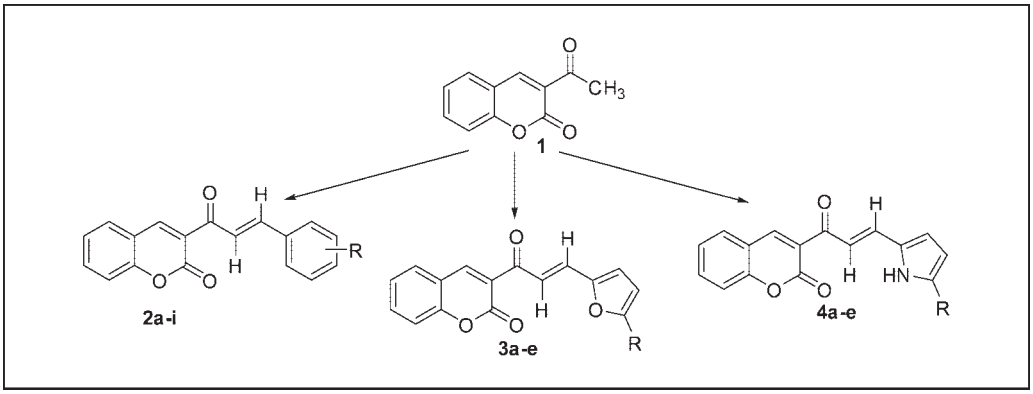
Microwave-Assisted Synthesis and Evaluation of Antimicrobial Activity of 3-{3-(s-Aryl and s-Heteroaromatic)acryloyl}-2*H*-chromen-2-one Derivatives

Olayinka O. Ajani[a]* and Obinna C. Nwinyi[b]

[a]Chemistry Department, College of Science and Technology, Covenant University, Ota, Ogun State, Nigeria
[b]Department of Biological Science, College of Science and Technology, Covenant University, Ota, Ogun State, Nigeria
*E-mail: wajanfresh@yahoo.com

Received July 13, 2009
DOI 10.1002/jhet.298
Published online 8 January 2010 in Wiley InterScience (www.interscience.wiley.com).



The exploration of potential utilization of microwaves as an energy source for heterocyclic synthesis was herein investigated using condensation of 3-acetylcoumarin (**1**) with aromatic and heteroaromatic aldehydes to afford the corresponding aromatic chalcones (**2a–j**) and heteroaromatic chalcones (**3a–e** and **4a–e**), respectively, in good to excellent yield within 1–3 min. The chemical structures were confirmed by analytical and spectral data. All the synthesized compounds were screened for their antibacterial activity and 3-{3-(4-dimethylaminophenyl)acryloyl}-2*H*-chromen-2-one (**2i**) was discovered to be the most active at minimum inhibitory concentration (MIC) value of 7.8 μg/mL.

J. Heterocyclic Chem., **47**, 179 (2010).

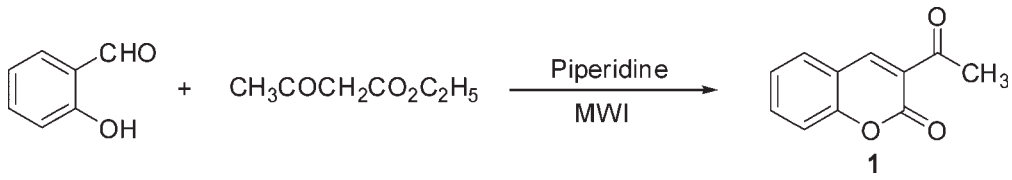
INTRODUCTION

Over the years, coumarins have been established as well-known naturally occurring oxygen-heterocyclic compounds isolated from various plants [1–4]. They are the family of lactones containing benzopyrone skeletal framework that have enjoyed isolation from plant as well as total synthesis in the laboratory. The plant extracts containing coumarin-related heterocycles are employed as herbal remedies in traditional systems of medicine. The synthesis of coumarin (2-oxo-2*H*-chromene) derivatives has attracted considerable attention of organic and medicinal chemists due to its wide usage in food additives [5], fragrances, pharmaceuticals, and agrochemicals [6]. Furthermore, the pharmacological and biochemical properties as well as therapeutic applications of coumarins depend upon the pattern of substitution [7]. In view of this, coumarins have attracted intense interest in recent years because of their diverse pharmacological properties. Hence, coumarins have been reported to possess, among others, anticoagulant [8,9], antitubercular [10], antileucemic [11], antimicrobial [12,13], anti-inflammatory [14,15], anti-HIV [16], analgesic [17,18], anticancer [19], antitumoral [20], anticonvulsant [21,22], antiplatelet [23], antifungal [24,25] antiviral [26,27], antibacterial [28–31], and antimalarial [32] activities.

Some coumarin derivatives can be utilized beneficially for the synthesis of valuable heterocyclic ring systems. In like fashion, chalcones are essential building blocks [33] and valuable reactive intermediates for the synthesis of various heterocyclic compounds [34–36] as well as metal complexes [37–39] of high-biological relevance. Many techniques have been employed in the synthesis of coumarin frameworks [40,41] and chalcone moieties [42,43]. However, microwave-assisted approach toward the synthesis of coumarin chalcones has not been extensively explored.

The continuing drive to develop more economical and environmentally friendly chemical processes has spurred synthetic chemists to seek more versatile methods such as microwave method, for running reactions with less waste and short reaction time [44,45]. On the basis of the experimental data from various studies, chemists

Scheme 1. Microwave assisted synthesis of 3-acetylcoumarin, **1**.



have found that microwave-enhanced chemical reaction rates can be faster than those of conventional heating methods by as much as a 1000-fold [46].

In view of our current trust in the microwave-assisted organic synthesis [47] and various findings mentioned earlier, there is merit in developing a facile route for the formation of coumarins incorporated with chalcone templates *via* microwave synthetic approach to investigate the antimicrobial properties of such targeted library.

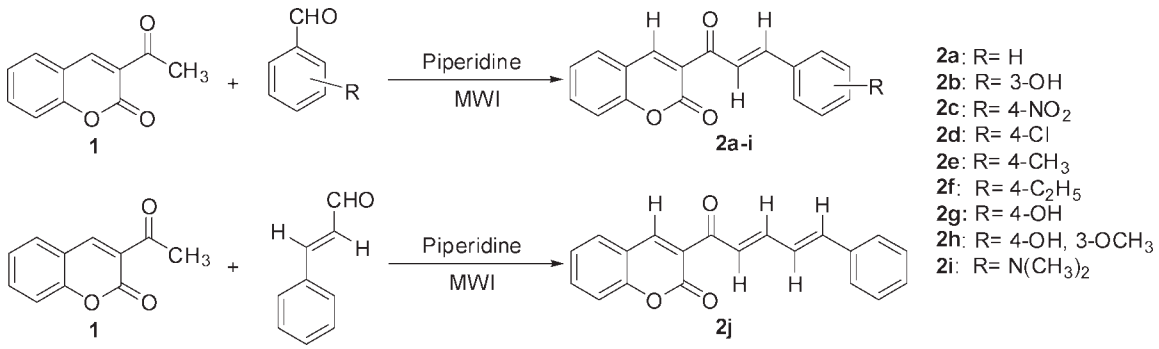
RESULTS AND DISCUSSION

Chemistry. In a continuing effort to obtain new antimicrobial drug candidates, the synthesis of s-phenyl- and s-furan-2-ylcoumarin derivatives were attempted in the presence of catalytic amount of piperidine in a solvent less medium. 3-Acetylcoumarin, **1**, used as the essential precursor in this study, was synthesized by the reaction of salisaldehyde with ethyl acetoacetate in the presence of catalytic amount of piperidine (Scheme 1). Furthermore, 3-acetylcoumarin, **1** was made to undergo condensation reaction with substituted benzaldehdye to afford chalcones 3-{3-(s-aryl)acryloyl)}-2*H*-chromen-2-one, **2a–i**, whereas the replacement of benzaldehyde with cinnamaldehyde resulted in the formation of chalcone 3-(5-phenylpenta-2,4-dienoyl)-2*H*-chromen-2-one **2j** under microwave irradiation (Scheme 2). The reaction of **1** with heteroaromatic aldehyde; furfural and pyrrole-2-carbaladehyde furnished chalcones 3-{3-(s-heteroaromatic) acryloyl)}-2*H*-chromen-2-one **3a–e** and **4a–e**, respectively (Scheme 3) in moderate yields.

