Synthesis and Antimicrobial Studies of Some Quinolinylpyrimidine Derivatives

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The quinolinylpyrimidine derivatives were prepared by the condensation of quinolinyl chalcones with urea (or thiourea) under basic conditions by using both conventional and microwave heating. Their IR, ^{1}H NMR, ^{13}C NMR, mass spectra and CHN analyses confirmed the prepared compounds. The newly prepared quinolinylpyrimidine derivatives were screened for antimicrobial activities against the bacterial strains *viz. S. aureus, Shigella, Salmonela, P. aeroginosa, B. Subtilus* and *E. coli* and found considerably active against *S. aureus, P. aeroginosa* and *E. coli*.

Keywords: Quinolinyl chalcone; Quinolinylpyrimidine; Antimicrobial.

INTRODUCTION

Quinoline derivatives are useful heterocyclic aromatic compounds and are widely used in medicinal chemistry. Many 4-hydroxy-1,2-dihydro-2-quinilinones have a wide spectrum of pharmacological applications such as anti-tumor,[1] anti HSV,[2] anti-convulsion[3] and anti-inflammatory[4] activities. Quinolinyl chalcones have been found to possess antimalarial, antibacterial and antifungal properties[5] and have also shown cytotoxicity in K-562 human leukemia cell lines.[6]

Chalcone derivatives are important starting materials for the syntheses of different classes of heterocyclic compounds such as pyrazolines, thiophenes and pyrimidines, etc. Most of these compounds are highly bioactive and are widely used in pharmaceutics. Since the late 1980s, a tremendous interest in the pyrimidine derivatives has been observed, as evidenced by the growing number of publications.[7,8] Many biologically active compounds found in the literature have pyrimidone, pyrazole or quinoline constituents in their structures.[9-12] Recently, pyrimidine derivatives were found to be associated with biological activities such as antimalarial,[13,14] antibacterial[15] and anticancer activities.[16]

Pyrimidoquinolines are important compounds because of their biological properties such as antimalarial,[17] anticancer,[16] antimicrobial[18,19] and anti-inflammatory[20,21] activities. Furthermore, many synthetic pharmacophores possessing antibacterial,[22] antifungal[23] and antimycotic[24] activities are based on the pyrimidyl structures. The development of pyrimidine-based antitumour[25] and antiviral[26] drugs have inspired chemists all over the world to prepare a new series of pyrimidine-based compounds and to study their biological activities.

Numerous methods have been reported to prepare pyrimidine derivatives.[27-30] However, these reported methods suffered from drawbacks such as longer reaction time, complicated work-up procedure, use of acids and bases and hazardous solvents. Microwaves in conjunction with solid supports have lead to high yield, remarkable enhancement in reaction rate and high catalytic activity.[31] The solventless approach using microwaves provides an opportunity to conduct reactions in open vessels, thus avoiding the risk of the development of high pressure.[32]

Keeping in view the potential biological activities of 4-hydroxyquinolinones and pyrimidines, it was perceived that if both the heterocyclic moieties were synthesized in a single nucleus, the new compounds would likely possess significant biological activity. In the present study and as part of our project, we have planned to prepare quinoline based pyrimidine derivatives using both conventional as well as microwave-induced heating methods and to study their antimicrobial effects against different bacterial

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strains.

RESULTS AND DISCUSSION

The chalcones were prepared by the Claisen Schmidt condensation using both conventional as well as ultrasonic assisted methods (Scheme I), and the prepared compounds along with the percentage yields are given in Table 1.

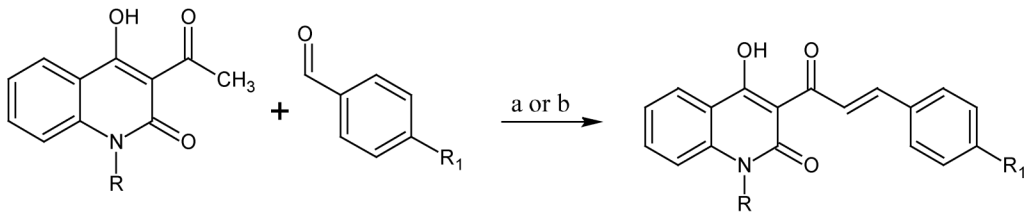
It is found that the ultrasonic-assisted method is energetically favourable, requires less time and provides better yields. Probably, a Cannizzaro reaction is reduced, which enhanced the yields of chalcone derivatives.

