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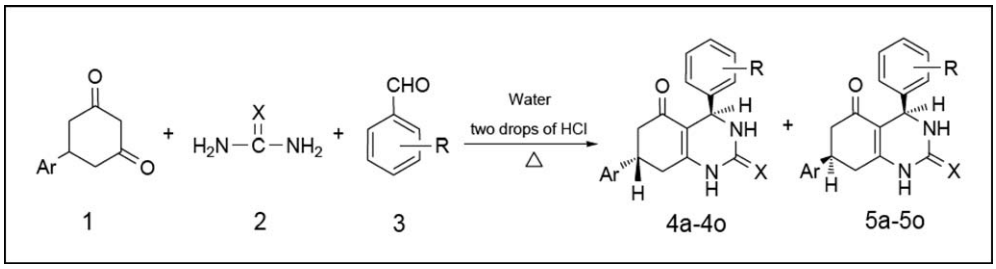

A green and convenient approach to the synthesis of novel 4,7-diaryl-2-oxo(thio)-1,2,3,4,5,6,7,8-octahydroquinazoline-5-one derivatives from appropriate aromatic aldehydes and 5-aryl-1,3-cyclohexanedione with urea or thiourea in the presence of dilute HCl as catalyst in water is described. This method provides several advantages such as environmental friendliness, low cost, high yields, and simple workup procedure. The structures of all compounds were characterized by elemental analysis, IR, MS, and ^{1}H NMR. The crystal and molecular structure of 4-(4′-chlorophenyl)-7-(4′-methoxyphenyl)-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione **5m** have been determined by single crystal X-ray diffraction analysis. The crystal of compound **5m** belongs to monoclinic with space group $P\text{-}2_1/c$, $a = 1.4353$ (4) nm, $b = 1.4011$ (4) nm, $c = 0.9248$ (3) nm, $\alpha = 90.00°$, $\beta = 101.242$ (6)°, $\gamma = 90.00°$, $Z = 4$, $V = 1.8241$ (9) nm^3, $R_1 = 0.0448$, and $wR_2 = 0.1022$.

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INTRODUCTION

Recently, much attention has been focused on the synthesis of octahydroquinazolinone due to their significant biological activities, such as against staphylococcus aureus, escherichiacoli, pseudomonas aeruginosa [1], and calcium antagonist activity [2,3]. Many methods have been developed for the preparation of quinazolinone derivatives which include the three-component coupling of an aldehyde with ethyl acetoacetate and ammonia in acetic acid or in refluxing alcohol [4,5], or using microwaves [6], ionic liquids [7], or refluxing at high temperature with many catalysts [8–14]. However, many of these reagents or catalysts are expensive, harmful, and difficult to handle especially on a large scale.

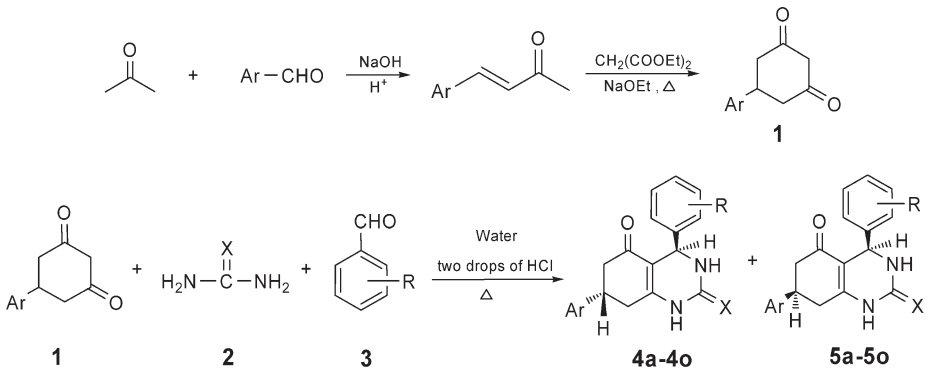
In this article, we report a clean and highly efficient route for the one-pot synthesis of the title compounds using dilute HCl as catalyst in water. This novel method is not only environmental friendliness but also consistently gives the corresponding products in good yields. We also obtained the single crystal **5m**, and the three-dimensional structure was confirmed by the X-ray diffraction analysis.

