An Efficient Synthesis of 2-Hydroxy-7,8-dihydroquinolin-5(6*H*)-ones and 7,8-Dihydroquinoline-2,5(1*H*,6*H*)-diones from Morita–Baylis–Hillman Adduct Acetates

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Abstract: A series of 2-hydroxy-7,8-dihydroquinolin-5(6*H*)-ones and 7,8-dihydroquinoline-2,5(1*H*,6*H*)-diones have been synthesized in good to excellent yields from Morita–Baylis–Hillman adduct acetates, cyclohexane-1,3-diones and ammonium acetate or primary amines in one pot under solvent-free conditions.

Key words: 2-hydroxy-7,8-dihydroquinolin-5(6*H*)-ones, 7,8-dihydroquinoline-2,5(1*H*,6*H*)-diones, Morita–Baylis–Hillman adduct acetates, cyclohexane-1,3-diones, solvent-free conditions

Nitrogen- and oxygen-containing heterocycles, such as carbostyrils, dihydroquinolinones and quinoline derivatives, are important core structures in organic chemistry because of their presence in many natural products[1,2a] and their various biological activity,[2] such as antitumor,[3] antipsychotic,[4] antibacterial,[5] cardiac[6] and cytotoxic activities.[7]

During the last decade, the applications of Morita–Baylis–Hillman adducts have attracted considerable interest.[8] The Morita–Baylis–Hillman reaction has been approved as an atom-economical, environment-friendly, carbon–carbon bond-forming reaction providing densely functionalized molecules whose applications in many organic transformation methodologies have been well documented.[9,10] Several reports on the preparation of dihydroquinolinones have been published.[11,12] Kim and co-workers[13] reported that 3-benzyl-7,8-dihydroquinolin-5(6*H*)-ones can be obtained from Morita–Baylis–Hillman adducts and 3-aminocyclohex-2-enone in butan-1-ol upon refluxing for 18 hours, followed by treatment with DBU; however, this method has several drawbacks, including harsh reaction conditions, low reaction efficiency and low chemoselectivity. Therefore, developing efficient, 'green' and convenient methodologies for the synthesis of dihydroquinolinones is still of interest and highly desirable.

In our ongoing studies on the application of Morita–Baylis–Hillman adduct acetates for the construction of oxygen- and nitrogen-fused heterocycles, we wish to report a new methodology for the synthesis of 2-hydroxy-7,8-dihydroquinolin-5(6*H*)-ones **4** and 7,8-dihydroquinoline-2,5(1*H*,6*H*)-diones **6** under solvent-free conditions.

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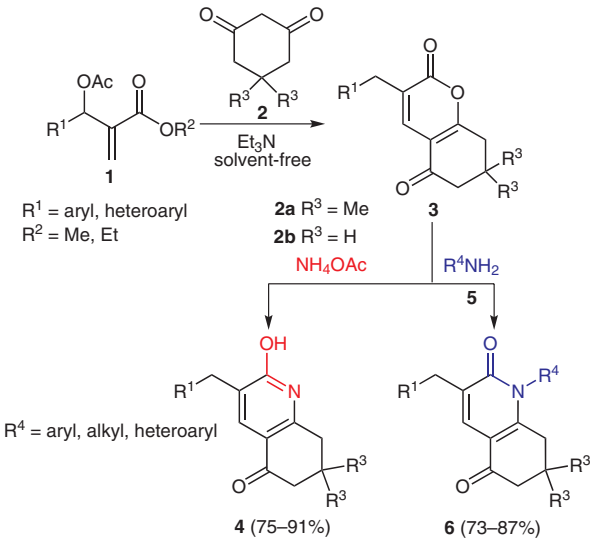
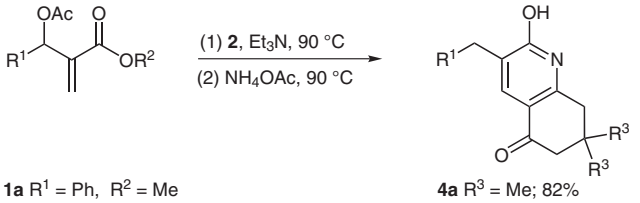
Recently, a direct conversion of Morita–Baylis–Hillman adduct acetates into 3-substituted 7,8-dihydro-6*H*-chromene-2,5-diones **3** in excellent isolated yields under solvent-free conditions has been successfully achieved in our laboratory.[14] It occurred to us that we should be able to synthesize the target compounds **4** and **6** in a one-pot, three-component process under solvent-free conditions. Our synthetic rationale is described in Scheme 1.



Scheme 1

Firstly, a three-component reaction of the Morita–Baylis–Hillman adduct acetate **1a** (R^1 = Ph, R^2 = Me), 5,5-dimethylcyclohexane-1,3-dione (**2a**) and ammonium acetate was carried out in one pot using triethylamine as base under solvent-free conditions at 90 °C for 12 hours. Unfortunately, the desired product **4a** was obtained in only 35% yield. Thus, we changed the method and first carried out reaction of a mixture of the Morita–Baylis–Hillman adduct acetate **1a**, 5,5-dimethylcyclohexane-1,3-dione (**2a**) and triethylamine under solvent-free conditions at 90 °C. TLC showed that the starting material **1a** was consumed within three hours to produce the intermediate 3-benzyl-7,7-dimethyl-7,8-dihydro-6*H*-chromene-2,5-dione (**3a**).[14] Then, ammonium acetate was added to the above mixture and the reaction was further stirred for one hour. After the mixture was cooled to 0 °C, the reaction was quenched with a solution of ethanol–water (4:1) and,

finally, 3-benzyl-2-hydroxy-7,7-dimethyl-7,8-dihydroquinolin-5(6*H*)-one (**4a**) was isolated in 82% yield (Scheme 2). More importantly, the workup procedure is very convenient, and the products can be isolated by simple filtration and washed with commercially available ethanol. Our protocol avoids the use of toxic organic solvents during the reaction and isolation process, and thus is superior to the previous methods.[13]



1a R^1 = Ph, R^2 = Me
1b R^1 = 3-$O_2NC_6H_4$, R^2 = Me

4a R^3 = Me; 82%
4b R^3 = Me; 91%

Scheme 2

Encouraged by these results and the workup operation, and with a view to understanding the generality of this reaction, we successfully extended the same strategy to a series of Morita–Baylis–Hillman adduct acetates; the results are summarized in Table 1. The reaction was compatible with a variety of Morita–Baylis–Hillman adduct acetates **1** with electron-donating or electron-withdrawing groups on the aromatic ring. The substrates with electron-donating groups afforded much lower yields and needed longer reaction times than those with electron-withdrawing groups. Heterocyclic compounds could also afford the corresponding products **4f**, **4g** in high yield. On the other hand, an ethyl ester in substrates **1** gives a lower yield than that of the methyl ester; steric effects may play an important role and resulted in moderate yield of the product (Table 1, entry 2).

