An Expedient Approach for the Synthesis of Bioactive Pyrazole, Isoxazole and Benzodiazepine-Substituted Quinolin-2(1*H*)-one Derivatives

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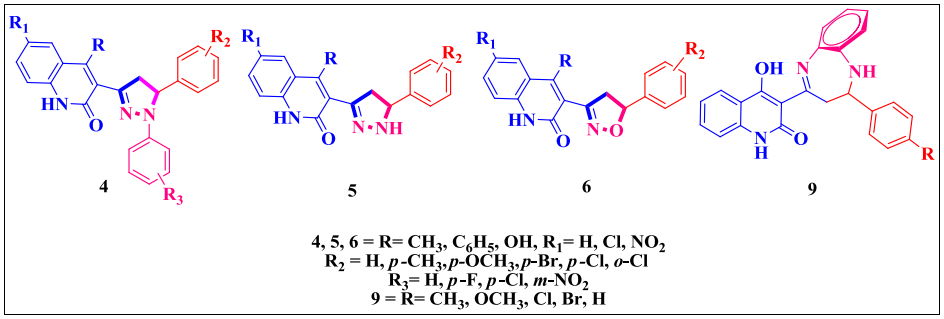
Additional supporting information may be found in the online version of this article at the publisher's web-site.
Received July 9, 2013
DOI 10.1002/jhet.2192
Published online 00 Month 2014 in Wiley Online Library (wileyonlinelibrary.com).



A sequence of functionalized pyrazole, isoxazole and benzodiazepine-substituted quinolone derivatives were synthesized in good yield starting from readily available starting precursors. These approaches lead to the synthesis of hitherto unknown compounds with a varied substitution pattern by both conventional and microwave-assisted method. A good number of analogues were evaluated for their *in vitro* cytotoxicity against human cervical and colon cancer cell lines by MTT protocol. Almost all the selected compounds showed remarkable cytotoxic activities. Among them, compound **4g** and **4i** emerged as the most promising scaffolds. These scaffolds will be used for further molecular level studies.

INTRODUCTION

The recent literatures are enriched with progressive findings about the synthesis and pharmacological action of substituted and fused heterocycles [1,2]. Among them, quinolines are one of the important nitrogen heterocycles that have shown extensive applications in pharmaceuticals [3,4] and found to have widespread occurrences in natural products [5]. Moreover, pyrazole-substituted moieties are found to be a core unit of numerous drug candidates [6,7], including Celebrex [8], Viagra [9], zaleplon [10], and allopurino [11–13]. In recent times, pyrazole-bearing quinoline systems have attracted great interest for their well-known biological activities including high-affinity interleukin [14], antioxidants [15,16], acetyl cholinesterase [17], anticancer [18,19], and DNA gyrase inhibitors [20]. In addition, the aforementioned activities of dihydroquinolone derivatives have also been reported to have central nervous system disorders [21,22], antimicrobial agents [23], and so on. Moreover, quinolone-substituted pyrazoline and isoxazoline analogues are found to have a good molluscicidal activities [24] with $LC_{50} = 0.7876$ and $LC_{50} = 0.7765$, and NMDA receptor antagonist [25] for the treatment of neurological condition makes this class of molecule distinctive among medicinal chemists and made them attractive targets for synthesis. In our previous study, 3-acetyl-4-hydroxyquinolin-2-one has been used as a lead precursor to synthesize fused pyrimidine and pyrazoloquinolone derivatives as antioxidants [16]. In continuation of our earlier work on the synthesis and antioxidant activities of quinolone-based heterocycles, we herein report the synthesis of 3-acetyl-4-methyl/phenyl-substituted quinolin-2-one systems as a lead for the synthesis of a library of pyrazole-substituted and isoxazole-substituted quinolones by microwave-assisted approach, and evaluation of their cytotoxicity for three human cancer cells have been investigated and presented.

RESULTS AND DISCUSSION

The starting precursor 3-acetylquinolin-2-one **1a–d** was achieved by the route as depicted by the literature method [26,27]. In fact, various aromatic aldehydes **2a–f** reacted smoothly with the solution of 3-acetylquinolin-2(1*H*)-one **1a–d** in the presence of sodium hydroxide at room temperature for 7–10 h to afford the corresponding quinolone-based α,β-unsaturated systems (**3a–l**) in excellent yield (Scheme 1; Table 1). The synthetic pathway used to achieve the target compounds that have been delineated in Schemes 2 and 3 resulted in poor to moderate yield of the desired cyclized products (**4a–p**, **5a–d**, **6a–e**), probably

Scheme 1. Synthesis of quinolone-based α,β-unsaturated carbonyl systems **3a–l**. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

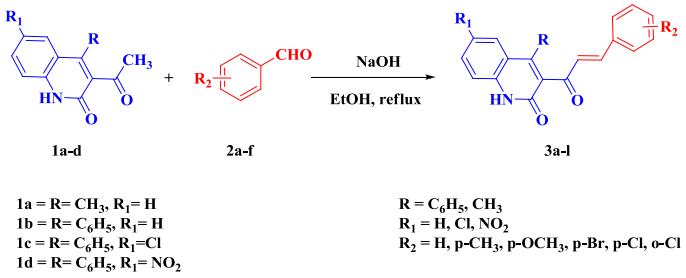


Table 1

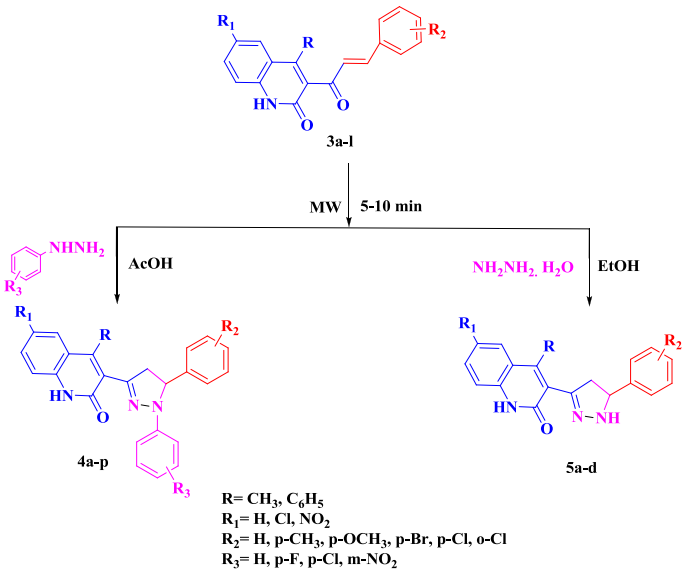
Synthesis of quinolone-based α,β-unsaturated carbonyl compounds **3a–l**.

Product	R	R_1	R_2	Yield in 10–12 h (%)[a]
3a	CH_3	H	*p*-Br	79
3b	CH_3	H	*p*-OCH_3	90
3c	C_6H_5	Cl	*o*-Cl	84
3d	CH_3	H	*p*-Cl	86
3e	C_6H_5	Cl	*p*-Cl	78
3f	C_6H_5	Cl	H	86
3g	C_6H_5	NO_2	*p*-Cl	77
3h	C_6H_5	Cl	*p*-OCH_3	84
3i	C_6H_5	H	*o*-Cl	75
3j	C_6H_5	H	*p*-CH_3	78
3k	C_6H_5	H	H	82
3l	C_6H_5	H	*p*-OCH_3	86

[a]Isolated yield from the conventional method.

because of the low neucleophilicity or poor solubility. In light of these findings, it was decided to perform the reaction, a trial under microwave irradiation. The effort not only improved the yield dramatically but also reduced the reaction time to 5–10 min compared with the conventional heating protocol to afford the desired compound (Table 2). So, the obtained quinolin-2(1*H*)-one-based α,β-unsaturated systems **3** were prepared from 4-substituted 3-acetyl-quinolin-2(1*H*)-one with various aromatic aldehydes and were then treated with phenyl hydrazine/hydrazine hydrate and hydroxylamine hydrochloride in the presence of catalytic amount of acetic acid or ethanol in a microwave-assisted, one-pot protocol to give the titled compound in good yield. The microwave reaction was carried out in Biotage initiator, and the absorption level was kept high with a prestirring of 20–30 s. Initially, the power was kept zero, followed by a gradual increase, and then the reaction proceeded at a constant power of 360 W with temperature of 120°C. Almost all the compounds were isolated with excellent yield by this method, and most of them were pure enough for further analysis without going for column chromatography. Therefore, the microwave-assisted method was chosen to be an ideal technique for preparing libraries in terms of greener approach compared

Scheme 2. Synthesis of pyrazole-substituted quinolone analogues **4a–p** and **5a–d**. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]



Scheme 3. Synthesis of isoxazole-substituted quinolone analogues **6a–e**. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

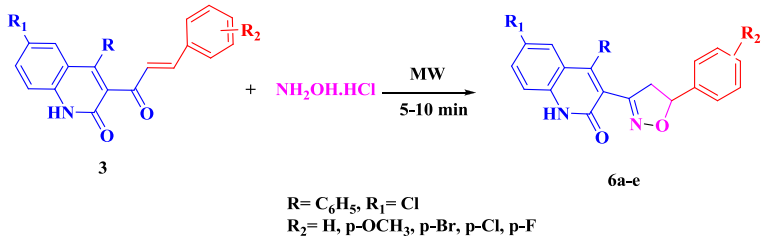


Table 2

Conventional and microwave-assisted approach toward the synthesis of analogues **4a–p**, **5a–d**, and **6a–e**.

