hz), 7.58 (1H, dd, H_7, J=8.6 Hz), 7.61 (1H, s, H_5), 7.90 (1H, d, H_8, J=8.6 Hz), 8.08 (1H, d, H_β, J=15.8 Hz), 8.31 (1H, s, H_4). MS (*m*/*z*): 325 (M^+, 38.1%), 290 (M^+-Cl, 100%). *Anal.* Calcd for $C_{19}H_{16}NO_2Cl$: C, 70.05; H, 4.95; N, 4.30. Found: C, 69.99; H, 4.94; N, 4.22.

(2*E*)-1-(1-Benzofuran-2-yl)-3-(2-chloro-6-methylquinolin-3-yl)prop-2-en-1-one 1o 56% yield. Off white solid. mp 162 °C. IR (KBr) cm^{-1}: 1660 (C=O), 1592 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.47 (3H, s, Me), 7.28 (1H, t, Ar-H), 7.36 (1H, d, H_α, J=15.8 Hz), 7.42—7.53 (4H, m, Ar-H), 7.62 (1H, s, H_5), 7.68 (1H, dd, H_7, J=8.5 Hz), 7.83 (1H, d, H_8, J=8.6 Hz), 8.04 (1H, d, H_β, J=15.6 Hz), 8.11 (1H, s, H_4). MS (*m*/*z*): 348 (M^+, 12.5%), 313 (M^+-Cl, 100%). *Anal.* Calcd for $C_{21}H_{14}NO_2Cl$: C, 72.52; H, 4.06; N, 4.03. Found: C, 72.49; H, 3.98; N, 4.01.

(2*E*)-3-(2-Chloro-6-methylquinolin-3-yl)-1-(2,3-dihydro-1,4-benzodioxin-6-yl)prop-2-en-1-one 1p 46% yield. Off white solid. mp 158—160 °C. IR (KBr) cm^{-1}: 1658 (C=O), 1595 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.54 (3H, s, Me), 4.32 (4H, m, Dioxane Ring), 6.96 (1H, d, Ar-H, J=8.8 Hz), 7.42 (1H, m, Ar-H), 7.55 (1H, d, H_α, J=15.7 Hz), 7.58 (1H, dd, H_7, J=8.6 Hz), 7.62 (1H, s, H_5), 7.70 (1H, m, Ar-H), 7.90 (1H, d, H_8, J=8.6 Hz), 8.15 (1H, d, H_β, J=15.7 Hz), 8.36 (1H, s, H_4). MS (*m*/*z*): 365 (M^+, 24.1%), 330 (M^+-Cl, 100%). *Anal.* Calcd for $C_{21}H_{16}NO_3Cl$: C, 68.95; H, 4.41; N, 3.83. Found: C, 68.91; H, 4.36; N, 3.79.

(2*E*)-3-(2-Chloro-6-methylquinolin-3-yl)-1-(1-naphthyl)prop-2-en-1-one 1q 97% yield. Bright yellow solid. mp 138 °C. IR (KBr) cm^{-1}: 1659 (C=O), 1587 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.53 (3H, s, Me), 7.38 (1H, d, H_α, J=15.9 Hz), 7.53—7.60 (5H, m, Ar-H), 7.85 (1H, d, Ar-H, J=6.8 Hz), 7.90 (1H, d, H_7, J=8.6 Hz), 7.93 (1H, s, H_5), 8.02 (1H, d, H_8, J=8.1 Hz), 8.04 (1H, d, H_β, J=16.2 Hz), 8.37 (1H, s, H_4), 8.39 (1H, d, Ar-H, J=8.3 Hz). MS (*m*/*z*): 357 (M^+, 17.2%), 322 (M^+-Cl, 100%). *Anal.* Calcd for $C_{23}H_{16}NOCl$: C, 77.20; H, 4.51; N, 3.91. Found: C, 77.13; H, 4.47; N, 3.85.