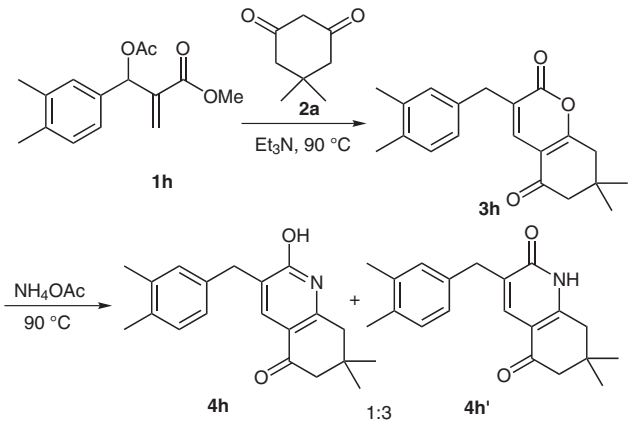
Interestingly, when the Morita–Baylis–Hillman adduct acetate **1h** was used as the substrate (Scheme 3), the unexpected mixed products **4h** and **4h′** were obtained (Table 1, entry 10), in a ratio of about 1:3, which have been identified by ^{1}H and ^{13}C NMR spectroscopy and MS data. However, when the Morita–Baylis–Hillman adduct acetate **1o**, derived from pentanal and methyl acrylate, was used as the substrate, the unexpected exclusive product **4o** was obtained by a three-component reaction in 55% yield (Scheme 4), even though the intermediate **3o** has never been detected or isolated during the reaction,[14] which cannot be explained at this stage.

With the above optimized reaction conditions, we synthesized the 3-(arylmethyl)-7,8-dihydroquinoline-2,5(1*H*,6*H*)-diones **6** via treatment with a series of primary amines **5** (Scheme 1). The reactions were also efficient and afforded the desired products in good yields; the results are summarized in Table 2. It can be seen that the reaction afforded the product in good yield when the reaction time in step 2 was extended; moreover, the primary amines **5** with electron-withdrawing groups required a much longer reaction time in step 2.

Table 1 Synthesis of 2-Hydroxy-7,8-dihydroquinolin-5(6*H*)-ones **4** from Morita–Baylis–Hillman Adduct Acetates **1**[a]

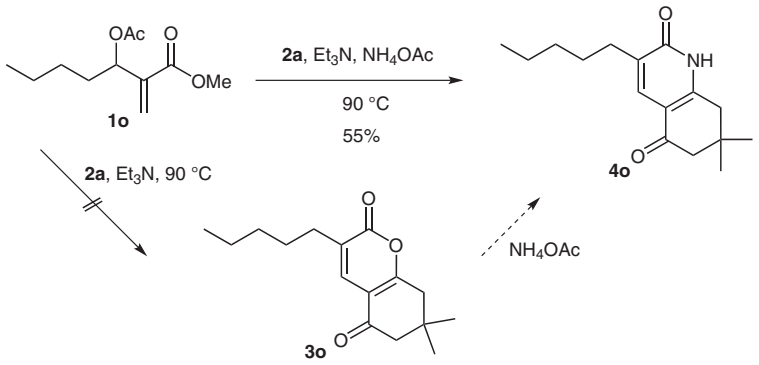
Entry	R^1	R^2	R^3	Time[b] (h)	Product	Yield[c] (%)
1	Ph	Me	Me	3.5 (1)	**4a**	82
2	Ph	Et	Me	4.5 (1)	**4a**	75
3	Ph	Me	Me	3.5 (1)	**4a**	73[d]
4	3-$O_2NC_6H_4$	Me	Me	3.0 (1)	**4b**	91
5	2-ClC_6H_4	Me	Me	3.5 (1)	**4c**	85
6	2-Cl-6-FC_6H_3	Me	Me	3.0 (1)	**4d**	88
7	4-FC_6H_4	Me	Me	3.5 (1)	**4e**	87
8	furan-2-yl	Me	Me	6.5 (1)	**4f**	75
9	thien-2-yl	Me	Me	4.5 (1)	**4g**	83
10	3,4-$Me_2C_6H_3$	Me	Me	7.0 (1)	**4h**, **4h′**	80[e]
11	3,4-$(OCH_2O)C_6H_3$	Me	Me	4.5 (1)	**4i**	80
12	3-$MeOC_6H_4$	Me	Me	3.5 (1)	**4j**	79
13	4-FC_6H_4	Me	H	3.5 (1)	**4k**	85
14	3-$O_2NC_6H_4$	Me	H	3.0 (1)	**4l**	90
15	Ph	Me	H	3.5 (1)	**4m**	82
16	3-$MeOC_6H_4$	Me	H	4.0 (1)	**4n**	78

[a] All reactions were carried out on Morita–Baylis–Hillman adduct acetates (1 mmol) with cyclic β-diketones (1.2 mmol) in the presence of triethylamine (1.2 mmol) at 90 °C under solvent-free conditions; ammonium acetate (3 mmol) was added subsequently.
[b] Reaction times for step 1 and step 2 (in brackets).
[c] Isolated yields based on the Morita–Baylis–Hillman adduct acetates.
[d] Ammonia was used instead of ammonium acetate.
[e] Isolated total yield.



Scheme 3

According to all of these results, a possible mechanism for the formation of compounds **4** (except for **4o**) and **6** from Morita–Baylis–Hillman adduct acetates **1** can be illustrated as shown in Scheme 5. A possible mechanism for the formation of compound **4o** can be described as per Scheme 6.