Product	R	R_1	R_2	R_3	Method A[a] yield 8–10 h (%)	Method B[b] yield 7–10 min (%)
4a	CH_3	H	4-OCH_3	H	55	75
4b	CH_3	H	4-Br	4-F	46	78
4c	CH_3	H	4-Br	4-Cl	48	72
4d	CH_3	H	2-Cl	H	52	84
4e	C_6H_5	H	4-CH_3	H	50	79
4f	C_6H_5	Cl	4-Cl	3-NO_2	55	82
4g	C_6H_5	Cl	H	4-F	44	80
4h	C_6H_5	Cl	2-Cl	H	56	74
4i	C_6H_5	H	4-OCH_3	H	52	76
4j	C_6H_5	H	4-CH_3	3-NO_2	40	68
4k	C_6H_5	H	H	H	58	80
4l	C_6H_5	Cl	H	H	42	75
4m	CH_3	H	H	H	57	78
4n	C_6H_5	Cl	4-OCH_3	H	45	86
4o	CH_3	H	4-Br	3-NO_2	52	85
4p	C_6H_5	NO_2	4-Cl	H	55	78
5a	CH_3	H	4-Br	—	45	75
5b	C_6H_5	Cl	4-OCH_3	—	54	74
5c	C_6H_5	H	4-Br	—	48	71
5d	C_6H_5	H	4-CH_3	—	55	74
6a	C_6H_5	Cl	4-Br	—	67	70
6b	C_6H_5	Cl	H	—	58	75
6c	C_6H_5	Cl	4-OCH_3	—	62	83
6d	C_6H_5	H	4-Cl	—	66	78
6e	C_6H_5	H	4-F	—	60	75

[a]Isolated yield from the conventional method.
[b]Isolated yield from the microwave-assisted approach.

with the conventional way of synthesis. To the best of our knowledge, the synthesis of 4-phenyl/4-methyl pyrazole-substituted and isoxazole-substituted quinolin-2(1*H*)-one derivative has been described scarcely in the literature.

A library of 25 compounds has been synthesized as summarized in Table 2 including 12 intermediates, and as is evident, the presence of electron-withdrawing/electron-donating substitutions did not seem to have any significant limitation on the overall reactivity, giving the desired product in quantitative yields. Both analytical and spectral data (^{1}H, ^{13}C NMR, and mass spectra) of all the synthesized compounds were in full agreement with the proposed structures. For instance, the ^{1}H NMR spectrum of **3b** in deuterated dimethyl sulfoxide (Scheme 1) furnished doublet of doublet at δ 6.94–6.97 attributed to the olefinic (CH=CH) group with coupling constant 16.5 and 9.0 Hz. The coupling constant $J = 16.5$ Hz indicated the *E* configuration of α,β-unsaturated compounds. In the ^{13}C NMR, the signal at δ 195.8 was due to the carbonyl carbon adjacent to olefinic bond, and the signal near 161.9 was due to the amide-C=O function. The signals around δ 15.99 and 55.84 were attributed to the methyl and methoxy functions, respectively. In the IR spectra, the stretching frequency of olefin and amide carbonyl functions appeared at 1597 and 1658 cm^{-1}, respectively. Elemental analyses and spectral data of **3a–l** are consistent with the proposed structures. The ^{1}H NMR spectrum of **4a** (Scheme 2) showed multiple of signals around δ 3.9 and 3.1 assignable

to methylene protons, and the signal at δ 5.35 was due to the —CH proton of the pyrazole moiety. The singlet peak that appeared at δ 3.7 and 2.6 were due to the "OCH_3" and "CH_3" function groups, respectively. The signals that appeared around δ 6.7–7.8 were attributed to the aromatic protons of **4a**. Another singlet peak around δ 11.84 was due to the "NH" function of **4a**. The same was factual for all other compounds of the series. In the ^{13}C NMR, the signal that appeared at δ 62.5 was due to the methylene proton of the pyrazole motif, and the disappearance of the peak due to the unsaturated —C═O function in **4a** confirmed the formation of the pyrazole motif. In the IR spectra, the carbonyl stretching frequency was absent because of the cyclization as confirmed in the formation of **4a**. The mass spectrum shows the M^+ ion peak at 410.2 and was in consistent with the proposed structure. Similarly, compounds **5a–d** (Scheme 2) and **6a–e** (Scheme 3) were well characterized by the straightforward method, which is highlighted in Supporting Information.

Synthesis and characterization of benzodiazepine-based quinoline systems. The intermediate (**7**) and its starting precursor were synthesized as per the literature method [28]. In this juncture, Scheme 4 disclosed the synthesis of benzodiazepine-substituted quinolines **9a–e** in good yield, accomplished from various derivatives of 3-cinnamoyl-4-hydroxyquinolin-2(1*H*)-ones (**7**). For example, the ^1H NMR Spectrum of **9a** furnished a singlet at δ 3.70 assignable to the "OCH_3" function. The signals at δ 6.2, 5.1, and 4.40 were attributed to the benzodiazepine ring unit, confirming the formation of **9a**. The signals that appeared around δ 6.8–7.9 was due to the aromatic protons, and the broad singlet around δ 10.6 and the sharp singlet at δ 16.2 were attributed to the "NH" and "OH" functions, respectively. The compound **9a** was further confirmed by their ^{13}C NMR, IR, and elemental analysis. Compound **9e** was unambiguously determined by single crystal X-ray analysis (Fig. 1). Fascinatingly, the same reaction could not be performed for the intermediates (**3a–I**), which might be because of the steric hindrance of the phenyl group present at the fourth position of the quinoline-2-one systems.

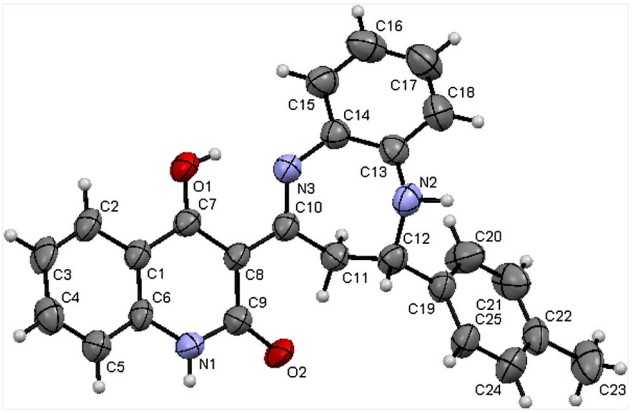
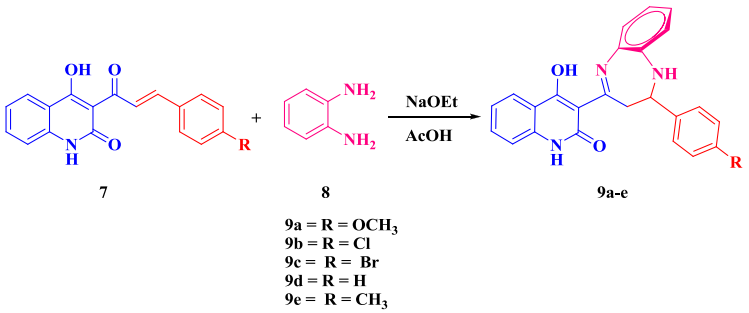


Figure 1. Ortep view of compound **9e**. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

BIOLOGICAL EVALUATION

The novel compounds were evaluated for their cytotoxicity against human cancer cell lines through a preliminary MTT assay [29]. The response parameter (IC_{50}) was calculated, which corresponds to the compound concentration causing 50% mortality in net cells. Among the selected compounds, **4g** and **4i** were found to be promising against three human cancer cell lines, which could be comparable with the reference drug adriamycin. Furthermore, compound **4i** was considered to be more potent against human cervical (HeLa) and colon (HCT-116, HCT-8) cancer cell lines with the IC_{50} values of 2.4, 2.2, and 5.6 μM (Table 3), followed by compound **4g** that showed a considerable cytotoxicity against cervical (HeLa) and colon (HCT-116, HCT-8) cancer cell lines with the IC_{50} values of 4.14, 8.6, and 7.6 μM, respectively. An interesting change in IC_{50} values was observed when substituting a hydrogen atom by a fluorine atom and methoxy function on the compounds belonging to the series **4** suggesting to be a methoxy group, and the fluoro function was favored in controlling the growth of cells. Compared with **4i** and **4g**, it was observed that compounds **4a**, **4b**, **4c**, **4d**, **5a**, **5b**, **6a**, and **6b** showed moderate cytotoxicity against the proliferation of cells. On the other hand, analogues **4f** and **4j** displayed less cytotoxicity against both the cell lines. As a result, from the structural point of

Scheme 4. Synthesis of benzodiazepine-substituted quinolone analogues **9a–e**. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]



7 **8** **9a-e**

9a = R = OCH_3
9b = R = Cl
9c = R = Br
9d = R = H
9e = R = CH_3

Table 3

Cytotoxicity expressed by IC_{50} in μM of compounds for cancer cell lines.

		MTT IC_{50} (μM)		
Entry	Product	HeLa[a]	HCT 116[b]	HCT-8[c]
1	**4a**	33.26 ± 0.20	29.2 ± 0.28	NT
2	**4b**	22.55 ± 0.40	18.55 ± 0.20	33.25 ± 0.33
3	**4c**	15.50 ± 0.52	23.33 ± 0.34	20.20 ± 0.24
4	**4d**	NT	NT	22.20 ± 0.28
5	**4f**	> 100	98.5 ± 0.76	NT
6	**4g**	4.14 ± 0.10	8.6 ± 0.16	7.6 ± 0.18
7	**4i**	2.4 ± 0.14	2.2 ± 0.12	5.6 ± 0.16
8	**4j**	87.73 ± 0.85	88.54 ± 0.58	NT
9	**5a**	46.45 ± 0.66	48.23 ± 0.24	NT
10	**5b**	40.11 ± 0.45	40.45 ± 0.30	NT
11	**6a**	15.22 ± 0.22	22.21 ± 0.32	18.12 ± 0.44
12	**6c**	12.20 ± 0.34	15.05 ± 0.22	NT
Adriamycin		6.3 ± 0.22	8.7 ± 0.20	7.2 ± 0.32

NT, not tested.
[a]Data are presented as IC_{50} values for cervical (HeLa) cancer cells.
[b]Colon HCT-116 cancer cells.
[c]Colon HCT-8 cancer cells.

view, the marked activity seems to be due to the electron-withdrawing capability of the group attached to the pyrazole and quinoline ring fragments, as it could make the molecules more acidic [30,31], whereas quinolinone-bearing isoxazole ring fragments **6a** showed that the IC_{50} values are 15.22, 22.21, and 18.12 μM and **6c** showed that the IC_{50} values are 12.20 and 15.05 μM, which showed reasonable antiproliferative activity against the aforementioned cell lines. Our studies obviously suggest that pyrazole-substituted quinolin-2(1*H*)-one derivative with an electron-withdrawing substituent on aryl ring could be an attractive template for the identification of novel cytotoxic agents.