(2*E*)-3-(2-Chloro-6-methylquinolin-3-yl)-1-(2-naphthyl)prop-2-en-1-one 1r 65% yield. Off white solid. mp 138 °C. IR (KBr) cm^{-1}: 1654 (C=O), 1589 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.53 (3H, s, Me), 7.35 (1H, d, H_α, J=16.1 Hz), 7.53—7.56 (2H, m, Ar-H), 7.60 (1H, dd, H_7, J= 8.1 Hz), 7.63 (1H, s, H_5), 7.86—7.93 (4H, m, Ar-H), 8.03 (1H, dd, H_8, J=8.6 Hz), 8.06 (1H, d, H_β, J=16.1 Hz), 8.44 (1H, s, H_4), 8.46 (1H, s, Ar-H). MS (*m*/*z*): 357 (M^+, 1.7%), 127 ($M^+-C_{13}H_9NOCl$, 100%). *Anal.* Calcd for $C_{23}H_{16}NOCl$: C, 77.20; H, 4.51; N, 3.91. Found: C, 77.18; H, 4.48; N, 3.91.

(2*E*)-1-(9-Anthryl)-3-(2-chloro-6-methylquinolin-3-yl)prop-2-en-1-one 1s 86% yield. Deep yellow solid. mp 232—233 °C. IR (KBr) cm^{-1}: 1662 (C=O), 1586 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.54 (3H, s, Me), 7.32 (1H, d, H_α, J=16.1 Hz), 7.47—7.57 (4H, m, Ar-H), 7.60 (1H, dd, H_7, J=8.5 Hz), 7.63 (1H, s, H_5), 7.77 (1H, d, H_β, J=16.1 Hz), 7.84 (1H, d, H_8, J=8.6 Hz), 7.92—7.95 (2H, m, Ar-H), 8.05—8.07 (2H, m, Ar-H), 8.31 (1H, s, H_4), 8.56 (1H, s, Ar-H). MS (*m*/*z*): 407 (M^+, 83%), 177 ($M^+-C_{13}H_9NOCl$, 100%). *Anal.* Calcd for $C_{27}H_{18}NOCl$: C, 79.50; H, 4.45; N, 3.43. Found: C, 7979.46; H, 4.41; N, 3.39.

(2*E*)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-thien-3-ylprop-2-en-1-one 2a 82% yield. Yellowish grey solid. mp 182 °C. IR (KBr) cm^{-1}: 1648 (C=O), 1593 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 3.94 (3H, s, OMe), 7.11 (1H, d, H_5, J=2.6 Hz), 7.39 (1H, d, H_4', J=2.9 Hz), 7.45 (1H, d, H_α, J=15.7 Hz), 7.60 (1H, dd, H_7, J=9.1 Hz), 7.69 (1H, d, H_5', J=4.6 Hz), 7.91 (1H, d, H_8, J=9.2 Hz), 8.17 (1H, d, H_β, J=15.9 Hz), 8.20 (1H, dd, H_2', J=2.2 Hz), 8.36 (1H, s, H_4). MS (*m*/*z*): 329 (M^+, 19.7%), 294 (M^+-Cl, 100%). *Anal.* Calcd for $C_{17}H_{12}NO_2ClS$: C, 61.91; H, 3.67; N, 4.25. Found: C, 61.90; H, 3.61; N, 4.23.

(2*E*)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-(3-methylthien-2-yl)prop-2-en-1-one 2b 64% yield. Greenish yellow solid. mp 180 °C. IR (KBr) cm^{-1}: 1654 (C=O), 1594 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.67 (3H, s, Me), 3.94 (3H, s, OMe), 7.02 (1H, d, H_4', J=4.9 Hz), 7.13 (1H, d, H_5, J=2.6 Hz), 7.36 (1H, d, H_8, J=9.2 Hz), 7.40 (1H, d, H_α, J=15.5 Hz), 7.49 (1H, d, H_5', J=4.9 Hz), 7.58 (1H, dd, H_7, J=8.6 Hz), 7.90 (1H, d, H_8, J=9.2 Hz), 8.17 (1H, d, H_β, J=15.4 Hz), 8.33 (1H, s, H_4). MS (*m*/*z*): 343 (M^+, 63.5%), 308 (M^+-Cl, 100%). *Anal.* Calcd for $C_{18}H_{14}NO_2ClS$: C, 62.88; H, 4.10; N, 4.07. Found: C, 62.75; H, 4.02; N, 4.03.

