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ORIGINAL ARTICLE

Synthesis of (*E*)-2-amino-*N*′-benzylidenehexahydroquinoline-3-carbohydrazide

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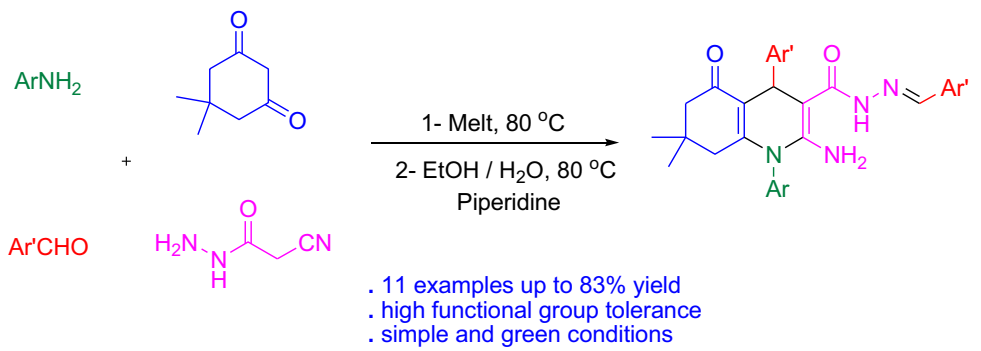
Abstract

A one-pot, multi-component protocol for the synthesis of a new class of functionalized quinoline carbohydrazide derivatives via reaction of various anilines, dimedone, aromatic aldehydes, and cyanoacetohydrazide is described. The reactions are completed in the presence of catalytic amount of piperidine, respectively, in melt conditions and then in ethanol/water (1:1) as green solvent at 80 °C. Mild conditions, green medium, short reaction times, simple workup and purification process with no chromatographic technique, and good yields are the main advantages of this method.

Graphical abstract



Keywords Multi-component protocol · Quinoline carbohydrazide derivatives · Anilines · Dimedone · Aromatic aldehydes · Cyanoacetohydrazide

Introduction

Multi-component reactions (MCRs) and their improvement are of considerable interest in the current research projects [1]. They have been extensively used in the total synthesis of natural products, as well as the design and discovery of biologically active molecules and various heterocyclic compounds [2].

For more than a century, heterocycles have constituted one of the largest areas of researches in organic chemistry [3–5]. Among the heterocycles, *N*-containing heterocycles represent a highly important class of compounds which are widely used in materials science, agrochemistry, and medicinal chemistry [6]. Therefore, *N*-containing heterocycles are especially considered "privileged" structures for the synthesis and development of new drugs [7]. Enaminones and related compounds are versatile synthetic intermediates in organic chemistry that combine the ambient nucleophilicity of enamine and the electrophilicity of enones [8]. They are widely used for the synthesis of a variety of heterocy-

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cles especially *N*-heterocyclic compounds in the past several years [9–14].

Quinoline is one of the most popular *N*-heterocyclic compounds incorporated into the structures of many pharmaceuticals [15]. The biological activity of quinoline compounds has been found in the form of antitumor [9, 16], antimalarial, antibacterial, antiplasmodial, antiproliferative, anticancer [10, 13], antiasthmatic, antihypertensive and anti-inflammatory [17] properties. Therefore, the synthesis of quinoline and its derivatives has been of great interest in organic and medicinal chemistry [18, 19].

In continuation of our research interests regarding the development of new methods in heterocyclic synthesis [20–23], herein we report an efficient synthesis of functionalized quinoline carbohydrazide derivatives through a multi-component reaction of various anilines, dimedone, aromatic aldehydes, and cyanoacetohydrazide, respectively, in melt conditions and then in EtOH/H_2O (1:1) as a green medium at 80 °C. To the best of our knowledge, there are no reports on the synthesis of these compounds in the literature.

Results and discussion

The one-pot, multi-component reactions of enaminones derived from the addition of various anilines **1** to dimedone **2** under solvent-free conditions at 80 °C, with aromatic aldehydes **3** and cyanoacetohydrazide **4** in the presence of catalytic amount of piperidine, in EtOH/H_2O (1:1) as a green solvent at 80 °C, led to the corresponding quinoline carbohydrazide derivatives **5a-k**, in good yields (Scheme 1).

We explored the scope of this reaction by varying the structure of the aromatic aldehyde and aniline components. The reaction proceeded very cleanly under the same reaction conditions to afford a series of functionalized quinoline carbohydrazide derivatives **5a–k** in 68–83% yields. The reaction proceeds with good yields when ethanol/water (1:1) was used as the solvent at reflux. The product **5** was insoluble in ethanol/water (1:1), so easily be purified by filtration and washing with ethanol/water, and column chromatography was unnecessary. Product **5** was soluble in pure ethanol, so workup and purification was a complicated and time-consuming process. Also due to the lack of solubility of starting materials in water, the reaction was not complete in pure water. In the absence of a catalyst, the reaction did not yield any product even after long reaction times. The results are shown in Table 1.

The structures of compounds **5a–k** (Table 1) were confirmed by IR, ^{1}H NMR, ^{13}C NMR, and mass spectra. The IR spectrum of **5a** exhibited absorption bands due to NH_2 and NH groups (3449, 3385 and 3287 cm^{-1}) and absorption bands due to C=O group (1638 cm^{-1}), and as well as 1489 and 1265 cm^{-1} due to the Ar and C–N groups.