A series of quinolinylpyrimidine derivatives have been prepared by using both conventional and microwave-induced heating. The compounds were prepared by the condensation of quinolinyl chalcones with urea (or thiourea) in basic media under prolonged refluxing conditions or under microwave irradiations (Scheme II).

The prepared compounds are given in Table 2 along with the reaction times and percentage yields. In conclusion, when both methods were compared, it was found that method B is extraordinarily less time consuming and product yields are approximately double those of method A.

The structures of prepared quinolinylpyrimidine derivatives have been elucidated by spectroscopic data and elemental analyses. IR spectra of the prepared compound showing a wide absorption band in the region of 3700-3250 cm^{-1} are attributed to OH and NH of the pyrimidyl derivatives. In the ^1H NMR spectra of these compounds both doublets for H_α and H_β are missing which reveal that the enone system of chalcones in the reactants has vanished. In the mass spectra (ESI) of the prepared compounds, (M-1) peak was observed as the base peak in general, and in some cases an exceptional (M+23) peak observed, probably due to $[M+Na]^+$. Similar results have been reported by Li et al.[33]

Scheme I



1a-e

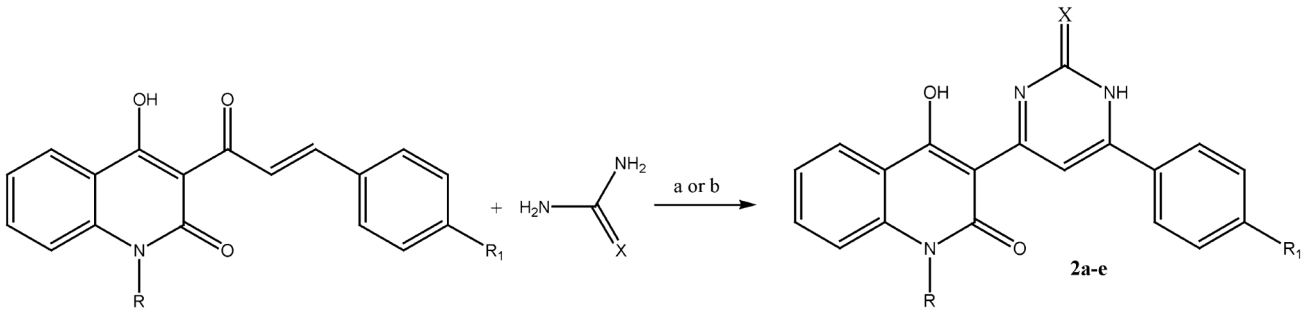
Compd.	R	R_1
1-a	Et	Cl
1-b	Me	Cl
1-c	Me	H
1-d	Ph	Cl
1-e	Ph	OMe

Reagents and conditions:- a Butanol+ I-2 drop piperidine and reflux
b neutral alumina and ultrasonic waves

Table 1. Prepared quinolinyl chalcones

Compound	R	R_1	Conventional Method A		Ultrasonic irradiation Method B	
			Time (hrs) of reflux	Yield (%)	Time (minutes) at 60 °C	Yield (%)
1-a	Et	Cl	6	27	85	65
1-b	Me	Cl	6	26	80	72
1-c	Me	H	6	38	85	74
1-d	Ph	Cl	6	36	90	75
1-e	Ph	OMe	6	28	85	65

Scheme II



Compd.	R	R_1	X
2-a	Et	Cl	O
2-b	Me	Cl	O
2-c	Me	H	O
2-d	Ph	Cl	S
2-e	Ph	OMe	S

Reagents and conditions:- a Alcoholic KOH and reflux,
b Basic alumina and microwave irradiation

Table 2. Quinolinylpyrimidine derivatives

Compound	R	R1	X	Reflux Time (hrs.) Method A	Yield %	MWI Time (minutes) Method B	Yield %
2-a	Et	Cl	O	10	40	4.5	85
2-b	Me	Cl	O	10	39	4.5	82
2-c	Me	H	O	8	38	4.0	80
2-d	Ph	Cl	S	8	38	4.0	82
2-e	Ph	OMe	S	8	45	4.5	85

The elemental analyses are found to be close to the calculated values.