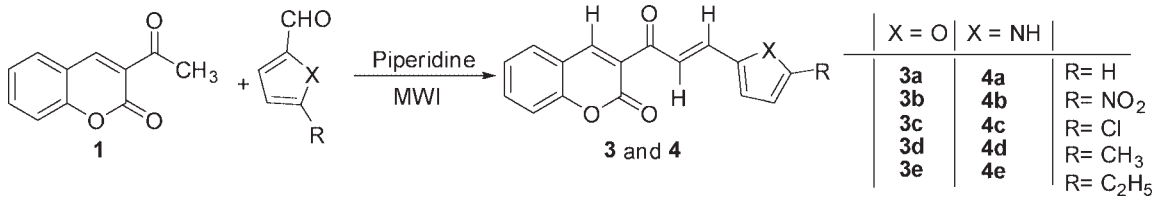
Preliminary optimization of reaction conditions was done by comparing the synthesis of **2a** in the presence of two solvents and solvent-free media (Table 1). It was observed that the solvent free medium gave the most suitable condition for the synthesis of **2a**, and therefore, it was used in all subsequent experiments. The effect of temperature was studied by carrying out the synthesis of **2a** at different temperatures; 50, 100, and 140°C (Table 2) using neat reaction condition in solvent free media. It was discovered that yield is a function of temperature, since the yield increased as the reaction temperature was raised. In fact, **2a** had the highest yield (97%) at 140°C. The results show that neat preparation of **2a** in solvent free medium at 140°C provides an efficient way to access diverse, highly functionalized coumarin containing chalcones. Hence, these optimum conditions were applied for the synthesis of a series of 3-{3-(s-aryl and (s-heteroaryl)acryloyl}-2*H*-chromen-2-one derivatives **2a–j**, **3a–e**, and **4a–e**, respectively. The melting points of the compounds varied between 119 and 289°C for all the compounds except **3c** and **4e** which did not melt even at 300°C. The progress of the reaction was monitored by TLC spotting with R_f values ranging between 0.44 and 0.85 in acetone/methanol (3:1, v/v) solvent system.

The structures of newly synthesized compounds were elucidated by IR, UV, NMR, mass spectral studies, and elemental analysis. The IR spectrum, of **2a**, for instance, exhibited the absorption band at 1740 cm^{-1} due to the presence of C=O (ester) which was confirmed by the presence of C—O of lactone at 1363 cm^{-1}. The band at 1673 cm^{-1} and 1606 cm^{-1} depicted the presence of C=O (conjugated ketone) and C=C (aromatic), respectively. The UV–visible spectrum of **2a** gave rise to wavelength (λ_{max}) at 224 nm and 348 nm with log ε

Scheme 2. Microwave assisted synthesis of various s-arylchalcones, **2a–j**.



Scheme 3. Microwave assisted synthesis of various s-heteroaromatic chalcones, **3a–e** and **4a–e**.



values of 3.99 and 3.47, respectively, whereas a shoulder was observed at 375 nm. The wavelength at 224 nm was as a result of $\pi \rightarrow \pi^*$ transition of phenyl ring, whereas 348 nm was as a result of $n \rightarrow \pi^*$ transition of the enone attached to coumarin moiety at 3-position, whereas a bathochromic shift observed as a shoulder at 375 nm was due to the presence of extensive conjugation of the π-electron systems. In ^{1}H-NMR spectrum (CD_3OD) of **2a**, a doublet at δ 7.03 (1H, J = 8.5 Hz, CO—CH=C); a multiplet at δ 7.33–7.84 (9H, which was made up of four protons of benzofused coumarin and five phenyl protons); a doublet at δ 7.82 (1H, J = 8.5 Hz, CO—C=CH) and a singlet at δ 8.57 (1H, Coumarin-H) were all observed down field of TMS scale. The ^{13}C-NMR spectrum showed peaks at δ 183.7 ppm due to C=O (conjugated ketone), whereas the peak at δ 159.4 ppm was due to the presence of C=O (ester). Other peaks which were observed between δ 153.0 and 116.1 ppm were due to sixteen sp^2 hybridized carbon atoms. The mass spectrum of **2a** showed the molecular ion peak at m/z 276 corresponding to its molecular weight. The base peak was observed at 173, whereas other daughter fragment noticed at m/z 199 was due to loss of phenyl free radical. The result of elemental analysis (Table 3) did not only correlate well with the molecular masses of the compounds but also showed a consistent minimum difference of not more than ±0.40 between % calculated and % found for the carbon, hydrogen, and nitrogen of the prepared compounds.

Antibacterial activities. The antibacterial activity of 21 synthesized compounds, **1**–**4e**, was determined *in vitro* by agar well diffusion technique [48]. The media were inoculated with test organisms and a solution of the tested compound in DMSO solvent. The zones of inhibition were measured after 24 h of incubation. The *in vitro* general sensitivity testing of the prepared compounds, **1**–**4e** was carried out against five gram positive bacteria [*Bacillus anthracis* (LIO), *Bacillus stearothermophilus* (NCIB 8222), *Bacillus subtilis* (NCIB 3610), *Bacillus cereus* (NCIB 6349), *Staphylococcus aureus* (NCIB 8588)] and five gram negative bacteria [*Escherichia coli* (NCIB 86), *Klebsiella pneumonia* (NCIB 418), *Pseudomonas aeruginosa* (NCIB 950), *Pseudomonas fluorescence* (NCIB 3756), *Shigella dysenteriae* (LIO)] as well as the standard drug streptomycin (Table 4). It was observed that the zones of inhibition of **1**, **2a**, **2d**, **2f**, **2g** on growth of various bacteria varied between 10 mm and 23 mm, whereas that of **2b**, **2c**, **2j**, **3a**, **4c** was between 10 mm and 21 mm. Others include **3b**, **3d**, **4d**, **4e** with zones of inhibition of 11–23 mm and **2e**, **2i**, **3c**, **4a** with inhibition zones of 15–31 mm.

In like fashion, the zones of inhibition of **2h** on the bacteria growth ranged between 14 mm and 18 mm, whereas that of **3e** ranged between 14 mm and 22 mm. Furthermore, streptomycin standard was active on all bacteria with the zones of inhibition ranging from 17 mm to 28 mm, except on *E. coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* where resistance was noticed. Compared with streptomycin, compounds **2e**, **2i**, and **4a** revealed larger zones of inhibition against *Bacillus stearothermophilus* (*i.e.*, >23 mm) and *Bacillus subtilis* (*i.e.*, >27 mm), whereas **2d** and **4e** showed the same zones of inhibition as streptomycin upon *Bacillus cereus* (23 mm).

However, high degree of resistance as well as small zones of inhibition were observed upon the screening of synthesized compounds against *Bacillus cereus*, *Staphylococcus aureus, Pseudomonas aeruginosa*, *Pseudomonas fluorescence*, and *Shigella dysenteriae*. In view of these, minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) tests were selectively carried out on the remaining five

Table 1

Synthesis of 3-cinnamoyl-2*H*-chromen-2-one, **2a**, in different solvents at 140°C.

Entry	Solvent	Time/mins	Yield/%
1	Ethanol	1	52
2	Chloroform	1	45
3	Solvent free	1	97

Table 2

Synthesis of 3-cinnamoyl-2*H*-chromen-2-one, **2a**, at different temperatures.

Entry	Solvent	Temperature/°C	Yield/%
1	Solvent free	140	97
2	Solvent free	100	83
3	Solvent free	50	58

Table 3

Physicochemical properties of compounds synthesized (**1–4e**).