(2*E*)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-(4-methylthien-2-yl)prop-2-en-1-one 2c 74% yield. Greenish yellow solid. mp 146 °C. IR (KBr) cm^{-1}: 1656 (C=O), 1594 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.33 (3H, s, Me), 3.94 (3H, s, OMe), 7.02 (1H, d, H_4', J=4.9 Hz), 7.12 (1H, d, H_5, J=2.5 Hz), 7.31 (1H, s, H_5'), 7.40 (1H, dd, H_7, J=9.3 Hz), 7.44 (1H, d, H_α, J=15.6 Hz), 7.70 (1H, s, H_3'), 7.91 (1H, d, H_8, J=9.2 Hz), 8.19 (1H, d, H_β, J=15.6 Hz), 8.35 (1H, s, H_4). MS (*m*/*z*): 343 (M^+, 21.4%), 308 (M^+-Cl, 100%). *Anal.* Calcd for $C_{18}H_{14}NO_2ClS$: C, 62.88; H, 4.10; N, 4.07. Found:

C, 62.79; H, 4.04; N, 4.04.

(2*E*)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-(5-methylthien-2-yl)prop-2-en-1-one 2d 57% yield. Yellowish grey solid. mp 152—153 °C. IR (KBr) cm^{-1}: 1648 (C=O), 1588 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.54 (3H, s, Me), 3.93 (3H, s, OMe), 7.06 (1H, d, H_4', J=4.4 Hz), 7.11 (1H, d, H_5, J=2.6 Hz), 7.33 (1H, d, H_α, J=15.6 Hz), 7.42 (1H, dd, H_7, J=9.2 Hz), 7.68 (1H, d, H_3', J=4.4 Hz), 7.90 (1H, d, H_8, J=9.2 Hz), 8.12 (1H, d, H_β, J=15.6 Hz), 8.36 (1H, s, H_4). MS (*m*/*z*): 343 (M^+, 29.6%), 308 (M^+-Cl, 100%). *Anal.* Calcd for $C_{18}H_{14}NO_2ClS$: C, 62.88; H, 4.10; N, 4.07. Found: C, 62.81; H, 4.03; N, 4.01.

(2*E*)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-(2,5-dimethylthien-3-yl)prop-2-en-1-one 2e 94% yield. Off white solid. mp 116 °C. IR (KBr) cm^{-1}: 1648 (C=O), 1585 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.44—2.72 (s, Me×2), 3.93 (3H, s, OMe), 7.09 (1H, s, H_4'), 7.10 (1H, d, H_5, J=2.9), 7.33 (1H, d, H_α, J=15.7 Hz), 7.39 (1H, dd, H_7, J=9.2 Hz), 7.90 (1H, d, H_8, J=9.2 Hz), 8.07 (1H, d, H_β, J=15.7 Hz), 8.31 (1H, s, H_4). MS (*m*/*z*): 357 (M^+, 56.4%), 322 (M^+-Cl, 100%). *Anal.* Calcd for $C_{19}H_{16}NO_2ClS$: C, 63.77; H, 4.51; N, 3.91. Found: C, 63.62; H, 4.44; N, 3.85.

(2*E*)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-(3-chlorothien-2-yl)prop-2-en-1-one 2f 67% yield. Greyish green solid. mp 136—138 °C. IR (KBr) cm^{-1}: 1651 (C=O), 1594 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 3.94 (3H, s, OMe), 7.08 (1H, d, H_4', J=5.2 Hz), 7.12 (1H, d, H_5, J=2.7 Hz), 7.41 (1H, dd, H_7, J=9.2 Hz), 7.61 (1H, d, H_5', J=5.2 Hz), 7.83 (1H, d, H_α, J=15.5 Hz), 7.91 (1H, d, H_8, J=9.2 Hz), 8.22 (1H, d, H_β, J=15.6 Hz), 8.36 (1H, s, H_4). MS (*m*/*z*): 363 (M^+, 24.9%), 328 (M^+-Cl, 100%). *Anal.* Calcd for $C_{17}H_{11}NO_2Cl_2S$: C, 56.06; H, 3.04; N, 3.84. Found: C, 56.02; H, 3.01; N, 3.78.