RESULTS AND DISCUSSION

The synthetic pathway is shown in Scheme 1. The 5-aryl-1,3-cyclohexanedione were obtained from aromatic aldehyde, acetone, and diethyl malonate according to the literature [15] method with slightly modification. The 4,7-diaryl-2-oxo(thio)-1,2,3,4,5,6,7,8-octahydroquinazoline-5-one derivatives were obtained by the Biginelli condensation reaction of 5-aryl-1,3-cyclohexanedione with urea or thiourea and substituted benzaldehydes using two drops of concentrated HCl as catalyst in water. As shown in Table 1, the reaction proceeded smoothly to afford the corresponding products in good yields. All aromatic aldhydes containing electron-withdrawing groups (such as halide) or electron-donating groups (such as methoxy) were used and reacted well to give the corresponding product in good yields under these conditions, so we conclude that the nature of the substituents on the aromatic ring had no obvious effect on the reaction.

Taking the reaction of benzaldehyde for example, we investigated the effect of the amount of catalyst on the reaction, which plays a crucial role in the success of the

Scheme 1



a: Ar=C_6H_5, X=O, R=H; b: Ar=C_6H_5, X=O, R=2-Cl; c: Ar=C_6H_5, X=O, R=4-Cl;
d: Ar=C_6H_5, X=O, R=3-OCH_3; e: Ar=C_6H_5, X=O, R=4-OCH_3; f: Ar=C_6H_5, X=S, R=H;
g: Ar=C_6H_5, X=S, R=2-Cl; h: Ar=C_6H_5, X=S, R=4-Cl; i: Ar=C_6H_5, X=S, R=3-OCH_3;
j: Ar=C_6H_5, X=S, R=4-OCH_3; k: Ar=4-$OCH_3C_6H_4$, X=O, R=H; l: Ar=4-$OCH_3C_6H_4$, X=O, R=2-Cl;
m: Ar=4-$OCH_3C_6H_4$, X=O, R=4-Cl; n: Ar=4-$OCH_3C_6H_4$, X=O, R=4-OCH_3; o: Ar=4-$OCH_3C_6H_4$, X=S, R=H;

reaction in terms of the rate and the yields. It was found that the reaction could not be carried out without the catalyst, and with two drops of concentrate HCl(about 0.1 mL) in 20 mL water at 70–80°C for 2 h, the reaction could afford the corresponding product in good yields. But with the catalyst increased, the yields show a decreasing trend. These data indicated that two drops of concentrate HCl in 20 mL water is quite suitable for this reaction.

The data of ^{1}H NMR, MS, and IR shown in the experimental section are in accordance with the chemical structures of the target compounds. In the ^{1}H NMR spectrum of compound **4f**, the single proton peak at δ 5.20 was the characteristic absorption proton peak of the 4-H, two broad single peaks at δ 7.88 and δ 9.66 were observed. They disappeared after D_2O exchange and therefore were attributed to the two *N*-H of the amino group. Because of the existence of intramolecular hydrogen bond between one proton of the amino group and the oxygen atom of the carbonyl group nearby (Table 3), its proton peak was drifted to δ 9.66.

The structures of these compounds were further supported by their IR spectra. Server typical absorption bands at 1711 cm^{-1} for (C═O), 3275 cm^{-1} for (*N*═H) were observed.

Table 1

Synthesis of 4,7-diaryl-2-oxo(thio)-1,2,3,4,5,6,7,8-octahydroquinazoline-5-one.

Entry	Ar	X	R	M.P. (°C)	Yield (%)	Approximate ratio (4:5)[a]
4a	C_6H_5	O	H	278–279	50	–
5a	C_6H_5	O	H	278–280	26	–
4b+5b	C_6H_5	O	2-Cl	280–282	80	5:3
4c+5c	C_6H_5	O	4-Cl	282–284	77	5:2
4d+5d	C_6H_5	O	3-OCH_3	280–281	85	2:1
4e	C_6H_5	O	4-OCH_3	270–272	57	–
5e	C_6H_5	O	4-OCH_3	272–274	26	–
4f	C_6H_5	S	H	250–251	50	–
5f	C_6H_5	S	H	251–252	29	–
4g+5g	C_6H_5	S	2-Cl	242–244	84	3:1
4h+5h	C_6H_5	S	4-Cl	250–251	81	7:3
4i+5i	C_6H_5	S	3-OCH_3	244–245	80	3:2
4j+5j	C_6H_5	S	4-OCH_3	247–248	86	2:1
4k+5k	4-$OCH_3C_6H_4$	O	H	252–254	88	2:1
4l+5l	4-$OCH_3C_6H_4$	O	2-Cl	259–260	86	7:3
4m	4-$OCH_3C_6H_4$	O	4-Cl	286–287	56	–
5m	4-$OCH_3C_6H_4$	O	4-Cl	284–286	28	–
4n+5n	4-$OCH_3C_6H_4$	O	4-OCH_3	254–256	83	3:2
4o+5o	4-$OCH_3C_6H_4$	S	H	234–235	81	5:3

[a] It was speculated from the integration area of the special position H in the ^{1}H NMR spectrum.