CONCLUSION

In conclusion, we have synthesized a new series of pyrazole-substituted, isoxazole-substituted, and benzodiazepine-substituted quinolin-2-(1*H*)-one analogues. The yield of the products was enhanced by the microwave-assisted approach rather than the conventional way of synthesis. The selected compounds were evaluated for cytotoxicity against cervical (HeLa) and colon cancer (HCT-116, HCT-8) cell lines. Most of them were found to be a promise against the aforementioned cell lines, and these classes of compounds have scope for further development toward becoming potential candidates as cytotoxic agents. Overall, the substituted heterocyclic framework provides a useful basis for the development of a new class of bioactive compounds.

EXPERIMENTAL

The melting points were taken using open capillary tubes and were uncorrected. ^1H and ^{13}C NMR spectra were recorded in Indian Institute of Science (IISC), Bangalore and Indian Institute of Technology, Chennai. Bruker (Advance) 400-MHz instrument in DMSO-d_6 using TMS as internal standard. Chemical shifts are given in parts per million (δ-scale), and the coupling constants are given in Hertz. IR spectra were recorded on a JASCO FT IR instrument (KBr) pellet in case of solids and $CHCl_3$ in case of viscous liquids. Elemental analyses were performed on a Perkin Elmer 2400 Series II Elemental CHNS analyzer. Single crystal X-ray structure was performed in a Bruker APEX-II CCD diffractometer (crystal type: Monoclinic). Molecular mass of the structures were performed in Agilent mass spectrometric system. Organic reactions were performed in Biotage Initiator EXP EU microwave synthesizer. The human cervical cancer cell line (HeLa) was obtained from the National Centre for Cell Science (NCCS), Pune, and grown in Eagles Minimum Essential Medium containing 10% fetal bovine serum (FBS). All cells were maintained at 37°C, 5% CO_2, 95% air, and 100% relative humidity. Maintenance of cultures was passaged weekly, and the culture medium was changed twice a week.

General procedure for the synthesis of quinoline-2(1*H*)-one based α,β-unsaturated systems (3a–l). Equimolar amount of 4-phenyl/methyl-3-acetylquinolin-2(1*H*)-one **1(a–d)** (0.01 mmol) and appropriate aromatic aldehydes **2(a–f)** (0.01 mmol) were dissolved in ethanol, and 0.1 mmol aq. NaOH was added dropwise over a period of half an hour at 0°C. After the addition, stirring was continued overnight. Then, the reaction mixture was poured into 500 g of crushed ice after confirmation by the TLC. The precipitate thus formed was neutralized with dil. HCl and filtered off, dried, and chromatographed on a silica gel column chromatography (8:2) *n*-hexane:EtOAc to obtain a pale yellow powder, and the products were characterized by ^1H, ^{13}C, and IR spectra.

General procedure for the synthesis of dihydro-1*H*-pyrazol-3-yl)-4-quinolin-2(1*H*)-one or (4a–p)

Conventional method A. Quinoline-2(1*H*)-one-based α,β-unsaturated carbonyl compound **3** (0.01 mmol) and substituted phenyl hydrazine hydrochloride (0.03 mmol) were mixed in acetic acid and were refluxed over a period of 8–9 h. After the reaction was over as evidenced by the TLC, the reaction

mixture was cooled to room temperature. Then, it was poured into 500 g of crushed ice after evaporation of the one-third of the solvent. The precipitate thus formed was filtered off, washed with excess of water, and dried; subsequently, the mixture was chromatographed on a silica gel column chromatography on *n*-hexane:EtOAc (7:3) to obtain a reddish yellow powder.

Microwave-assisted synthesis B. Quinoline-2(1*H*)-one-based α,β-unsaturated carbonyl compound **3** (0.01 mmol) and phenyl hydrazine hydrochloride (0.03 mmol) were powdered, mixed with 2–5 drops of AcOH, and introduced in an open borosil glass vessel. The reaction proceeded at a constant power of 360 W with temperature of 120°C for 5 min with constant interval. After completion (TLC), the reaction mixture was brought to room temperature and poured into 300 g of crushed ice. The crude product was recrystallized to obtain the title compound, which was found to be in good purity (TLC) and yield.

3-(5-(4-Methoxyphenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-methylquinolin-2(1H)-one (4a). Pale yellow solid (75%); mp 222–225°C; IR (KBr) υ_{max} 2847.38, 1740.44, 1645.95, 1501.31, 1389.46, 998.94, 748.24 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 11.84 (s, 1H, 1-NH), 7.85 (d, 1H, J = 8.04 Hz, ArH), 7.53 (t, 1H, J = 7.84 Hz, Ar—H), 7.23–7.36 (m, 4H, Ar—H), 7.13 (t, 2H, J = 7.8 Hz, Ar—H), 6.91–6.95 (m, 4H, Ar—H), 6.71 (t, 1H, J = 7.28, Hz, ArH), 5.35 (dd, 1H, J_1 = 6.86 Hz, J_2 = 12.12 Hz, Pyr-H), 3.91 (dd, 1H, J_1 = 17.8 Hz, J_2 = 12.2 Hz, Pyr-H), 3.72 (s, 3H, —OCH_3), 3.11 (dd, 1H, J_1 = 17.68 Hz, J_2 = 6.86 Hz, Pyr-H), 2.62 (s, 3H, —CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.6, 158.4, 146.7, 144.7, 137.8, 134.6, 130.6, 128.8, 127.2, 125.6, 123.9, 112, 119.6, 118.5, 115.3, 114.2, 112.9, 62.5, 55.0, 46.4, 16.3; MS *m/z* 409.5 (M^+). *Anal*. Calcd for $C_{26}H_{23}N_3O_2$ (409) C, 76.26; H, 5.66; N, 10.26; Found: C, 76.28; H, 5.59; N, 10.21%.

3-(5-(4-Bromophenyl)-1-(4-fluorophenyl)-4,5-dihydro-1H-pyrazol-3-yl)-4-methylquinolin-2 (1H)-one (4b). Orange solid (78%); mp 215–218°C; IR (KBr) υ_{max} 2857.24, 1656.55, 1508.06, 1218.79, 821.53, 752.10, 640.25 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 11.85 (s, 1H, 1-NH), 7.83 (d, 1H, J = 8 Hz, ArH), 7.69 (d, 1H, J = 6.3 Hz, Ar—H), 7.54 (t, 3H, J = 8 Hz, Ar—H), 7.34 (d, 3H, J = 8 Hz, Ar—H), 7.23 (t, 1H, J = 6.8 Hz, Ar—H), 7.00 (t, 1H, J = 8.56 Hz, Ar—H), 6.92 (t, 2H, J = 7.44 Hz, Ar—H) 5.38 (dd, 1H, J_1 = 12.00 Hz, J_2 = 8.56 Hz, Pyr-H), 3.94 (dd, 1H, J_1 = 15.72 Hz, J_2 = 12.00 Hz, Pyr-H), 3.16 (dd, 1H, J_1 = 17.76 Hz, J_2 = 8.56 Hz, Pyr-H), 2.60 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.2, 157.4, 155.4, 147.6, 46.8, 142.4, 141.8, 138.3, 132.3, 131.7, 131.0, 128.9, 126.1, 124.1, 122.5, 122.5, 120.9, 120; *Anal*. Calcd for $C_{25}H_{19}BrFN_3O$ (475) C, 63.04; H, 4.02; N, 8.82; Found: C, 63.10; H, 4.06; N, 8.85%.

3-(5-(4-Bromophenyl)-1-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl)-4-methylquinolin-2(1H)-one (4c). Orange solid (72%) mp 217–220°C; IR (KBr) υ_{max} 2850.27, 1658.48, 1596.77, 1496.49, 1007.62, 819.59, 753.06 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 11.89 (s, 1H, 1-NH), 7.85 (d, 1H, J = 8.4 Hz, Ar—H), 7.53–7.57 (m, 3H, Ar—H), 7.30–7.35 (m, 3H, Ar—H), 7.25 (t, 1H, J = 7.6 Hz, Ar—H), 7.20 (d, 2H, J = 8.8 Hz, Ar—H), 6.91 (d, 2H, J = 9.2, Hz, Ar—H), 5.46 (dd, 1H, J_1 = 12.00 Hz, J_2 = 6.4 Hz, Pyr-H), 3.95 (dd, 1H, J_1 = 22.40 Hz, J_2 = 11.00 Hz, pyr-H), 3.15 (dd, 1H, J_1 = 17.60 Hz, J_2 = 6.40 Hz, Pyr-H), 2.60 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.1, 148.4, 146.8, 142.1, 138.3, 132.3, 131.7, 131.2, 128.8, 126.2, 124, 122.6, 121, 120, 115.8, 114.8, 62.7, 46.8, 16.9; *Anal*. Calcd for $C_{25}H_{19}BrClN_3O$ (491) C, 60.93; H, 3.89; N, 8.53; Found: C, 60.98; H, 3.86; N, 8.49%.