Comp no.	Molecular formula	Mol. wt.	Yield (%)	M.P. (°C)	R_f[a]	Color	Elem. Anal. %Calcd. (%Found)		
							C	H	N
1	$C_{11}H_8O_3$	188	92.6	119–121	0.52	yellow	70.2(70.1)	4.3(4.4)	–
2a	$C_{18}H_{12}O_3$	276	97.0	142–143	0.50	yellow	78.3(78.1)	4.3(4.5)	–
2b	$C_{18}H_{12}O_4$	292	89.1	139–140	0.61	yellow	74.0(74.4)	4.1(3.9)	–
2c	$C_{18}H_{11}NO_5$	321	78.3	170–172	0.69	orange	67.3(67.2)	3.4(3.2)	4.4(4.6)
2d	$C_{18}H_{11}ClO_3$	310.5	77.1	222–223	0.59	yellow	69.7(69.4)	3.5(3.7)	–
2e	$C_{19}H_{14}O_3$	290	92.5	161–163	0.54	yellow	78.6(78.3)	4.8(4.5)	–
2f	$C_{20}H_{16}O_3$	304	95.1	172–174	0.66	cream	78.9(78.6)	5.3(5.1)	–
2g	$C_{18}H_{12}O_4$	292	97.8	246–249	0.68	yellow	74.0(73.8)	4.1(4.3)	–
2h	$C_{19}H_{14}O_5$	322	77.1	230–231	0.70	yellow	70.8(70.9)	4.3(4.1)	–
2i	$C_{20}H_{17}NO_3$	319	81.6	217–218	0.71	red	75.2(74.9)	5.3(5.0)	4.4(4.7)
2j	$C_{20}H_{14}O_3$	302	73.3	184–186	0.63	yellow	79.5(79.3)	4.6(4.4)	–
3a	$C_{16}H_{10}O_4$	266	87.2	135–137	0.57	brown	72.2(72.4)	3.8(3.5)	–
3b	$C_{16}H_9NO_6$	311	66.8	194–196	0.81	yellow	61.7(61.4)	2.9(3.1)	4.5(4.3)
3c	$C_{16}H_9ClO_4$	300.5	59.2	> 300	0.44	green	63.9(64.1)	3.0(2.8)	–
3d	$C_{17}H_{12}O_4$	280	74.8	200–201	0.49	green	72.9(72.6)	4.3(4.5)	–
3e	$C_{18}H_{14}O_4$	294	66.5	240–241	0.85	orange	73.5(73.8)	4.8(4.7)	–
4a	$C_{16}H_{11}NO_3$	265	71.4	209(dec)	0.69	black	72.5(72.4)	4.2(4.4)	5.3(5.5)
4b	$C_{16}H_{10}N_2O_5$	310	63.7	268–269	0.85	yellow	61.9(62.2)	3.2(3.3)	9.0(9.2)
4c	$C_{16}H_{10}NClO_3$	299.5	55.8	288–289	0.55	yellow	64.1(61.5)	3.3(3.5)	4.7(4.5)
4d	$C_{17}H_{13}NO_3$	279	50.1	214–216	0.77	orange	73.1(73.5)	4.7(4.6)	5.0(4.8)
4e	$C_{18}H_{15}NO_3$	293	50.8	> 300	0.83	yellow	73.7(73.3)	5.1(5.0)	4.8(4.6)

[a] Solvent system: CH_3COCH_3:CH_3OH (3:1, v/v) solvent system.

Table 4

Result of antibacterial screening (sensitivity testing) on bacteria with zones of inhibition (in mm).

Comp. no.	Bacteria									
	B.a	*B.c*	*B.s*	*B.su*	*S.a*	*E.c*	*K.p*	*P.a*	*P.f*	*S.d*
1	10	10	11	23	–	14	12	13	10	–
2a	–	14	18	20	–	10	23	–	10	–
2b	–	–	20	–	–	17	19	–	–	–
2c	12	–	–	21	14	10	16	–	–	–
2d	17	23	23	16	10	14	–	16	–	–
2e	18	20	24	31	18	16	29	21	15	18
2f	21	15	–	23	–	15	19	11	10	–
2g	–	–	20	23	–	18	10	–	–	–
2h	18	18	15	11	–	16	14	–	–	–
2i	18	25	25	28	–	31	22	17	–	15
2j	–	10	20	20	–	21	16	–	12	18
3a	–	–	14	10	10	21	17	–	–	–
3b	11	8	–	11	–	19	23	–	–	–
3c	–	–	15	19	–	31	18	15	–	–
3d	13	–	12	18	–	17	23	15	13	11
3e	15	–	20	14	15	13	22	17	–	–
4a	18	–	31	28	–	16	15	–	–	–
4b	12	–	–	13	–	9	15	12	–	–
4c	18	–	12	15	13	21	13	13	–	10
4d	15	13	16	14	–	14	23	–	–	11
4e	17	23	22	–	–	13	–	11	–	–
str	20	23	23	27	21	–	–	–	22	17

–Indicates bacteria are resistant to the compounds >1000 μg/mL.

B.a, Bacillus anthracis (LIO)$^{G+}$; *B.c, Bacillus cereus* (NCIB 6349)$^{G+}$; *B.s, Bacillus stearothermophilus* (NCIB 8222)$^{G+}$; *B.su, Bacillus subtilis* (NCIB 3610)$^{G+}$; *S.a, Staphylococcus aureus* (NCIB 8588)$^{G+}$; *E.c, Escherichia coli* (NCIB 86)$^{G-}$; *K.p, Klebsiella pneumonia* (NCIB 418)$^{G-}$; *P.a, Pseudomonas aeruginosa* (NCIB 950)$^{G-}$; *P.f, Pseudomonas fluorescence* (NCIB 3756)$^{G-}$; *S.d, Shigella dysenteriae* (LIO)$^{G-}$; str, streptomycin; $^{G+}$, Gram positive; $^{G-}$, Gram negative.

Table 5

Results of MIC and MBC of synthesized compounds on some selected bacteria (in μg/mL).

	Bacteria									
	B. anthracis		*B. stearotherm*		*B. subtilis*		*E. coli*		*K. pneumonia*	
Comp. no.	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
1	31.2	62.4	31.2	62.4	15.6	15.6	31.2	31.2	31.2	31.2
2a	–	–	15.6	15.6	7.8	7.8	31.2	62.4	7.8	31.2
2b	–	–	7.8	31.2	–	–	15.6	15.6	7.8	15.6
2c	31.2	62.4	–	–	7.8	7.8	31.2	62.4	15.6	62.4
2d	15.6	62.4	7.8	31.2	15.6	15.6	15.6	31.2	–	–
2e	7.8	15.6	7.8	15.6	7.8	7.8	15.6	31.2	7.8	31.2
2f	7.8	31.2	–	–	7.8	7.8	15.6	15.6	15.6	62.4
2g	–	–	7.8	7.8	7.8	7.8	15.6	15.6	31.2	62.4
2h	15.6	15.6	15.6	62.4	31.2	31.2	31.2	31.2	31.2	63.4
2i	7.8	7.8	7.8	15.6	7.8	7.8	7.8	7.8	7.8	7.8
2j	–	–	15.6	62.4	7.8	7.8	7.8	15.6	15.6	31.2
3a	–	–	31.2	31.2	31.2	31.2	7.8	7.8	7.8	15.6
3b	31.2	62.4	–	–	31.2	31.2	15.6	15.6	15.6	15.6
3c	–	–	31.2	93.6	7.8	7.8	7.8	7.8	15.6	31.2
3d	31.2	62.4	31.2	31.2	15.6	15.6	15.6	31.2	7.8	15.6
3e	15.6	31.2	7.8	15.6	31.2	62.4	31.2	62.4	7.8	31.2
4a	7.8	31.2	7.8	7.8	7.8	31.2	15.6	62.4	31.2	62.4
4b	31.2	31.2	–	–	15.6	31.2	31.2	31.2	7.8	15.6
4c	7.8	15.6	31.2	31.2	15.6	15.6	7.8	31.2	31.2	93.6
4d	15.6	62.6	15.6	31.2	15.6	31.2	15.6	15.6	7.8	31.2
4e	15.6	31.2	7.8	15.6	–	–	31.2	31.2	–	–
str	7.8	15.6	15.6	15.6	7.8	7.8	–	–	–	–