Table 2

Crystallographic data for crystallographic data for complex **5m.**

Empirical formula	C_{21} H_{19} Cl N_2 O_3
Formula weight	382.83
Wavelength (nm)	0.071073
Crystal system	Monoclinic
Space group	$P2_1/c$
a (nm)	1.4353(4)
b (nm)	1.4011(4)
c (nm)	0.9248(3)
α (°)	90.00
β (°)	101.242(6)
γ (°)	90.00
Volume (nm^3)	1.8241(9)
Z	4
Calculated density (g cm^{-3})	1.394
Absorption coefficient (mm^{-1})	0.234
F (000)	800
Final R indices [I > 2sigma (I)]	$R_1 = 0.0448$, $wR_2 = 0.1022$
R indices (all data)	$R_1 = 0.0769$, $wR_2 = 0.1162$

CRYSTAL STRUCTURE

A summary of the crystal data and structure refinement is presented in Table 2. A perspective view of compound **5m** with atomic numbering scheme was shown in Figure 1. In compound **5m**, The dihedral angle between the bond lengths and bond angles are generally normal in the phenyl and quinoline ring and the quinoline ring [C(7), C(8), C(9), C(10), C(11), C(12), C(13), C(14), N(1), N(2)] with plane equation 4.0780 (0.0027) x + 10.7892 (0.0071) y + 4.6691 (0.0053) z = 8.9674, The benzene ring a [C(1), C(2), C(3), C(4), C(5), C(6)] with plane equation 10.4240 (0.0095) x + 3.3441 (0.0130) y − 7.1571 (0.0059) z = 11.7828 is 88.76°. The benzene ring b [C(15), C(16), C(17), C(18), C(19), C(20)] is coplanar with the conjunction C(14), whose plane equation is − 2.5083 (0.0140) x + 11.9234 (0.0087) y − 4.1769 (0.0084) z = 0.8635. The dihedral angles between the benzene ring b and quinoline ring plane is 59.09°. The packing diagram of the **5m** in a unit cell was shown in Figure 2. X-ray analysis reveals that there are intramolecular and intermolecular hydrogen bonds in the crystal. The intermolecular hydrogen bond N(1)–H(1)···O(2) is 2.861(4) Å, the structural analysis indicates that these molecular interactions play the role of further stabilizing the structure. The bond lengths and bond angles of primary hydrogen bonds were listed in Table 3.

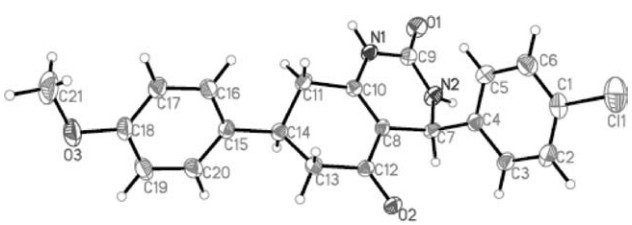


Figure 1. Molecular structure of compound **5m**.

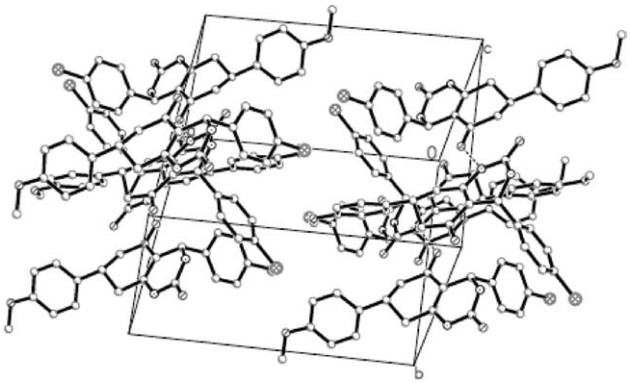


Figure 2. Packing diagram of compound **5m** in unit-cell.