Antibacterial activity of novel prepared quinolinyl pyrimidine derivatives

A novel prepared series of quinolinylpyrimidine derivatives was screened for the antibacterial activities against *S. aureus, Shigella, Salmonela, P. aeroginosa, B. Subtilus* and *E. coli*. Antibacterial tests were carried out by using disc diffusion method.[34] Antimicrobial activity was evaluated by measuring the diameter (mm) of zone inhibition around each disc and average results are recorded in Table 3.

The effects of newly prepared quinolinylpyrimidine derivatives on biological testing were found to be comparatively less active than the control. When the responses of the quinolinylpyrimidine compounds are compared against different tested bacterial species it is observed that *S. aureus*, *P. aeroginosa* and *E. coli* strains are effectively inhibited. The other species are not inhibited by these compounds or are minutely inhibited at very high concentrations.

EXPERIMENTAL

All the chemicals used were obtained from Merck (Germany) and were used as received. Melting points were recorded on a Gallenkemp apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker AVANCE 300 (300.13 MHz for ^{1}H NMR and 75.5 MHz for ^{13}C NMR). The ^{1}H NMR spectra are referenced with respect to the non-deuterated residual solvent in the sample. IR spectra were recorded on a Perkin Elmer spectrum –IX. Mass spectra were recorded on a Bruker Esquire 3000 + ion trap with ESI ionization. Elemental analyses were performed on a

Table 3. *In vitro* antimicrobial activity of newly prepared quinolinylpyrimidine derivatives

Compound	Conc. μg/disc	*S. aureus*	*Shigella*	*Salmonela*	*P. aeroginosa*	*B. Subtilus*	*E. coli*
	100	5	-	-	4	-	2
2-a	200	12	-	-	9	-	8
	600	21	3	1	19	1	12
	100	6	-	-	4	-	-
2-b	200	16	1	-	10	-	5
	600	24	4	2	18	2	14
	100	3	-	-	5	-	1
2-c	200	7	-	-	11	-	6
	600	16	1	2	22	1	12
	100	7	-	1	10	-	2
2-d	200	9	-	3	14	1	8
	600	15	3	5	23	7	15
	100	5	-	-	7	-	-
2-e	200	7	-	-	12	-	7
	600	12	1	12	19	1	11
Ofloxacin	50	25	27	25	25	25	26

Average zone inhibition values are given in millimeters, '—' no inhibition

Perkin-Elmer 2400-CHN Analyzer. Microwave irradiations were carried out in a Q-PRO M microwave synthesis system with power output 800 watts. An ultrasonic bath LC 30 H was used for ultrasonic irradiation. Reaction monitoring and purity of the compounds were checked on silica gel coated aluminum plates (Merck).

General Procedure

Conventional heating (method A)

A mixture of chalcone (1 mmol), urea or thiourea (1 mmol) dissolved in ethanol (20 mL, 95%) and potassium hydroxide (1 g) in water (3 mL) was taken in a flask and heated under reflux for the times given in Table 2. Completion of reaction was monitored by thin layer chromatography (TLC). The reaction mixture was concentrated under vacuum. The precipitates were filtered under suction and washed with water. The crude product was purified by silica gel column chromatography with ethyl acetate/n-hexane.

Microwave-assisted by solid support basic alumina (method B)

A mixture of chalcone (1 mmol), urea or thiourea (1 mmol) dissolved in ethanol (10 mL, 95%) and potassium hydroxide (0.5 g) in water (2 mL) was taken in a beaker (100 mL). Basic alumina (2 g) was slowly added with constant stirring to the above mixture and the solvent was removed under vacuum. The mixture was subjected to microwave-induced radiations in an alumina bath for thirty seconds. The completion of reaction was monitored by TLC. The product was extracted with ethanol (20 mL × 2) and concentrated to one-fourth under vacuum. Precipitates were filtered under suction and washed with water. The crude product was purified by silica gel column chromatography with ethyl acetate/n-hexane.

Antimicrobial Activity

The prepared compounds (1.5 g) were dissolved in chloroform (25 mL) to obtain the solutions (60 mg/mL) and further concentrations (20 and 10 mg/mL) were obtained by dilution method. The solutions were sterilized by filtration by 0.45 μm Millipore filters. Antimicrobial tests were then carried out by using the disc diffusion method. One hundred microliters of suspension containing 10^8 CFU/mL of bacteria were spread on Muller-Hinton agar (MHA) medium. The discs (6 mm in diameter) were impregnated with 10 μL of the solutions (60, 20, 10 mg/mL). Negative controls were prepared by using the same solvent (chloroform), employed to dissolve the test compounds. A known antibiotic, Ofloxacin 10 μL of solution (5 mg/mL), was used as positive reference standard. The loaded discs were then placed in the above-prepared plates. The inoculated plates were incubated at 37 ^{o}C for 24 hours. Antimicrobial activity was evaluated by measuring the diameter (mm) of zone inhibition. Each assay in this experiment was repeated

thrice.

