Synthesis and Characterization of Benzochromeno[2,3-*b*] tetrahydroquinolinone Derivatives

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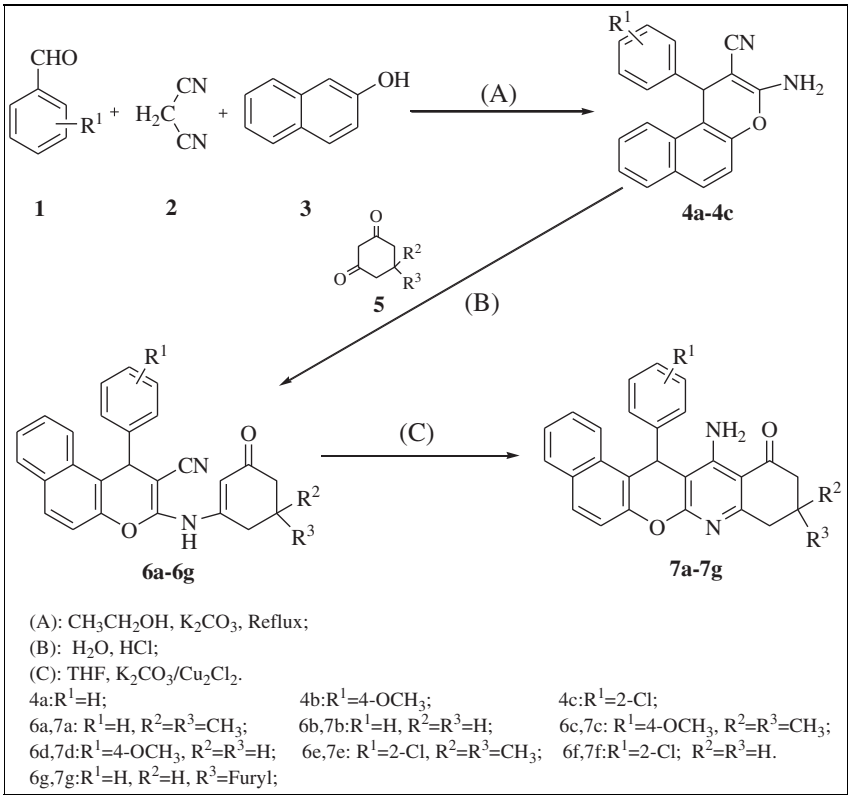

We report on a novel method for the preparation of a new series of benzochromeno[2,3-*b*]tetrahydroquinolin-1-one derivatives. The title compounds are prepared by the 5-substituted-1,3 -cyclohexanedione and 3-amino-1-aryl-1*H*-benzo[*f*]chromene-2-carbonitrile or 2-amino-4-aryl-4*H*-benzo[*h*]chromene-3-carbonitrile using dilute HCl, K_2CO_3, and Cu_2Cl_2 as catalysts. The method has the advantages of simple operation, high efficiency, and low toxicity. The structures of all compounds are characterized by elemental analysis, IR, MS, and ^{1}H NMR spectra. Two single crystals are characterized by using X-ray diffraction.

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INTRODUCTION

Alzheimer's disease is the most prevalent of the neurodegenerative diseases and main cause of dementia in elderly people [1]. Various therapeutic approaches have now been attempted to treat Alzheimer's disease by using agents such as acetylcholinesterase inhibitors, muscarinic agonists, or acethylcholine releasers [2]. Particularly, clinical trials of many acetylcholinesterase inhibitors have been conducted. Among them, 9-amino-1,2,3,4-tetrahydroacridine(Tacrine, THA) is the first cholinesterase inhibitor approved in the USA for symptomatic treatment of Alzheimer's disease [3]. It is a centrally acting reversible cholinesterase inhibitor [4], but the poor selectivity of this drug for acetylcholinesterase resulted in a number of side effects, especially hepatotoxicity [5]. Even though, considerable amount of THA derivatives and its analogues were synthesized to find compounds with reduced side effects [6]. This study is focused to analogues of THA.

Herein, we tried to use 1,3-cyclohexanedione and chromenes for the synthesis of benzochromeno-[2,3-*b*] tetrahydroqu-inolin-1-one derivatives.

Hydrochloric acid has emerged as an inexpensive, non-toxic, nonmetallic, readily available and environmental catalyst for various organic transformations, which has been reviewed recently. Designing organic reaction in aqueous media is another attractive area in chemistry [7]. Herein, we

tried to use hydrochloric acid as a catalyst to synthesize benzochromeno[2,3-*b*]tetrahydroquinolin-1-one derivatives in aqueous media.

RESULTS AND DISCUSSION

Initially, a one-pot synthesis of 3-amino-1-aryl-1*H*-benzo [*f*]chromene-2-carbonitrile **4** was achieved when aromatic aldehydes, malononitrile, and 2-naphthol were heated at 80°C using K_2CO_3 as catalyst in ethanol [8]. Thus, compound **4** reacted with 5-substituted-1,3-cyclohexanedione using dilute hydrochloric acid (50 mmol/L) as catalyst in aqueous media to give compound **6**. And the title compound **7** was obtained in THF using K_2CO_3/Cu_2Cl_2 as catalysts. The synthetic pathways are shown in Scheme 1.

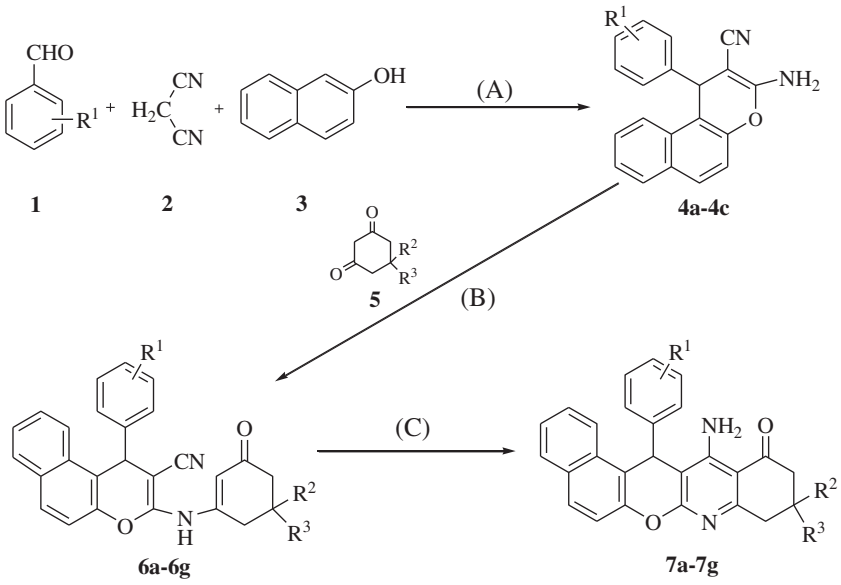
Then, we extended our investigations by using 1-naphthol as the starting materials instead of 2-naphthol. We found that it also easily reacted with aromatic aldehydes and malononitrile in good yields. The compounds **6′** and **7′** were prepared following the method given for **6** and **7**. The synthetic pathways are shown in Scheme 2.