CONCLUSIONS

In summary, we have described a general and highly efficient procedure for the one-pot preparation of 4,7-diaryl-2-oxo(thio)-1,2,3,4,5,6,7,8-octahydroquinazoline-5-one derivatives catalyzed by two drops of concentrate HCl in water. It is possible to apply tenets of green chemistry to the generation of interesting products using aqueous media methods that are less expensive and less toxic than those with organic solvent. Catalyst is very cheap, nontoxic and used in very small amount. Moreover, the procedure offers several advantages including high yields, low-cost, operational simplicity, cleaner reactions, and minimal environmental effects, which make it a useful and attractive process for the synthesis of these compounds.

EXPERIMENTAL

Melting points were determined on an electro-thermal apparatus and the temperature was not calibrated. Microanalysis was performed by the Perkin–Elmer 2400 Microanalytical Service. Infrared spectra were recorded as thin films on KBr using a Perking-Elmer 1700 spectrophotometer. The NMR spectra were recorded by a Bruker ARX-300 spectrometer. Sample solutions were prepared in $CDCl_3$ or DMSO containing TMS as an internal reference. Mass spectra were recorded by JMS-DX300 at 70 eV.

All chemical reagents were commercially available and purified with standard methods before use. 5-aryl-1,3-cyclohexanedione were obtained from aromatic aldehyde, acetone, and

Table 3

Inter and intramolecular interaction distances (Å) for the compound **5m**.

D–H···A	D–H	H···A	D···A	D–H···A	Symmetry
N(1)–H(1)···O(2)	0.900	1.98	2.861	165.68	*x*, *y*, *z*

diethyl malonate according to the literature [15] method with slightly modification. A mixture of an 5-aryl-1,3-cyclohexanedione (**1**, 5 mmol), urea or thiourea(**2**, 5 mmol), aromatic aldehyde (**3**, 5 mmol) and two drops of 37% HCl (0.1 mL) in water (20 mL) were stirred at 70–80°C for 2 h. Then the mixture was cooled to room temperature; solid was filtered off and washed with water. The crude products were purified by recrystallization from ethanol (95%).

Data of compounds are shown below. ***4a.*** ^{1}H NMR (DMSO, 300 MHz) δ: 2.26–2.60 (m, 3H, 6-H + 8-H), 2.70–2.83 (m, 1H, 6-H), 3.41–3.47 (m, 1H, 7-H), 5.13 (s, 1H, 4-H), 6.85–7.32 (m, 10H, Ph-H), 7.72 (s, 1H, 3-NH), 9.50 (s, 1H, 1-NH); IR (KBr) ν: 3240, 1712, 1671, 1619, 1507 cm^{-1}; MS (70eV) *m/z* (%): 319.17 (M + 1, 100); Anal. Calcd. for $C_{20}H_{18}N_2O_2$: C 75.45, H 5.70, N 8.80; found C 75.37, H 5.62, N 8.87.

5a. ^{1}H NMR (DMSO, 300 MHz) δ: 2.36–2.66 (m, 3H, 6-H + 8-H), 2.71–2.86 (m, 1H, 6-H), 3.41–3.47 (m, 1H, 7-H), 5.16(s, 1H, 4-H), 6.80–7.33 (m, 10H, Ph-H), 7.78 (s, 1H, 3-NH), 9.56 (s, 1H, 1-NH); IR (KBr) ν: 3243, 1715, 1671, 1629, 1508 cm^{-1}; MS (70eV) *m/z* (%): 319.17 (M + 1, 100); Anal. Calcd. for $C_{20}H_{18}N_2O_2$: C 75.45, H 5.70, N 8.80; found C 75.53, H 5.65, N 8.67.

4b + 5b. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.25–2.79 (m, 4H, 6-H + 8-H), 3.37–3.47 (m, 1H, 7-H), 5.58 and 5.62 (each s, 1H, 4-H), 7.07–7.49 (m, 9H, Ph-H), 7.71 and 7.75 (each s, 1H, 3-NH), 9.60 and 9.62 (each s, 1H, 1-NH); IR (KBr) ν: 3255, 1693, 1632, 1500 cm^{-1}; MS (70eV) *m/z* (%): 352.50 (M, 100); Anal. Calcd. for $C_{20}H_{17}ClN_2O_2$: C 68.09, H 4.86, N 7.94; found C 68.21, H 4.77, N 7.81.