(*2E*)-1-(1-Ethyl-4-hydroxyquinolin-2(1*H*)-one-3yl)-3-(4-chlorophenyl)-2-propen-1-one (1-a)

The title compound (**1-a**) was prepared from 3-acetyl-1-ethyl-4-hydroxyquinolin-2(1*H*)-one (2.31 g, 0.01 mol) and 4-chlorobenzaldehyde (1.40 g, 0.01 mol) by both methods and purified by column chromatography with n-hexane: ethyl acetate (1:1) as eluent. M.p. 166-168 ^{o}C, IR (KBr, ν_{max} in cm^{-1}) 3700-3000 (hydrogen bonded OH), 1644 (C=O), 1614 (Lactam), 1538 (C=C), ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.57 (d, *J* = 15.6 Hz, 1H, H_β), 8.17 (d, *J* = 8.1 Hz, 1H, H_5), 7.8 (d, *J* = 15.6 Hz, 1H, H_α), 7.62 (m, 3H, H_6, H_7, H_8), 7.28 (br-m, 4H, protons of chlorophenyl), 4.2 (q, *J* = 7.2 Hz, 2H, N-C$\underline{H}_2$CH$_3$), 1.3 (t, *J* = 7.2 Hz, 3H, proton of NCH$_2$C$\underline{H}_3$) ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 194.2 (CO), 176.0, 161.3, 143.2, 140.0, 136.4, 134.9, 133.7, 130.1, 129.1, 126.4, 125.8, 121.9, 116.2, 114.1, 105.6, 37.2, 12.8. Mass spectra (ESI) 354 (M+1, 100%), 356 (M+1+2, 33%). Anal. Calcd for $C_{20}H_{16}ClNO_3$: (353.80): C, 67.9; H, 4.56; N, 3.96. Found: C, 67.54; H, 4.48; N, 3.92.

(*2E*)-1-(1-Methyl-4-hydroxyquinolin-2(1*H*)-one-3-yl)-3-(4-chlorophenyl)-2-propen-1-one (1-b)

The title compound (**1-b**) was prepared from 3-acetyl-4-hydroxy-1-methylquinolin-2(1*H*)-one (2.17 g, 0.01 mol) and 4-chlorobenzaldehyde (1.40 g, 0.01 mol) by both methods and purified by column chromatography with solvents n-hexane: ethyl acetate (3:1) as eluent. M.p. 182-184 ^{o}C, IR (KBr, ν_{max} in cm^{-1}) 3680-3000 (hydrogen bonded OH), 1645, 1610 (Lactam), 1537 (C=C), ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.51 (d, *J* = 15.6 Hz, 1H, H_β), 8.22 (d, *J* = 8.5 Hz, 1H, H_5), 7.84 (br-m, 4H, H_α, H_6, H_7, H_8), 7.52 (m, 4H, protons of chlorophenyl), 3.23 (s, 3H, N-CH$_3$), ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 193.8 (CO), 176.2, 160.4, 145.3, 141.2, 135.3, 133.8, 131.5, 130.7, 128.9, 127.6, 126.4, 125.9, 118.6, 116.2, 109.3, 28.4, Mass spectra (ESI) *m/z* 340 (M+1, 60%). Anal. Calcd for $C_{19}H_{14}ClNO_3$: (339.77): C, 67.16; H, 4.15; N, 4.12. Found: C, 65.9; H, 4.00; N, 3.98%.