^{1}H NMR spectrum ($CDCl_3$) of **5a** revealed two singlets for the NH_2 (amine) and NH (amide) groups (δ 6.84, 8.69 ppm, respectively), two singlets for the methine and imine protons (δ 5.06, 7.73 ppm, respectively), two singlets for two CH_3 groups (δ 0.68, 0.94 ppm), characteristic multiplets for two CH_2 groups (δ 2.01–2.25 ppm), and multiplets for the aromatic region (δ 7.21–7.57 ppm) which completely in accord with the assigned structure. The ^{1}H-decoupled ^{13}C NMR spectrum ($CDCl_3$) of **5a** showed 25 distinct resonances which were consistent with the proposed structure.

The EI-MS of **5a** displayed the molecular ion peak at *m/z* 682, which was in agreement with the proposed structure.

A plausible mechanism for the formation of product **5** is shown in Scheme 2. It is reasonable to assume that the reaction involves the initial formation of enaminone intermediate **6** between the aniline **1** and dimedone **2**. Apparently, the condensation of cyanoacetohydrazide **4** with aromatic aldehyde **3** furnishes adduct **7**. Intermediate **6** is activated by piperidine for the next addition reaction with aromatic aldehyde **3** to afford **9**. Then, Michael addition reaction between intermediate **9** and adduct **7** affords **10** which undergoes cyclization by nucleophilic addition of the secondary amino group to cyano group, followed by successive imine-enamine tautomerization led to the formation of product **5**.

Scheme 1 Synthesis of quinoline carbohydrazide derivatives

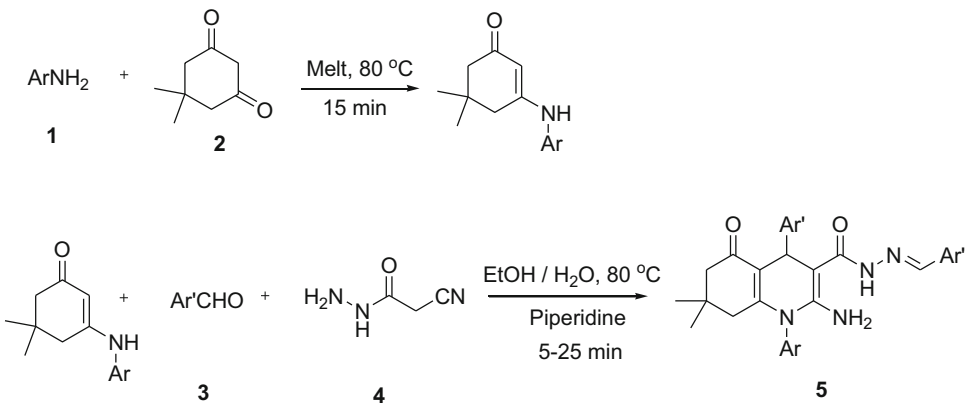


Table 1 Synthesis of products **5a–k**

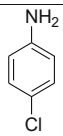
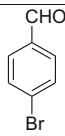
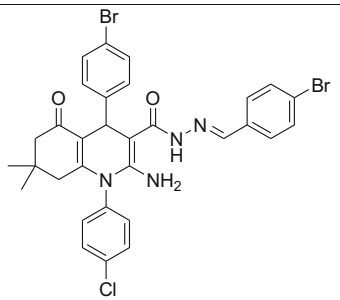
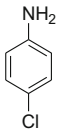
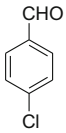
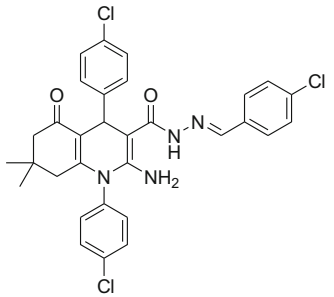
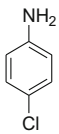
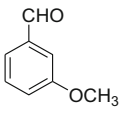
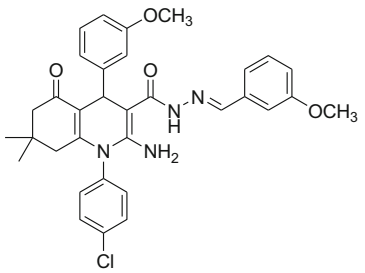
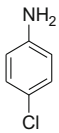
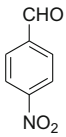
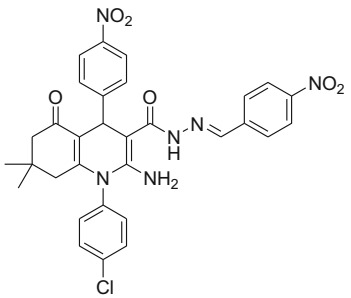
Entry	$ArNH_2$[a]	Ar'CHO[a]	Product	Time (min)	Yield (%)
1			 **5a**	5	76
2			 **5b**	5	74
3			 **5c**	20	68
4			 **5d**	10	81