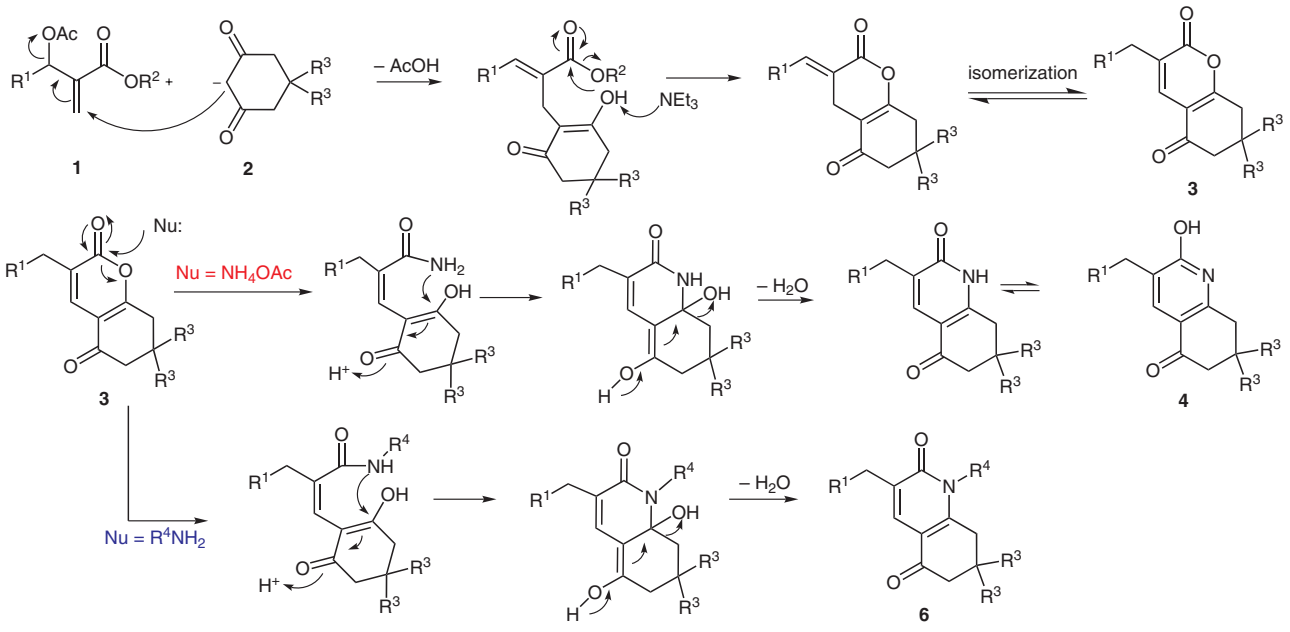


Scheme 4

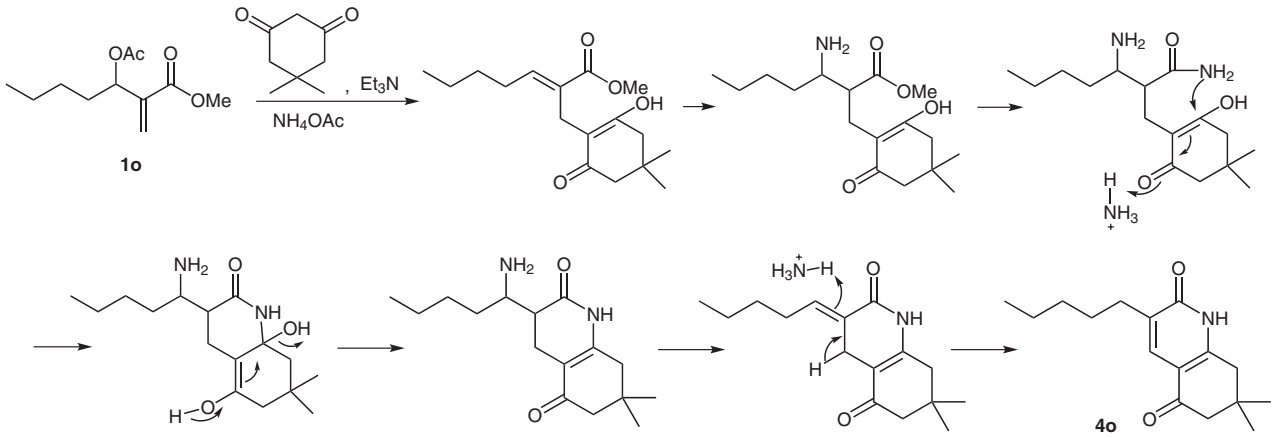
Table 2 Synthesis of 7,8-Dihydroquinoline-2,5(1*H*,6*H*)-diones **6** from Morita–Baylis–Hillman Adduct Acetates **1**[a]

Entry	R^1	R^2	R^3	R^4 of Amine **5**	Time[b] (h)	Product	Yield[c] (%)
1	4-FC_6H_4	Me	Me	*n*-Bu	3.0 (3)	**6a**	85
2	3-$O_2NC_6H_4$	Me	Me	Ph	3.0 (2)	**6b**	83
3	3-$O_2NC_6H_4$	Me	Me	4-Tol	3.0 (2)	**6c**	85
4	3-$O_2NC_6H_4$	Me	Me	4-$MeOC_6H_4$	3.0 (1)	**6d**	87
5	3-$O_2NC_6H_4$	Me	Me	4-ClC_6H_4	3.0 (3)	**6e**	81
6	3-$O_2NC_6H_4$	Me	Me	3,4-$F_2C_6H_3$	3.0 (3)	**6f**	73
7	3-$O_2NC_6H_4$	Me	Me	4-phenylthiazol-2-yl	3.0 (2)	**6g**	82

[a] All reactions were carried out on Morita–Baylis–Hillman adduct acetates (1 mmol) with 5,5-dimethylcyclohexane-1,3-dione (**2a**; 1.2 mmol) in the presence of triethylamine (1.2 mmol) at 90 °C under solvent-free conditions; an amine **5** (3 mmol) was added subsequently.
[b] Reaction times for step 1 and step 2 (in brackets).
[c] Isolated yields based on the Morita–Baylis–Hillman adduct acetates.



Scheme 5



Scheme 6

In summary, we have developed a simple, efficient and 'green' strategy for the synthesis of various 7,8-dihydroquinolinones from Morita–Baylis–Hillman adduct acetates, cyclic β-diketones and ammonium acetate or primary amines in one pot under solvent-free conditions. Merits of the present process are the simple experimental procedure, especially the workup operation, environmental friendliness, and high yields and purity of products.