5-Substituted-1,3-cyclohexanedione reacted with compound **4** using dilute HCl as catalyst in water. Taking **7a** for example, various trial reactions were investigated to choose the best reaction conditions; the result is summarized in Tables 1. and 2. We have noted that the reaction temperature should be higher than 80°C. We guessed that there were two types of 5-substituted-1,3-cyclohexanedione in the water: ketenes and enol. When the reaction temperature was higher than 80°C, 5-substituted-1,3-cyclo-hexanedione was in the type of enol. It has also been observed that the amount and concentration of catalyst played a crucial role in the success of the reaction in terms of the rate and the yields. The reaction could not be carried out in the absence of the catalyst. It was found that the best conditions were at 80–100°C and the ratio of 5-substituted-1,3-cyclohexanediones (mmol) : compound **4a** (mmol):50 mmol/L HCl (mmol) was 5:5:2.

Under the optimized conditions, various substituted aromatic aldehydes were reacted with malononitrile and naphthol to obtain the corresponding products (Tables 3. and 4.), and the reactions were all successful. From these observations, we may conclude that the nature of the substituent on the aromatic rings does not have any significant role in determining the course of the reaction.

Crystal structure. A summary of the crystal data and structure refinement is presented in Table 5. A perspective view of compound **6c** with atomic numbering scheme is shown in Figure 1. In compound **6c**, The dihedral angle between the bond lengths and bond angles are generally normal in the phenyl and quinoline ring, and the quinoline

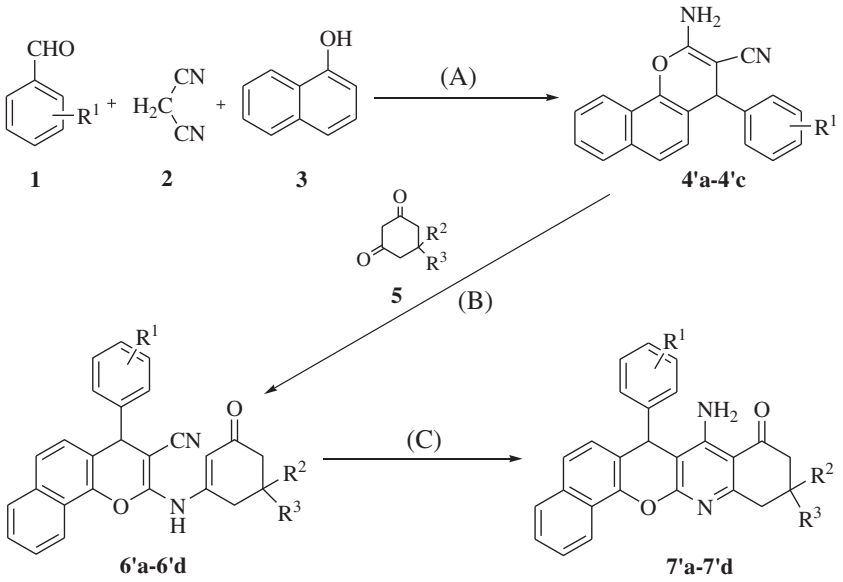
Scheme 1. The synthetic route of benzo[*f*]chromeno[2,3-*b*]tetrahydroquinolin-1-one derivatives.



(A): CH_3CH_2OH, K_2CO_3, Reflux;
(B): H_2O, HCl;
(C): THF, K_2CO_3/Cu_2Cl_2.

4a:R^1=H; 4b:R^1=4-OCH_3; 4c:R^1=2-Cl;
6a,7a: R^1=H, R^2=R^3=CH_3; 6b,7b:R^1=H, R^2=R^3=H; 6c,7c: R^1=4-OCH_3, R^2=R^3=CH_3;
6d,7d:R^1=4-OCH_3, R^2=R^3=H; 6e,7e: R^1=2-Cl, R^2=R^3=CH_3; 6f,7f:R^1=2-Cl; R^2=R^3=H.
6g,7g:R^1=H, R^2=H, R^3=Furyl;

Scheme 2. The synthetic route of benzo[*h*]chromeno[2,3-*b*]-tetrahydroquinolin-1-one derivatives.



(A): CH_3CH_2OH, K_2CO_3, Reflux;
(B): H_2O, HCl;
(C): THF, K_2CO_3/Cu_2Cl_2.
4'a:R^1=H; 4'b:R^1=4-OCH_3; 4'c:R^1=2-Cl;
6'a,7'a: R^1=H, R^2=R^3=CH_3; 6'b,7'b:R^1=H, R^2=R^3=H; 6'c,7'c: R^1=4-OCH_3, R^2=R^3=H;
6'd,7'd:R^1=2-Cl, R^2=R^3=H;

Table 1

The reaction temperature of synthesis of compound 7**a**.

Entry	Reaction temperature (°C)	Time (h)	Yield (%)
1	40	4	3.8
2	50	4	8.8
3	60	4	12.8
4	70	4	30.6
5	80	4	50.4
6	90	4	50.6
7	100	4	50.6

Table 2

Compound 7**a** synthesis catalyzed by the various amount of hydrochloric acid(50 mmol/L HCl).

Entry	Amount of HCl (mL)	Time (h)	Yield (%)
1	0	4	0
2	20	4	36.8
3	30	4	42.8
4	40	4	50.6
5	50	4	45.6
6	60	4	42.2
7	70	4	39.8

Table 3

The melting point and yield of benzochromene derivatives.