Table 1 continued

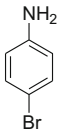
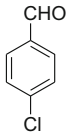
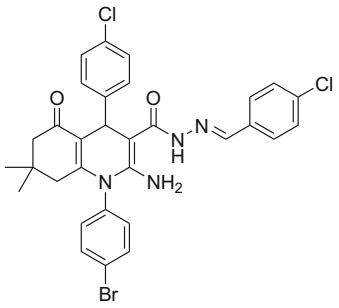
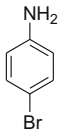
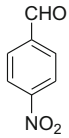
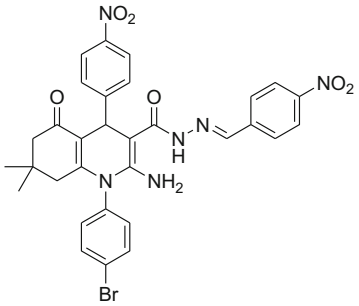
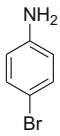
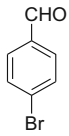
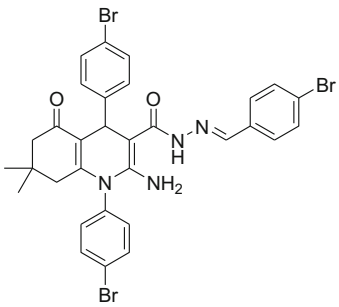
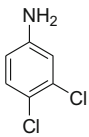
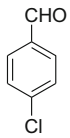
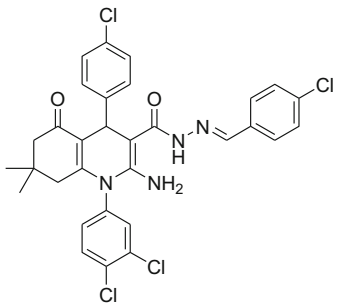
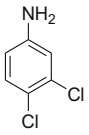
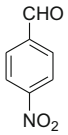
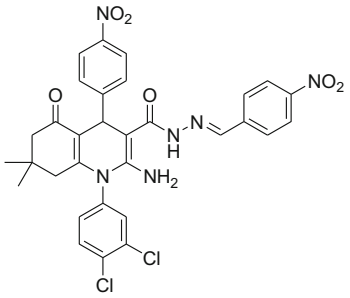
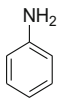
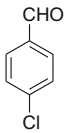
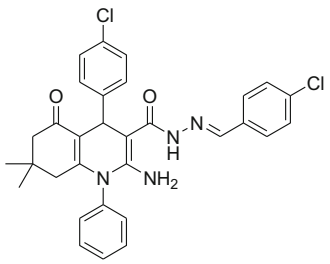
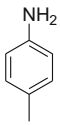
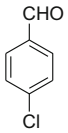
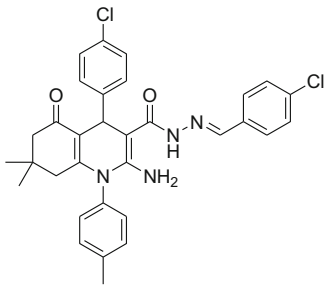
Entry	$ArNH_2$[a]	Ar'CHO[a]	Product	Time (min)	Yield (%)
5			 **5e**	5	75
6			 **5f**	15	83
7			 **5g**	5	78
8			 **5h**	10	72

Table 1 continued

Entry	$ArNH_2$[a]	Ar'CHO[a]	Product	Time (min)	Yield (%)
9			 **5i**	15	79
10			 **5j**	25	70
11			 **5k**	10	73

[a]Aromatic aldehydes (2 mmol), cyanoacetohydrazide (1 mmol), dimedone (1 mmol), and various anilines (1 mmol) were used. The reactions were run in EtOH/H_2O (1:1), at 80 °C

Conclusion

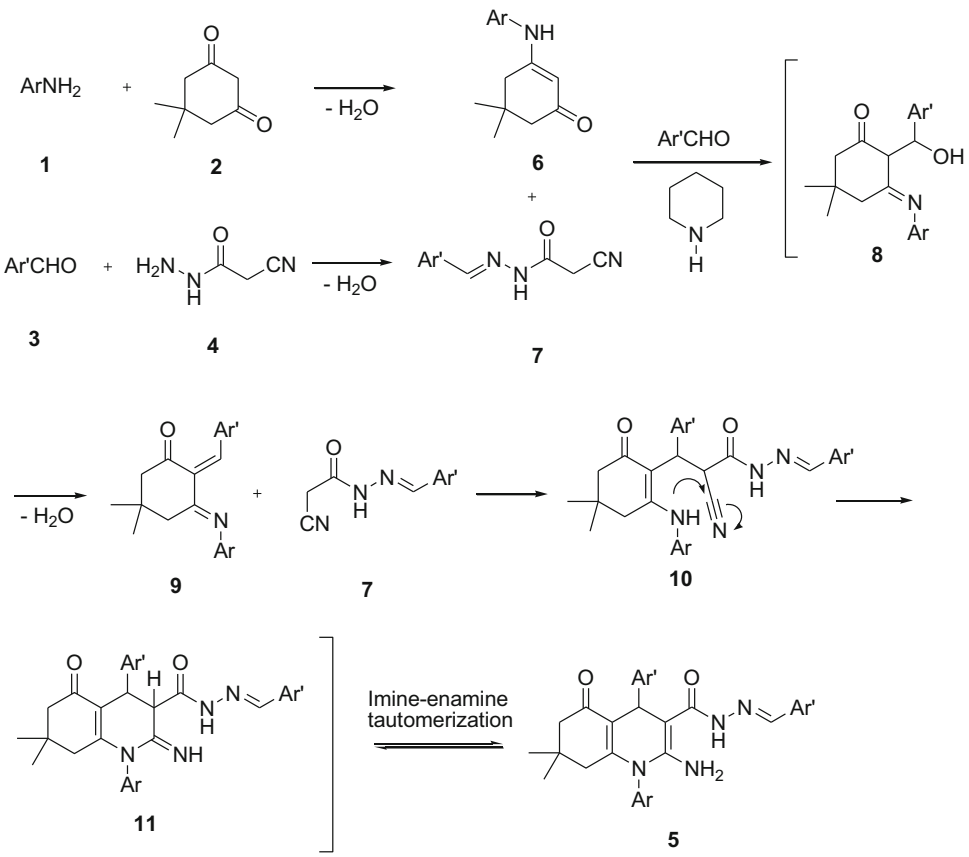
In summary, we have developed an efficient, one-pot, multi-component approach to the synthesis of functionalized quinoline carbohydrazide derivatives based on the reaction of enaminones derived from the addition of various anilines to dimedone under solvent-free conditions at 80 °C, with aromatic aldehydes and cyanoacetohydrazide in the presence of catalytic amount of piperidine, in EtOH/H_2O (1:1) at 80 °C. The significant features of this method are green methodology, easy workup, readily available starting materials, high atom economy, short reaction times, compatibility with various functional groups, and good product yields.