Starting materials and solvents were purchased from common commercial sources and were used without additional purification. Melting points were determined with a Büchi B-540 capillary melting point apparatus and are uncorrected. IR spectra were recorded on a Nicolet Avatar-370 instrument. ^{1}H and ^{13}C NMR spectra were recorded on Varian (400 MHz) and Avance III (500 MHz) instruments using TMS as an internal standard. Mass spectra were measured with a Finnigan Trace DSQ instrument. Elemental analyses were performed on a VarioEL-3 instrument. All spectroscopic data of the products were identical to data from authentic samples.

3-(Arylmethyl)-2-hydroxy-7,8-dihydroquinolin-5(6*H*)-ones 4 and 3-(Arylmethyl)-7,8-dihydroquinoline-2,5(1*H*,6*H*)-diones 6; General Procedure

A mixture of a Morita–Baylis–Hillman adduct acetate **1** (1 mmol), a cyclic β-diketone **2** (1.2 mmol) and Et_3N (1.2 mmol) was stirred at 90 °C for the indicated time (Tables 1 and 2). Then, NH_4OAc (3 mmol) or a primary amine **5** (3 mmol) was added to the mixture, and the reaction mixture was further stirred for the given time (Tables 1 and 2). The mixture was cooled, the reaction was quenched with EtOH–H_2O (4:1; 5 mL) and the mixture was stirred at 0 °C for 3 h. Finally, the product **4** or **6** was isolated by simple filtration and washed with cooled EtOH.

3-Benzyl-2-hydroxy-7,7-dimethyl-7,8-dihydroquinolin-5(6*H*)-one (4a)

White solid; mp 218.6–220.2 °C; R_f = 0.30 (hexane–EtOAc, 1:1).

IR (KBr): 3423, 3134, 1683, 1630, 1397, 1216 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.11 (s, 6 H, CH_3), 2.39 (s, 2 H, CH_2), 2.70 (s, 2 H, CH_2), 3.84 (s, 2 H, CH_2), 7.18–7.22 (m, 1 H, ArH), 7.25–7.30 (m, 4 H, ArH), 7.85 (s, 1 H, ArH), 13.11 (br s, 1 H, OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.3 (2 C), 33.2, 36.1, 40.2, 50.9, 113.7, 126.3, 128.4 (2 C), 129.0 (2 C), 130.1, 135.5, 139.1, 152.7, 165.8, 194.1.

MS (ESI): *m*/*z* (%) = 282 (100) [M$^+$ + 1].

Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.65; H, 6.64; N, 5.11.

2-Hydroxy-7,7-dimethyl-3-(3-nitrobenzyl)-7,8-dihydroquinolin-5(6*H*)-one (4b)

White solid; mp 236.4–238.1 °C; R_f = 0.20 (hexane–EtOAc, 1:1).

IR (KBr): 3423, 3134, 1635, 1527, 1401, 1225 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.00 (s, 6 H, CH_3), 2.32 (s, 2 H, CH_2), 2.68 (s, 2 H, CH_2), 3.87 (s, 2 H, CH_2), 7.58 (t, *J* = 8.0 Hz, 1 H, ArH), 7.74 (t, *J* = 8.0 Hz, 2 H, ArH), 8.05–8.08 (m, 1 H, ArH), 8.15 (s, 1 H, ArH), 12.15 (br s, 1 H, OH).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 28.2 (2 C), 33.1, 35.2, 40.6, 50.5, 112.0, 121.7, 123.7, 130.0, 130.2, 134.5, 136.1, 142.7, 148.2, 154.7, 163.5, 193.9.

MS (ESI): *m*/*z* (%) = 327 (100) [M$^+$ + 1].

Anal. Calcd for $C_{18}H_{18}N_2O_4$: C, 66.25; H, 5.56; N, 8.58. Found: C, 65.99; H, 5.37; N, 8.60.

3-(2-Chlorobenzyl)-2-hydroxy-7,7-dimethyl-7,8-dihydroquinolin-5(6*H*)-one (4c)

White solid; mp 224.8–226.7 °C; R_f = 0.25 (hexane–EtOAc, 1:1).

IR (KBr): 3427, 3124, 1669, 1636, 1400, 1209 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.12 (s, 6 H, CH_3), 2.39 (s, 2 H, CH_2), 2.76 (s, 2 H, CH_2), 3.97 (s, 2 H, CH_2), 7.16–7.20 (m, 2 H, ArH), 7.31 (t, *J* = 5.0 Hz, 1 H, ArH), 7.35–7.38 (m, 1 H, ArH), 7.74 (s, 1 H, ArH), 13.09 (br s, 1 H, OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.2 (2 C), 33.2, 33.4, 40.2, 50.9, 113.6, 126.7, 128.0, 128.3, 129.6, 131.4, 134.5, 135.6, 136.3, 152.7, 165.6, 194.0.

MS (ESI): *m*/*z* (%) = 316 (100) [M$^+$ + 1].

Anal. Calcd for $C_{18}H_{18}ClNO_2$: C, 68.46; H, 5.75; N, 4.44. Found: C, 68.14; H, 5.97; N, 4.56.

3-(2-Chloro-6-fluorobenzyl)-2-hydroxy-7,7-dimethyl-7,8-dihydroquinolin-5(6*H*)-one (4d)

White solid; mp 281.8–284.1 °C; R_f = 0.25 (hexane–EtOAc, 1:1).

IR (KBr): 3420, 3125, 1673, 1636, 1401, 1210 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.14 (s, 6 H, CH_3), 2.39 (s, 2 H, CH_2), 2.81 (s, 2 H, CH_2), 4.03 (s, 2 H, CH_2), 6.99–7.03 (m, 1 H, ArH), 7.18–7.23 (m, 2 H, ArH), 7.56 (s, 1 H, ArH), 13.16 (br s, 1 H, OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.7 (d, *J* = 3.8 Hz), 28.2 (2 C), 33.2, 40.2, 51.0, 113.6, 114.1 (d, *J* = 22.5 Hz), 124.4 (d, *J* = 17.5

Hz), 125.4 (d, *J* = 2.5 Hz), 127.1, 128.6 (d, *J* = 10.0 Hz), 134.6, 135.9 (d, *J* = 7.5 Hz), 152.6, 161.9 (d, *J* = 247.5 Hz), 165.5, 193.9.

MS (ESI): *m*/*z* (%) = 334 (100) [$M^+ + 1$].

Anal. Calcd for $C_{18}H_{17}ClFNO_2$: C, 64.77; H, 5.13; N, 4.20. Found: C, 64.54; H, 5.13; N, 4.28.