3-(5-(2-Chlorophenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-methylquinolin-2-(1H)-one (4d). Pale yellow solid (77%); mp 222–225°C; IR(KBr) υ_{max} 3412.42, 2851.24, 1645.95, 1597.73, 1501.31, 1431.89, 1389.46, 1124.3, 873.59, 750.17 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 11.87 (s, 1H, 1-NH), 7.85 (d, 1H, J = 8.08 Hz, Ar—H), 7.52–7.57 (m, 3H, Ar—H), 7.41 (s, 1H, Ar—H), 7.32–7.34 (m, 3H, Ar—H), 7.25 (t, 2H, J = 8 Hz, Ar—H), 6.86 (d, 2H, J = 7.96 Hz, Ar—H), 6.75 (t, 1H, J = 7.2 Hz, Ar—H), 5.62 (dd, 1H, J_1 = 12.28 Hz, J_2 = 6.72 Hz, Pyr-H), 4.07 (dd, 1H, J_1 = 17.60 Hz, J_2 = 12.36 Hz, Pyr-H), 3.11 (dd, 1H, J_1 = 17.76 Hz, J_2 = 6.88 Hz, Pyr-H), 2.62 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 133, 132.4, 131.4, 130.5, 128.7, 127.9, 127.4, 125.5, 124.6, 123.7, 123.2, 122, 120.2, 119.6, 119.3, 118.8, 115.4, 112.7, 107.2, 62.3, 59.7, 46.2, 20.7, 16.3, 14; MS *m/z* 413 (M^+): *Anal*. Calcd for $C_{25}H_{20}ClN_3O$ (413) C, 72.55; H, 4.87; N, 10.15; Found: C, 72.59; H, 4.84; N, 10.12%.

4-Phenyl-3-(1-phenyl-5-p-tolyl-4,5-dihydro-1H-pyrazol-3-yl) quinolin-2(1H)-one (4e). White solid (79%) mp 216–218°C; IR(KBr) υ_{max} 3437.49, 2835.8, 1656.55, 1598.7, 1503.24, 1243.86, 1031.73, 829.24 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) 11.89 (s, 1H, 1-NH), 8.26 (s, 1H, Ar—H), 8.14 (d, 1H, J = 7.8 Hz), 7.82–7.88 (m, 3H, Ar—H), 7.67–7.71 (q, 4H, Ar—H), 7.17 (t, 2H, J = 7.4 Hz, Ar—H), 6.96 (d, 2H, J = 7.88 Hz, Ar—H), 6.75 (t, 1H, J = 7.24 Hz), 5.65 (dd, 1H, J_1 = 15.50 Hz, J_2 = 5.80 Hz, Pyr-H), 4.00 (dd, 1H, J_1 = 17.8 Hz, J_2 = 12.32 Hz, Pyr-H), 3.20 (dd, 1H, J_1 = 17.60 Hz, J_2 = 6.48 Hz, Pyr-H), 2.63 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 137.8, 132.8, 131.03, 130.6, 129, 125.7, 123.5, 122.4, 122, 120.9, 119.1, 115.5, 112.9, 62, 46.1, 40.6, 16.3; *Anal*. Calcd for $C_{31}H_{25}N_3O$ (455) C, 81.73; H, 5.53; N, 9.22; Found: C, 81.78; H, 5; N, 9.15%.

6-Chloro-3-(5-(4-chlorophenyl)-1-(3-nitrophenyl)-4,5-dihydro-1H-pyrazol-3-yl)-4-phenyl quinolin-2(1H)-one (4f). White solid (82%) mp 218–220°C; IR (KBr) υ_{max} 3302.5, 3146.29, 2852.2, 1644.98, 1388.5, 1209.15, 1090.55, 818.63 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.35 (s, 1H, 1-NH), 7.62 (d, 1H, J = 8.76 Hz, ArH), 7.54 (d, 2H, J = 7.44 Hz, Ar—H), 7.43–7.50 (m, 5H, Ar—H), 7.37 (s, 1H, Ar—H), 7.24–7.30 (m, 4H, Ar—H), 6.91 (d, 2H, J = 9.44 Hz, Ar—H), 6.86 (d, 1H, J = 7.6 Hz, ArH), 5.49 (dd, 1H, J_1 = 12.2 Hz, J_2 = 4.76 Hz, Pyr-H), 3.96 (dd, 1H, J_1 = 7.96 Hz, J_2 = 12.6 Hz, Pyr-H), 2.94 (dd, 1H, J_1 = 18.08 Hz, J_2 = 4.92 Hz, Pyr-H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.8, 149.9, 148.9, 147.8, 144.6, 140.6, 137.5, 135.8, 132.6, 131.4, 130.3, 130.21, 129.3, 128.9, 128.2, 126.5, 126.4, 125.2, 121.4, 118.7, 117.9, 113.1, 107.2, 61.8, 46.8; *Anal*. Calcd for $C_{30}H_{20}Cl_2N_4O_3$ (554) C, 64.87; H, 3.63; N, 10.09; Found: C, 64.80; H, 3.65; N, 10.12%.

6-Chloro-3-(1-(4-fluorophenyl)-5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-phenylquinolin-2 (1H)-one (4g). Pale yellow solid (80%) mp 225–227°C; IR (KBr) υ_{max} 3155.11, 3022.87, 2854.13, 1659.45, 1509.03, 1209.15 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6). δ 11.55 (s, 1H, 1-NH), 7.62 (m, 2H, Ar—H), 7.45 (t, 1H, J = 9.6 Hz, Ar—H), 7.36 (d, 2H, J = 7.68 Hz, Ar—H), 6.93–7.32 (m, 8H, Ar—H), 6.83 (t, 2H, J = 9.5 Hz, Ar—H), 6.53 (d, 2H, J = 7.56 Hz, Ar—H), 5.17 (dd, 1H, J_1 = 19.76 Hz, J_2 = 9.60 Hz, Pyr-H), 3.89 (dd, 1H, J_1 = 18.64 Hz, J_2 = 15.36 Hz, Pyr-H), 2.88 (dd, J_1 = 18.80 Hz, J_2 = 6.76 Hz Pyr-H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.9, 159.9, 157.48, 154.9, 149.1, 147.4, 146.4, 145.1, 142.8, 141.2, 138.2, 136.1, 134.1, 133.1, 131.3, 130.9, 129.2, 128.8, 128.6, 127.8, 127.6, 126.5, 125.8, 121.5, 121, 118.1, 117.8, 115.3, 114.4, 63.5, 47; *Anal*. Calcd for $C_{30}H_{21}ClFN_3O$ (493) C, 72.95; H, 4.29; N, 8.51. Found: C, 72.92; H, 4.35; N, 8.52%.

6-Chloro-3-(5-(2-chlorophenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-phenylquinolin-2(1H)-one (4h). Pale yellow solid (74%) mp 214–216°C; IR (KBr) υ_{max} 3437.49, 3151.11, 3022.87, 2853.17, 1651.73, 1597.73, 1501.31, 1394.28, 1213.97 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.29 (s, 1H, 1-NH), 7.59 (d, 1H, J = 6.32 Hz, ArH), 7.33–7.55 (m, 6H, Ar—H), 7.26 (t, 1H, J = 7.56 Hz, Ar—H), 7.12–7.20 (m, 3H, Ar—H), 7.04 (q, 2H, Ar—H), 6.90 (d, 1H, J = 2.36 Hz, Ar—H), 6.65 (t, 1H, J = 7.36 Hz, Ar—H), 6.47 (d, 2H, J = 7.72 Hz, Ar—H), 5.65 (dd, 1H, J_1 = 16.28 Hz, J_2 = 5.12 Hz, Pyr-H), 3.98 (dd, 1H, J_1 = 14.00 Hz, J_2 = 5.24 Hz, Pyr-H), 2.81 (dd, 1H, J_1 = 15.5 Hz, J_2 = 12.24 Hz, Ar—H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.4, 148.8, 144.7, 138.5, 136.9, 135.5, 130.6, 129.6, 129, 128.7, 128.3, 127.6, 127, 125.9, 125.1, 121.1, 117.4, 112.3, 79.1, 59.5, 44.8; MS *m/z* 510.2 (M^+). *Anal*. Calcd for $C_{30}H_{21}Cl_2N_3O$ (509) C, 70.59; H, 4.15; N, 8.23; Found: C, 70.54; H, 4.19; N, 8.28%.

3-(5-(4-Methoxyphenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-phenylquinolin-2(1H)-one (4i). Orange solid (76%); mp 225–228°C; IR (KBr) υ_{max} 3437.49, 2835.8, 1656.55, 1598.7, 1503.24, 1243.86, 1031.73, 829.24, 752.10, 611.32 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 11.85 (s, 1H, 1-NH), 7.44–7.52 (m, 5H, Ar—H), 7.34 (d, 1H, J = 8.5 Hz, ArH), 7.22–7.25 (m, 2H, Ar—H), 7.07–7.14 (m, 3H, Ar—H), 6.96 (t, 2H, J = 6.5 Hz, Ar—H), 6.80 (t, 1H, J = 10 Hz, Ar—H), 6.73 (d, 2H, J = 6 Hz, Ar—H), 6.70 (d, 1H, J = 7 Hz, Ar—H), 5.13 (dd, 1H, J_1 = 12.50 Hz, J_2 = 6.50 Hz, Pyr-H), 3.96 (dd, 1H, J_1 = 17.50 Hz, J_2 = 12.50 Hz, Pyr-H), 3.79 (s, 3H, OCH_3), 2.97 (dd, 1H, J_1 = 17.5 Hz, J_2 = 12.00 Hz, Pyr-H); ^{13}C NMR (100 MHz, DMSO-d_6) 160.1, 158.7, 149.2, 144.5, 137.8, 133.5, 132.1, 131.4, 120.1, 124.5, 124.5, 122.3, 121, 119.6, 118.1, 114.1, 111.6, 61.1, 45.1, 44.6, 15.1; *Anal*. Calcd for $C_{31}H_{25}N_3O_2$ (471) C, 78.96; H, 5.10; N, 8.24 Found: C, 78.91; H, 5.15; N, 8.28%.