Experimental section

General remarks

The dimedone, various anilines, aromatic aldehydes, cyanoacetohydrazide, piperidine, and other chemicals and solvents were obtained from Merck and Aldrich and were used without further purification. NMR spectra were recorded with a Bruker DRX-300 Avance instrument (300 MHz for ^1H and 75.4 MHz for ^{13}C) with $CDCl_3$ and DMSO as solvent. Chemical shifts are given in ppm (δ), and coupling constant (J) is reported in hertz (Hz). Melting points were measured with an electrothermal 9100 apparatus. Mass spectra were recorded with an Agilent 5975C VL MSD with Triple-Axis Detector operating at an ionization potential of 70 eV. IR spectra were measured with Bruker Tensor 27 spec-

Scheme 2 Proposed mechanism for the formation of product **5**



trometer. Elemental analyses for C, H and N were performed using a PerkinElmer 2004 series [II] CHN elemental analyzer.

General procedure for the synthesis of product 5

A mixture of aniline **1** (1 mmol) and dimedone **2** (1 mmol, 0.140 g) was melted at 80 °C for 15 min. Then, ethanol/water (1:1, 5 mL) and one-drop piperidine were added, and the solution was stirred for 5 min at 80 °C. Next, aromatic aldehyde **3** (2 mmol) and cyanoacetohydrazide **4** (1 mmol, 0.099 g) were added and the solution was stirred at 80 °C for the time given in Table 1. Upon completion as monitored by TLC, the reaction mixture was allowed to cool to room temperature, and the precipitates were filtered and washed with ethanol/water (1:1) to give product **5** in good yields.

(31E)-N′-(4-bromobenzylidene)-2-amino-4-(4-bromophenyl)-1-(4-chlorophenyl)-1,4,5,6,7,8-hexahydro-7,7-dimethyl-5-oxoquinoline-3-carbohydrazide **(5a, $C_{31}H_{27}Br_2ClN_4O_2$)** Yellow solid: M.p.: 212–214 °C, yield: 0.518 g (76%); IR (KBr) (ν_{max}/cm^{-1}): 3449, 3385, 3287 (NH_2, NH), 1638 (C=O), 1562 (C=O), 1489 (Ar), 1265 (C–N); MS (EI, 70 eV): *m/z* (%) = 682 (M^+, 0.03), 623 (6), 458 (68): 431 (18), 301 (26), 198 (28), 168 (31), 127 (20), 89 (100), 63 (25); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.68 (3H, *s*, CH_3), 0.94 (3H, *s*, CH_3), 2.01–2.25 (4H, *m*, $2CH_2$), 5.06 (1H, *s*, CH), 6.84 (2H, *s*, NH_2), 7.21–7.57 (12H, *m*, Ar), 7.73 (1H, *s*, CH), 8.69 (1H, *s*, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 26.3 (CH_3), 29.7 (CH_3), 32.2 ($C(CH_3)_2$), 33.4 (CH), 41.8 (CH_2), 49.9 (CH_2), 79.0, 114.5, 120.6, 123.9, 128.7, 129.0, 130.9, 131.3, 131.7, 131.9, 132.9, 134.4, 136.5, 143.5, 144.4, 149.1, 152.2, 165.8 (C=O), 195.8 (C=O); Anal. Calc. for $C_{31}H_{27}Br_2ClN_4O_2$ (682.83): C, 54.53; H, 3.99, N, 8.21. Found: C, 54.9; H, 3.5; N, 7.9.