– Indicates bacteria are resistant to the compounds >100 μg/mL.
MIC, minimum inhibitory concentration, i.e. the lowest concentration to completely inhibit bacterial growth; MBC, minimum bactericidal concentration, i.e. the lowest concentration to completely kill bacteria.

microorganisms comprising three gram +ve (*Bacillus anthracis, Bacillus subtilis*, and *Bacillus stearothermophilus*) and two gram –ve (*Escherichia coli* and *Klebsiella pneumonia*e) bacterial strains (Table 5). MIC is defined as the lowest concentration of the compounds that completely inhibit the growth of microorganism, whereas MBC is the lowest concentration at which 99.9% of the inoculum was killed. The MIC values of the compounds varied between 7.8 and 31.2 μg/mL, whereas that of streptomycin was between 7.8 and 15.6 μg/mL. The MBC of few compounds was found to be the same as MIC but in most of the compounds, it was twofold or threefold or fourfold higher than their corresponding MIC values. In the long run, **2i** emerged as the most active antibacterial agent at 7.8 μg/mL.

CONCLUSIONS

It was discovered that microwave-assisted approach is highly efficient procedure for the preparation of various coumarin chalcones, especially in the solvent-free media. By visualizing the antimicrobial data, the results revealed that the compounds exhibited high potency as antibacterial agents. The most active compound was 3-{(3-(4-dimethylamino phenyl)acryloyl}-2*H*-chromen-2-one (**2i**) with an MIC value of 7.8 μg/mL. Thus, 3-(substituted aryl and substituted heteroaromatic)acryloyl)-2*H*-chromen-2-one derivatives synthesized as well as the starting material may seem promising for further activity optimization studies.

EXPERIMENTAL

General condition (chemical synthesis). Melting points were determined with open capillary tube on a Gallenkamp (variable heater) melting point apparatus and were uncorrected. Infra red spectra were recorded as KBr disc using a Shimadzu IR-740 Spectrophotometer, whereas UV–visible spectra were recorded on a Heλiosεα v2.02 Unicam Spectrophotometer using methanol solvent. ^{1}H- and ^{13}C-NMR were run on a Jeol EX 400 Spectrometer using deuteriated methanol with tetramethylsilane as the internal standard and δ values recorded in ppm. Mass spectra were run on Finnigan MAT 312 machine. All compounds were routinely checked by TLC on silica gel G plates using CH_3COCH_3:CH_3OH (3:1, v/v) solvent system and the developed plates were visualized under UV light. The elemental analysis (C, H, N) of compounds were performed using a Carlo Erba-1108 elemental analyzer. The microwave-assisted syntheses were carried out in a CEM Discover monomode oven using sealed tube, with magnetic stirring, and the temperature control was fixed at 140°C. All reagents used

were obtained from Sigma-Aldrich Chemicals, except piperidine and furfural derivatives which were obtained from BDH Chemical Limited. Solvents used were of analytical grade and, when necessary, were purified and dried by standard method.

3-Acetylcoumarin (1). To a mixture of salicyaldehyde (0.86 mL, 81.89 mmoles) and ethyl acetoacetate (11.5mL, 90.13 mmoles) was added catalytic amount of piperidine (0.2 mL, 1.64 mmoles) and swirled thoroughly. The mixture was irradiated in microwave oven at 400 W for 1 min. The solid product was filtered, dried, and recrystallized from methanol to afford pure 3-acetyl coumarin **1** in appropriate yield (Table 3). λ_{max} (Log ε): 216 (5.29), 236 (4.65), 288 (4.57), 327 (4.57), 348 (4.49), 355 (4.24), 369 (4.01). IR (KBr): 2925 (CH aliphatic), 1746 (C=O ester), 1685 (C=O), 1606 (C=C), 1369 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 2.27 (s, 3H, CH_3), 7.42–7.84 (m, 4H, Benzofused coumarin-H), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 198.7 (C=O), 159.4 (C=O), 153.0, 137.4, 131.2, 128.3, 127.9, 125.4, 118.1, 116.1, 29.6 (CH_3) ppm. MS: m/z 188 (M^+, 80%), 145 (100%), 94 (50%).

General procedure for synthesis of (2a–j). To an equimolar mixture of 3-acetylcoumarin, **1** (1 g, 5.3 mmoles) and substituted benzaldehyde (5.3 mmoles) was added piperidine (0.2 mL, 1.64 mmoles) drop wisely with continuous stirring until homogeneity was achieved. The mixture was irradiated in microwave oven at 400 W for 1–3 min. The crude product was filtered, dried, and recrystallized from appropriate solvent to afford **2a–j** in varied yields (Table 3).

3-Cinnamoyl-2H-chromen-2-one (2a). Reagents: Compound **1** (1.0 g, 5.3 mmoles), benzaldehyde (0.5 mL, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 3 min, 140°C. Purification: recrystallization (ethanol). λ_{max} (Log ε): 224 (3.99), 348 (3.47), 375 (3.01s). IR (KBr): 1740, 1673, 1606, 1363 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 7.03 (d, 1H, J = 8.5 Hz, CO—CH=C), 7.33–7.84 (m, 9H, Benzofused coumarin-4H and Ar-5H), 7.82 (d, 1H, J = 8.5 Hz, CO—C=CH), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7 (C=O), 159.4 (C=O), 153.0, 147.2, 142.2, 135.2, 134.2, 128.6, 128.6, 128.5, 128.5, 128.3, 127.9, 127.9, 125.4, 125.4, 118.1, 116.1 ppm. MS: m/z 276 (M^+, 75%), 199 (60%), 173 (100%).

3-(3-(3-Hydroxyphenyl)acryloyl)-2H-chromen-2-one (2b). Reagents: Compound **1** (1.0 g, 5.3 mmoles), *m*-hydroxybenzaldehyde (0.65 g, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 2 min, 140°C. Purification: recrystallization (methanol). λ_{max} (Log ε): 208 (3.82), 280 (3.32), 348 (3.46), 361 (3.46), 369 (3.45). IR (KBr): 3302, 1703, 1648, 1600, 1375 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 5.35 (s, 1H, OH, D_2O exchangeable), 6.70 (s, 1H, Ar-H), 6.83 (d, 1H, Ar-H), 7.03 (d, 1H, J = 8.8 Hz, CO—CH=C), 7.16 (d, 1H, Ar-H), 7.42–7.84 (m, 4H, Benzofused coumarin-H), 7.53 (t, 1H, Ar-H), 7.96 (d, 1H, J = 8.8 Hz, CO—C=CH), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7 (C=O), 159.4 (C=O), 158.4, 153.0, 147.2, 142.2, 135.4, 134.2, 130.0, 128.3, 127.9, 125.4, 125.4, 121.1, 118.1, 117.6, 116.1, 115.1 ppm. MS: m/z 292 (M^+, 30%), 275 (50%), 199 (25%), 145 (100%).

3-(3-(4-Nitrophenyl)acryloyl)-2H-chromen-2-one (2c). Reagents: Compound **1** (1.0 g, 5.3 mmoles), *p*-nitrobenzaldehyde (0.80 g, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 1 min, 140°C. Purification: recrystallization (methylated spirit). λ_{max} (Log ε): 220 (4.22), 328 (3.76), 368 (3.87). IR (KBr): 1740, 1673, 1606, 1364, 738 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 7.32 (d, 1H, J = 8.5 Hz, CO—CH=C), 7.96 (d, 1H, J = 8.5 Hz, CO—C=CH), 7.42–7.84 (m, 4H, Benzofused coumarin-H), 8.03 (d, 2H, Ar-H), 8.21 (d, 2H, Ar-H), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7 (C=O), 159.4 (C=O), 153.0, 147.2, 147.1, 142.2, 141.3, 134.2, 129.0, 129.0, 128.3, 127.9, 125.4, 125.4, 123.8, 123.8, 118.1, 116.1 ppm. MS: m/z 321 (M^+, 70%), 275 (47%), 145 (100%).