Entry	R^1	R^2	R^3	mp (°C)	Yield (%)
4a	H	/	/	>260	91.4
4b	H	/	/	190–192	90.8
4c	4-OCH_3	/	/	256–258	92.2
4′a	H	/	/	206–208	90.6
4′b	H	/	/	188–190	88.6
4′c	4-OCH_3	/	/	238–240	91.6
6a	H	CH_3	CH_3	218–220	60.6
6b	H	H	H	236–238	62.8
6c	4-OCH_3	CH_3	CH_3	190–192	57.6
6d	4-OCH_3	H	H	216–218	58.2
6e	2-Cl	CH_3	CH_3	242–244	60.6
6f	2-Cl	H	H	206–208	63.6
6g	H	H	Furyl	224–226	46.6
6′a	H	CH_3	CH_3	246–248	55.8
6′b	H	H	H	238–240	56.2
6′c	4-OCH_3	H	H	214–216	54.8
6′d	2-Cl	H	H	256–258	58.6

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

Table 4

The melting point and yield of benzochromene[2,3-*b*]quinolinone derivatives.

Entry	R^1	R^2	R^3	mp (°C)	Yield (%)
7a	H	CH_3	CH_3	>260	50.6
7b	H	H	H	>260	51.8
7c	4-OCH_3	CH_3	CH_3	256–258	48.6
7d	4-OCH_3	H	H	202–204	49.8
7e	2-Cl	CH_3	CH_3	248–250	51.6
7f	2-Cl	H	H	192–194	51.8
7g	H	H	Furyl	234–236	36.8
7′a	H	CH_3	CH_3	226–228	50.8
7′b	H	H	H	196–198	52.8
7′c	4-OCH_3	H	H	232–234	47.8
7′d	2-Cl	H	H	202–204	51.2

Table 5

Crystallographic data for crystallographic data for complex **6c**.

Complex	**$C_{29}H_{26}N_20_3.C_2H_5OH$**
Empirical formula	C_{31} H_{32} N_2 O_4
Formula weight	496.59
Wavelength (Å)	0.71073
Space group	*P* 21/c
Crystal system	triclinic
a (Å)	10.969(2)
b (Å)	15.260(3)
c (Å)	18.208(3)
α (°)	90.00
β (°)	120.213(10)
γ (°)	90.00
Volume (Å^3), Z	2633.8(9), 4
D_{calc} (g/cm^3)	1.252
Absorption coefficient	0.931
F(0 0 0)	407
Crystal size (mm^3)	0.25 × 0.15 × 0.10
Transmission max/min	0.986/0.991
θ range for data collection (°)	2.2-26.8
Limiting indices	$-13 \le h \le 13$, $-18 \le k \le 16$, $-13 \le l \le 22$
Reflection collected	5177
Independent reflections	3932
(R_{int})	0.0365
Goodness-of-fit(GOF)on F^2	1.004
R_1	0.0455, 0.0570
wR_2	0.1359, 0.1418
Largest difference in peak and hole (e Å^{-3})	0.19 and −0.31

(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 **6c** in a unit cell is 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 are listed in Table 6.

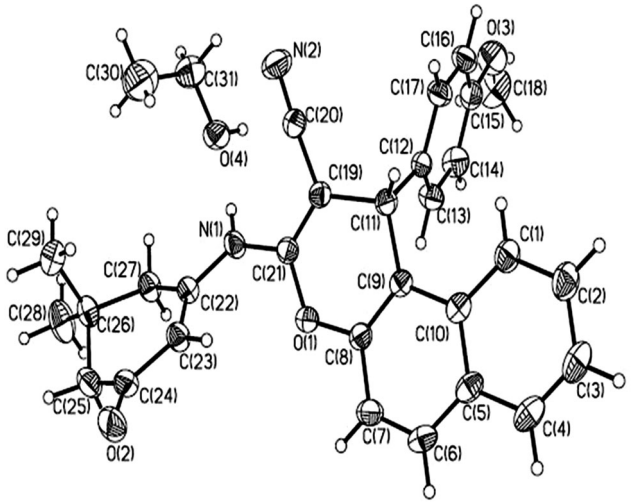


Figure 1. ORTEP plot of compound **6c**. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

The data of ^{1}H NMR, MS, and IR shown in the experimental section were in accordance with the chemical structures of the target compounds. And finally, the structures as well as the relative stereochemistry of compounds **6c** (Fig. 1.) and **7d** (Fig. 3.) were confirmed by X-ray crystallographic analysis. From the structure, it was found that the cyclohexyl ring adopted a half-boat conformation in case of compound **6c**. The existence of the solvent ethanol moleculars in the crystal links all molecules into a three-dimensional supermolecular structure by the intermolecular N—H···O and O—H···O hydrogen bonds. And compound **7d** is a plane structure.

CONCLUSION

In summary, a novel methodology is reported for the synthesis of new benzochromeno[2,3-*b*]tetrahydroquinolin-1-one derivatives. Although it needs two steps, we used nontoxic solvent and catalyst in the first step, and there was no need to handle intermediates **6** for the next step. Compared with the methods in the past, the new method has many advantages such as reduced pollution, good yields, and lower cost. In addition, the optimum conditions are under investigation here. The reaction temperature should be higher than 80°C, and the most suitable ratio of 5-substituted-1, 3-cyclohexanediones (mmol) : compound **4a** (mmol) : 50 mmol/L HCl (mL) is 5: 5: 2.

EXPERIMENTAL

Melting points were determined on an electrothermal apparatus, and the temperature was not calibrated. Micro-analysis was

Table 6

Inter- and intramolecular interaction distances (Å) for the compound **6c**.

D–H···A	*D–H*	*H···A*	*D···A*	*D–H···A*	**Symmetry**
N(1) – H(1A)···O(4)	0.86	1.92	2.7732	174.9	x, y, z
O(4) – H(4B)···O(2)	0.82	1.84	2.6548	177.0	x,-y + 1/2,z + 1/2

performed by the Perkin-Elmer (Waltham, Massachusetts) 2400 Microanalytical Service. Infrared spectra were recorded as thin films on KBr using a Perkin-Elmer (Waltham, Massachusetts) 1700 spectrophotometer. The ^{1}H NMR spectra were recorded by a Bruker (Switzerland) ARX-300 spectrometer. Sample solutions were prepared in $CDCl_3$ or DMSO-d_6 containing TMS as an internal standard. Mass spectra were recorded by Agilent-6110 (Santa Clara, California).

All chemical reagents were commercially available and purified with standard methods before use. Solvents were dried in routine ways and redistilled. 5-Substituted-1,3-cyclo-hexanedione **1** were obtained from aromatic aldehyde, acetone, and dimethyl molanate according to the literature method with slight modification.