(31E)-N′-(4-chlorobenzylidene)-2-amino-1,4-bis(4-chlorophenyl)-1,4,5,6,7,8-hexahydro-7,7-dimethyl-5-oxoquinoline-3-carbohydrazide **(5b, $C_{31}H_{27}Cl_3N_4O_2$)** Yellow solid: M.p.: 234–236 °C, yield: 0.439 g (74%); IR (KBr) (ν_{max}/cm^{-1}): 3432, 3282 (NH_2, NH), 1646 (C=O), 1592 (C=O), 1487 (Ar), 1266 (C–N); MS (EI, 70 eV): *m/z* (%) = 593 (M^+, 0.08), 535 (8), 438 (15), 412 (46), 370 (3), 301 (13), 276 (44), 249 (22), 185 (47), 165 (100), 138 (47), 111 (59), 89 (58), 63 (15); ^{1}H NMR (300 MHz, DMSO): δ = 0.68 (3H, *s*, CH_3), 0.99 (3H, *s*, CH_3), 1.55–2.25 (4H, *m*, $2CH_2$), 5.30 (1H, *s*, CH), 7.28 (4H, *d*, $^3J_{HH}$ = 7.8 Hz, Ar), 7.34 (2H, *s*, NH_2), 7.42 (4H, *d*, $^3J_{HH}$ = 8.4 Hz, Ar), 7.58 (2H, *d*, $^3J_{HH}$ = 7.8 Hz, Ar), 7.64 (2H, *d*, $^3J_{HH}$ = 8.1 Hz, Ar), 8.29 (1H, *s*, CH), 10.70 (1H, *s*, NH); ^{13}C NMR (75.4 MHz, DMSO): δ = 26.1 (CH_3), 29.7 (CH_3), 32.3 ($C(CH_3)_2$), 32.4 (CH), 41.4 (CH_2), 49.9 (CH_2), 79.7, 114.0, 116.1, 128.4, 128.5, 129.2, 129.4, 130.7, 132.5, 133.9, 134.4, 134.7,

135.5, 142.9, 146.9, 150.3, 152.7, 166.4 (C=O), 195.2 (C=O); Anal. Calc. for $C_{31}H_{27}Cl_3N_4O_2$ (593.9): C, 62.69; H, 4.58, N, 9.43. Found: C, 63.1; H, 4.9; N, 9.0.

(30E)-N′-(3-methoxybenzylidene)-2-amino-1-(4-chlorophenyl)-1,4,5,6,7,8-hexahydro-4-(3-methoxyphenyl)-7,7-dimethyl-5-oxoquinoline-3-carbohydrazide **(5c, $C_{33}H_{33}ClN_4O_4$)** Yellow solid: M.p.: 200–202 °C, yield: 0.397 g (68%); IR (KBr) (ν_{max}/cm^{-1}): 3414, 3345, 3241 (NH_2, NH), 1624 (C=O), 1479 (Ar), 1267 (C–N); MS (EI, 70 eV): *m/z* (%) = 585 (M^+, 0.03), 525 (8), 408 (20), 366 (6), 249 (54), 221 (12), 193 (100), 161 (38), 121 (35), 92 (19), 89 (10), 68 (43), 63 (7); ^{1}H NMR (300 MHz, DMSO): δ = 0.64 (3H, *s*, CH_3), 0.89 (3H, *s*, CH_3), 1.58–2.26 (4H, *m*, $2CH_2$), 3.67 (3H, *s*, OCH_3), 3.75 (3H, *s*, OCH_3), 5.28 (1H, *s*, CH), 6.64–7.67 (14H, *m*, Ar and NH_2), 8.30 (1H, *s*, CH), 10.65 (1H, *s*, NH); ^{13}C NMR (75.4 MHz, DMSO): δ = 26.1 (CH_3), 28.5 (CH_3), 32.9 ($C(CH_3)_2$), 33.4 (CH), 41.5 (CH_2), 50.0 (CH_2), 55.2 (OCH_3), 55.5 (OCH_3), 80.2, 97.6, 110.8, 111.1, 114.3, 119.8, 120.1, 124.7, 129.5, 130.7, 132.4, 135.7, 137.0, 138.6 144.0, 149.6, 150.1, 152.5, 159.3, 159.9, 160.1, 166.4 (C=O), 195.8 (C=O); Anal. Calc. for $C_{33}H_{33}ClN_4O_4$ (585.09): C, 67.74; H, 5.68, N, 9.58. Found: C, 67.3; H, 5.9; N, 9.2.

(30E)-N′-(4-nitrobenzylidene)-2-amino-1-(4-chlorophenyl)-1,4,5,6,7,8-hexahydro-7,7-dimethyl-4-(4-nitrophenyl)-5-oxoquinoline-3-carbohydrazide **(5d, $C_{31}H_{27}ClN_6O_6$)** Yellow solid: M.p.: 210–212 °C, yield: 0.498 g (81%); IR (KBr) (ν_{max}/cm^{-1}): 3464, 3386, 3247 (NH_2, NH), 1639 (C=O), 1562 (C=O), 1513 (Ar), 1265 (C–N); MS (EI, 70 eV): *m/z* (%) = 615 (M^+, 0.01), 298 (50), 251 (22), 176 (100), 130 (28), 76 (27); ^{1}H NMR (300 MHz, DMSO): δ = 0.62 (3H, *s*, CH_3), 0.87 (3H, *s*, CH_3), 1.59–2.34 (4H, *m*, $2CH_2$), 5.50 (1H, *s*, CH), 7.48–7.82 (10H, *m*, Ar and NH_2), 8.13 (2H, *d*, $^3J_{HH}$ = 8.7 Hz, Ar), 8.22 (2H, *d*, $^3J_{HH}$ = 8.7 Hz, Ar), 8.41 (1H, *s*, CH), 11.05 (1H, *s*, NH); ^{13}C NMR (75.4 MHz, DMSO): δ = 26.1 (CH_3), 29.7 (CH_3), 32.3 ($C(CH_3)_2$), 33.4 (CH), 41.5 (CH_2), 49.8 (CH_2), 79.0, 113.3, 123.9, 124.4, 127.7, 128.8, 130.7, 132.5, 134.9, 135.3, 141.6, 142.0, 146.1, 147.6, 150.9, 153.3, 155.6, 166.3 (C=O), 195.2 (C=O); Anal. Calc. for $C_{31}H_{27}ClN_6O_6$ (615.04): C, 60.54; H, 4.42, N, 13.66. Found: C, 60.8; H, 4.0; N, 13.5.