3-(1-(3-Nitrophenyl)-5-p-tolyl-4,5-dihydro-1H-pyrazol-3-yl)-4-phenylquinolin-2(1H)-one (4j). Orange solid (68%); mp 211–212°C; IR (KBr) $\upsilon_{max:}$ 3846.33, 3079.76, 2888.84, 1651.73, 1523.49, 114.65, 1006.66, 808.03, 702.92 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.18 (s, 1H, 1-NH), 7.40–7.53 (m, 8H, Ar—H), 7.24 (d, 2H J = 8.8 Hz, Ar—H), 7.09 (t, 1H, J = 8.76 Hz, Ar—H), 7.04 (d, 3H, J = 7.36 Hz, Ar—H), 6.87 (d, 1H, J = 7.96 Hz, Ar—H), 6.81 (d, 2H, J = 5.6 Hz, Ar—H), 5.32 (dd, 1H, J_1 = 12.36 Hz, J_2 = 4.80 Hz, Pyr-H), 3.97 (dd, 1H, J_1 = 19.16 Hz, J_2 = 12.00 Hz, Pyr-H), 2.91 (dd, 1H, J_1 = 17.16 Hz, J_2 = 4.8 Hz, Pyr-H), 2.21 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161, 148.8, 145.1, 137.1, 136.5, 130.2, 129.9, 128.9, 128.3, 127.8, 126.3, 124.1, 122.5, 118.7, 115.8, 112.6, 107.1, 62.4, 47.1, 21.1; *Anal*. Calcd for $C_{31}H_{24}N_4O_3$ (500) C, 74.38; H, 4.83; N, 11.19; Found: C, 74.41; H, 4.85; N, 11.23%.

3-(1,5-Diphenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-phenylquinolin-2(1H)-one (4k). Pale yellow solid (80%); mp 220–222°C; IR (KBr) υ_{max} 3154.97, 2935.13, 2846.42, 1660.41, 1597.73, 1500.35, 1389.46, 1306.54, 1214.93, 1123.3 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.09 (s, 1H, 1-NH), 7.43–7.50 (m, 5H, Ar—H), 7.39 (d, 1H, J = 7.6 Hz, Ar—H), 7.15–7.24 (m, 4H, Ar—H), 7.10 (t, 1H, J = 8 Hz, Ar—H), 6.99–7.02 (m, 3H, Ar—H), 6.91 (d, 2H, J = 6.8 Hz, Ar—H), 6.58 (t, 3H, J = 7.6 Hz, Ar—H), 5.20 (dd, 1H, J_1 = 12.80 Hz, J_2 = 6.00 Hz, Pyr-H), 3.88 (dd, J_1 = 17.8 Hz, J_2 = 12.40 Hz, Pyr-H), 2.81 (dd, 1H, J_1 = 6 Hz, J_2 = 17.6 Hz, Pyr-H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.7, 150.1, 144.9, 144.1, 142.6, 138.2, 136.1, 130.7, 129.7, 128.7, 128.5, 128.1, 127.9, 127.2, 125.8, 124.2, 122.1, 119.7, 118.2, 115.3, 112.6, 62.3, 46.4; *Anal*. Calcd for $C_{30}H_{23}N_3O$ (441) C, 81.61; H, 5.25; N, 9.52; Found: C, 81.56; H, 5.29; N, 9.50%.

6-Chloro-3-(1,5-diphenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-phenylquinolin-2(1H)-one (4l). White solid (75%) mp 218–222°C; IR (KBr) υ_{max} 3153.04, 2917.77, 1650.77, 1597.73, 1500.35, 1393.32, 828.27, 748.24 cm^{-1};^1H NMR (400 MHz, DMSO-d_6) δ 12.24 (s, 1H, 1-NH), 7.42–7.62 (m, 6H, Ar—H), 7.39 (t, 2H, J = 7.6 Hz, ArH), 7.17–7.24 (m, 4H, Ar—H), 6.99 (t, 2H, J = 7.6 Hz, ArH), 6.89–6.90 (m, 3H, Ar—H), 6.60 (d, 1H, J = 7.2 Hz, ArH), 6.55 (d, 2H, J = 8Hz, ArH), 5.26 (dd, 1H, J_1 = 15.88 Hz, J_2 = 6.24 Hz, Pyr-H), 3.86 (dd, 1H, J_1 = 12.16 Hz, J_2 = 7.52 Hz, Pyr-H), 2.82 (dd, 1H, J_1 = 14.00 Hz, J_2 = 5.42 Hz, Pyr-H); ^{13}CNMR(100 MHz, DMSO-d_6) δ 160.5, 148.8, 144.4, 143.8, 142.4, 136.9, 135.5, 130.5, 129.7, 128.4, 127.2, 125.9, 125.4, 121.1, 118.3, 117.4, 112.6, 62.3, 46.3; *Anal*. Calcd for $C_{30}H_{22}ClN_3O$ (475) C, 75.70; H, 4.66; N, 8.83; Found: C, 75.72; H, 4.61; N, 8.80%.

3-(1,5-Diphenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-methylquinolin-2(1H)-one (4m). Off white solid (78%) mp 222–225°C; IR (KBr) υ_{max} 3155.94, 2847.38, 1655.59, 1597.73, 1500.35, 1387.53, 997.98 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 11.83 (s, 1H, 1-NH), 7.84 (d, 1H, J = 8 Hz, Ar—H), 7.51 (d, 1H, J = 8 Hz, Ar—H), 7.24–7.37 (m, 7H, Ar—H), 7.13 (t, 2H, J = 8.8 Hz, ArH), 6.92 (d, 2H, J = 8 Hz, Ar—H), 6.71 (t, 1H, J = 7.2 Hz, Ar—H), 5.36 (dd, 1H, J_1 = 12.40 Hz, J_2 = 5.50 Hz, Pyr-H), 3.95 (dd, 1H, J_1 = 17.80 Hz, J_2 = 12.00 Hz, Pyr-H), 3.12 (dd, 1H, J_1 = 17.80 Hz, J_2 = 7.20 Hz, Pyr-H), 2.61 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 134.1, 133.1, 132.4, 130.1, 128.7, 127.9, 128.4, 126.3, 125.3, 124.5, 122.1, 122.1, 120.1, 119.6, 118.2, 115.2, 111.6, 106.1, 62.2, 58.2, 47, 20.7, 16.3; *Anal.* Calcd for $C_{25}H_{21}N_3O$ (379) C, 79.13; H, 5.58; N, 10.56; Found: C, 79.15; H, 5.58; N, 10.51%.

6-Chloro-3-(5-(4-methoxyphenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-phenylquinolin-2(1H)-one (4n). Orange solid: (85%) mp 228–232°C; (KBr) υ_{max} 4011.46, 3155.94, 2923.56, 1653.66, 1596.77, 1501.31, 1247.72, 1034.62, 829.24, 746.32, 702.92 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.2 (s, 1H, 1-NH), 7.56 (d, 1H, J = 8.8 Hz, Ar—H), 7.40–7.52 (m, 4H, Ar—H), 7.36 (s, 1H, Ar–H), 7.24 (d, 1H, J = 7.2 Hz, Ar—H), 6.98 (q, 2H, Ar—H), 6.90 (d, 1H, J = 2.4 Hz, Ar—H), 6.75–6.83 (m, 4H, Ar—H) 6.56 (d, 3H, J = 8 Hz, Ar—H), 5.18 (dd, 1H, J_1 = 12.40 Hz, J_2 = 5.60 Hz, Pyr-H), 3.84 (dd,1H, J_1 = 21.80 Hz, J_2 = 12.40 Hz, Pyr-H), 3.69 (s, 3H, —OCH_3), 2.79 (dd, 1H, J_1 = 16.00 Hz, J_2 = 7;.60 Hz, Pyr-H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161, 158.7, 149.2, 144.3, 137.4, 136.8, 132.4, 131, 130.7, 128.9, 128.6, 127.5, 126.3, 124.5, 122.3, 121, 118.6, 117, 114.1, 112,4, 62, 46.1, 44.6, 16.5; *Anal*. Calcd for $C_{31}H_{24}ClN_3O_2$ (505) C, 73.58; H, 4.78; N, 8.30; Found: C, 73.57; H, 4.76; N, 8.32%.

3-(5-(4-Bromophenyl)-1-(3-nitrophenyl)-4,5-dihydro-1H-pyrazol-3-yl)-4-methylquinolin-2(1H)-one (4o). Orange solid (87%); mp 224–226°C; IR (KBr) υ_{max} 2857.24, 1654.55, 1508.23,1277.79, 825.53, 750.10, 645.25 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 11.89 (s,1H, 1-NH), 7.85 (d,1H, J = 8.4 Hz, ArH), 7.49–7.62 (m, 3H, Ar—H), 7.34 (d, 3H, J = 10.2 Hz, Ar—H), 7.25 (t, 1H, J = 7.6 Hz, Ar—H), 7.20 (d, 2H, J = 8.8Hz, Ar—H), 6.91 (d, 2H, J = 9.2 Hz, Ar—H), 5.46 (dd, 1H, J_1 = 12 Hz, J_2 = 6.40 Hz, Pyr-H), 3.95 (dd,1H, J_1 = 20.40 Hz, J_2 = 11.00 Hz, Pyr-H), 3.15 (dd,1H, J_1 = 17.60 Hz, J_2 = 6.40 Hz, Pyr-H), 2.60 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161. 2, 157.4, 155.4, 147.6, 146.8, 142.4, 141.8, 138.2, 132.3,

131.7, 131.1, 128.9, 126.1, 124.1, 122.5, 122.5, 120.9, 120.1; *Anal.* Calcd for $C_{25}H_{19}BrN_4O_3$ (503) C, 59.65; H, 3.80; N, 11.13; Found: C, 59.60; H, 3.83; N, 11.10%.