(*2E*)-1-(1-Methyl-4-hydroxyquinolin-2(1*H*)-one-3-yl)-3-phenyl-2-propen-1-one (1-c)

The title compound (**1-c**) was prepared from 3-acetyl-4-hydroxy-1-methylquinolin-2(1*H*)-one (2.17 g, 0.01 mol) and benzaldehyde (1.06 g, 0.01 mol) by both methods and purified by column chromatography with n-hexane: ethyl acetate (1:1) as eluent. M.p. 168-170 ^{o}C (Lit. m.p. 170-1 ^{o}C[35]), IR (KBr, ν_{max} in cm^{-1}) 3680-3000 (hydrogen bonded OH), 1640 (C=O), 1605 (lactam), 1536 (C=C), ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.62 (d, *J* = 15.9 Hz, 1H, H_β), 8.19 (d, *J* = 1.8 Hz, 1H, H_5), 7.86 (d, *J* = 15.9 Hz, 1H, H_α), 7.61 (m, 3H, H_6, H_7, H_8), 7.21 (m, 3H, H_2', H_4', H_6'), 7.16 (m, 2H, H_3', H_5'), 3.59 (s, 3H, N-CH$_3$). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 193.1 (CO), 176.0, 145.9, 141.6, 135.2, 134.8, 130.6, 129.1, 128.8, 126.3, 125.3, 125.1, 122.2, 114.2, 29.5. Mass spectra (ESI) *m/z* 306 (M+1, 75%). Anal. Calcd for $C_{19}H_{15}NO_3$: (305.33): C, 74.74; H, 4.95; N, 4.59. Found: C, 73.9; H, 4.86; N, 4.35.

(2*E*)-1-(1-Phenyl-4-hydroxyquinolin-2(1*H*)-one-3-yl)-3-(4-chlorophenyl)-2-propen-1-one (1-d)

The title compound (**1-d**) was prepared from 3-acetyl-4-hydroxy-1-phenylquinolin-2(1*H*)-one (2.79 g, 0.01 mol) and 4-chlorobenzaldehyde (1.40 g, 0.01 mol) by both methods and purified by column chromatography with n-hexane: ethyl acetate (3:1) as eluent. M.p. 240-242 ^{o}C, IR (KBr, ν_{max} in cm^{-1}) 3700-3000 (hydrogen bonded OH), 1648 (C=O), 1610 (lactam) 1537 (C=C), ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.62 (d, *J* = 15.6 Hz, 1H, H_β), 8.29 (d, *J* = 1.2 Hz, 1H, H_5), 7.89 (d, *J* = 15.6 Hz, 1H, H_α), 7.65 (m, 5H, protons of N-phenyl), 7.48 (m, 2H, H_6, H_7), 7.43 (m, 5H, H_8, 4 protons of chlorophenyl). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 193.1 (CO), 175.8, 151.3, 142.3, 135.4, 134.7, 132.9, 130.5, 128.9, 127.6, 125.4, 124.1, 122.4, 121.3, 118.6, 117.6, 114.5, 113.2, 110.2, Mass spectra (ESI) *m/z* 402 (M+1, 100%). Anal. Calcd for $C_{24}H_{16}ClNO_3$: (401.08): C, 71.73; H, 4.01; N, 3.49. Found: C, 72.36; H, 3.95; N, 3.32.

(*2E*)-1-(1-Phenyl-4-hydroxyquinolin-2(1*H*)-one-3-yl)-3-(4-methoxyphenyl)-2-propen-1-one (1-e)

The title compound (**1-e**) was prepared from 3-acetyl-4-hydroxy-1-phenylquinolin-2(1*H*)-one (2.79 g, 0.01 mol) and 4-methoxybenzaldehyde (1.36 g, 0.01 mol) by both methods and purified by column chromatography with n-hexane: ethyl acetate (3:1) as eluent. M.p. 262-264 ^{o}C (Lit. m.p 260 ^{o}C[35]), IR (KBr, ν_{max} in cm^{-1}) 3700-3000 (hydrogen bonded OH), 1648 (C=O), 1610 (lactam), 1568 (C=C), ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.52 (d, *J* = 15.6 Hz, 1H, H_β), 8.24 (d, *J* = 8.1 Hz, 1H, H_5), 7.94 (d, *J* = 15.6 Hz, 1H, H_α), 7.54 (br-m, 5H, H_6, H_7, H_8, H_2', H_6'), 7.43 (br-m, 3H, H_3', H_4', H_5'), 7.19 (m, 4H, protons of 4-methoxyphenyl), 3.81 (s, 3H, protons of OCH$_3$), ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 194.6 (CO), 176.8, 152.1, 145.3, 135.8, 132.9, 130.6, 129.7, 128.6, 126.7, 125.1, 123.5, 121.2, 119.2, 118.0, 116.9, 114.5, 112.7, 55.3, Mass spectra (ESI)

m/z 398 (M+1, 65%). Anal. Calcd for $C_{25}H_{19}NO_4$: (397.13): C, 75.55; H, 4.82; N, 3.52. Found: C, 76.42; H, 4.68; N, 3.82.