4c + 5c. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.61–2.86 (m, 4H, 6-H + 8-H), 3.32–3.47 (m, 1H, 7-H), 5.45 and 5.52 (each s, 1H, 4-H), 7.07–7.49 (m, 9H, Ph-H), 8.13 and 8.17 (each s, 1H, 3-NH), 9.50 and 9.52 (each s, 1H, 1-NH); IR (KBr) ν: 3310, 1720, 1678, 1614, 1491 cm^{-1}; MS (70eV) *m/z* (%): 351.17 (M-1, 100); Anal. Calcd. for $C_{20}H_{17}ClN_2O_2$: C 68.09, H 4.86, N 7.94; found C 68.15, H 4.95, N 7.82.

4d + 5d. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.46–2.84 (m, 4H, 6-H + 8-H), 3.38–3.53 (m, 1H, 7-H), 5.43 and 5.53 (each s, 1H, 4-H), 6.71–7.49 (m, 9H, Ph-H), 8.00 and 8.03 (each s, 1H, 3-NH), 9.00 and 9.05 (each s, 1H, 1-NH); IR (KBr) ν: 3325, 1711, 1674, 1621, 1489 cm^{-1}; MS (70eV) *m/z* (%): 347.17 (M-1, 100); Anal. Calcd. for $C_{21}H_{20}N_2O_3$: C 72.40, H 5.79, N 8.04; found C 72.48, H 5.70, N 8.13.

4e. ^{1}H NMR (DMSO, 300 MHz) δ: 2.36–3.10 (m, 4H, 6-H + 8-H), 3.39–3.50 (m, 1H, 7-H), 3.70 (s, 3H, -OCH_3), 5.13 (s, 1H, 4-H), 6.76–7.38 (m, 9H, Ph-H), 7.73 (s, 1H, 3-NH), 9.51 (s, 1H, 1-NH); IR (KBr) ν: 3215, 1715, 1638, 1598, 1510 cm^{-1}; MS (70eV) *m/z* (%): 349.49 (M + 1, 100); Anal. Calcd. for $C_{21}H_{20}N_2O_3$: C 72.40, H 5.79, N 8.04; found C 72.25, H 5.65, N 7.92.

5e. ^{1}H NMR (DMSO, 300 MHz) δ: 2.36–2.86 (m, 4H, 6-H + 8-H), 3.41–3.47 (m, 1H, 7-H), 5.16 (s, 1H, 4-H), 6.80–7.33 (m, 9H, Ph-H), 7.78 (s, 1H, 3-NH), 9.56 (s, 1H, 1-NH); IR (KBr) ν: 3218, 1715, 1628, 1600, 1511 cm^{-1}; MS (70eV) *m/z* (%): 349.49 (M + 1, 100); Anal. Calcd. for $C_{21}H_{20}N_2O_3$: C 72.40, H 5.79, N 8.04; found C 72.48, H 5.68, N 8.12.

4f. ^{1}H NMR (DMSO, 300 MHz) δ: 2.27–2.83 (m, 4H, 6-H + 8-H), 3.10–3.30 (m, 1H, 7-H), 5.20 (s, 1H, 4-H), 7.20–7.40 (m, 9H, Ph-H), 7.88 (s, 1H, 3-NH), 9.66 (s, 1H, 1-NH); IR (KBr) ν: 3275, 1711, 1680, 1624, 1509 cm^{-1}; MS (70eV) *m/z* (%): 334.18 (M-1, 100); Anal. Calcd. for $C_{20}H_{18}N_2OS$: C 71.83, H 5.42, N 8.38; found C 71.75, H 5.50, N 8.24.

5f. ^{1}H NMR (DMSO, 300 MHz) δ: 2.38–2.86 (m, 4H, 6-H + 8-H), 3.36–3.48 (m, 1H, 7-H), 5.18 (s, 1H, 4-H), 7.18–7.41 (m, 9H, Ph-H), 7.83 (s, 1H, 3-NH), 9.60 (s, 1H, 1-NH); IR (KBr) ν: 3276, 1709, 1683, 1624, 1512 cm^{-1}; MS (70eV) *m/z* (%): 334.18 (M-1, 100); Anal. Calcd. for $C_{20}H_{18}N_2OS$: C 71.83, H 5.42, N 8.38; found C 71.95, H 5.51, N 8.22.