3-(4-Fluorobenzyl)-2-hydroxy-7,7-dimethyl-7,8-dihydroquinolin-5(6*H*)-one (4e)

White solid; mp 201.7–203.0 °C; R_f = 0.30 (hexane–EtOAc, 1:1).

IR (KBr): 3423, 3137, 1684, 1632, 1611, 1508, 1398, 1217 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.13 (s, 6 H, CH_3), 2.40 (s, 2 H, CH_2), 2.70 (s, 2 H, CH_2), 3.81 (s, 2 H, CH_2), 6.94–6.98 (m, 2 H, ArH), 7.22–7.27 (m, 2 H, ArH), 7.84 (s, 1 H, ArH), 13.04 (br s, 1 H, OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.2 (2 C), 33.2, 35.4, 40.2, 50.9, 113.7, 115.1, 115.3, 130.2 (d, *J* = 82.5 Hz), 130.4, 134.7, 134.8, 135.5, 152.8, 161.5 (d, *J* = 224.5 Hz), 165.7, 194.0.

MS (EI): *m*/*z* (%) = 299 (100) [M^+].

Anal. Calcd for $C_{18}H_{18}FNO_2$: C, 72.22; H, 6.06; N, 4.68. Found: C, 72.01; H, 6.04; N, 4.78.

3-(Furan-2-ylmethyl)-2-hydroxy-7,7-dimethyl-7,8-dihydroquinolin-5(6*H*)-one (4f)

White solid; mp 216.9–218.7 °C; R_f = 0.35 (hexane–EtOAc, 1:1).

IR (KBr): 3422, 3129, 1671, 1637, 1400, 1206 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.13 (s, 6 H, CH_3), 2.40 (s, 2 H, CH_2), 2.75 (s, 2 H, CH_2), 3.89 (s, 2 H, CH_2), 6.13 (d, *J* = 3.0 Hz, 1 H, ArH), 6.30–6.35 (m, 1 H, ArH), 7.33 (d, *J* = 1.0 Hz, 1 H, ArH), 7.86 (s, 1 H, ArH), 12.99 (br s, 1 H, OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.2 (2 C), 28.3, 33.2, 40.3, 50.9, 106.8, 110.3, 113.7, 127.1, 135.8, 141.6, 152.2, 152.9, 165.5, 193.9.

MS (ESI): *m*/*z* (%) = 272 (100) [$M^+ + 1$].

Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.79; H, 6.33; N, 5.14.

2-Hydroxy-7,7-dimethyl-3-(thien-2-ylmethyl)-7,8-dihydroquinolin-5(6*H*)-one (4g)

White solid; mp 227.2–229.1 °C; R_f = 0.25 (hexane–EtOAc, 1:1).

IR (KBr): 3414, 3135, 1647, 1617, 1400, 1218 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.13 (s, 6 H, CH_3), 2.41 (s, 2 H, CH_2), 2.79 (s, 2 H, CH_2), 4.05 (s, 2 H, CH_2), 6.91–6.94 (m, 2 H, ArH), 7.13 (d, *J* = 4.5 Hz, 1 H, ArH), 7.92 (s, 1 H, ArH), 13.10 (br s, 1 H, OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.3 (2 C), 30.1, 33.2, 40.3, 51.0, 113.8, 124.0, 125.8, 126.9, 129.4, 135.6, 141.3, 153.0, 165.5, 194.0.

MS (ESI): *m*/*z* (%) = 286 (100) [$M^+ - 1$].

Anal. Calcd for $C_{16}H_{17}NO_2S$: C, 66.87; H, 5.96; N, 4.87. Found: C, 66.52; H, 5.84; N, 4.68.

3-(3,4-Dimethylbenzyl)-2-hydroxy-7,7-dimethyl-7,8-dihydroquinolin-5(6*H*)-one (4h)

White solid; mp 216.0–218.5 °C; R_f = 0.30 (hexane–EtOAc, 1:1).

IR (KBr): 3433, 3133, 1637, 1595, 1400, 1236 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.11 (s, 6 H, CH_3), 2.21 (s, 6 H, CH_3), 2.39 (s, 2 H, CH_2), 2.73 (s, 2 H, CH_2), 3.77 (s, 2 H, CH_2), 7.04 (s, 3 H, ArH), 7.82 (s, 1 H, ArH), 12.92 (br s, 1 H, OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.4, 19.8, 28.2 (2 C), 33.2, 35.5, 40.3, 51.0, 113.7, 126.5, 129.7, 130.3, 130.6, 134.5, 135.3, 136.4, 136.5, 152.5, 165.7, 194.1.

MS (ESI): *m*/*z* (%) = 308 (100) [$M^+ - 1$].

Anal. Calcd for $C_{20}H_{23}NO_2$: C, 77.64; H, 7.49; N, 4.53. Found: C, 77.53; H, 7.49; N, 4.51.

3-(3,4-Dimethylbenzyl)-7,7-dimethyl-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (4h′)

White solid; mp 196.8–198.0 °C; R_f = 0.35 (hexanes–EtOAc, 1:1).

IR (KBr): 3423, 3134, 1635, 1528, 1401, 1233 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.12 (s, 6 H, CH_3), 2.30 (s, 6 H, CH_3), 2.31 (s, 2 H, CH_2), 2.36 (s, 2 H, CH_2), 3.71 (s, 2 H, CH_2), 7.22 (d, *J* = 7.5 Hz, 1 H, ArH), 7.31 (dd, *J* = 8.5, 8.0 Hz, 2 H, ArH), 7.85 (s, 1 H, ArH), 8.24 (s, 1 H, NH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.8, 19.9, 24.8, 28.3 (2 C), 32.9, 41.1, 50.5, 109.5, 124.2, 128.1, 130.0, 132.3, 132.6, 136.9, 138.6, 139.6, 148.3, 166.3, 195.8.

MS (ESI): *m*/*z* (%) = 308 (100) [$M^+ - 1$].

Anal. Calcd for $C_{20}H_{23}NO_2$: C, 77.64; H, 7.49; N, 4.53. Found: C, 77.49; H, 7.58; N, 4.53.

3-(1,3-Benzodioxol-5-ylmethyl)-2-hydroxy-7,7-dimethyl-7,8-dihydroquinolin-5(6*H*)-one (4i)

White solid; mp 206.8–208.2 °C; R_f = 0.30 (hexanes–EtOAc, 1:1).