General procedure for the synthesis of 3-amino-1-aryl-1*H*-benzo[*f*]chromene-2-carbonitrile (4a–4c). To a solution of corresponding aldehyde (10 mmol), malononitrile (10 mmol) and 2-naphthol (10 mmol) in ethanol (50 mL) were added K_2CO_3 (0.0828 g) at room temperature. The mixture was stirred at 80°C for 4 h, and then, the reaction mixture was cooled to room temperature. The solid was isolated by filtration, washed with cold ethanol, and recrystallized from methanol.

General procedure for the synthesis of 2-amino-4-aryl-4*H*-benzo[*h*]-chromene-3-carbonitrile (4′a–4′c). The compounds **4′a–4′c** were synthesized according to the method of the compounds **4a–4c**.

General procedure for the synthesis of 3-(5-substituted-3-oxocyclohex-1-enylamino) 1-aryl-1*H*-benzo[*f*]-chromene-2-carbonitrile (6a–6g). 3-Amino-1-aryl-1*H*-benzo[*f*]chromene-2-carbonitrile (5 mmol) and 5-substituted-1,3-cyclo-hexan- edione (6 mmol) were suspended in water (1 mL/mmol) containing 50 mmol/L HCl. The mixture was refluxed for 4 h. At the end of the reaction, the mixture was chilled to room temperature, and the compound was filtered off. The yellow powder was recrystallized from ethyl acetate.

General procedure for the synthesis of 2-(5-substituted-3-oxocyclohex-1-enylamino)-4-aryl-4*H*- benzo-[*h*]chromene-3-carbonitrile(6′a–6′d). The compounds **6′a–6′d** were synthesized according to the method given for the compounds **6a–6d**.

General procedure for the synthesis of 14-amino-2,3,4,13-tertrahydro-3-substituted-13-aryl-1*H* -benzo-[*f*]chromene[2,3-*b*]quinolin-1-one (7a–7g). The mixture of the last step was added to THF (1 mL/mmol) that contains K_2CO_3 (2.5 mmol) and Cu_2Cl_2 (1.25 mmol). The reaction mixture was refluxed for 2 h. Then, the precipitate was filtered off and washed with ethanol. The yellow powder was purified by silica gel flash

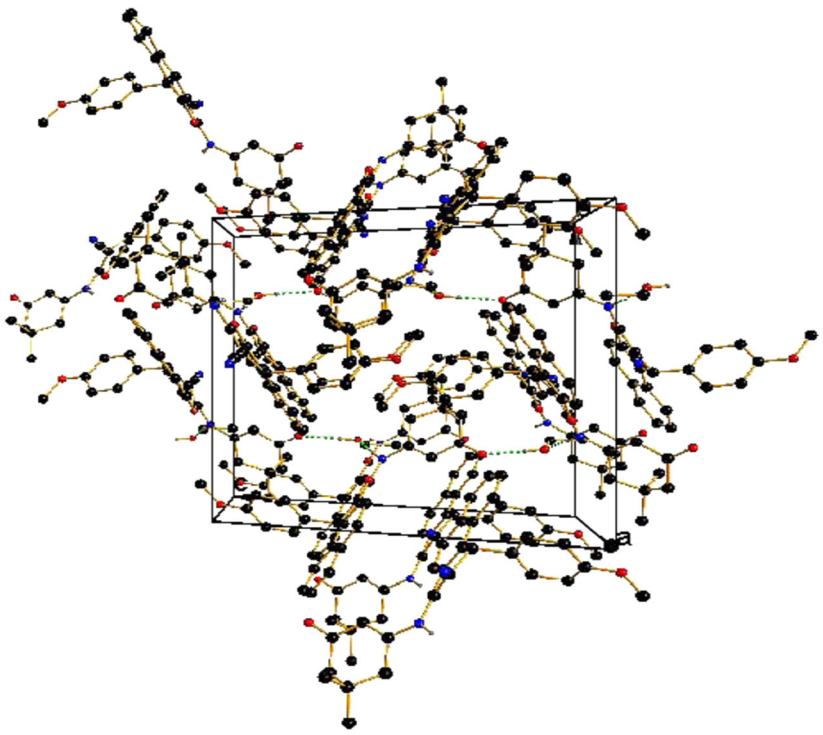


Figure 2. Packing diagram of compound **6c** in unit-cell. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

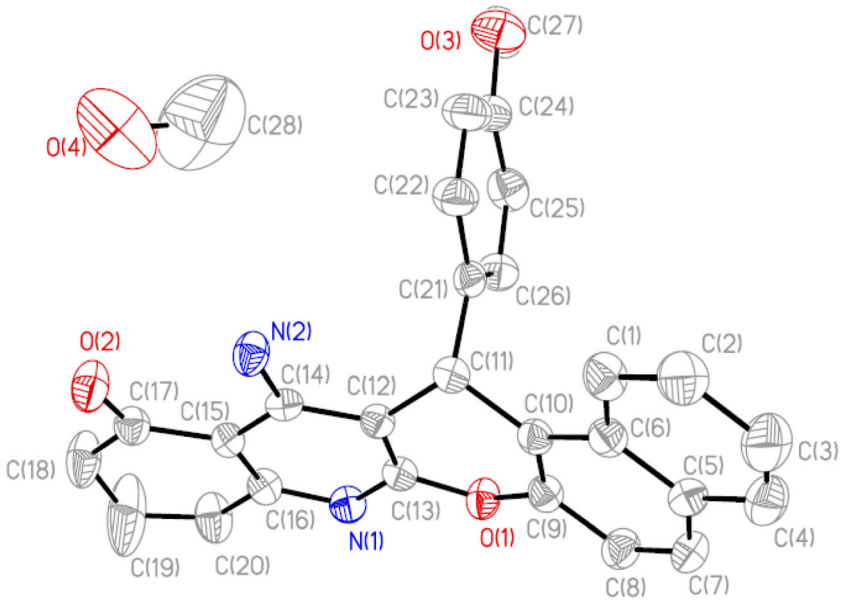


Figure 3. ORTEP plot of compound **7d**. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

chromatography using ethyl acetate/hexane mixture (1:2, v/v) as eluent to give pure compounds.