3-(5-(4-Chlorophenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-6-nitro-4-phenylquinolin-2(1H)-one (4p). Orange solid (72%); mp 218–223°C; IR (KBr) υ_{max} 3299.61, 3152.08, 2993.94, 1906.29, 1646.91, 1528.31, 1489.74, 1335.46, 1095.37, 831.16, 754.03, 696.17 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.35 (s, 1H, 1-NH), 8.26 (d, 1H, J = 6.8 Hz, ArH), 8.09 (s, 1H, H-NO_2), 7.39–7.49 (m, 4H, ArH), 7.34 (d, 1H, J = 8.9 Hz, ArH), 7.16–7.20 (m, 3H, ArH), 7.04 (t, 2H, J = 7.8 Hz, ArH), 6.88 (d, 2H, J = 8.35 Hz, ArH), 6.70 (t, 1H, J = 7.3 Hz, ArH), 6.62 (d, 2H, J = 7.95 Hz, ArH), 5.13 (dd, 1H, J_1 = 12.40 Hz, J_2 = 5.55 Hz, Pyr-H), 3.85 (dd, 1H, J_1 = 17.00 Hz J_2 = 12.50 Hz, Pyr-H), 2.86 (dd, 1H, J_1 = 7.45 Hz, J_2 = 5.65 Hz, Pyr-H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.2, 150, 147.8, 147.2, 143.7, 140.1, 138.8, 135.1, 131.7, 130.1, 129.3, 128.2, 126.5, 125.4, 121.5, 118.7, 116.9, 107.1, 61.8, 46.8; *Anal.* Calcd for $C_{30}H_{21}ClN_4O_3$ (520) C, 69.48; H, 4.06; N, 10.75; Found: C, 69.46; H, 3.98; N, 10.71%.

General procedure for the synthesis of 4,5-dihydro-1*H*-pyrazol-3-yl)quinolin-2(1*H*)-one (5a–d)

Conventional method A. Substituted α,β-unsaturated carbonyl compounds **3** (0.01 mmol) and hydrazine hydrate (0.03 mmol) were taken in ethanol and were refluxed over a period of 6–7 h. After the reaction was over as evidenced by the TLC, the reaction mixture was cooled to room temperature. Then, it was poured into 300 g of crushed ice after evaporation of the one-third of the solvent. The precipitate thus formed was filtered off, washed with excess of water, and dried, and then the mixture was chromatographed on a silica gel column chromatography on *n*-hexane:EtOAc (7:3) to obtain a pale yellow powder.

Microwave-assisted synthesis B. Quinoline-2(1*H*)-one-based α,β-unsaturated carbonyl compound **3** (0.01 mmol) and phenyl hydrazine hydrochloride (0.03 mmol) were powdered, mixed with two to five drops of EtOH, and introduced in an open borosil glass vessel. The reaction proceeded at a constant power of 360 W with temperature 120°C for 5 min with constant interval. After completion (TLC), the reaction mixture was brought to room temperature and poured into 300 g of crushed ice after evaporation of the one-third of the solvent. The crude product was recrystallized to obtain the title compound, which was found to be in good purity (TLC) and yield (Table 2).

3-(5-(4-Bromophenyl)-4,5-dihydro-1H-pyrazol-3-yl)-4-methyl quinolin-2(1H)-one (5a). Yellow solid (75%) mp 225–226°C; IR (KBr) υ_{max} 3324.68, 3158.83, 2843.52, 1663.30, 1486.85, 1428.03, 1263.15 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 11.55 (s, 1H, 1-NH), 7.23 (d, 1H, J = 7.76 Hz, Ar—H), 7.34 (s, 1H, Pyr-NH), 7.45–7.52 (m, 3H, Ar—H), 7.33 (d, 2H, J = 9.46 Hz, Ar—H), 7.87 (d, 1H, J = 8.9 Hz, Ar—H), 7.14 (t, 1H, J = 8.00 Hz, Ar—H), 4.82 (t, 1H, J = 9.28 Hz, Pyr-H), 2.87 (dd, 1H, J_1 = 17.88 Hz, J_2 = 9.28 Hz, Pyr-H), 2.04 (dd, 1H, J_1 = 18.44 Hz, J_2 = 8.80 Hz, Pyr-H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.4, 148.8, 146.2, 142.8, 138.1, 131.6, 130.3, 128.6, 126.7, 123.2, 121.7, 120.2, 116.5, 114.8, 64.1, 62.5, 45.8; *Anal.* Calcd for $C_{18}H_{14}ClN_3O_2$ (339) C, 63.63; H, 4.15; N, 12.37 Found: C, 63.60; H, 4.17; N, 12.33%.

6-Chloro-4-phenyl-3-(5-phenyl-4,5-dihydro-1H-pyrazol-3-yl) quinolin-2(1H)-one (5b). White solid (74%) mp 228–230°C; IR (KBr) υ_{max} 3313.11, 3149.19, 2992.98, 1652.70, 1486.85, 1404.89, 1088.62 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.24 (s, 1H, Q-NH), 7.47–7.58 (m, 4H, Ar—H), 7.40 (d, 1H, J = 8.96 Hz, Ar—H), 7.32 (d, 1H, J = 6.0 Hz, Ar—H),7.28 (d, 2H, J = 8.92 Hz, Ar—H), 7.20 (d, 2H, J = 8.32 Hz, Ar—H), 6.88 (d, 1H, J = 3.56 Hz, Ar—H), 4.58 (t, 1H, J = 10.72 Hz, Pyr-H), 3.25 (dd, 1H, J_1 = 17.28 Hz, J_2 = 10.72 Hz, Pyr-H), 2.52 (dd, 1H, J_1 = 16.80 Hz, J_2 = 9.56 Hz, Pyr-H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 161.1, 149.2, 146.1, 143.1, 137.5, 135.8, 131.8, 130.8, 128.3, 127, 125.3, 121.3, 118.9, 117, 63.2, 61.8, 46.5, 45.1, 43.8; *Anal.* Calcd for $C_{24}H_{18}ClN_3O$ (399), C, 72.09; H, 4.54; N, 10.51 Found: C, 72.05; H, 4.58; N, 10.49%.

3-(5-(4-Bromophenyl)-4, 5-dihydro-1H-pyrazol-3-yl)-4-phenyl quinolin-2(1H)-one (5c). Orange solid (80%); mp 231–232°C; IR (KBr) υ_{max} 2994.91, 2850.27, 1644.02, 1431.89, 1376.93, 1270.86 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H, Q-NH), 7.45–7.51 (m, 4H, ArH), 7.39 (d, 1H, J = 8.6 Hz, ArH), 7.31 (d, 1H, J = 6.88 Hz, ArH), 7.20 (s, 1H, ArH), 7.01–7.09 (m, 5H, ArH), 6.97 (t, 2H, J = 6.88 Hz, ArH), 4.52 (t, 1H, J = 9.68 Hz, Pyr-H), 3.40 (dd, 1H, J_1 = 20.24 Hz, J_2 = 12.52 Hz, Pyr-H), 3.19 (dd, 1H, J_1 = 16.36 Hz, J_2 = 11.40 Hz, Pyr-H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 134.8, 134.7, 133.9, 133.8, 133.2, 132.9, 132.4, 132.3, 131.3, 131.3, 130.7, 127.9, 127.8, 126.3, 126.2, 120.7, 120.5, 67.5, 49.8, 45.3, 25.3; *Anal.* Calcd for $C_{24}H_{18}BrN_3O$ (443) C, 64.88; H, 4.08; N, 9.46. Found: C, 64.85; H, 4.01; N, 9.41%.

4-Phenyl-3-(5-p-tolyl-4,5-dihydro-1H-pyrazol-3-yl)quinolin-2(1H)-one (5d). Pale yellow powder (74%); mp 218–222°C; IR (KBr) υ_{max} 3359.39, 2848.35, 1648.84, 1512.88, 1345.11, 855.27, 758.85, 701.96, 607.46 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.10 (s, 1H, Q-NH), 8.10 (d, 2H, J = 11.24 Hz, ArH), 7.45–7.54 (m, 5H, ArH), 7.39 (d, 1H, J = 7.88 Hz, ArH), 7.33–7.35 (m, 4H, ArH), 7.19 (d, 1H, J = 6.0 Hz, ArH),7.09(t, 1H J = 9 Hz, ArH), 7.99 (d, 1H, J = 10.12 Hz, ArH), 4.73 (t, 1H, J = 7.88 Hz, Pyr-H), 4.03 (dd, 1H, J_1 = 16.08 Hz, J_2 = 9.68 Hz, Pyr-H), 3.16 (dd, 1H, J_1 = 16.44 Hz, J_2 = 9.76 Hz, Pyr-H), 2.08 (s, 1H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.7, 150.6, 147.2, 138.8, 136.3, 131.9, 130.6, 129.8, 129, 128.3, 127.7, 127.4, 126.6, 123, 121.6, 119.7, 116.9, 114.8, 63.5, 61.4, 46.8, 45.5, 43.6; *Anal.* Calcd for $C_{25}H_{21}N_3O$ (379), C, 79.13; H, 5.58; N, 11.07. Found: C,79.11; H, 5.55; N, 11.05%.