IR (KBr): 3413, 3138, 2961, 1636, 1401, 1249 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.13 (s, 6 H, CH_3), 2.40 (s, 2 H, CH_2), 2.74 (s, 2 H, CH_2), 3.75 (s, 2 H, CH_2), 5.91 (s, 2 H, CH_2), 6.71–6.75 (m, 2 H, ArH), 6.80 (s, 1 H, ArH), 7.82 (s, 1 H, ArH), 12.99 (br s, 1 H, OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.2 (2 C), 33.2, 35.7, 40.3, 51.0, 100.8, 108.2, 109.6, 113.7, 122.0, 130.3, 132.8, 135.3, 146.1, 147.6, 152.6, 165.7, 194.1.

MS (ESI): *m*/*z* (%) = 324 (100) [$M^+ - 1$].

Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.31. Found: C, 69.97; H, 6.04; N, 4.37.

2-Hydroxy-3-(3-methoxybenzyl)-7,7-dimethyl-7,8-dihydroquinolin-5(6*H*)-one (4j)

White solid; mp 158.6–159.6 °C; R_f = 0.30 (hexanes–EtOAc, 1:1).

IR (KBr): 3425, 3137, 3025, 2958, 1684, 1634, 1397, 1217 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.12 (s, 6 H, CH_3), 2.39 (s, 2 H, CH_2), 2.72 (s, 2 H, CH_2), 3.77 (s, 3 H, OCH_3), 3.82 (s, 2 H, CH_2), 6.74 (d, *J* = 8.0 Hz, 1 H, ArH), 6.87 (dd, *J* = 10.5, 8.0 Hz, 2 H, ArH), 7.20 (t, *J* = 8.0 Hz, 1 H, ArH), 7.85 (s, 1 H, ArH), 13.05 (br s, 1 H, OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.2 (2 C), 33.2, 36.1, 40.2, 51.0, 55.1, 111.2, 113.7, 115.3, 121.4, 129.4, 130.0, 135.6, 140.7, 152.7, 159.6, 165.8, 194.1.

MS (ESI): *m*/*z* (%) = 310 (100) [$M^+ - 1$].

Anal. Calcd for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.36; H, 6.78; N, 4.41.

3-(4-Fluorobenzyl)-2-hydroxy-7,8-dihydroquinolin-5(6*H*)-one (4k)

White solid; mp 208.0–210.0 °C; R_f = 0.25 (hexanes–EtOAc, 1:1).

IR (KBr): 3413, 3137, 1675, 1639, 1401, 1192 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.13 (t, *J* = 6.5 Hz, 2 H, CH_2), 2.54 (t, *J* = 6.5 Hz, 2 H, CH_2), 2.82 (t, *J* = 6.5 Hz, 2 H, CH_2), 3.79 (s, 2 H, CH_2), 6.93–6.97 (m, 2 H, ArH), 7.21–7.26 (m, 2 H, ArH), 7.84 (s, 1 H, ArH), 12.85 (br s, 1 H, OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.4, 26.8, 35.3, 37.2, 114.7, 115.1, 115.3, 130.3 (d, *J* = 27.5 Hz), 130.5, 134.7, 134.7, 135.8, 154.1, 160.6, 163.9 (d, *J* = 343.8 Hz), 194.1.

MS (ESI): *m*/*z* (%) = 272 (100) [M^+ + 1].

Anal. Calcd for $C_{16}H_{14}FNO_2$: C, 70.84; H, 5.20; N, 5.16. Found: C, 70.66; H, 5.22; N, 5.32.

2-Hydroxy-3-(3-nitrobenzyl)-7,8-dihydroquinolin-5(6*H*)-one (4l)

White solid; mp 247.4–249.5 °C; R_f = 0.20 (hexanes–EtOAc, 1:1).

IR (KBr): 3410, 3134, 1684, 1635, 1401, 1233 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.19 (t, *J* = 6.5 Hz, 2 H, CH_2), 2.57 (t, *J* = 6.5 Hz, 2 H, CH_2), 2.90 (t, *J* = 6.5 Hz, 2 H, CH_2), 3.91 (s, 2 H, CH_2), 7.43 (t, *J* = 7.5 Hz, 1 H, ArH), 7.60 (d, *J* = 7.5 Hz, 1 H, ArH), 7.97 (s, 1 H, ArH), 8.04–8.27 (m, 1 H, ArH), 8.28 (s, 1 H, ArH), 13.12 (br s, 1 H, OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.4, 26.9, 36.2, 37.1, 114.7, 121.6, 124.3, 128.7, 129.2, 135.1, 136.3, 141.3, 148.2, 154.9, 165.2, 194.1.

MS (ESI): *m*/*z* (%) = 297 (100) [M^+ – 1].

Anal. Calcd for $C_{16}H_{14}N_2O_4$: C, 64.42; H, 4.73; N, 9.39. Found: C, 64.12; H, 4.93; N, 9.40.

3-Benzyl-2-hydroxy-7,8-dihydroquinolin-5(6*H*)-one (4m)

White solid; mp 205.8–206.9 °C; R_f = 0.30 (hexanes–EtOAc, 1:1).

IR (KBr): 3415, 3136, 1639, 1606, 1401, 1224 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.12 (t, *J* = 6.5 Hz, 2 H, CH_2), 2.53 (t, *J* = 6.5 Hz, 2 H, CH_2), 2.81 (t, *J* = 6.5 Hz, 2 H, CH_2), 3.83 (s, 2 H, CH_2), 7.18–7.21 (m, 1 H, ArH), 7.24–7.28 (m, 4 H, ArH), 7.85 (s, 1 H, ArH), 12.94 (br s, 1 H, OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.5, 26.8, 36.0, 37.2, 114.7, 126.4, 128.4 (2 C), 129.1 (2 C), 130.4, 135.8, 139.1, 154.1, 165.4, 194.2.

MS (ESI): *m*/*z* (%) = 252 (100) [M^+ – 1].

Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.99; H, 6.12; N, 5.51.

2-Hydroxy-3-(3-methoxybenzyl)-7,8-dihydroquinolin-5(6*H*)-one (4n)

White solid; mp 175.3–176.6 °C; R_f = 0.15 (hexanes–EtOAc, 1:1).