3-(3-(4-Chlorophenyl)acryloyl)-2H-chromen-2-one (2d). Reagents: Compound **1** (1.0 g, 5.3 mmoles), *p*-chlorobenzaldehyde (0.74 g, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 1.5 min, 140°C. Purification: recrystallization (methanol). ^{1}H-NMR (CD_3OD, 400 Hz): δ 7.03 (d, 1H, J = 8.5 Hz, CO—CH=C), 7.82 (d, 1H, J = 8.5 Hz, CO—C=CH), 7.44 (d, 2H, Ar-H), 7.68 (d, 2H, Ar-H), 7.42–7.84 (m, 4H, Benzofused coumarin-H), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7, 159.4, 153.0, 147.2, 142.2, 134.2, 133.5, 133.3, 129.0, 129.0, 128.7, 128.7, 128.3, 127.9, 125.4, 125.4, 118.1, 116.1 ppm. MS: m/z 310.5 (M^+, 80%), 275 (40%).

3-(3-(3-p-Tolylacryloyl)-2H-chromen-2-one (2e). Reagents: Compound **1** (1.0 g, 5.3 mmoles), *p*-methylbenzaldehyde (0.65 g, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 2 min, 140°C. Purification: recrystallization (methanol). ^{1}H-NMR (CD_3OD, 400 Hz): δ 2.34 (s, 3H, CH_3), 7.18 (d, 2H, Ar-H), 7.03 (d, 1H, J = 8.5 Hz, CO—CH=C), 7.42–7.84 (m, 4H, Benzofused coumarin-H), 7.59 (d, 2H, Ar-H), 7.82 (d, 1H, J = 8.5 Hz, CO—C=CH), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7, 159.4, 153.0, 147.2, 142.2, 137.6, 134.2, 132.2, 128.9, 128.9, 128.5, 128.5, 128.3, 127.9, 125.4, 125.4, 118.1, 116.1, 21.3 (CH_3) ppm. MS: m/z 290 (M^+, 50%), 199 (100%).

3-(3-(4-Ethylphenyl)acryloyl)-2H-chromen-2-one (2f). Reagents: Compound **1** (1.0 g, 5.3 mmoles), *p*-ethylbenzaldehyde (0.72 mL, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 2 min, 140°C. Purification: recrystallization (methanol). ^{1}H-NMR (CD_3OD, 400 Hz): δ 1.25 (t, 3H, J = 7.0 Hz, CH_3), 2.60 (q, 2H, J = 7.0 Hz, CH_2), 6.77 (d, 2H, Ar-H), 7.03 (d, 1H, J = 8.5 Hz, CO—CH=C), 7.42–7.84 (m, 6H, Benzofused coumarin-4H and Ar-2H), 7.82(d, 1H, J = 8.5 Hz, CO—C=CH), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7, 159.4, 153.0, 142.2, 143.5, 142.2, 134.2, 132.4, 128.5, 128.5, 128.3, 127.9, 127.6, 127.6, 125.4, 125.4, 118.1, 116.1, 28.2 (CH_2), 14.5 (CH_3). MS: m/z 304 (M^+, 80%), 285 (35%), 145 (100%).

3-(3-(4-Hydroxyphenyl)acryloyl)-2H-chromen-2-one (2g). Reagents: Compound **1** (1.0 g, 5.3 mmoles), *p*-hydroxybenzaldehyde (0.65 g, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 3 min, 140°C. Purification: recrystallization (ethanol). λ_{max} (Log ε): 211 (3.52), 336 (3.41), 368 (3.56). IR (KBr): 3241, 1734, 1685, 1612, 1375 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 5.35 (s, 1H, OH, D_2O exchangeable), 6.65 (d, 2H, Ar-H), 7.03 (d, 1H, J = 8.5 Hz, CO—CH=C), 7.42–7.84 (m, 4H, Benzofused coumarin-H), 7.56 (d, 2H, Ar-H), 7.82 (d, 1H, J = 8.5 Hz, CO—C=CH), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7, 159.4, 157.7 (C—OH), 153.0, 147.2, 142.2, 134.2, 130.6, 130.6, 128.3, 127.9, 127.8, 125.4, 125.4, 118.1, 116.1, 115.8 ppm. MS: m/z 292 (M^+, 40%), 275 (75%), 199 (50%), 145 (100%).

3-(3-(4-Hydroxy-3-methoxyphenyl)acryloyl)-2H-chromen-2-one (2h). Reagents: Compound **1** (1.0 g, 5.3 mmoles), vanillin

(0.81 g, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 1 min, 140°C. Purification: recrystallization (ethanol). λ_{max} (Log ε): 208 (4.03), 244 (3.91), 352 (3.42). IR (KBr): 1740, 1685, 1600, 1338 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 3.83 (s, 3H, OCH_3), 5.35 (s, 1H, OH, D_2O exchangeable), 6.79 (d, 1H, Ar-H), 6.99 (d, 1H, Ar-H), 7.03 (d, 1H, J = 8.5 Hz, CO—CH=C), 7.16 (s, 1H, Ar-H), 7.42–7.84 (m, 4H, Benzofused coumarin-H), 7.82 (d, 1H, J = 8.5 Hz, CO—C=CH), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7 (C=O), 159.4 (C=O), 153.0, 149.1 (*C*—OCH_3), 147.9 (C—OH), 147.2, 142.2, 134.2, 128.3, 127.9, 127.6, 125.4, 125.4, 122.9, 118.1, 116.8, 116.1, 111.9, 56.1 (OCH_3) ppm. MS: m/z 323 (M^+, 68%), 275 (60%), 199 (50%).

3-(3-(4-Dimethylaminophenyl)acryloyl)-2H-chromen-2-one (2i). Reagents: Compound **1** (1.0 g, 5.3 mmoles), 4-(*N*,*N*-dimethylamino)benzaldehyde (1.27 g, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 2.5 min, 140°C. Purification: recrystallization (ethanol). λ_{max} (Log ε): 208 (4.00), 327 (3.90s), 344 (3.97), 448 (3.84). IR (KBr): 1746, 1685, 1594, 1375 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 3.06 (s, 6H, 2×CH_3), 6.71 (d, 2H, Ar-H), 7.03 (d, 1H, J = 8.5 Hz, CO—CH=C), 7.72 (d, 2H, Ar-H), 7.42–7.84 (m, 4H, Ar-H), 7.82 (d, 1H, J = 8.5 Hz, CO—C=CH), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7 (C=O), 159.4 (C=O), 153.0, 150.3, 147.2, 142.2, 134.2, 129.7, 129.7, 128.3, 127.9, 125.4, 125.4, 124.7, 118.1, 116.1, 111.7, 111.7, 41.3 (2×CH_3) ppm. MS: m/z 319 (M^+, 70%), 199 (100%).

3-(5-Phenylpenta-2,4-dienoyl)-2H-chromen-2-one (2j). Reagents: Compound **1** (1.0 g, 5.3 mmoles), cinnamaldehyde (0.67 mL, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 1 min, 140°C. Purification: recrystallization (ethanol). λ_{max} (Log ε): 212 (3.72), 300 (3.49), 330 (3.49), 347 (3.53), 360 (3.53), 366 (3.53), 369 (4.01). IR (KBr): 1740, 1648, 1612, 1375 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 6.69 (d, 1H, J = 8.5 Hz, CO—CH=C), 6.71 (d, 1H, J = 8.5 Hz, 9.2 Hz, CO—C=C—CH), 7.02 (d, 1H, J = 9.2 Hz, COC=C—C=CH), 7.52 (d, 1H, J = 8.5 Hz, 9.2 Hz, CO—C=CH), 7.33–7.84 (m, 9H, Benzofused coumarin-4H and Ar-5H), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7 (C=O), 159.4 (C=O), 153.0, 151.9, 147.2, 141.0, 135.2, 134.2, 128.6, 128.6, 128.5, 128.5, 128.3, 127.9, 127.9, 125.4, 125.2, 121.2, 118.1, 116.1 ppm. MS: m/z 302 (M^+, 55%).