(2*E*)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-(5-chlorothien-2-yl)prop-2-en-1-one 2g 95% yield. Yellowish grey solid. mp 178—180 °C. IR (KBr) cm^{-1}: 1654 (C=O), 1594 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 3.91 (3H, s, OMe), 6.95 (1H, d, H_4', J=4.1 Hz), 7.11 (1H, d, H_5, J=2.7 Hz), 7.36 (1H, dd, H_7, J=9.2 Hz), 7.42 (1H, d, H_α, J=15.6 Hz), 7.50 (1H, d, H_3', J=4.1 Hz), 7.89 (1H, d, H_8, J=9.2 Hz), 8.12 (1H, d, H_β, J=15.6 Hz), 8.36 (1H, s, H_4). MS (*m*/*z*): 363 (M^+, 13.7%), 328 (M^+-Cl, 100%). *Anal.* Calcd for $C_{17}H_{11}NO_2Cl_2S$: 56.06; H, 3.04; N, 3.84. Found: C, 56.01; H, 2.98; N, 3.79.

(2*E*)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-(2,5-dichlorothien-3-yl)prop-2-en-1-one 2h 96% yield. Greyish green solid. mp 144 °C. IR (KBr) cm^{-1}: 1664 (C=O), 1591 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 3.94 (3H, s, OMe), 7.11 (1H, d, H_5, J=2.7 Hz), 7.16 (1H, s, H_4'), 7.41 (1H, dd, H_7, J=9.2 Hz), 7.46 (1H, d, H_α, J=15.7 Hz), 7.91 (1H, d, H_8, J=9.2 Hz), 8.14 (1H, d, H_β, J=15.7 Hz), 8.33 (1H, s, H_4). MS (*m*/*z*): 397 (M^+, 14.3%), 362 (M^+-Cl, 100%). *Anal.* Calcd for $C_{17}H_{10}NO_2Cl_3S$: C, 51.21; H, 2.53; N, 3.51. Found: C, 51.19; H, 2.42; N, 3.46.

(2*E*)-1-(3-Bromothien-2-yl)-3-(2-chloro-6-methoxyquinolin-3-yl)prop-2-en-1-one 2i 73% yield. Greyish green solid. mp 148—150 °C. IR (KBr) cm^{-1}: 1650 (C=O), 1591 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 3.94 (3H, s, OMe), 7.12 (1H, d, H_5, J=2.7 Hz), 7.16 (1H, d, H_4', J=5.1 Hz), 7.41 (1H, dd, H_7, J=9.2 Hz), 7.59 (1H, d, H_5', J=5.1 Hz), 7.83 (1H, d, H_α, J=15.6 Hz), 7.91 (1H, d, H_8, J=9.2 Hz), 8.22 (1H, d, H_β, J=15.6 Hz), 8.36 (1H, s, H_4). MS (*m*/*z*): 408 (M^+, 16.2%), 374 (M^+-Cl, 100%). *Anal.* Calcd for $C_{17}H_{11}NO_2ClSBr$: C, 49.96; H, 2.71; N, 3.43. Found: C, 49.92; H, 2.70; N, 3.33.

(2*E*)-1-(5-Bromothien-2-yl)-3-(2-chloro-6-methoxyquinolin-3-yl)prop-2-en-1-one 2j 84% yield. Yellowish grey solid. mp 178 °C. IR (KBr) cm^{-1}: 1654 (C=O), 1589 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 3.91 (3H, s, OMe), 6.95 (1H, d, H_4', J=4.1 Hz), 7.10 (1H, d, H_5, J=2.6 Hz), 7.36 (1H, dd, H_7, J=9.2 Hz), 7.42 (1H, d, H_α, J=15.6 Hz), 7.45 (1H, d, H_3', J=4.1 Hz), 7.89 (1H, d, H_8, J=9.2 Hz), 8.13 (1H, d, H_β, J=15.6 Hz), 8.36 (1H, s, H_4). MS (*m*/*z*): 409 (M^+, 20.4%), 374 (M^+-Cl, 100%). *Anal.* Calcd for $C_{17}H_{11}NO_2ClSBr$: C, 49.96; H, 2.71; N, 3.43. Found: C, 49.87; H, 2.68; N, 3.41.