IR (KBr): 3430, 3131, 1640, 1401, 1452, 1228 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.12 (t, *J* = 6.5 Hz, 2 H, CH_2), 2.53 (t, *J* = 6.5 Hz, 2 H, CH_2), 2.82 (t, *J* = 6.5 Hz, 2 H, CH_2), 3.77 (s, 3 H, OCH_3), 3.80 (s, 2 H, CH_2), 6.72–6.75 (m, 1 H, ArH), 6.83–6.86 (m, 2 H, ArH), 7.20 (t, *J* = 8.0 Hz, 1 H, ArH), 7.86 (s, 1 H, ArH), 12.95 (br s, 1 H, OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.5, 26.8, 36.0, 37.2, 55.2, 111.3, 114.7, 115.2, 121.5, 129.4, 130.2, 135.9, 140.7, 154.2, 159.6, 165.4, 194.2.

MS (ESI): *m*/*z* (%) = 282 (100) [M^+ – 1].

Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94. Found: C, 71.83; H, 6.26; N, 5.05.

7,7-Dimethyl-3-pentyl-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (4o)

A mixture of Morita–Baylis–Hillman adduct acetate **1o** (1 mmol), 5,5-dimethylcyclohexane-1,3-dione (**2a**; 1.2 mmol), Et_3N (1.2 mmol) and NH_4OAc (3 mmol) was stirred at 90 °C until TLC monitoring indicated complete consumption of adduct **1o**. Brine was added and the suspension was extracted twice with EtOAc. The organic phase was dried over Na_2SO_4, then concentrated to give the crude product. Column chromatography (silica gel, hexane–EtOAc, 4:1→ 6:1 gradient elution) gave the desired product **4o** in 55% isolated yield (144 mg).

White solid; mp 142.5–143.3 °C; R_f = 0.40 (hexanes–EtOAc, 2:1).

IR (KBr): 3238, 3161, 2956, 2930, 1692, 1613, 1390, 1239 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.0 Hz, 3 H, CH_3), 1.11 (s, 6 H, CH_3), 1.33–1.41 (m, 2 H, CH_2), 1.45–1.51 (m, 2 H, CH_2), 2.19–2.33 (m, 2 H, CH_2), 2.34 (s, 2 H, CH_2), 2.35 (s, 2 H, CH_2), 3.33–3.34 (m, 2 H, CH_2), 7.01–7.05 (m, 1 H, ArH), 8.65 (s, 1 H, NH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.9, 22.5, 22.6, 28.3, 28.4 (2 C), 30.2, 32.9, 40.9, 50.5, 109.6, 125.4, 144.6, 149.1, 165.8, 196.2.

MS (ESI): *m*/*z* (%) = 262 (100) [M^+ + 1].

Anal. Calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.44; H, 8.98; N, 5.47.

1-*n*-Butyl-3-(4-fluorobenzyl)-7,7-dimethyl-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (6a)

A mixture of the Morita–Baylis–Hillman adduct acetate **1** (R^1 = 4-FC_6H_4, R^2 = Me; 1 mmol), 5,5-dimethylcyclohexane-1,3-dione (**2a**; 1.2 mmol) and Et_3N (1.2 mmol) was stirred at 90 °C until TLC monitoring indicated complete consumption of the Morita–Baylis–Hillman adduct acetate. Then, *n*-$BuNH_2$ (3 mmol) was added to the reaction mixture which was further stirred at 70 °C for 3 h (the progress of the reaction was monitored by TLC). Brine was added and the suspension was extracted twice with EtOAc. The organic phase was dried over Na_2SO_4, then concentrated to give the crude product. Column chromatography (silica gel, hexane–EtOAc, 2:1→ 4:1 gradient elution) gave the desired product **6a** in 85% isolated yield (302 mg).

Viscous yellowish oil; R_f = 0.55 (hexane–EtOAc, 1:1).

IR (neat): 3041, 2960, 2872, 1644, 1423, 1220 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.99 (t, *J* = 7.5 Hz, 3 H, CH_3), 1.14 (s, 6 H, CH_3), 1.41–1.49 (m, 2 H, CH_2), 1.61–1.68 (m, 2 H, CH_2), 2.39 (s, 2 H, CH_2), 2.77 (s, 2 H, CH_2), 3.80 (s, 2 H, CH_2), 4.04 (t, *J* = 7.5 Hz, 2 H, CH_2), 6.94–6.98 (m, 2 H, ArH), 7.23–7.28 (m, 2 H, ArH), 7.75 (s, 1 H, ArH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.7, 19.3 (d, *J* = 231.3 Hz), 28.5, 30.8, 32.9, 36.1, 40.7, 44.4, 49.9, 58.4, 113.4, 115.1, 115.3, 129.8, 130.5 (d, *J* = 8.8 Hz), 132.9, 134.7, 134.8, 152.8, 160.6, 162.8 (d, *J* = 66.2 Hz), 194.2.

MS (ESI): *m*/*z* (%) = 356 (100) [M^+ + 1].

Anal. Calcd for $C_{22}H_{26}FNO_2$: C, 74.34; H, 7.37; N, 3.94. Found: C, 74.54; H, 7.17; N, 3.94.

7,7-Dimethyl-3-(3-nitrobenzyl)-1-phenyl-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (6b)

White solid; mp 175.0–177.3 °C; R_f = 0.35 (hexanes–EtOAc, 1:1).

IR (KBr): 3132, 1651, 1518, 1402, 1209 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.01 (s, 6 H, CH_3), 2.29 (s, 2 H, CH_2), 2.38 (s, 2 H, CH_2), 3.94 (s, 2 H, CH_2), 7.16 (t, *J* = 7.5 Hz, 2 H, ArH), 7.44 (t, *J* = 8.0 Hz, 1 H, ArH), 7.49–7.52 (m, 1 H, ArH), 7.54–7.57 (m, 2 H, ArH), 7.68 (d, *J* = 4.0 Hz, 1 H, ArH), 7.93 (s, 1 H, ArH), 8.05–8.12 (m, 1 H, ArH), 8.13 (s, 1 H, ArH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.2 (2 C), 33.0, 36.7, 42.2, 50.1, 113.2, 121.6, 123.8, 127.6 (2 C), 129.3 (2 C), 129.4, 130.2 (2 C), 134.1, 135.6, 137.5, 141.0, 148.3, 154.2, 163.3, 194.1.

MS (ESI): *m*/*z* (%) = 403 (100) [M^+ + 1].

Anal. Calcd for $C_{24}H_{22}N_2O_4$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.46; H, 5.52; N, 6.84.

7,7-Dimethyl-3-(3-nitrobenzyl)-1-*p*-tolyl-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (6c)
White solid; mp 187.4–189.1 °C; R_f = 0.35 (hexane–EtOAc, 1:1).