General procedure for synthesis of (3a–e) and (4a–e). A catalytic amount of piperidine (0.2 mL, 1.64 mmoles) was cautionly added to a well-ground mixture of 3-acetyl coumarin **1**(1.0 g, 5.3 mmoles) and substituted heteroaromatic aldehyde (5.3 mmoles). The reaction mixture was irriadiated in microwave oven at an emitted power of 400 W for an appropriate time. Then, it was poured in crushed ice and the product was filtered and recrystallized from appropriate solvent to give **3a**–**e** and **4a**–**e**.

3-(3-(Furan-2-yl)acryloyl)-2H-chromen-2-one (3a). Reagents: Compound **1** (1.0 g, 5.3 mmoles), furfural (0.33 mL, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 3 min, 140°C. Purification: recrystallization (methylated spirit). λ_{max} (Log ε): 220 (3.88), 348 (3.49), 368 (3.65). IR (KBr): 1734, 1648, 1606, 1380 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 6.87 (t, 1H, Furan-H), 7.03 (d, 1H, J = 8.7 Hz, CO—CH=C), 7.42–7.84 (m, 5H, Benzofused coumarin-4H & Furan-1H), 7.66 (d, 1H, J = 8.7 Hz, CO—C=CH), 8.17 (d, 1H, Furan-H), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7 (C=O), 159.4 (C=O), 153.0, 151.5, 147.2, 143.7, 138.9, 134.2, 129.3, 128.3, 127.9, 125.4, 118.1, 116.1, 113.8, 112.7. MS: m/z 266 (M^+, 25%), 199 (75%), 68 (33%).

3-(3-(5-Nitrofuran-2-yl)acryloyl)-2H-chromen-2-one (3b). Reagents: Compound **1** (1.0 g, 5.3 mmoles), 5-nitrofurfural (0.47 mL, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 1.5 min, 140°C. Purification: recrystallization (aqueous ethanol, 1:1). λ_{max} (Log ε): 216 (4.03), 372 (3.77). IR (KBr): 1734, 1685, 1600, 1376 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 7.03 (d, 1H, J = 8.7 Hz, CO—CH=C), 7.42–7.85 (m, 5H, Benzofused coumarin-4H & Furan-1H), 7.66 (d, 1H, J = 8.7 Hz, CO—C=CH)), 7.94 (d, 1H, Furan-H), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7 (C=O), 159.4 (C=O), 155.4, 153.8, 153.0, 147.2, 138.9, 134.2, 129.3, 128.3, 127.9, 125.4, 118.1, 117.5, 116.1, 114.5. MS: m/z 311 (M^+, 20%), 265 (45%).

3-(3-(5-Chlorofuran-2-yl)acryloyl)-2H-chromen-2-one (3c). Reagents: Compound **1** (1.0 g, 5.3 mmoles), 5-chlorofurfural (0.69 g, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 1 min, 140°C. Purification: recrystallization (ethanol). λ_{max} (Log ε): 216 (4.28), 368 (4.41), 388 (3.95). IR (KBr): 1744, 1648, 1605, 1380 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 6.89 (d, 1H, J = 9.3 Hz, Furan-H), 7.03 (d, 1H, J = 8.7 Hz, CO—CH=C), 7.24 (d, 1H, J = 9.3 Hz, Furan-H), 7.42–7.84 (m, 4H, Benzofused coumarin-H), 7.66 (d, 1H, J = 8.7 Hz, CO—C=CH), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7 (C=O), 159.4 (C=O), 153.0, 151.9, 147.2, 138.9, 138.7, 134.2, 129.3, 128.3, 127.9, 125.4, 118.1, 116.1, 114.1, 109.8. MS: m/z 300.5 (M^+, 60%), 199 (80%), 103.5 (38%).

3-(3-(5-Methylfuran-2-yl)acryloyl)-2H-chromen-2-one (3d). Reagents: Compound **1** (1.0 g, 5.3 mmoles), 5-methylfurfural (0.53 mL, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 2.5 min, 140°C. Purification: recrystallization (methylated spirit). λ_{max} (Log ε): 208 (4.03), 244 (3.91), 352 (3.42). IR (KBr): 1740, 1685, 1600, 1338 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 2.30 (s, 3H, CH_3), 6.43 (d, 1H, J = 9.5 Hz, Furan-H), 7.03 (d, 1H, J = 8.5 Hz, CO—CH=C), 7.28 (d, 1H, J = 9.5 Hz, Furan-H), 7.42–7.84 (m, 4H, Benzofused coumarin-H), 7.66 (s, 1H, CO—C=CH). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7, 159.4, 157.6, 153.0, 152.4, 147.2, 138.9, 134.2, 129.3, 128.3, 127.9, 125.4, 118.1, 117.5, 116.1, 109.5, 13.8 (CH_3). MS: m/z 280 (M^+, 83%), 265 (52%), 68 (30%).

3-(3-(5-Ethylfuran-2-yl)acryloyl)-2H-chromen-2-one (3e). Reagents: Compound **1** (1.0 g, 5.3 mmoles), 5-ethyl-2-furaldehyde (0.63 mL, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 2 min, 140°C. Purification: recrystallization (methylated spirit). λ_{max} (Log ε): 212 (4.07), 248 (3.84), 368 (3.42). IR (KBr): 1734, 1648, 1606, 1380 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 1.25 (t, 3H, J = 6.0 Hz, CH_3), 2.44 (q, 2H, J = 6.0 Hz, CH_2), 6.43 (d, 1H, J = 10.0 Hz, Furan-H), 7.03 (d, 1H, J = 8.6 Hz, CO—CH=C), 7.28 (d, 1H, J = 10.0 Hz, Furan-H), 7.42–7.84 (m, 4H, Benzofused coumarin-H), 7.66 (d, 1H, J = 8.6 Hz, CO—C=CH), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7 (C=O), 159.4 (C=O), 157.4, 153.0, 151.8, 147.2, 138.9, 134.2, 129.3, 128.3, 127.9, 125.4, 120.0, 118.1, 116.1, 108.7, 21.4 (CH_2), 12.7 (CH_3). MS: m/z 294 (M^+, 40%). 280 (45%).

3-(3-(1H-Pyrrol-2-yl)acryloyl-2H-chromen-2-one (4a). Reagents: Compound **1** (1.0 g, 5.3 mmol), pyrrole-2-carboxaldehyde (0.50 g, 5.3 mmol), piperidine (0.2 mL). Conditions: MWI for

2.5 min, 140°C. Purification: recrystallization (DMF/ethanol, 1:9). λ_{max} (Log ε): 212 (4.16), 344 (3.62). IR (KBr): 3445, 1685, 1600, 1348 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 5.00 (s, 1H, NH, D_2O exchangeable), 6.15 (t, 1H, J = 12.5 Hz, 15 Hz, Pyrrolo-H), 6.51 (d, 1H, J = 12.5 Hz, Pyrrolo-H), 6.95 (d, 1H, J = 15 Hz, Pyrrolo-H), 7.03 (d, 1H, J = 8.0 Hz CO—CH=C), 7.42–7.84 (m, 4H, Benzofused coumarin-H), 7.66 (d, 1H, J = 8.0 Hz, CO—C=CH), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7, 159.4, 153.0, 147.2, 143.4, 134.2, 129.8, 129.3, 128.3, 127.9, 125.4, 118.3, 118.1, 116.1, 111.9, 108.2. MS: m/s 266 (M^+, 62%), 199 (100%), 67 (48%).