3-[6-(4-Chlorophenyl)-1,2-dihydro-2-oxopyrimidin-4-yl]-4-hydroxy-1-ethylquinolin-2(1*H*)-one (2-a)

The title compound (**2-a**) was prepared from 3-[(*E*)-3-(4-chlorophenyl)acryloyl]-1-ethyl-4-hydroxyquinolin-2(1*H*)-one (0.35 g, 1 mmol) and urea (0.06 g, 1 mmol) by both methods and purified by column chromatography with ethyl acetate/n-hexane (3:2) as eluent. M.p. 282-284 ºC, IR (KBr, ν_{max} in cm^{-1}): 3738-3450, 1663, 1632, 1594, 1533, ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.24 (dd, *J* = 1.8, 7.8 Hz, 1H, H_5), 7.88-7.50 (br-m, 3H, H_6, H_7, H_8), 7.41-7.24 (br-m, 4H, protons of *p*-chlorophenyl), 7.05 (m, 1H, methine proton, 4.24 (q, *J* = 7.2 Hz, 2H, N-C$\underline{H}_2$CH$_3$), 1.30 (t, *J* = 7.2 Hz, 3H, N-CH$_2$C$\underline{H}_3$), ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 194.9 (CO), 180.5, 168.9, 144.8, 138.2, 137.98, 135.86, 133.95, 133.59, 131.55, 129.5, 124.4, 118.07, 114.3, 18.6, Mass spectrum (ESI) *m/z* 394 (M+1, 25%), 396 (M+1+2, 10%), 376 (M-OH, 25%). Anal. Calcd for $C_{21}H_{16}ClN_3O_3$: (393.08): C, 64.05; H, 4.09; N, 10.67. Found: C, 63.85; H, 4.02; N, 10.23.

3-[6-(4-Chlorophenyl)-1,2-dihydro-2-oxopyrimidin-4-yl]-4-hydroxy-1-methylquinolin-2(1*H*)-one (2-b)

The title compound (**2-b**) was prepared from 3-[(*E*)-3-(4-chlorophenyl)acryloyl]-4-hydroxy-1-methylquinolin-2(1*H*)-one (0.34 g, 1 mmol) and urea (0.06 g, 1 mmol) by the above-described methods and purified by column chromatography with ethyl acetate/n-hexane (2:1) as eluent. M.p. >300 ºC, IR (KBr, ν_{max} in cm^{-1}): 3724-3450, 1643, 1599.4, 1519.2, ^{1}H NMR (300 MHz, $CDCl_3$) δ: δ 8.04 (dd, *J* = 1.5, 7.8 Hz, 1H, H_5), 7.65-7.56 (br-m, 3H, H_6, H_7, H_8), 7.45-7.17 (m, 4H, *p*-chlorophenyl), 7.03 (m, 1H, methine proton), 3.32 (s, 3H, NC$\underline{H}_3$), ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 189.6, 174.9, 164.0, 141.3, 136.0, 133.7, 133.1, 132.5, 131.0, 129.4, 129.2, 126.3, 124.5, 119.7, 113.7, 109.4, 28.3, Mass spectrum (ESI) *m/z* 402 (M+23, 20%), 378 (M-1, 20%), 380 (M+1, 10%), 362 (M-OH, 100%). Anal. Calcd for $C_{20}H_{14}ClN_3O_3$: (379.07): C, 63.25; H, 3.72; N, 11.06. Found: C, 62.96; H, 3.64; N, 10.93.

3-[6-Phenyl-1,2-dihydro-2-oxopyrimidin-4-yl]-4-hydroxy-1-methylquinolin-2(1*H*)-one (2-c)