General procedure for the synthesis of 14-amino-2,3,4,13-tertrahydro-3-substituted-13-aryl-1*H*-benzo-[*h*]chromene[2,3-*b*] quinolin-1-one (7′a–7′d). The compounds **7′a–7′d** were synthesized following the method given for the compounds **7a–7g**.

Data of compounds are shown in the succeeding sections.

***3-Amino-1-phenyl-1H*-benzo[*f*]-chromene-2-carbonitrile (4a).** Yield: 91.4%, mp > 260°C; ^{1}H NMR (DMSO-d_6, 300 Hz) δ: 5.29 (s, 1H, 4H), 6.97–7.14 (m, 3H, Ph-H), 7.17 (br s, 2H, NH_2), 7.19–7.95 (m, 8H, Ph-H), IR (KBr) υ: 3340 (NH), 2183 (C≡N); MS (ESI) *m/z*: 299.1 (M + 1). *Anal*. Calcd for $C_{20}H_{14}N_2O$: C 80.52, H 4.73, N 9.39; found C 80.40, H 4.74, N 9.41.

***3-Amino-1-(4-methoxy-phenyl)-1H*-benzo[*f*]chromene-2-carbonitrile (4b).** Yield: 90.8%, mp 190–192°C; ^{1}H NMR ($CDCl_3$, 300 Hz) δ: 3.74 (s, 3H, OCH_3), 5.21 (s, 1H, 4-H), 6.77–7.13 (m, 4H, Ph-H),7.19 (br s, 2H, NH_2), 7.23–7.86 (m, 10H, Ph-H), IR (KBr) υ: 3323 (NH), 2193 (C ≡ N); MS (ESI) *m/z*: 329.1 (M + 1). *Anal*. Calcd for $C_{21}H_{16}N_2O_2$: C 76.81, H 4.91, N 8.53; found C 76.45, H 4.94, N 8.56.

***3-Amino-1-(2-chlorophenyl)-1H*-benzo[*f*]chromene-2-carbonitrile (4c).** Yield: 92.2%, mp 256–258°C; ^{1}H NMR (DMSO, 300 Hz) δ: 5.71 (s, 1H, 4-H), 6.97–7.05 (m, 4H, Ph-H), 7.17–7.21 (m, 4H, NH_2 + Ph-H), 7.32–7.99 (m, 5H, Ph-H), IR (KBr) υ: 3348 (NH), 2179 (C≡N); MS (ESI) *m/z*: 333.0 (M + 1). *Anal*. Calcd for $C_{20}H_{13}ClN_2O$: C 72.18, H 3.94, N 8.42; found C 71.89, H 3.99, N 8.47.

***2-Amino-4-phenyl-4H*-benzo[*h*]-chromene-3-carbonitrile (4′a).** Yield: 90.6%, mp 206–208°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 4.89 (s, 1H, 4-H), 7.08–7.33 (m, 8H, NH_2 + Ph-H), 7.54–8.23 (m, 11H, Ph-H), IR (KBr) υ: 3385 (NH), 2179 (C≡N); MS (ESI) *m/z*: 299.1 (M + 1). *Anal*. Calcd for $C_{20}H_{14}N_2O$: C 80.52, H 4.73, N 9.39; found C 80.41, H 4.74, N 9.43.

***2-Amino-4-(4-methoxy-phenyl)-4H*-benzo[*h*]-chromene-3-carbonitrile (4′b).** Yield: 88.6%, mp 188–190°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.79 (s, 3H, OCH_3) 4.84 (s, 1H, 4-H), 6.84–7.16 (m, 6H, Ph-H), 7.18 (br s, 2H, NH_2), 7.52–8.19 (m, 4H, Ph-H), IR (KBr) υ: 3356 (NH), 2138 (C≡N); MS (ESI) *m/z*: 329.2 (M + 1). *Anal*. Calcd for $C_{21}H_{16}N_2O_2$: C 76.81, H 4.91, N 8.53; found C 76.47, H 4.93, N 8.57.

***2-Amino-4-(2-chlorophenyl)-4H*-benzo[*h*]-chromene-3-carbonitrile (4′c).** Yield: 91.6%, mp 238–240°C; ^{1}H NMR ($CDCl_3$, 300 Hz) δ: 5.57 (s, 1H, 4-H), 7.06–7.19 (m, 4H, Ph-H), 7.20 (br s, 2H, NH_2), 7.27–7.81 (m, 6H, Ph-H), IR (KBr) υ: 3368 (NH), 2098 (C≡N); MS (ESI) *m/z*: 333.1 (M + 1). *Anal*. Calcd for $C_{20}H_{13}ClN_2O$: C 72.18, H 3.94, N 8.42; found C 71.88, H 3.98, N 8.48.

***3-(5,5-Dimethyl-3-oxocyclohex-1-enylamino)-1-phenyl-1H*-benzo[*f*]chromene-2-carbonitrile (6a).** Yield: 60.6%, mp 218–220°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.13, 1.14 (each s, each 3H, CH_3), 2.28–2.34 (m, 2H, 4′-H), 2.38–2.43 (m, 2H, 6′-H), 5.33 (s, 1H, 1-H), 5.99 (s, 1H, 2′-H), 6.39 (brs, 1H, NH), 7.19–7.89 (m, 11H, Ph-H), IR (KBr) υ: 3285 (NH), 1619 (C=O), 2216 (C≡N); MS (ESI) *m/z*: 421.1 (M + 1). *Anal*. Calcd for $C_{20}H_{24}N_2O_2$: C 79.98, H 5.75, N 6.66; found C 79.89, H 5.83, N 6.71.

***3-(3-Oxocyclohex-1-enylamino)-1-phenyl-1H*-benzo[*f*]chromene-2-carbonitrile (6b).** Yield: 62.8%, mp 236–238°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.03–2.12 (m, 2H, 5′-H), 2.39–2.46 (m, 2H, 6′-H), 2.51–2.61 (m, 2H, 4′-H), 5.32 (s, 1H, 1-H), 5.95 (s, 1H, 2′-H), 6.54 (brs, 1H, NH), 7.19–7.96 (m, 11H, Ph-H), IR (KBr) υ: 3213 (NH), 1658 (C=O), 2257 (C≡N); MS (ESI) *m/z*: 393.2 (M + 1). *Anal*. Calcd for $C_{26}H_{20}N_2O_2$: C 79.57, H 5.14, N 7.14; found C 79.45, H 5.17, N 7.19.