4g + 5g. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.60–2.99 (m, 3H, 6-H + 8-H), 3.47–3.66 (m, 1H, 6-H), 3.69–3.96 (m, 1H, 7-H), 5.44 and 5.54 (each s, 1H, 4-H), 6.56–7.41 (m, 9H, Ph-H), 9.70 and 9.76 (each s, 1H, 3-NH), 12.40 and 12.47 (each s, 1H, 1-NH); IR (KBr) ν: 3293, 1693, 1632, 1500 cm^{-1}; MS (70eV) *m/z* (%): 368.50 (M, 100); Anal. Calcd. for $C_{20}H_{17}ClN_2OS$: C 65.12, H 4.65, N 7.59; found C 65.32, H 4.47, N 7.53.

4h + 5h. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.60–3.08 (m, 4H, 6-H + 8-H), 3.33–3.56 (m, 1H, 7-H), 5.44 and 5.51 (each s, 1H, 4-H), 7.12–7.57 (m, 9H, Ph-H), 12.08 and 12.11 (each s, 1H, 3-NH), 12.40 and 12.45 (each s, 1H, 1-NH); IR (KBr) ν: 3276, 1695, 1640, 1502 cm^{-1}; MS (70eV) *m/z* (%): 369.19 (M + 1, 100); Anal. Calcd. for $C_{20}H_{17}ClN_2OS$: C 65.12, H 4.65, N 7.59; found C 65.05, H 4.53, N 7.67.

4i + 5i. ^{1}H NMR (DMSO, 300 MHz) δ: 2.34–2.90 (m, 4H, 6-H + 8-H), 3.27–3.47 (m, 1H, 7-H), 3.79 (s, 1H, -OCH_3), 5.21 and 5.24 (each s, 1H, 4-H), 6.76–7.36 (m, 9H, Ph-H), 9.70 and 9.76 (each s, 1H, 3-NH), 10.65 and 10.72 (each s, 1H, 1-NH); IR (KBr) ν: 3301, 1680, 1624, 1501 cm^{-1}; MS (70eV) *m/z* (%): 365.04 (M + 1, 100); Anal. Calcd. for $C_{21}H_{20}N_2O_2S$: C 69.20, H 5.53, N 7.69; found C 69.08, H 5.50, N 7.77.

4j + 5j. ^{1}H NMR (DMSO, 300 MHz) δ: 2.30–2.96 (m, 4H, 6-H + 8-H), 3.43–3.49 (m, 1H, 7-H), 3.71 (s, 1H, -OCH_3), 5.13 and 5.17 (each s, 1H, 4-H), 6.77–7.43 (m, 9H, Ph-H), 9.66 and 9.73 (each s, 1H, 3-NH), 10.61 and 10.68 (each s, 1H, 1-NH); IR (KBr) ν:3255, 1644, 1609, 1562, 1510 cm^{-1}; MS (70eV) *m/z* (%): 364.15 (M, 100); Anal. Calcd. for $C_{21}H_{20}N_2O_2S$: C 69.20, H 5.53, N 7.69; found C 69.32, H 5.47, N 7.58.

4k + 5k. ^{1}H NMR (DMSO, 300 MHz) δ: 2.25–2.85 (m, 4H, 6-H + 8-H), 3.10–3.30 (m, 1H, 7-H), 3.70 (s, 1H, -OCH_3), 5.17 and 5.18 (each s, 1H, 4-H), 6.80–7.32 (m, 10H, Ph-H), 7.75 and 7.80 (each s, 1H, 3-NH), 9.79 and 9.55 (each s, 1H, 1-NH); IR (KBr) ν: 3270, 1714, 1606, 1597, 1514 cm^{-1}; MS (70eV) *m/z* (%): 347.34 (M-1, 100); Anal. Calcd. for $C_{21}H_{20}N_2O_3$: C 72.40, H 5.79, N 8.04; found C 72.32, H 5.87, N 8.12.