3-(3-(5-Nitro-1H-pyrrol-2-yl)acryloyl)-2H-chromen-2-one (4b). Reagents: Compound **1** (1.0 g, 5.3 mmoles), 5-nitro-1*H*-pyrrole-2-carboxaldehyde (0.74 g, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 2.5 min, 140°C. Purification: recrystallization (DMF/ethanol, 1:9). λ_{max} (Log ε): 210 (3.93), 368 (3.52). IR (KBr): 3302, 1740, 1685, 1600, 1338 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 5.0 (s, 1H, NH; D_2O exchangeable), 6.75 (d, 1H, J = 12.3 Hz, Pyrrolo-H), 7.03 (d, 1H, J = 7.5 Hz, CO—CH=C), 7.42–7.84 (m, 4H, Benzofused coumarin-4H), 7.46 (d, 1H, J = 12.3 Hz, Pyrrolo-H), 7.66 (d, 1H, J = 7.5 Hz, CO—C=CH), 8.57 (d, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7 (C=O), 159.4 (C=O), 153.0, 147.2, 143.4, 139.9, 134.2, 134.0, 129.3, 128.3, 127.9, 125.4, 118.1, 116.1, 112.5, 109.3. MS: m/z 311 (M^+, 55%), 67 (35%).

3-(3-(5-Chloro-1H-pyrrol-2-yl)acryloyl)-2H-chromen-2-one (4c). Reagents: Compound 1 (1.0 g, 5.3 mmoles), 5-chloro-1*H*-pyrrole-2-carboxaldehyde (0.69 g, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 2.5 min, 140°C. Purification: recrystallization (DMF/ethanol, 3:7). λ_{max} (Log ε): 212 (4.29), 252 (3.84), 350 (3.42s). IR (KBr): 3241, 1734, 1685, 1612, 1375, 980 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 5.0 (s, 1H, NH; D_2O exchangeable), 6.40 (d, 1H, J = 11.2 Hz, Pyrrolo-H), 6.51 (d, 1H, J = 11.2 Hz, Pyrrolo-H), 7.03 (d, 1H, J = 8.1 Hz, CO—CH=C), 7.42–7.84 (m, 4H, Benzofused coumarin-H), 7.66 (d, 1H, J = 8.1 Hz, CO—C=CH), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7, 159.4, 153.0, 147.2, 143.4, 134.2, 129.8, 129.3, 128.3, 127.9, 125.4, 121.8, 118.1, 116.3, 116.1, 112.1. MS: m/z 300.5 (M^+, 55%).

3-(3-(5-Methyl-1H-pyrrol-2-yl)acryloyl)-2H-chromen-2-one (4d). Reagents: Compound **1** (1.0 g, 5.3 mmoles), 5-methyl-1*H*-pyrrole-2-carboxaldehyde (0.58 g, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 2.5 min, 140°C. Purification: recrystallization (methanol). λ_{max} (Log ε): 220 (3.87), 368 (4.15), 388 (3.72). IR (KBr): 3302, 2929, 1734, 1648, 1600, 1375 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 2.14 (s, 3H, CH_3), 5.0 (s, 1H, NH; D_2O exchangeable), 6.07 (d, 1H, J = 11.5 Hz, Pyrrolo-H), 6.35 (d, 1H, J = 11.5 Hz, Pyrrolo-H), 7.03 (d, 1H, J = 8.1 Hz, CO—CH=C), 7.42–7.84 (m, 4H, Benzofused coumarin-H), 7.66 (d, 1H, J = 8.1 Hz, CO—C=CH), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7 (C=O), 159.4 (C=O), 153.0, 147.2, 143.4, 134.2, 130.1, 129.5, 129.3, 128.3, 127.9, 125.4, 118.1, 116.1, 112.0, 106.5, 17.3 (CH_3).

3-(3-(5-ethyl-1H-pyrrol-2-yl)acryloyl)-2H-chromen-2-one (4e). Reagents: Compound **1** (1.0 g, 5.3 mmoles), 5-ethyl-1*H*-pyrrole-2-carboxaldehyde (0.65 g, 5.3 mmoles), piperidine (0.2 mL). Conditions: MWI for 2.5 min, 140°C. Purification: recrystallization (methylated spirit). λ_{max} (Log ε): 220 (4.11), 250 (3.91), 368 (3.42). IR (KBr): 3241, 1746, 1740, 1650, 1594, 1375 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 Hz): δ 1.24 (t, 3H, J = 7.2 Hz, CH_3), 3.11 (q, 2H, J = 7.2 Hz, CH_2), 5.0 (s, 1H, NH; D_2O exchangeable), 6.07 (d, 1H, J = 11.5 Hz, Pyrrolo-H), 6.35 (d, 1H, J = 11.5 Hz, Pyrrolo-H), 7.03 (d, 1H, J = 8.2 Hz, CO—CH=C), 7.42–7.84 (m, 4H, Benzofused coumarin-H), 7.66 (d, 1H, J = 8.2 Hz, CO—C=CH), 8.57 (s, 1H, Coumarin-H). ^{13}C-NMR (CD_3OD, 400 Hz): δ 183.7 (C=O), 159.4 (C=O), 153.0, 147.2, 143.4, 136.1, 134.2, 129.5, 129.3, 128.3, 127.9, 125.4, 118.1, 116.1, 112.0, 107.7, 21.4 (CH_2), 13.7 (CH_3).

Antibacterial activity assays. Most of the organisms used were standard bacteria of National Collection for Industrial Bacteria (NCIB), whereas few others were Locally Isolated Organisms (LIO). The organisms were *Bacillus cereus* (NCIB 6349), *Bacillus stearothermophilus* (NCIB 8222), *Bacillus subtilis* (NCIB 3610), *Bacillus anthracis* (LIO), *Bacillus polymyxa* (LIO), *Corynebacterium pyogenes* (LIO), *Streptococcus faecalis* (NCIB775), *Staphylococcus aureus* (NCIB 8588), *Clostridium sporogenes* (LIO), *Escherichia coli* (NCIB 86), *Pseudomonas fluorescence* (NCIB 3756), *Klebsiella pneumonia* (NCIB 418), *Shigella dysenteriae* (LIO), *Pseudomonas aeruginosa* (NCIB 950), and *Candida albican* (LIO).

Antibacterial sensitivity testing of compounds, 1–4e. All the synthesized compounds (**1–4e**) and streptomycin were screened for antibacterial activity on nine gram positive and five gram negative bacterial strains using agar well diffusion method [48]. The medium employed was diagnostic sensitivity test agar (Biotech Ltd.). With the aid of a sterile 1 mL pipette, about 0.2 mL of the broth culture of test organism was added to 18 mL sterile molten diagnostic sensitivity test agar (Biotech Ltd.) which had already cooled down to 45°C. This was well mixed and poured into previously sterilized Petri dishes, which had been properly labeled according to the test organisms. The medium was then allowed to set. With the aid of a sterile cork borer, the required numbers of holes were bored into the medium. The wells were made of about 5 mm to the edge of the plate. The wells were then filled up aseptically with the solution of the compound in DMSO using Pasteur pipettes. Streptomycin was used as the standard antibacterial agent at a concentration of 1000 μg/mL. The plates were allowed to stand for about 1 h on the bench for proper diffusion of the antibacterial agents into the medium and then incubated uprightly at 37°C for 24 h. Care was taken not to stockpile the plates. Clear zones of inhibition in millimetres indicated the relative susceptibility of the bacteria to the compounds (**1–4e**) and streptomycin standard.

Determination of MIC and MBC. The minimum inhibitory concentration (MIC) was done using the method of Russell and Furr [48]. Based on the level of resistance of some organisms and large zones of inhibition experienced in others, minimum inhibitory concentration (MIC) was selectively done for five gram positive and five gram negative bacterial strains. Different concentrations (7.8 and 100.0 μg/mL) of the compounds and standard were prepared using a twofold dilution which was prepared in a sterile plate with the aid of sterile pipette and then mixed with 18 mL of molten nutrient agar. This was then allowed to set. The surface of the nutrient agar plate was allowed to dry before streaking with overnight broth cultures of the bacterial strains. The plates were then labeled accordingly and incubated at 37°C for up to 72 h. They were subsequently examined for the presence or absence of growth.

The lowest concentration preventing the growth of bacteria was taken as the minimum inhibitory concentration of the compounds. This procedure was likewise repeated for the streptomycin (standard).