***3-(5,5-Dimethyl-3-oxocyclohex-1-enylamino)-1-(4-methoxy-phenyl)-1H*-benzo[*f*]chromene-2-carbonitrile (6c).** Yield: 57.6%, mp 190–192°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.13 (m, 6H, CH_3), 2.28–2.43 (m, 4H, 4′ + 6′-H), 3.73 (s, 3H, OCH_3), 5.27 (s, 1H, 1-H), 5.98 (s, 1H, 2′-H), 6.47 (brs, 1H, NH), 6.82–7.87 (m, 10H, Ph-H), IR (KBr) υ: 3318 (NH), 1582 (C=O), 2263 (C≡N); MS (ESI) *m/z*: 451.2 (M + 1). *Anal*. Calcd for $C_{29}H_{26}N_2O_3$: C 77.31, H 5.82, N 6.22; found C 77.19, H 5.89, N 6.30.

***3-(3-Oxocyclohex-1-enylamino)-1-(4-methoxy-phenyl)-1H*-benzo[*f*]chromene-2-carbonitrile (6d).** Yield: 58.2%, mp 216–218°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.04–2.14 (m, 2H,

5′-H), 2.41–2.46 (m, 2H, 6′-H), 2.48–2.61 (m, 2H, 4′-H), 3.74 (s, 3H, OCH_3), 5.32 (s, 1H, 1-H), 5.93 (s, 1H, 2′-H), 6.52 (brs, 1H, NH), 7.19–8.06 (m, 11H, Ph-H), IR (KBr) υ: 3238 (NH), 1668 (C=O), 2287 (C≡N); MS (ESI) *m/z*: 423.2 (M + 1). *Anal*. Calcd for $C_{27}H_{22}N_2O_3$: C 76.76, H 5.25, N 6.63; found C 76.52, H 5.32, N 6.69.

***3-(5,5-Dimethyl-3-oxocyclohex-1-enylamino)-1-(2-chlorophenyl)-1H*-benzo[*f*]chromene-2-carbonitrile (6e)**. Yield: 60.6%, mp 242–244°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.14, 1.15 (each s, each 3H, CH_3), 2.30–2.46 (m, 4H, 4′ + 6′-H), 5.94 (s, 1H, 1-H), 6.06 (s, 1H, 2′-H), 6.74 (brs, 1H, NH), 7.06–7.49 (m, 10H, Ph-H), IR (KBr) υ: 3264 (NH), 1654 (C=O), 2263 (C≡N); MS (ESI) *m/z*: 455.2 (M + 1). *Anal*. Calcd for $C_{28}H_{23}ClN_2O_2$: C 73.92, H 5.10, N 6.16; found C 73.78, H 5.18, N 6.23.

***3-(3-Oxocyclohex-1-enylamino)-1-(2-chlorophenyl)-1H*-benzo[*f*]chromene-2-carbonitrile (6f)**. Yield: 63.6%, mp 206–208°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.06–2.14 (m, 2H, 5′-H), 2.41–2.45 (m, 2H, 6′-H), 2.53–2.54 (m, 2H, 4′-H), 5.98–6.01 (m, 2H, 1 + 2′-H), 6.41 (brs, 1H, NH), 6.92–7.86 (m, 10H, Ph-H), IR (KBr) υ: 3228 (NH), 1638 (C=O), 2247 (C≡N); MS (ESI) *m/z*: 427.1 (M + 1). *Anal*. Calcd for $C_{26}H_{19}ClN_2O_2$: C 73.15, H 4.49, N 6.56; found C 72.98, H 4.57, N 6.62.

***3-(5′-Furanly-3-oxocyclohex-1-enylamino)-1-phenyl-1H*-benzo[*f*]chromene-2-carbonitrile (6g)**. Yield: 46.6%, mp 224–226°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.05–2.87 (m, 4H, 6′-H, 4′-H), 3.49–3.59 (m, 1H, 5′-H), 5.32 (s, 1H, 1-H), 5.99 (s, 1H, 5′ + 5″-H), 6.09–6.12 (m, 1H, 5′ + 4″-H), 6.12–6.33 (5′ + 3″-H), 6.47 (brs, 1H, NH-H), 7.18–7.89 (m, 11H, Ph-H), IR (KBr) υ: 3228 (NH), 1638 (C=O), 2247 (C≡N); MS (ESI) *m/z*: 459.2 (M + 1). *Anal*. Calcd for $C_{30}H_{22}N_2O_3$: C 78.59, H 4.84, N 6.11; found C 78.40, H 4.91, N 6.19.

***2-(5,5-Dimethyl-3-oxocyclohex-1-enylamino)-4-phenyl-4H*-benzo[*h*]chromene-3-carbonitrile (6′a)**. Yield: 55.8%, mp 226–228°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.13, 1.14 (each s, each 3H, CH_3), 2.33 (s, 2H, 4′-H), 2.44 (s, 2H, 6′-H), 4.97 (s, 1H, 1-H), 6.08 (s, 1H, 2′-H), 6.90 (brs, 1H, NH-H), 7.22–7.83 (m, 11H, Ph-H), IR (KBr) υ: 3325 (NH), 1719 (C=O), 2256 (C≡N); MS (ESI) *m/z*: 421.2 (M + 1). *Anal*. Calcd for $C_{20}H_{24}N_2O_2$: C 79.98, H 5.75, N 6.66; found C 79.87, H 5.81, N 6.73.

***2-(3-Oxocyclohex-1-enylamino)-4-phenyl-4H*-benzo[*h*]chromene-3-carbonitrile (6b′)**. Yield: 56.2%, mp 238–240°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.06–2.14 (m, 2H, 5′-H), 2.43–2.47 (m, 2H, 6′-H), 2.56–2.61 (m, 2H, 4′-H), 4.96 (s, 1H, 1-H), 6.02 (s, 1H, 2′-H), 6.82 (brs, 1H, NH-H), 7.00–8.15 (m, 11H, Ph-H), IR (KBr) υ: 3283 (NH), 1658 (C=O), 2287 (C≡N); MS (ESI) *m/z*: 393.2 (M + 1). *Anal*. Calcd for $C_{26}H_{20}N_2O_2$: C 79.57, H 5.14, N 7.14; found C 79.42, H 5.18, N 7.18.