(30E)-N′-(4-chlorobenzylidene)-2-amino-1-(4-bromophenyl)-4-(4-chlorophenyl)-1,4,5,6,7,8-hexahydro-7,7-dimethyl-5-oxoquinoline-3-carbohydrazide **(5e, $C_{31}H_{27}BrCl_2N_4O_2$)** Yellow solid: M.p.: 200–202 °C, yield: 0.478 g (75%); IR (KBr) (ν_{max}/cm^{-1}): 3452, 3380, 3219 (NH_2, NH), 1636 (C=O), 1562 (C=O), 1488 (Ar), 1266 (C–N); MS (EI, 70 eV): *m/z* (%) = 638 (M^+, 0.06), 587 (16), 458 (100), 431 (27), 368 (27), 264 (56), 226 (44), 154 (32), 124 (55), 89 (80), 57 (38); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.68 (3H, *s*, CH_3), 0.95 (3H, *s*, CH_3), 2.01–2.32 (4H, *m*, $2CH_2$), 5.06 (1H, *s*, CH), 6.85 (2H, *s*, NH_2), 7.17 (2H, *d*, $^3J_{HH}$ = 8.1 Hz, Ar), 7.26–7.32(4H, *m*, Ar), 7.42 (2H, *d*, $^3J_{HH}$ = 8.1 Hz, Ar), 7.61 (2H, *d*, $^3J_{HH}$ = 8.7 Hz, Ar), 7.72 (1H, *s*, CH), 7.73 (2H, *d*, $^3J_{HH}$ = 8.4 Hz, Ar), 8.59 (1H, *s*, NH); ^{13}C NMR (75.4 MHz, DMSO): δ = 26.1 (CH_3), 29.8 (CH_3), 32.3 ($C(CH_3)_2$), 33.5 (CH), 41.4 (CH_2), 50.0 (CH_2), 79.6, 114.0, 123.4, 128.4, 128.5, 129.2, 129.4, 130.6, 132.8, 133.6, 133.9, 134.5, 136.0, 142.8, 146.9, 150.2, 152.6, 166.4 (C=O), 195.2 (C=O); Anal. Calc. for $C_{31}H_{27}BrCl_2N_4O_2$ (638.38): C, 58.32; H, 4.26, N, 8.78. Found: C, 58.8; H, 4.6; N, 8.5.

(30E)-N′-(4-nitrobenzylidene)-2-amino-1-(4-bromophenyl)-1,4,5,6,7,8-hexahydro-7,7-dimethyl-4-(4-nitrophenyl)-5-oxoquinoline-3-carbohydrazide **(5f, $C_{31}H_{27}BrN_6O_6$)** Yellow solid: M.p.: 217–219 °C, yield: 0.547 g (83%); IR (KBr) (ν_{max}/cm^{-1}): 3462, 3385, 3251 (NH_2, NH), 1637 (C=O), 1560 (C=O), 1513 (Ar), 1264 (C–N); MS (EI, 70 eV): *m/z* (%) = 659 (M^+, 0.93), 587 (9), 368 (13), 298 (47), 264 (25), 236 (19), 178 (100), 130 (31), 103 (26), 76 (39), 43 (27); ^{1}H NMR (300 MHz, DMSO): δ = 0.62 (3H, *s*, CH_3), 0.87 (3H, *s*, CH_3), 1.59–2.29 (4H, *m*, $2CH_2$), 5.50 (1H, *s*, CH), 7.43 (2H, *d*, $^3J_{HH}$ = 8.4 Hz, Ar), 7.52 (2H, *s*, NH_2), 7.68 (2H, *d*, $^3J_{HH}$ = 8.7 Hz, Ar), 7.78–7.82 (4H, *m*, Ar), 8.14 (2H, *d*, $^3J_{HH}$ = 8.7 Hz, Ar), 8.22 (2H, *d*, $^3J_{HH}$ = 8.7 Hz, Ar), 8.41 (1H, *s*, CH), 11.06 (1H, *s*, NH); ^{13}C NMR (75.4 MHz, DMSO): δ = 26.1 (CH_3), 29.7 (CH_3), 32.3 ($C(CH_3)_2$), 33.1 (CH), 41.5 (CH_2), 49.9 (CH_2), 79.0, 113.3, 123.6, 123.9, 124.5, 127.7, 128.8, 132.8, 133.7, 135.7, 141.6, 142.0, 146.1, 147.6, 150.8, 153.2, 155.5, 166.3 (C=O), 195.2 (C=O); Anal. Calc. for $C_{31}H_{27}BrN_6O_6$ (659.49): C, 56.46; H, 4.13, N, 12.74. Found: C, 56.9; H, 4.5; N, 12.3.