(2*E*)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-(5-iodothien-2-yl)prop-2-en-1-one 2k 91% yield. Yellowish grey solid. mp 184 °C. IR (KBr) cm^{-1}: 1648 (C=O), 1594 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 3.91 (3H, s, OMe), 6.92 (1H, d, H_4', J=4.1 Hz), 7.10 (1H, d, H_5, J=2.7 Hz), 7.36 (1H, dd, H_7, J=9.2 Hz), 7.43 (1H, d, H_α, J=15.5 Hz), 7.46 (1H, d, H_3', J=4.1 Hz), 7.89 (1H, d, H_8, J=9.2 Hz), 8.14 (1H, d, H_β, J=15.6 Hz), 8.36 (1H, s, H_4). MS (*m*/*z*): 455 (M^+, 11.2%), 237 ($M^+-C_{12}H_9NOCl$, 100%). *Anal.* Calcd for $C_{17}H_{11}NO_2ClSI$: C, 44.81; H, 2.43; N, 3.07. Found: C, 44.75; H, 2.39; N, 3.02.

(2*E*)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-(1*H*-pyrrol-2-yl)prop-2-en-1-one 2l 90% yield. Pale yellow solid. mp 172 °C. IR (KBr) cm^{-1}: 1648 (C=O), 1596 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.47 (3H, s, OMe), 6.34 (1H, dd, H_4', J=3.4 Hz), 6.64 (1H, d, H_3', J=3.4 Hz), 7.0 (1H, d, H_5', J=4.0 Hz), 7.44 (1H, d, H_α, J=15.5 Hz), 7.52 (1H, dd, H_7, J=8.6 Hz), 7.12 (1H, d, H_5, J=2.7 Hz), 7.90 (1H, d, H_8, J=8.6 Hz), 8.20 (1H, d, H_β, J=15.6 Hz), 8.34 (1H, s, H_4). MS (*m*/*z*): 311 (M^+, 13.3%), 276 (M^+-Cl, 100%). *Anal.* Calcd for $C_{17}H_{13}N_2O_2Cl$: C, 65.28; H, 4.19; N, 8.96. Found: C, 65.27; H, 4.11; N, 8.92.

(2*E*)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-(5-methyl-2-furyl)prop-2-en-1-one 2m 98% yield. Greenish yellow solid. mp 168 °C. IR (KBr) cm^{-1}: 1664 (C=O), 1594 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.45 (3H, s, Me), 3.93 (3H, s, OMe), 6.24 (1H, dd, H_4', J=3.0 Hz), 7.29 (1H, d, H_3', J=3.4 Hz), 7.45 (1H, d, H_α, J=15.8 Hz), 7.40 (1H, dd, H_7, J=9.1 Hz), 7.12 (1H, d, H_5, J=2.7 Hz), 7.90 (1H, d, H_8, J=8.2 Hz), 8.22 (1H, d, H_β, J=15.8 Hz), 8.36 (1H, s, H_4). MS (*m*/*z*): 327 (M^+, 28.7%), 292 (M^+-Cl, 100%). *Anal.* Calcd for $C_{18}H_{14}NO_3Cl$: C, 65.96; H, 4.31; N, 4.27. Found: C, 65.94; H, 4.31; N, 4.26.

(2*E*)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-(2,5-dimethyl-3-furyl)prop-2-en-1-one 2n 69% yield. Pale yellow solid. mp 122 °C. IR (KBr) cm^{-1}: 1649 (C=O), 1596 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 2.27—2.61 (s, Me×2), 3.93 (3H, s, OMe), 6.97 (1H, s, H_4'), 7.11 (1H, d, H_5, J=2.7 Hz), 7.24 (1H, d, H_α, J=15.9 Hz), 7.40 (1H, dd, H_7, J=9.2 Hz), 7.90 (1H, d, H_8, J=9.2 Hz), 8.12 (1H, d, H_β, J=15.8 Hz), 8.36 (1H, s, H_4). MS (*m*/*z*): 341 (M^+, 22.5%), 306 (M^+-Cl,100%). *Anal.* Calcd for $C_{19}H_{16}NO_3Cl$: C, 66.77; H, 4.72; N, 4.10. Found: C, 66.74; H, 4.68; N, 4.09.