***2-(3-Oxocyclohex-1-enylamino)-4-(4-methoxy-phenyl)-4H*-benzo[*h*]chromene-3-carbonitrile (6c′)**. Yield: 54.8%, mp 214–216°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.14–1.15 (m, 6H, CH_3), 2.24–2.43 (m, 4H, 4′ + 6′-H), 3.75 (s, 3H, OCH_3), 5.23 (s, 1H, 1-H), 5.61 (s, 1H, 2′-H), 6.57 (brs, 1H, NH), 6.78–7.86 (m, 10H, Ph-H), IR (KBr) υ: 3358 (NH), 1587 (C=O), 2268 (C≡N); MS (ESI) *m/z*: 451.1 (M + 1). *Anal*. Calcd for $C_{27}H_{22}N_2O_3$: C 76.76, H 5.25, N 6.63; found C 76.50, H 5.31, N 6.69.

***2-(3-Oxocyclohex-1-enylamino)-4-(2-chlorophenyl)-4H*-benzo[*h*]chromene-3-carbonitrile (6d′)**. Yield: 58.6%, mp 256–258°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.09–2.17 (m, 2H, 5′-H), 2.45–2.50 (m, 2H, 6′-H), 2.58–2.61 (m, 2H, 4′-H), 5.64 (s, 1H, 1-H), 6.08 (s, 1H, 2′-H), 6.73 (brs, 1H, NH), 7.01–7.63 (m, 10H, Ph-H), IR (KBr) υ: 3325 (NH), 1678 (C=O), 2247 (C≡N); MS (ESI) *m/z*: 426.4 (M + 1). *Anal*. Calcd for $C_{26}H_{19}ClN_2O_2$: C 73.15, H 4.49, N 6.56; found C 72.97, H 4.57, N 6.63.

***14-Amino-2,3,4,13-tertrahydro-3,3-dimethyl-13-phenyl-1H*-benzo[*f*]chromene[2,3-*b*]quinolin-1-one (7a)**. Yield: 50.6%, mp >260°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.09,1.10 (each s, each 3H, 6H, CH_3), 2.46 (s, 2H, 2-H), 2.87 (s, 2H,4-H), 5.58 (s, 1H, 13-H), 6.43 (br s, 1H, NH), 7.10–8.12 (m, 11H, Ph-H), 9.21 (br s, 1H, NH), IR (KBr) υ: 3296, 1561, 1142, 1093; MS (ESI) *m/z*: 421.2 (M + 1). *Anal*. Calcd for $C_{20}H_{24}N_2O_2$: C 79.98, H 5.75, N 6.66; found C 79.82, H 5.85, N 6.70.

***14-Amino-2,3,4,13-tertrahydro-13-phenyl-1H*-benzo[*f*]chromenequinolin-1-one (7b)**. Yield: 51.8%, mp >260°C; ^{1}H NMR ($CDCl_3$, 300 Hz) δ: 1.24–2.13 (m, 2H, 4-H), 2.55–2.64 (m, 2H,3-H), 2.92–3.10 (m, 2H, 2-H), 5.57 (s, 1H, 13-H), 6.45 (br s, 1H, NH), 7.10–8.13 (m, 11H, Ph-H), 9.23 (br s, 1H, NH), IR (KBr) υ: 3286, 1568, 1146, 1112; MS (ESI) *m/z*: 393.2 (M + 1). *Anal*. Calcd for $C_{26}H_{20}N_2O_2$: C 79.57, H 5.14, N 7.14; found C 79.43, H 5.19, N 7.17.

***14-Amino-2,3,4,13-tertrahydro-3,3-dimethyl-13-(4-methoxy-phenyl)-1H*-benzo[*f*]chromene[2,3-*b*]-quinolin-1-one (7c)**. Yield: 48.6%, mp 256–258°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.08,1.09 (each s, each 3H, 6H, CH_3), 2.46 (s, 2H, 2-H), 2.88 (s, 2H,4-H), 3.68 (s, 3H, OCH_3), 5.53 (s, 1H, 13-H), 6.41 (br s, 1H, NH), 7.27–8.11 (m, 10H, Ph-H), 9.20 (br s, 1H, NH), IR (KBr) υ: 3336, 1581, 1152, 1098; MS (ESI) *m/z*: 451.3 (M + 1). *Anal*. Calcd for $C_{29}H_{26}N_2O_3$: C 77.31, H 5.82, N 6.22; found C 77.17, H 5.89, N 6.29.

***14-Amino-2,3,4,13-tertrahydro-13-(4-methoxy-phenyl)-1H*-benzo[*f*]chromene[2,3-*b*]quinolin-1-one (7d)**. Yield: 49.8%, mp 202–204°C; ^{1}H NMR ($CDCl_3$, 300 Hz) δ: 2.07–2.11 (m, 2H, 4-H), 2.60–2.64 (m, 2H,3-H), 3.01–3.05 (m, 2H, 2-H), 3.69 (s, 3H, OCH_3), 5.54 (s, 1H, 13-H), 6.65 (br s, 1H, NH), 7.27–8.09 (m, 10H, Ph-H), 9.25 (brs, 1H, NH), IR (KBr) υ: 3296, 1608, 1186, 1120; MS (ESI) *m/z*: 423.2 (M + 1). *Anal*. Calcd for $C_{27}H_{22}N_2O_3$: C 76.76, H 5.25, N 6.63; found C 76.50, H 5.30, N 6.67.

***14-Amino-2,3,4,13-tertrahydro-3,3-dimethyl-13-(2-chlorophenyl)-1H*-benzo[*f*]chromene[2,3-*b*]-quinolin-1-one (7e)**. Yield: 51.6%, mp 248–250°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.42 (d, 6H, CH_3), 2.29–2.47 (m, 4H, 2-H, 4-H), 5.90 (m, 1H, 13-H), 6.46 (br s, 1H, NH), 7.08–7.83 (m, 10H, Ph-H), 9.18 (br s, 1H, NH), IR (KBr) υ: 3316, 1602, 1182, 1068; MS (ESI) *m/z*: 455.1 (M + 1). *Anal*. Calcd for $C_{28}H_{23}ClN_2O_2$: C 73.92, H 5.10, N 6.16; found C 73.77, H 5.20, N 6.25.