General procedure for the synthesis of 4,5-dihydroisoxazol-3-yl)quinolin-2(1*H*)-one (6a–e)

Conventional method A. Various substituted α,β-unsaturated carbonyl compounds **3** (0.01 mmol) and hydroxylamine hydrochloride (0.03 mmol) were taken in ethanol and were refluxed over a period of 7–8 h. After the reaction was over as evidenced by the TLC, the reaction mixture was cooled to room temperature. Then, it was poured into 500 g of crushed ice after evaporation of the one-third of the solvent. The precipitate thus formed was filtered off, washed with excess of water, and dried, and then the mixture was chromatographed on a silica gel column chromatography on *n*-hexane:EtOAc (8:2) to obtain a reddish yellow powder.

Microwave-assisted synthesis B. Equimolar amount of quinolin-2(1*H*)-one-based α,β-unsaturated carbonyl compound **3** (0.01 mmol) and hydroxylamine hydrochloride (0.03 mmol) were powdered, mixed with 2-5 drops of EtOH, and introduced in an open borosil glass vessel. The reaction proceeded at a constant power of 360 W with temperature of 120°C for 5 min with constant interval. After completion (TLC), the reaction mixture was brought to room temperature and poured into 300 g of crushed ice. The crude product was recrystallized to

obtain the title compound, which was found to be in good purity (TLC) and yield (Table 2).

3-(5-(4-Bromophenyl)-4,5-dihydroisoxazol-3-yl)-6-chloro-4-phenylquinolin-2(1H)-one (6a). Pale green solid (82%); mp 216–220°C; IR (KBr) υ_{max} 3304.43, 3150.15, 2827.13, 1900.50, 1646.91, 1482.99, 1262.18, 1084.76, 893.84, 703.89 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.21 (s, 1H, 1-NH), 7.61 (dd, 1H, $J_1 = 8.26$ Hz, $J_2 = 2.84$ Hz, ArH), 7.54–7.56 (m, 2H, ArH), 7.43–7.45 (m, 2H, ArH), 7.32 (d, 2H, $J = 8.56$ Hz, ArH), 7.25 (d, 1H, $J = 7.40$ Hz, ArH), 6.96 (d, 2H, $J = 8.00$ Hz, ArH), 6.90 (d, 1H, $J = 2.84$ Hz, ArH), 5.54 (dd, 1H, $J_1 = 11.72$ Hz, $J_2 = 6.88$ Hz, CH—H), 3.70 (dd, 1H, $J_1 = 17.12$ Hz, $J_2 = 11.44$ Hz, CH_2—H), 2.91 (dd, 1H, $J_1 = 13.84$ Hz, $J_2 = 7.44$ Hz, CH_2—H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.7, 153.5, 150.7, 140.9, 138.1, 134.9, 132.9, 131.7, 129.7, 129.1, 128.9, 128.9, 128.8, 128.2, 126.6, 126.3, 123, 121, 118.1, 80.8, 46.56; *Anal*. Calcd For $C_{24}H_{16}BrClN_2O_2$ (479) C, 60.08; H, 3.36; N, 5.84; Found: C, 60.12; H, 3.40; N, 5.82%.

6-Chloro-4-phenyl-3-(5-phenyl-4, 5-dihydroisoxazol-3-yl)quinolin-2(1H)-one (6b). Pale green solid (82%); mp 205–210°C; IR (KBr) υ_{max} 3301.54, 3148.22, 2829.06, 1642.09, 1481.06, 1370.18, 1258.32, 1258.32, 888.05, 759.81 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.31 (s, 1H, NH), 7.61 (dd, 1H, $J_1 = 9.12$ Hz, $J_2 = 2.40$ Hz, ArH), 7.55 (t, 2H, $J = 4.20$ Hz, ArH), 7.44–7.47 (m, 2H, ArH), 7.37 (d, 1H, $J = 6.00$ Hz, ArH), 7.26–7.27 (m, 4H, ArH), 6.91–6.97 (m, 3H, ArH), 5.50 (dd, 1H, $J_1 = 11.44$ Hz, $J_2 = 7.48$ Hz, CH—H), 3.69 (dd, 1H, $J_1 = 17.72$ Hz, $J_2 = 10.48$ Hz, CH_2—H), 2.94 (dd, 1H, $J_1 = 18.36$ Hz, $J_2 = 9.20$ Hz, CH—H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.4, 153.5, 150.3, 142.2, 138.1, 134.6, 131.6, 129.6, 129.1, 128.9, 128.3, 126.7, 126.5, 126.4, 123, 121.4, 118.2, 81.8, 46.2; *Anal*. Calcd For $C_{24}H_{17}ClN_2O_2$ (400) C, 71.91; H, 4.27; N, 6.99; Found: C, 71.87; H, 4.32; N, 7.02%.

6-Chloro-3-(5-(4-methoxyphenyl)-4,5-dihydroisoxazol-3-yl)-4-phenylquinolin-2(1H)-one (6c). Pale green solid (82%) mp 220–224°C; IR (KBr) υ_{max} 3150.15, 2990.09, 1903.40, 1649.80, 1481.06, 1368.25, 897.70, 702.92, 611.32, 550.57 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.31 (s, 1H, NH), 7.63 (t, 2H, $J = 8.48$ Hz, ArH), 7.27–7.32 (m, 3H, ArH), 7.19 (d, 2H, $J = 7.04$ Hz, ArH), 7.07 (d, 2H, $J = 9.00$ Hz, ArH), 6.97 (d, 1H, $J = 2.16$ Hz, ArH), 6.91 (d, 1H, $J = 2.24$ Hz, ArH), 6.84 (d, 2H, $J = 8.48$ Hz, ArH), 6.69 (d, 1H, $J = 9.55$ Hz, ArH), 5.45 (dd, 1H, $J_1 = 14.12$ Hz, $J_2 = 7.08$ Hz, CH—H), 3.85 (s, 3H, OCH_3), 3.66 (dd, 1H, $J_1 = 18.36$ Hz, $J_2 = 9.92$ Hz, CH—H), 2.91 (dd, 1H, $J_1 = 16.24$ Hz, $J_2 = 8.48$ Hz, CH—H);^{13}C NMR (100 MHz, DMSO-d_6) δ 194.1, 160.4, 159.9, 153.5, 150.4, 147.1, 146.7, 141.4, 138.8, 138.1, 137.6, 134.8, 134.1, 133.1, 132.1, 131.7, 131.3, 129.9, 129.1, 128.9, 126.9, 126.1, 123.2, 121.1, 118.2, 81.4, 46.2; *Anal*. Calcd for $C_{25}H_{19}ClN_2O_3$ (430) C, 69.69; H, 4.44; N, 6.50; Found: C, 69.58; H, 4.48; N, 6.47%.

3-(5-(4-Chlorophenyl)-4,5-dihydroisoxazol-3-yl)-4-phenylquinolin-2(1H)-one (6d). Pale green solid (78%); mp 210–215°C; IR (KBr) υ_{max} 3304.43, 3150.15, 2827.13, 1900.50, 1646.91, 1482.99, 1262.18, 1084.76, 893.84, 703.89 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.30 (s, 1H, 1-NH), 7.55 (dd, 1H, $J_1 = 8.12$ Hz, $J_2 = 2.55$ Hz, ArH), 7.53–7.58 (m, 2H, ArH), 7.40–7.44 (m, 2H, ArH), 7.22 (d, 2H, $J = 7.87$ Hz, ArH), 6.66 (d, 2H, $J = 7.50$ Hz, ArH), 6.57 (d, 1H, $J = 2.40$ Hz, ArH), 5.48 (dd, 1H, $J_1 = 10.72$ Hz, $J_2 = 6.76$ Hz, CH—H), 3.66 (dd, 1H, $J_1 = 16.12$ Hz, $J_2 = 10.20$ Hz, CH_2—H), 2.88 (dd, 1H, $J_1 = 11.84$ Hz, $J_2 = 7.10$ Hz, CH_2—H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.7, 155.2, 148.7, 141.9, 135.1, 133.9, 131.5, 130.7, 129.7, 128.1, 128.2, 126.6, 125.3, 122, 120.2, 117.1, 82.6, 46.5; *Anal*. Calcd For $C_{24}H_{17}ClN_2O_2$ (400) C, 71.91; H, 4.27; N, 6.99; Found: C, 71.88; H, 4.22; N, 7.02%.

3-(5-(4-Fluorophenyl)-4,5-dihydroisoxazol-3-yl)-4-phenylquinolin-2(1H)-one (6e). Pale green solid (75%); mp 210–215°C; IR (KBr) υ_{max} 3201.43, 2727.20, 1915.50, 1646.65, 1326.10, 1075.55, 895.80, 703.11 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.25 (s, 1H, 1-NH), 7.52 (dd, 1H, $J_1 = 8.56$ Hz, $J_2 = 2.50$ Hz, ArH), 7.49–7.58 (m, 2H, ArH), 7.39–7.43 (m, 2H, ArH), 7.16 (d, 2H, $J = 6.90$ Hz, ArH), 6.61 (d, 2H, $J = 7.25$ Hz, ArH), 6.43 (d, 1H, $J = 2.50$ Hz, ArH), 5.78 (dd, 1H, $J_1 = 11.72$ Hz, $J_2 = 7.67$ Hz, CH—H), 4.05 (dd, 1H, $J_1 = 17.12$ Hz, $J_2 = 9.45$ Hz, CH_2—H), 2.97 (dd, 1H, $J_1 = 10.39$ Hz, $J_2 = 7.41$ Hz, CH_2—H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.5, 154.2, 149.1, 142.2, 134.1, 133.9, 131.1, 129.9, 128.1, 125.5, 124.3, 121.1, 116.1, 83.6, 47.2; *Anal*. Calcd For $C_{24}H_{17}FN_2O_2$ (384) C, 74.99; H, 4.46; N, 7.29; Found: C, C, 75.05; H, 4.41; N, 7.32%.