To obtain minimum bactericidal concentration (MBC), 0.1 mL volume was taken from each tube and spread on agar plates. The number of c.f.u was counted after 18–24 h of incubation at 35°C.

REFERENCES AND NOTES

[1] Lévai, A.; Jekó, J. ARKIVOC 2009, vi, 63.

[2] Curir, P.; Galeotti, F.; Marcello, D.; Barile, E.; Lanzotti, V. J Nat Prod 2007, 70, 1668.

[3] Tran, Q. L.; Tezuka, Y.; Ueda, J.-Y.; Nguyen, N. T.; Maruyawa, Y.; Begum, K.; Kim, H. S.; Tran, Q. K.; Kadota, S. J Ethnopharmacol 2003, 86, 249.

[4] Yenjai, C.; Sripontan, S.; Sriprajun, P.; Kittakoop, P.; Jintasirikul, A.; Tanticharoen, M.; Thebtaranonth, Y. Planta Med 2000, 66, 277.

[5] Ragitha, B.; Kumar, N. V.; Someshwar, P.; Madhav, J. V.; Reddy, P. N.; Reddy, Y. T. ARKIVOC 2006, xii, 23.

[6] Dekić, S. V.; Dekić, V. S.; Vučić, B.; Dekić, B. R.; Dekić, M. S. Phys Chem Technol 2007, 5, 85.

[7] Kostova, I.; Raleva, S.; Genova, P.; Argirova, R. Bioinorg Chem Appl 2006, 2006, 68274.

[8] Anderson, D. M.; Shelley, S.; Crick, N.; Buraglio, M. J Clin Pharmacol 2002, 42, 1358.

[9] Tassies, D.; Freire, C.; Puoan, J.; Maragall, S.; Monteagudo, J.; Ordinas, A.; Reverter, J. C. Haematologica 2002, 87, 1185.

[10] Gürsoy, A.; Karali, N. Turk J Chem 2003, 27, 545.

[11] Kotali, A.; Lafazanis, I. S.; Papageorgiou, A.; Chrysogelou, E.; Liarliaris, T.; Sinakos, Z. Molbank 2008, M574, 1.

[12] Satyanarayana, V. S. V.; Sreevani, P.; Sivakumar, A.; Vijayakumar, V. ARKIVOC 2008, vii, 221.

[13] Raviraj, A. K.; Manohar, V. K. Indian J Chem 2005, 44B, 591.

[14] Kontogiorgis, C. A.; Savvoglou, K.; Hadjipavlou-Litina, D. J. J Enzyme Inhib Med Chem 2006, 21, 21.

[15] Srinivas, K. K.; Hager, E.; Pehit, C.; Davidson, N. E.; Khan, S. R. J Med Chem 2003, 46, 2831.

[16] Meteeva, N. N.; Kode, R. M.; Redda, K. K. J Heterocycl Chem 2002, 39, 1251.

[17] Jayashree, B. K.; Sameer, A.; Yogendra, N. Pharmacologyonline 2008, 2, 404.

[18] Venugopala, K. N.; Jayashree, B. S. Asian J Chem 2004, 16, 407.

[19] Lacy, A.; O'Kennedy, R. Curr Pharm Des 2004, 10, 3797.

[20] Al-Soud, Y. A.; Al-Sa'doni, H. H.; Amajaour, H. A. S.; Salih, K. S. M.; Mubarak, M. S.; Al-Masoudi, N. A.; Jaber, I. H. Z Naturforsch B 2008, 63, 83.

[21] Luszcski, J. J.; Andres-Mach, M.; Cisowswi, W.; Mazol, I.; Glowniak, K.; Czuczwar, S. J. Eur J Pharmacol 2009, 607, 107.

[22] Tosun, F.; Kizilay, Ç. A.; Erol, K.; Kiliç, F. S.; Kürkçüoğlu, M.; Başer, K. H. C. Food Chem 2008, 107, 990.

[23] Roma, G.; Di Braccio, M.; Grossi, G.; Piras, D.; Leoncini, G.; Bruzzese, D.; Grazia, S. M.; Fossa, P.; Mosta, L. J Med Chem 2007, 50, 2886.

[24] Montagner Souza, S. M. D.; Groposo, C.; Monache, F. D.; Smania, E. F. A.; Smania, A., Jr.; Z Naturforsch C 2008, 63, 21.

[25] Mouri, T.; Yano, T.; Kochi, S. I.; Ando, T.; Hori, M. J Pestic Sci 2005, 30, 209.

[26] Neyts, J.; De Clercq, E.; Singha, R.; Chang, Y. H.; Das, A. R.; Chakraborty, S. K.; Hong, S. C.; Tsay, S.-C.; Hsu, M.-H.; Hwu, J. R. J Med Chem 2009, 52, 1486.

[27] Hwu, J. R.; Singha, R.; Hong, S. C.; Chang, Y. H.; Das, A. R.; Vliengen, I.; De Clercq, E.; Neyts, J. Antiviral Res 2008, 77, 157.

[28] Govori, S. R.; Spahiu, S.; Haziri, A. FASEB J 2008, 22, 1061.

[29] Siddiqui, Z. N.; Asad, M.; Praveen, S. Med Chem Res 2008, 17, 318.

[30] Mashelkar, U. C.; Audi, A. A. J Indian Chem Soc 2005, 82, 254.

[31] Lee, S.; Shin, S.-D.; Kim, J. S.; Oh, K.-B.; Kang, S. S. Arch Pharm Res 2003, 26, 449.

[32] Lisgarten, J. N.; Potter, B. S.; Aymami, J.; Oketch-Rabah, H.; Palmer, R. A. J Chem Crystallogr 2003, 33, 149.

[33] Yun, J. M.; Kweon, M. H.; Kwon, H.; Wang, J. K.; Mukhtar, H. Carcinogenesis 2006, 27, 1454.

[34] Gaber, M.; Fayed, T. A.; El-Daly, S. A.; El-Sayed, Y. S. Photochem Photobiol Sci 2008, 7, 257.

[35] Larsen, M.; Kromann, H.; Kharazmi, A.; Nielsen, S. F. Bioorg Med Chem Lett 2005, 15, 4858.

[36] Anzari, F. L.; Umbreen, S.; Hussain, L.; Makhmoor, T.; Nawaz, S. A.; Lodhi, M. A.; Khan, S. N.; Shaheen, F.; Choudhary, M. I.; Rahman, A. U. Chem Biodivers 2005, 2, 487.

[37] Son, K. I.; Kang, S. Y.; Noh, D. Y. Bull Korean Chem Soc 2009, 30, 513.

[38] Schobert, R.; Biersack, B.; Dietrich, A.; Knauer, S.; Zoldakova, M.; Freuhauf, A.; Mueller, T. J Med Chem 2009, 52, 241.

[39] Devi, J. M.; Tharmaraj, P.; Ramakrishnan, S. K.; Ramachandran, K. Mater Lett 2008, 62, 852.

[40] Majumdar, K. C.; Mondal, S. Tetrahedron Lett 2008, 49, 2418.

[41] Yamamoto, Y.; Kirai, N. Org Lett 2008, 10, 5513.

[42] Saxena, O. M.; Faridi, U.; Kumar, J. K.; Luqman, S.; Darokar, M. P.; Shanker, K.; Chanotiya, C. S.; Gupta, M. M.; Negi, A. S. Steroids 2007, 72, 892.

[43] Tamilvanan, M.; Pandurangan, A.; Reddy, B. S. R.; Subramanian, K. Polym Int 2006, 56, 104.

[44] Lewis, I. Process Column 2005, 17, 1.

[45] Pivonka, D. E.; Empfiled, J. R. Appl Spectrosc 2004, 58, 41.

[46] Hayes, B. L. Aldrichim Acta 2004, 37, 66.

[47] Ajani, O. O.; Obafemi, C. A.; Ikpo, C. O.; Ajanaku, K. O.; Ogunniran, K. O.; James, O. O. Int J Phys Sci 2009, 4, 156.

[48] Russell, A. D.; Fur, J. R. J Appl Bacteriol UK 1977, 43, 253.