***14-Amino-2,3,4,13-tertrahydro-13-(2-chlorophenyl)-1H*-benzo[*f*]chromene[2,3-*b*]quinolin-1-one (7f)**. Yield: 51.8%, mp 192–194°C; ^{1}H NMR ($CDCl_3$, 300 Hz) δ: 2.08–2.11 (m, 2H, 4-H), 2.58–2.64 (m, 2H,3-H), 3.00–3.05 (m, 2H, 2-H), 5.54 (s, 1H, 13-H), 6.68 (br s, 1H, NH), 7.17–8.11 (m, 10H, Ph-H), 9.26 (brs, 1H, NH), IR (KBr) υ: 3316, 1668, 1192, 1108; MS (ESI) *m/z*: 423.2 (M + 1). *Anal.* Calcd for $C_{26}H_{19}ClN_2O_2$: C 73.15, H 4.49, N 6.56; found C 72.95, H 4.57, N 6.65.

***14-Amino-2,3,4,13-tertrahydro-3-furanly-13-(2-chlorophenyl)-1H*-benzo[*f*]chromene[2,3-*b*]-quinolin-1-one (7g)**. Yield: 36.8%, mp 234–236°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.53–3.28 (m, 4H, 6′-H, 4′-H), 3.58–3.61 (m, 1H, 5′-H), 5.34 (s, 1H, 1-H), 5.89 (s, 1H, 5′ + 5″-H), 6.13–6.18 (m, 1H, 5′ + 4″-H), 6.57 (brs, 1H, NH-H), 7.18–7.89 (m, 11H, Ph-H), 7.21–7.33 (m, 1H, 5′ + 3″-H), IR (KBr) υ: 3336, 1678, 1216, 1138; MS (ESI) *m/z*: 459.1 (M + 1). *Anal*. Calcd for $C_{30}H_{22}N_2O_3$: C 78.59, H 4.84, N 6.11; found C 78.38, H 4.93, N 6.19.

***14-Amino-2,3,4,13-tertrahydro-3,3-dimethyl-13-phenyl-1H-*benzo[*h*]chromene[2,3-*b*]quinolin-1-one (7′a)**. Yield: 50.8%, mp 226–228°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.10, 1.11 (each s, each 3H, 6H, CH_3), 2.47 (s, 2H, 2-H), 2.85 (s, 2H,4-H), 5.54 (s, 1H, 13-H), 6.49 (br s, 1H, NH), 7.15–8.11 (m, 11H, Ph-H), 9.23 (br s, 1H, NH), IR (KBr) υ: 3298, 1611, 1172, 1090; MS (ESI) *m/z*: 421.1 (M + 1). *Anal*. Calcd for $C_{26}H_{20}N_2O_2$: C 79.57, H 5.14, N 7.14; found C 79.41, H 5.20, N 7.19.

***14-Amino-2,3,4,13-tertrahydro-13-phenyl-1H-*benzo[*h*]chromene [2,3-*b*]quinolin-1-one (7′b)**. Yield: 52.8%, mp 196–198°C; ^{1}H NMR ($CDCl_3$, 300 Hz) δ: 1.18–2.13 (m, 2H, 4-H), 2.55–2.64 (m, 2H,3-H), 2.92–3.19 (m, 2H, 2-H), 5.91 (s, 1H, 13-H), 6.45 (br s, 1H, NH), 7.15–8.63 (m, 11H, Ph-H), 9.25 (br s, 1H, NH), IR (KBr) υ: 3316, 1618, 1186, 1113; MS (ESI) *m/z*: 392.5 (M + 1). *Anal*. Calcd for $C_{26}H_{20}N_2O_2$: C 79.57, H 5.14, N 7.14; found C 79.39, H 5.20, N 7.19.

***14-Amino-2,3,4,13-tertrahydro-13-(4-methoxy-phenyl)-1H-*benzo[*h*]chromene-[2,3-*b*]quinolin-1-one (7′c)**. Yield: 47.8%, mp 232–234°C; 1H NMR ($CDCl_3$, 300 Hz) δ: 2.06–2.17 (m, 2H, 4-H), 2.61–2.66 (m, 2H,3-H), 3.06–3.10 (m, 2H, 2-H), 3.75 (s, 3H, OCH_3), 5.10 (s, 1H, 13-H), 6.68 (br s, 1H, NH), 7.17–8.60 (m, 10H, Ph-H), 9.26 (br s, 1H, NH), IR (KBr) υ: 3306, 1638, 1176, 1108; MS (ESI) *m/z*: 423.2 (M + 1). *Anal*. Calcd for $C_{27}H_{22}N_2O_3$: C 76.76, H 5.25, N 6.63; found C 76.49, H 5.33, N 6.69.

***14-Amino-2,3,4,13-tertrahydro-13-(2-chlorophenyl)-1H-*benzo [*h*]chromene[2,3-*b*]quinolin-1-one (7′d)**. Yield: 50.8%, mp 202–204°C; ^{1}H NMR ($CDCl_3$, 300 Hz) δ: 2.08–2.13 (m, 2H, 4-H), 2.60–2.65 (m, 2H, 3-H), 3.01–3.06 (m, 2H, 2-H), 5.57 (s, 1H, 13-H), 6.74 (br s, 1H, NH), 7.17–8.23 (m, 10H, Ph-H), 9.28 (br s, 1H, NH), IR (KBr) υ: 3322, 1676, 1202, 1102; MS (ESI) *m/z*: 423.2 (M + 1). *Anal*. Calcd for $C_{26}H_{19}ClN_2O_2$: C 73.15, H 4.49, N 6.56; found C 72.95, H 4.57, N 6.65.

Determination of crystal structure. A colorless transparent crystal of size 0.25 × 0.15 × 0.10 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 ($\lambda = 0.071073$ nm) at 291(2) K. In the range of $2.2 < \theta < 26.8$, 3932 independent reflections were obtained in compound **6c**, and 3495 independent reflections were obtained in compound **7d**. 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. In the compound **6c**, the final convergence indices were $R = 0.0570$, $wR = 0.1418$, $w = 1/[s^2(F_0)^2 + (0.0964P)^2]$, $P = (F_0^2 + 2F_c^2)/3$, $S = 1.004$. The maximum and the minimum difference peak holes were 0.19 and -0.31 eÅ^{-3}, respectively. In the compound **7d**, the final convergence indices were $R = 0.1529$, $wR = 0.3696$, $w = 1/[s^2(F_0)^2 + (0.11542000P)^2 + 8.000P]$, $P = (F_0^2 + 2F_c^2)/3$, and $S = 1.031$. The maximum and the minimum difference peak holes were 0.77 and -0.24 eÅ^{-3}, respectively.

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