General procedure for the synthesis of benzo[*b*][1,4] diazepin-4-yl)quinolin-2(1*H*)-one (*9a–e*). Equimolar amount of substituted 3-cinnamoyl-4-hydroxyquinolin-2(1*H*)-one **7** (0.01 mmol) and *o*-phenylenediamine **8** (0.03 mmol) was taken in acetic acid and was refluxed over a period of 8–9 h. After the reaction was over as evidenced by the TLC, the reaction mixture was cooled to room temperature. Then, it was poured into 300 g of crushed ice after evaporation of the one-third of the solvent. The precipitate thus formed was filtered off, washed with excess of water, and dried, and then the mixture was chromatographed on a silica gel column chromatography on hexane:ethyl acetate (8:2) to obtain a pale green yellow powder.

4-Hydroxy-3-(2-(4-methoxyphenyl)-2,3-dihydro-1H-benzo[b][1,4]diazepin-4-yl)quinolin-2(1H)-one (9a). Pale green solid (77%); mp 210–215°C; IR (KBr) υ_{max} 3404.71, 3100.97, 2900.41, 1644.02, 1563.99, 1494.56, 1368.25, 1176.36, 1030.77, 753.06 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 16.20 (s, 1H, C4-OH), 10.66 (s,1H, C1-NH), 7.95 (d,1H, $J = 8.10$ Hz, Ar—H), 7.49 (t,1H, $J = 7.80$ Hz, Ar—H), 7.28 (d, 2H, $J = 8.42$ Hz, Ar—H), 7.14–7.21 (m, 3H, Ar—H), 7.09 (d, 2H, $J = 7.20$ Hz, Ar—H), 6.88–6.91(m, 3H, Ar—H), 6.22 (s,1H, CH—H), 5.13 (d,1H, $J = 8.40$ Hz, CH—H), 4.40 (s,1H, CH—H), 3.70 (s,3H, OCH_3), ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.4, 159.2, 141.9, 137.8, 133.7, 128.3, 127.4, 125.1, 121.3, 120.1, 114.2, 65.7, 55.5, 37.6; *Anal*. Calcd for $C_{25}H_{21}N_3O_3$ (411): C, 72.98; H, 5.14; N, 10.21; Found: C, 72.95; H, 5.09; N, 10.23%.

3-(2-(4-Chlorophenyl)-2,3-dihydro-1H-benzo[b][1,4]diazepin-4-yl)-4-hydroxyquino lin-2(1H)-one (9b). Pale green solid (75%); mp 223–225°C; IR (KBr) υ_{max} 3414.35, 2868.59, 1646.91, 1604.48, 1562.06, 1372.10, 1307.50, 882.27, 752.10 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 16.23 (s, 1H, C-4-OH), 10.66 (s, 1H, C^1-NH), 7.94 (d, 1H, $J = 8.56$ Hz, Ar—H), 7.47 (t, 1H, $J = 8.52$ Hz, Ar—H),7.05–7.37 (m, 9H, Ar—H), 6.89 (t, 1H, $J = 7.88$ Hz, Ar—H), 6.32 (s, 1H, CH—H), 5.21 (d, 1H, $J = 8.52$ Hz, CH—H), 4.17 (s, 1H, CH—H), ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.4, 144.2, 141.7, 133.5, 132.3, 128.7, 128.4, 128.3, 125.2, 121.3, 120.3, 115.5, 65.7, 36.8; *Anal*. Calcd for $C_{23}H_7ClN_3O_2$ (402): C, 68.57; H, 4.25; N, 10.43; Found: C, 68.50; H, 4.28; N, 10.39%.

3-(2-(4-Bromophenyl)-2,3-dihydro-1H-benzo[b][1,4]diazepin-4-yl)-4-hydroxyquinolin-2(1H)-one (9c). Green solid (80%); mp 217–220°C; IR (KBr) υ_{max} 3406.64, 2868.59, 1647.88, 1604.48, 1562.06, 1372.10, 883.23, 754.03 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 16.25 (s, 1H, C4-OH), 10.62 (s, 1H, C^1-NH), 7.93 (d, 1H, $J = 9.40$ Hz, Ar—H), 7.46–7.51(m, 3H,

Ar—H), 7.31 (d, 2H, $J = 7.04$ Hz, Ar—H), 7.15–7.20 (m, 3H, Ar—H), 7.05 (d, 2H, $J = 6.28$ Hz, Ar—H), 6.90 (t, 1H, $J = 8.60$ Hz, Ar—H), 6.32 (s, 1H, CH—H), 5.19 (d, 1H, $J = 9.44$ Hz, CH—H), 4.18 (s, 1H, CH—H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.1, 144.7, 141.2, 133.6, 132.1, 128.9, 126.3, 125.2, 121.3, 120.7, 120.3, 115.5, 65.4, 36.8; *Anal*. Calcd for $C_{24}H_{18}BrN_3O_2$ (460) C, 62.62; H, 3.94; N, 9.13; Found: C, 62.58; H, 3.96; N, 9.07%.

4-Hydroxy-3-(2-phenyl-2, 3-dihydro-1H-benzo[b][1,4]diazepin-4-yl)quinolin-2(1H)-one (9d). Pale green solid (72%); mp 205–210°C; IR (KBr) υ_{max} 3400.85, 2863.77, 1642.09, 1604.48, 1555.31, 1464.67, 1367.28, 876.48, 751.13, 487.90 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 16.23 (s,1H, C-4-OH), 10.69 (s,1H, C^1-NH), 7.94 (d,1H, $J = 8.76$ Hz, Ar—H), 7.48 (t,1H, $J = 8.76$ Hz, Ar—H), 7.25–7.37 (m, 4H, Ar—H), 7.05–7.23 (m, 6H, Ar—H), 6.89 (t,1H, $J = 7.44$ Hz, Ar—H), 6.29 (s,1H, CH—H), 5.18 7.93 (d,1H, $J = 10.12$ Hz, CH—H), 4.35 (s,1H, CH—H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.4, 145.6, 141.8, 128.8, 128.4, 127.8, 126.3, 125.1, 121.4, 120.2, 115.6, 37.44; *Anal*. Calcd for $C_{24}H_{19}N_3O_2$ (381): C, 75.57; H, 5.02; N, 11.02; Found: C, 75.60; H, 5.05; N, 10.98%.

***4-Hydroxy-3-(2-p-tolyl-2,3-dihydro-1H-benzo[b][1,4]diazepin-4-yl)quinolin-2(1H)*-one (9e).** Pale green solid (70%); mp 225–228°C; IR (KBr) υ_{max} 3325.64, 2913.91, 1645.95, 1602.56, 1565.92, 1460.81, 1360.53, 811.88, 754.03537.07 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 16.18 (s, 1H, C-4-OH), 10.67 (s, 1H, C^1-NH), 7.94 (d, 1H, $J = 8.10$ Hz, Ar—H), 7.49 (t, 1H, $J = 7.20$ Hz, Ar—H), 7.05–7.25 (m, 8H, Ar—H), 6.89 (t, 1H, $J = 7.20$ Hz, Ar—H), 6.26 (s, 1H, CH—H), 5.14 (d, 1H, $J = 9.00$ Hz, CH—H), 4.36 (s, 1H, CH—H), 2.24 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.4, 142.6, 141.8, 136.9, 133.5, 129.4, 128.4, 126.2, 125.1, 121.4, 120.2, 115.7, 66.1, 37.7, 21.1; *Anal*. Calcd for $C_{25}H_{21}N_3O_2$ (395) C,75.93; H,5.35; N, 10.63; Found: C, 75.89; H, 5.32; N, 10.57%; CCDC number for **9e**: CCDC 886309. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK. Fax: + 44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk.

***In vitro* cytotoxicity assay.** Cytotoxicity studies of the compounds along with adriamycin were carried out on human cervical cancer cells (HeLa), colon cancer cells (HCT-116), and colon cancer cell lines (HCT-8), which were obtained from the National Centre for Cell Science, Pune, India. Cell viability was carried out using the MTT assay method. The HeLa, HCT-8, and HCT-116 cells were grown in Eagles minimum essential medium containing 10% FBS. For the screening experiment, the cells were seeded into 96-well plates in 100 µL of the respective medium containing 10% FBS, at a plating density of 10,000 cells/well, and incubated at 37°C, under conditions of 5% CO_2, 95% air, and 100% relative humidity for 24 h prior to the addition of compounds. The compounds were dissolved in DMSO and diluted in the respective medium containing 1% FBS. After 24 h, the medium was replaced with the respective medium with 1% FBS containing the compounds at various concentrations and incubated at 37°C under conditions of 5% CO_2, 95% air, and 100% relative humidity for 48 h. Triplication was maintained, and the medium not containing the compounds served as the control. After 48 h, 10 µL of MTT (5 mg/mL) in phosphate buffered saline (PBS) was added to each well and incubated at 37°C for 4 h. The medium with MTT was then flicked off, and the formed formazan crystals were dissolved in 100 µL of DMSO. The absorbance was then measured at 570 nm using a micro plate reader. The percentage of cell inhibition was determined using the following formula, and a graph was plotted with the percentage of cell inhibition versus concentration. From this, the IC_{50} value was calculated:

$$\% \text{ inhibition} = [\text{mean OD of untreated cells (control)} / \text{mean OD of treated cells (control)}] \times 100.$$

Acknowledgments. The authors thank the Council of Scientific and Industrial Research CSIR-SRF (Ref No. 09/472(0145)/2K10–EMR-I) New Delhi, India, for the financial assistance. We acknowledge Dr Aathirajan, Professor, Cell Culture Laboratory, KMCH College of Pharmacy, Coimbatore for evaluating cytotoxicity. The authors thank SAIF, NMR Research Centre, Bangalore SAIF, IIT Chennai for spectral study.

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