4 l + 5 l. ^{1}H NMR (DMSO, 300 MHz) δ: 2.22–2.88 (m, 4H, 6-H + 8-H), 3.22–3.44 (m, 1H, 7-H), 3.72 (s, 1H, —OCH_3), 5.59 and 5.60 (each s, 1H, 4-H), 6.84–7.40 (m, 8H, Ph-H), 7.66 and 7.69 (each s, 1H, 3-NH), 9.56 and 9.62 (each s, 1H, 1-NH); IR (KBr) ν: 3291, 1717, 1636, 1596, 1498 cm^{-1}; MS (70eV) *m/z* (%): 383.12 (M + 1, 100); Anal. Calcd. for $C_{21}H_{19}ClN_2O_3$: C 65.88, H 5.00, N 7.32; found C 65.93, H 4.90, N 7.23.

4m. ^{1}H NMR (DMSO, 300 MHz) δ: 2.34–2.82 (m, 4H, 6-H + 8-H), 3.27–3.40 (m, 1H, 7-H), 3.72 (s, 1H, —OCH_3), 5.20 (s, 1H, 4-H), 6.85–7.27 (m, 8H, Ph-H), 7.80 (s, 1H, 3-NH), 9.57 (s, 1H, 1-NH); IR (KBr) ν:3331, 1723, 1611, 1600, 1509 cm^{-1}; MS (70eV) *m/z* (%): 381.26 (M-1, 100); Anal. Calcd. for $C_{21}H_{19}ClN_2O_3$: C 65.88, H 5.00, N 7.32; found C 65.82, H 5.07, N 7.25.

5m. ^{1}H NMR (DMSO, 300 MHz) δ: 2.40–2.75 (m, 4H, 6-H + 8-H), 3.35–3.43 (m, 1H, 7-H), 3.70 (s, 1H, -OCH_3), 5.18 (s, 1H, 4-H), 6.80–7.37 (m, 8H, Ph-H), 7.78 (s, 1H, 3-NH), 9.54

(s, 1H, 1-NH); IR (KBr) ν: 3335, 1723, 1610, 1603, 1512 cm^{-1}; MS (70eV) *m*/*z* (%): 381.26 (M-1, 100); Anal. Calcd. for $C_{21}H_{19}ClN_2O_3$: C 65.88, H 5.00, N 7.32; found C 65.81, H 5.08, N 7.22.

4n + 5n. ^{1}H NMR (DMSO, 300 MHz) δ: 2.34–2.82 (m, 4H, 6-H + 8-H), 3.35–3.43 (m, 1H, 7-H), 3.69 (s, 1H, —OCH_3), 3.72 (s, 1H, —OCH_3), 5.15 and 5.18 (each s, 1H, 4-H), 6.74–7.27 (m, 8H, Ph-H), 7.73 and 7.79 (each s, 1H, 3-NH), 9.48 and 9.54 (each s, 1H, 1-NH); IR (KBr) ν: 3341, 1712, 1637, 1608, 1515 cm^{-1}; MS (70eV) *m*/*z* (%): 377.33 (M-1, 100); Anal. Calcd. for $C_{22}H_{22}N_2O_4$: C 69.83, H 5.86, N 7.40; found C 69.92, H 5.78, N 7.31.

4o + 5o. ^{1}H NMR (DMSO, 300 MHz) δ: 2.28–2.87 (m, 3H, 6-H + 8-H), 3.16–3.31 (m, 1H, 6-H), 3.37–3.46 (m, 1H, 7-H), 3.71 (s, 1H, -OCH_3), 5.21 and 5.23 (each s, 1H, 4-H), 6.81–7.37 (m, 8H, Ph-H), 9.67 and 9.73 (each s, 1H, 3-NH), 10.60 and 10.67 (each s, 1H, 1-NH); IR (KBr) ν: 3358, 1701, 1595, 1567, 1502 cm^{-1}; MS (70eV) *m*/*z* (%): 365.14 (M + 1, 100); Anal. Calcd. for $C_{21}H_{20}N_2O_2S$: C 69.20, H 5.53, N 7.69; found C 69.33, H 5.46, N 7.75.

Determination of crystal structure. A colorless transparent crystal of size 0.30 mm × 0.20 mm × 0.15 mm was selected for the crystal structure measurement. The X-ray diffraction intensities were recorded by a Bruker SMART APEX CCD automatic diffractometer with graphite-monochromatized Mo Kα radiation (λ = 0.071073 nm) at 291(2)K. In the range of $2.05 < \theta < 25.99$, 9632 independent reflections were obtained. The structures were solved by direct methods using SHELXL-97 program. All the nonhydrogen atoms were refined on F^2 anisotropically with the full-matrix least squares method. Hydrogen atoms were added according to the theoretical methods.

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