The title compound (**2-c**) was prepared from 4-hydroxy-3-[(*E*)-3-(4-methoxyphenyl)acryloyl]-1-methylquinolin-2(1*H*)-one (0.34 g, 1 mmol) and urea (0.06 g, 1 mmol) by the above-described methods and purified by silica gel column chromatography using ethyl acetate/n-hexane (3:2) as eluent, mp 272-274 ºC, IR (KBr, ν_{max} in cm^{-1}): 3700-3440, 1615, 1587, 1552, ^{1}H NMR (300 MHz, $CDCl_3$) δ: δ 8.05 (dd, *J* = 1.5, 7.5 Hz, 1H, H_5), 7.67-7.54 (br-m, 3H, H_6, H_7, H_8), 7.41-7.20 (m 5H, protons of phenyl ring), 7.01 (m, 1H, methine proton), 3.35 (s, 3H, NC$\underline{H}_3$), ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 190.1 (CO), 164.1, 141.3, 137.2, 134.2, 132.8, 131.1, 129.2, 128.9, 127.8, 126.3, 124.5, 119.8, 113.7, 109.5, 28.4, Mass spectrum (ESI) *m/z* 368, (M+23, 10%), 344 (M-1, 35%), 328 (M-OH, 100%). Anal. Calcd for $C_{20}H_{15}N_3O_3$: (345.11): C, 69.56; H, 4.38; N, 12.17; O, 13.9. Found: C, 69.85; H, 4.26; N, 12.27.

3-[6-(4-Chlorophenyl)-1,2-dihydro-2-thiopyrimidin-4-yl]-4-hydroxy-1-phenylquinolin-2(1*H*)-one (2-d)

The title compound (**2-d**) was prepared from 3-[(*E*)-3-(4-chlorophenyl)acryloyl]-4-hydroxy-1-phenylquinolin-2(1*H*)-one (0.40 g, 1 mmol) and thiourea (0.08 g, 1 mmol) by the above-described methods and purified by silica gel column chromatography with ethyl acetate/n-hexane (4:1) as eluent. M.p. >300 ºC, IR (KBr, ν_{max} in cm^{-1}): 3664-3350, 1640, 1597.4, 1534.8, ^{1}H NMR (300 MHz, $CDCl_3$) δ: δ 15.02 (s, 1H, OH), 8.92 (br-s, 1H, NH), 8.20 (d, *J* = 7.5 Hz, 1H, H_5), 8.03 (d, *J* = 8.1 Hz, 2H, H_6, H_7), 7.62-7.38 (br-m, 6H, H_8, 5H of N-Phenyl), 7.31-7.11 (m, 4H, *p*-chlorophenyl), 6.36 (s, 1H, methine proton), ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 186.4, 174.2, 148.3, 133.9, 130.2, 129.4, 128.2, 127.3, 126.9, 126.0, 125.1, 124.3, 122.2, 120.7, 119.1, 114.7, 114.3, Mass spectrum (ESI) *m/z* 456 (M-1, 100%), 458 (M+1, 33%). Anal. Calcd for $C_{25}H_{16}ClN_3O_2S$: (457.06): C, 65.57; H, 3.52; N, 9.18. Found: C, 65.25; H, 3.42; N, 8.95.

3-[6-(4-Methoxyphenyl)-1,2-dihydro-2-thiopyrimidin-4-yl]-4-hydroxy-1-phenylquinolin-2(1*H*)-one (2-e)

The title compound (**2-e**) was prepared from 4-hydroxy-3-[(*E*)-3-(4-methoxyphenyl)acryloyl]-1-phenylquinolin-2(1*H*)-one (0.40 g, 1 mmol) and thiourea (0.08 g, 1 mmol) by the above-described methods and purified by column chromatography with ethyl acetate/n-hexane (3:1) as eluent. M.p. >300 °C, IR (KBr, ν_{max} in cm^{-1}): 3640-3250, 1645, 1600, 1550, ^{1}H NMR (300 MHz, $CDCl_3$) δ: 15.02 (s, 1H, OH), 8.86 (br-s, 1H, NH), 8.41 (s, 1H, H_5), 8.20 (t, *J* = 6.9 Hz, 1H, H-7), 8.02 (d, *J* = 8.7 Hz, 1H, H_6), 7.96 (d, *J* = 8.7 Hz, 1H, H_8), 7.61-7.42 (br-m, 5H, protons of N-phenyl ring), 7.30-7.11 (m, 4H, protons of 4-methoxy phenyl), 6.3 (m, 1H, methine proton, 3.8 (s, 3H, -OC$\underline{H}_3$), ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 187.3, 174.2, 150.2, 135.3, 131.2,

129.3, 128.4, 127.6, 126.7, 125.4, 124.1, 123.2, 122.5, 120.2, 119.1, 54.2, Mass spectrum (ESI) *m/z* 452 (M-1, 70%), 436 (M-OH), 100%). Anal. Calcd for $C_{26}H_{19}N_3O_3S$: (453.11): C, 68.86; H, 4.22; N, 9.27. Found: C, 68.90; H, 4.20; N, 9.43.

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