(2*E*)-1-(1-Benzofuran-2-yl)-3-(2-chloro-6-methoxyquinolin-3-yl)prop-2-en-1-one 2o 62% yield. Off white solid. mp 158 °C. IR (KBr) cm^{-1}: 1658 (C=O), 1587 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 3.87 (3H, s, OMe), 7.01 (1H, d, H_5, J=2.7 Hz), 7.29 (1H, t, Ar-H) 7.36 (1H, d, H_α, J=15.8 Hz), 7.42—7.52 (4H, m, Ar-H), 7.67 (1H, d, H_7, J=9.2 Hz), 7.82 (1H, d, H_8, J=9.2 Hz), 8.06 (1H, d, H_β, J=15.8 Hz), 8.10 (1H, s, H_4). MS (*m*/*z*): 363 (M^+, 10.5%), 328 (M^+-Cl, 100%). *Anal.* Calcd for $C_{21}H_{14}NO_3Cl$: C, 69.33; H, 3.88; N, 3.85. Found: C, 69.31; H, 3.82; N, 3.81.

(2*E*)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-(2,3-dihydro-1,4-benzodioxin-6-yl)prop-2-en-1-one 2p 92% yield. Off white solid. mp 163—164 °C. IR (KBr) cm^{-1}: 1658 (C=O), 1596 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 3.93 (3H, s, OMe), 4.34 (4H, m, Dioxane Ring), 6.94 (1H, d, Ar-H, J=8.1 Hz), 7.12 (1H, d, H_5, J=2.6 Hz), 7.36 (1H, d, Ar-H, J=3.9 Hz), 7.50 (1H, d, H_α, J=15.6 Hz), 7.58 (1H, dd, H_7, J=9.1 Hz), 7.70 (1H, m, Ar-H), 7.91 (1H, d, H_8, J=9.2 Hz), 8.18 (1H, d, H_β, J=15.6 Hz), 8.35 (1H, s, H_4). MS (*m*/*z*): 381 (M^+, 7.5%), 346 (M^+-Cl, 100%). *Anal.* Calcd for $C_{21}H_{16}NO_4Cl$: C, 66.06; H, 4.22; N, 3.67. Found: C, 66.02; H, 4.18; N, 3.63.

(2*E*)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-(1-naphthyl)prop-2-en-1-one 2q 90% yield. Pale yellow solid. mp 162 °C. IR (KBr) cm^{-1}: 1659 (C=O), 1587 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 3.92 (3H, s, OMe), 7.09 (1H, d, H_5, J=2.7 Hz), 7.38 (1H, d, H_α, J=15.9 Hz), 7.40 (1H, dd, H_7, J=9.2 Hz), 7.53—7.61 (3H, m, Ar-H), 7.83—7.92 (3H, m, Ar-H), 7.98 (1H, d, H_8, J=9.2 Hz), 8.03 (1H, d, H_β, J=16.1 Hz), 8.35 (1H, s, H_4), 8.40 (1H, d, Ar-H, J=8.3 Hz). MS (*m*/*z*): 373 (M^+, 57.0%), 338 (M^+-Cl, 100%). *Anal.* Calcd for $C_{23}H_{16}NO_2Cl$: C, 73.90; H, 4.31; N, 3.75. Found: C, 73.87; H, 4.27; N, 3.72.