(30E)-N′-(4-bromobenzylidene)-2-amino-1,4-bis(4-bromophenyl)-1,4,5,6,7,8-hexahydro-7,7-dimethyl-5-oxoquinoline-3-carbohydrazide **(5 g, $C_{31}H_{27}Br_3N_4O_2$)** Yellow solid: M.p.: 240–242 °C, yield: 0.567 g (78%); IR (KBr) (ν_{max}/cm^{-1}): 3449, 3281 (NH_2, NH), 1681 (C=O), 1588 (C=O), 1540 (Ar), 1256 (C–N); MS (EI, 70 eV): *m/z* (%) = 727 (M^+, 0.01), 669 (2), 499 (3), 434 (10), 365 (14), 337 (5), 276 (6), 249 (100), 209 (47), 182 (17), 155 (54), 127 (52), 89 (50), 63 (7); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.69 (3H, *s*, CH_3), 0.95 (3H, *s*, CH_3), 1.96–2.26 (4H, *m*, $2CH_2$), 5.03 (1H, *s*, CH), 6.85 (2H, *s*, NH_2), 7.15–7.90 (12H, *m*, Ar), 8.20 (1H, *s*, CH), 8.52 (1H, *s*, NH); ^{13}C NMR (75.4 MHz, DMSO): δ = 26.1 (CH_3), 29.7 (CH_3), 32.3 ($C(CH_3)_2$), 32.5 (CH), 41.5 (CH_2), 50.0 (CH_2), 79.6, 106.4, 116.2, 124.3, 126.8, 128.8, 129.6, 129.9, 131.3, 131.4, 132.3, 132.8, 133.5, 144.1, 148.7, 150.8, 158.6, 166.3 (C=O), 195.2 (C=O); Anal. Calc. for $C_{31}H_{27}Br_3N_4O_2$ (727.28): C, 51.19; H, 3.74, N, 7.70. Found: C, 51.7; H, 3.4; N, 7.5.

(30E)-N′-(4-chlorobenzylidene)-2-amino-1-(3,4-dichlorophenyl)-4-(4-chlorophenyl)-1,4,5,6,7,8-hexahydro-7,7-dimethyl-5-oxoquinoline-3-carbohydrazide **(5 h, $C_{31}H_{26}Cl_4N_4O_2$)** Yellow solid: M.p.: 202–204 °C, yield: 0.452 g (72%); IR (KBr) (ν_{max}/cm^{-1}): 3378, 3298 (NH_2, NH), 1695 (C=O), 1607 (C=O), 1524 (Ar), 1245 (C–N); MS (EI, 70 eV): *m/z* (%) = 628 (M^+, 0.13), 569 (7), 472 (9), 445 (13), 406 (8), 352 (21), 296 (9), 276 (45), 248 (15), 226 (8), 187 (6), 165 (100), 138 (21), 111 (6), 89 (25), 63 (8); ^{1}H NMR (300 MHz, DMSO): δ = 0.62 (3H, *s*, CH_3), 0.87 (3H, *s*, CH_3), 1.61–2.30 (4H, *m*, $2CH_2$), 5.29 (1H, *s*, CH), 7.27 (2H, *d*, $^3J_{HH}$ = 8.4 Hz, Ar), 7.40–7.46 (7H, *m*, Ar and NH_2), 7.58 (2H, *d*, $^3J_{HH}$ = 8.7 Hz, Ar), 7.82–7.85 (2H, *m*, Ar), 8.30 (1H, *s*, CH), 10.70 (1H, *s*, NH); ^{13}C NMR (75.4 MHz, DMSO): δ = 26.0 (CH_3), 29.8 (CH_3), 32.3 ($C(CH_3)_2$), 32.5 (CH), 41.4 (CH_2), 50.0 (CH_2), 79.7, 114.0, 128.3, 128.5, 129.2, 129.6, 130.6, 131.1, 132.3, 132.9, 133.0, 133.2, 133.9, 134.5, 136.5, 142.9, 146.9, 150.0, 152.5, 166.4 (C=O), 195.2 (C=O); Anal. Calc. for $C_{31}H_{26}Cl_4N_4O_2$ (628.38): C, 59.25; H, 4.17, N, 8.92. Found: C, 58.9; H, 4.6; N, 8.5.