(2*E*)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-(2-naphthyl)prop-2-en-1-one 2r 55% yield. Light grey solid. mp 140 °C. IR (KBr) cm^{-1}: 1659 (C=O), 1586 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 3.95 (3H, s, OMe), 7.15 (1H, d, H_5, J=2.7 Hz), 7.41 (1H, dd, H_7, J=9.2 Hz), 7.55—7.64 (2H, m, Ar-H), 7.73 (1H, d, H_α, J=15.7 Hz), 7.89—8.00 (4H, m, Ar-H), 8.11 (1H, dd, H_8 J=9.2 Hz), 8.23 (1H, d, H_β, J=15.7 Hz), 8.42 (1H, s, H_4), 8.56 (1H, s, Ar-H). MS (*m*/*z*): 373 (M^+, 34.9%), 338 (M^+-Cl, 100%). *Anal.* Calcd for $C_{23}H_{16}NO_2Cl$: C, 73.90; H, 4.31; N, 3.75. Found: C, 73.88; H, 4.27; N, 3.71.

(2*E*)-1-(9-Anthryl)-3-(2-chloro-6-methoxyquinolin-3-yl)prop-2-en-1-one 2s 97% yield. Deep yellow solid. mp 220—222 °C. IR (KBr) cm^{-1}: 1660 (C=O), 1588 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 3.92 (3H, s, OMe), 7.11 (1H, d, H_5, J=2.7 Hz), 7.40 (1H, d, H_α, J=16.1 Hz), 7.47—7.56 (4H, m, Ar-H), 7.84 (1H, dd, H_7, J=7.2 Hz), 7.90—7.93 (2H, m, Ar-H), 7.96 (1H, d, H_β, J=16.1 Hz), 8.03 (1H, d, H_8, J=7.4 Hz), 8.54 (1H, s, Ar-H), 8.06—8.08 (2H, m, Ar-H). MS (*m*/*z*): 423 (M^+, 16.3%), 177 ($M^+-C_{13}H_9NO_2Cl$, 100%). *Anal.* Calcd for $C_{27}H_{18}NO_2Cl$: C, 76.50; H, 4.28; N, 3.30. Found: C, 76.42; H, 4.27; N, 3.27.

Antileishmanial Assay The title compounds (**1a**—**s**, **2a**—**s**) were tested for the antileishmanial activity using *L. major* promastigotes as parasites for *in vitro* screening. Parasites were cultured at 24 °C in Shaking incubator on M 199 medium containing foetal bovine serum (10%); *N*-2-hydroxyethylpiperazine-*N*′-2-ethanesulfonic acid (HEPES) (25 mM), and penicillin and streptomycin (0.22 mg each).[39]

Each compound (1 mg) was dissolved in 1 ml of dimethyl sulfoxide (DMSO) and Amphotericin B (1 mg) taken in DMSO (1 ml) was used as a positive control. Parasites were taken from lag phase of their growth and

were centrifuged at 3000 rpm for 3 min. The parasite density was maintained at 2×10^6 cells/ml by diluting with fresh culture medium. In 96-well plates, 180 μl of medium was added in different wells. The experimental compound (20 μl) was added in medium and serially diluted. Parasite culture (100 μl) was added in all wells. In negative controls, DMSO was serially diluted in medium while the positive control contained varying concentrations of standard antileishmanial compound *i.e.* Amphotericin B. The plates were incubated for 72 h at 24 °C. The culture was examined microscopically on an improved neubaur counting chamber and IC_{50} values of compounds possessing antileishmanial activity were calculated. All assays were run in duplicate. The results are summarized in Table 2.

Antimicrobial Assay The *in vitro* antimicrobial activity was done by the reported method.[40] All the title compounds were screened for antibacterial activity against *Escherichia coli*, *Micrococus luteus* and *Staphylococus aureus* using Chloramphenicol (1.00 mmol/ml) as standard. The antifungal activity was investigated against *Aspergillus flavus*, *Aspergillus niger* and *Curvuliaria lunata* using Flucanazole (1.00 mmol/ml) as standard. At the end of 24 h and 48 h for bacteria and fungi respectively, the inhibition was recorded measuring the diameter of the inhibition zone. Each experiment was repeated thrice and the average of the three independednt determinations was recorded. The results are summarized in Table 3.

Acknowledgement The author is grateful to Higher Education Commission, Pakistan and Institute of Chemistry, University of the Punjab, Lahore, for financial assistance. We are also thankful to International Centre for Chemical and Biological Sciences, HEJ Research Institute of Chemistry, University of Karachi, Karachi, for spectral measurements.

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