(30E)-N′-(4-nitrobenzylidene)-2-amino-1-(3,4-dichlorophenyl)-1,4,5,6,7,8-hexahydro-7,7-dimethyl-4-(4-nitrophenyl)-5-oxoquinoline-3-carbohydrazide **(5i, $C_{31}H_{26}Cl_2N_6O_6$)** Yellow solid: M.p.: 222–224 °C, yield: 0.513 g (79%); IR (KBr) (ν_{max}/cm^{-1}): 3461, 3379, 3243 (NH_2, NH), 1641 (C=O), 1558 (C=O), 1513 (Ar), 1264 (C–N); MS (EI, 70 eV): *m/z* (%) = 649 (M^+, 0.05), 456 (52), 430 (10), 298 (33), 251 (14), 176 (100), 130 (23), 89 (34), 63 (21); ^{1}H NMR (300 MHz, DMSO): δ = 0.62 (3H, *s*, CH_3), 0.87 (3H, *s*, CH_3), 1.64–2.27 (4H, *m*, $2CH_2$), 5.48 (1H, *s*, CH), 7.63 (2H, *s*, NH_2), 7.48–7.93 (7H, *m*, Ar), 8.13 (2H, *d*, $^3J_{HH}$ = 8.7 Hz, Ar), 8.23 (2H, *d*, $^3J_{HH}$ = 8.7 Hz, Ar), 8.42 (1H, *s*, CH), 11.06 (1H, *s*, NH); ^{13}C NMR (75.4 MHz, DMSO): δ = 26.0 (CH_3), 29.7 (CH_3), 32.3 ($C(CH_3)_2$), 33.3 (CH), 41.4 (CH_2), 49.9 (CH_2), 79.1, 113.3, 123.8, 124.4, 127.7, 129.0, 131.1, 132.3, 133.0, 133.4, 136.2, 141.8, 141.9, 146.1, 147.6, 150.6, 153.1, 155.5, 166.3 (C=O), 195.2 (C=O); Anal. Calc. for $C_{31}H_{26}Cl_2N_6O_6$ (649.48): C, 57.33; H, 4.03, N, 12.94. Found: C, 57.8; H, 4.5; N, 12.7.

(29E)-N′-(4-chlorobenzylidene)-2-amino-4-(4-chlorophenyl)-1,4,5,6,7,8-hexahydro-7,7-dimethyl-5-oxo-1-phenylquinoline-3-carbohydrazide **(5j, $C_{31}H_{28}Cl_2N_4O_2$)** Yellow solid: M.p.: 204–206 °C, yield: 0.391 g (70%); IR (KBr) (ν_{max}/cm^{-1}): 3446, 3281 (NH_2, NH), 1680 (C=O), 1587 (C=O), 1537 (Ar), 1252 (C–N); MS (EI, 70 eV): *m/z* (%) = 559 (M^+, 0.06), 499 (9), 418 (5), 377 (100), 351 (28), 279 (38), 226 (23), 181 (15), 154 (53), 138 (26), 111 (25), 89 (45), 63 (5); ^{1}H NMR (300 MHz, DMSO): δ = 0.60 (3H, *s*, CH_3), 0.84 (3H, *s*, CH_3), 1.53–2.24 (4H, *m*, $2CH_2$), 5.32 (1H, *s*, CH), 7.22 (2H, *s*, NH_2), 7.28–7.60 (13H, *m*, Ar), 8.30 (1H, *s*, CH), 10.71 (1H, *s*, NH); ^{13}C NMR (75.4 MHz, DMSO): δ = 26.2 (CH_3), 29.7 (CH_3), 32.3 ($C(CH_3)_2$), 32.3 (CH), 41.5 (CH_2), 49.9 (CH_2), 79.6, 113.9, 128.4, 128.5, 129.2, 129.4, 129.5, 130.1, 130.5, 130.6, 133.9, 134.5 136.6, 142.8, 147.0, 150.5, 152.8, 166.4 (C=O), 195.2 (C=O); Anal. Calc. for $C_{31}H_{28}Cl_2N_4O_2$ (559.49): C, 66.55; H, 5.04, N, 10.01. Found: C, 66.9; H, 5.5; N, 10.2.

(29E)-N′-(4-chlorobenzylidene)-2-amino-4-(4-chlorophenyl)-1,4,5,6,7,8-hexahydro-7,7-dimethyl-5-oxo-1-p-tolylquinoline-3-carbohydrazide **(5k, $C_{32}H_{30}Cl_2N_4O_2$)** Yellow solid: M.p.: 226–228 °C, yield: 0.418 g (73%); IR (KBr) (ν_{max}/cm^{-1}): 3454, 3284 (NH_2, NH), 1683 (C=O), 1594 (C=O), 1544 (Ar), 1257 (C–N); MS (EI, 70 eV): *m/z* (%) = 573 (M^+, 0.02), 513 (11), 432 (10), 391 (100), 365 (20), 343 (8), 307 (13), 281 (21), 240 (14), 182 (32), 154 (20), 124 (18), 89 (32), 63 (8); ^{1}H NMR (300 MHz, DMSO): δ = 0.60 (3H, *s*, CH_3), 0.85 (3H, *s*, CH_3), 1.53–2.24 (4H, *m*, $2CH_2$), 2.48 (3H, *s*, CH_3), 5.31 (1H, *s*, CH), 7.23 (2H, *s*, NH_2), 7.27–7.60 (12H, *m*, Ar), 8.29 (1H, *s*, CH), 10.66 9.42 (1H, *s*, NH); ^{13}C NMR (75.4 MHz, DMSO): δ = 21.2 (CH_3), 26.2 (CH_3), 29.7 (CH_3), 32.2 ($C(CH_3)_2$), 32.4 (CH), 41.5 (CH_2), 50.0 (CH_2), 79.6, 113.9, 123.5, 128.3, 128.5, 129.2, 129.4, 130.1, 130.4, 131.2, 133.9, 134.5, 139.6, 142.8, 147.0, 150.7, 152.9, 166.4 (C=O), 195.2 (C=O); Anal. Calc. for $C_{32}H_{30}Cl_2N_4O_2$ (573.51): C, 67.02; H, 5.27, N, 9.77. Found: C, 67.4; H, 5.8; N, 9.5.

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