IR (KBr): 3128, 1649, 1618, 1403, 1209 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.01 (s, 6 H, CH_3), 2.32 (s, 2 H, CH_2), 2.38 (s, 2 H, CH_2), 2.42 (s, 3 H, CH_3), 3.93 (s, 2 H, CH_2), 7.03 (d, *J* = 7.5 Hz, 2 H, ArH), 7.34 (d, *J* = 7.5 Hz, 2 H, ArH), 7.43 (t, *J* = 7.5 Hz, 1 H, ArH), 7.68 (d, *J* = 7.0 Hz, 1 H, ArH), 7.93 (s, 1 H, ArH), 8.05 (d, *J* = 7.5 Hz, 1 H, ArH), 8.13 (s, 1 H, ArH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.2, 28.2 (2 C), 33.0, 36.7, 42.2, 50.1, 113.2, 121.6, 123.9, 127.3 (2 C), 129.2, 129.3, 130.8 (2 C), 134.0, 134.8, 135.7, 139.5, 141.1, 148.3, 154.5, 163.5, 194.2.

MS (ESI): *m*/*z* (%) = 415 (100) [M^+ – 1].

Anal. Calcd for $C_{25}H_{24}N_2O_4$: C, 72.10; H, 5.81; N, 6.73. Found: C, 72.26; H, 5.75; N, 6.60.

1-(4-Methoxyphenyl)-7,7-dimethyl-3-(3-nitrobenzyl)-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (6d)
White solid; mp 153.4–154.7 °C; R_f = 0.35 (hexane–EtOAc, 1:1).

IR (KBr): 3133, 2651, 2574, 1732, 1401, 1223 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.02 (s, 6 H, CH_3), 2.33 (s, 2 H, CH_2), 2.38 (s, 2 H, CH_2), 3.87 (s, 3 H, CH_3), 3.94 (s, 2 H, CH_2), 7.05 (d, *J* = 9.0 Hz, 4 H, ArH), 7.43 (t, *J* = 7.5 Hz, 1 H, ArH), 7.68 (d, *J* = 7.5 Hz, 1 H, ArH), 7.92 (s, 1 H, ArH), 8.06 (d, *J* = 8.5 Hz, 1 H, ArH), 8.13 (s, 1 H, ArH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.3 (2 C), 33.0, 36.8, 42.4, 50.1, 55.6, 113.3, 115.4 (2 C), 121.6, 123.9, 128.7 (2 C), 129.2, 129.3, 130.0, 134.0, 135.7, 141.1, 148.4, 154.7, 160.0, 163.6, 194.2.

MS (ESI): *m*/*z* (%) = 431 (100) [M^+ – 1].

Anal. Calcd for $C_{25}H_{24}N_2O_5$: C, 69.43; H, 5.59; N, 6.48. Found: C, 69.27; H, 5.68; N, 6.61.

1-(4-Chlorophenyl)-7,7-dimethyl-3-(3-nitrobenzyl)-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (6e)
White solid; mp 206.7–209.3 °C; R_f = 0.35 (hexane–EtOAc, 1:1).

IR (KBr): 3132, 2573, 1735, 1637, 1401, 1223 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.03 (s, 6 H, CH_3), 2.29 (s, 2 H, CH_2), 2.39 (s, 2 H, CH_2), 3.94 (s, 2 H, CH_2), 7.11 (d, *J* = 8.0 Hz, 2 H, ArH), 7.44 (t, *J* = 7.5 Hz, 1 H, ArH), 7.53 (d, *J* = 8.0 Hz, 2 H, ArH), 7.67 (d, *J* = 7.0 Hz, 1 H, ArH), 7.93 (s, 1 H, ArH), 8.06 (d, *J* = 8.0 Hz, 1 H, ArH), 8.12 (s, 1 H, ArH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.3 (2 C), 33.1, 36.7, 42.3, 50.1, 113.5, 121.7, 123.8, 129.2 (2 C), 129.3, 129.4, 130.5 (2 C), 134.3, 135.6, 135.7, 135.9, 140.9, 148.4, 153.8, 163.2, 194.0.

MS (ESI): *m*/*z* (%) = 435 (100) [M^+ – 1].

Anal. Calcd for $C_{24}H_{21}ClN_2O_4$: C, 65.98; H, 4.84; N, 6.41. Found: C, 65.87; H, 4.95; N, 6.41.

1-(3,4-Difluorophenyl)-7,7-dimethyl-3-(3-nitrobenzyl)-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (6f)
White solid; mp 195.1–197.0 °C; R_f = 0.30 (hexane–EtOAc, 1:1).

IR (KBr): 3131, 1654, 1401, 1271 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.04 (s, 6 H, CH_3), 2.31 (s, 2 H, CH_2), 2.39 (s, 2 H, CH_2), 3.93 (s, 2 H, CH_2), 6.94 (d, *J* = 8.0 Hz, 1 H, ArH), 7.04 (t, *J* = 7.5 Hz, 1 H, ArH), 7.36 (d, *J* = 8.0 Hz, 1 H, ArH), 7.45 (t, *J* = 8.0 Hz, 1 H, ArH), 7.67 (d, *J* = 7.5 Hz, 1 H, ArH), 7.93 (s, 1 H, ArH), 8.07 (d, *J* = 8.0 Hz, 1 H, ArH), 8.11 (s, 1 H, ArH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.2 (d, *J* = 3.8 Hz, 2 C), 33.1, 36.7, 42.2, 50.2, 113.5, 117.7, 117.9, 118.7, 118.9, 121.7, 123.8, 124.7, 129.4, 129.5, 133.4, 134.4, 135.6, 140.7, 149.1 (d, *J* = 182.5 Hz), 152.8 (d, *J* = 208.8 Hz), 163.1, 193.8.

MS (ESI): *m*/*z* (%) = 437 (100) [M^+ – 1].

Anal. Calcd for $C_{24}H_{20}F_2N_2O_4$: C, 65.75; H, 4.60; N, 6.39. Found: C, 65.59; H, 4.71; N, 6.46.

7,7-Dimethyl-3-(3-nitrobenzyl)-1-(4-phenylthiazol-2-yl)-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (6g)
White solid; mp 169.4–170.5 °C; R_f = 0.35 (hexane–EtOAc, 1:1).

IR (KBr): 3129, 1662, 1560, 1532, 1401, 1344 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.05 (s, 6 H, CH_3), 2.42 (s, 2 H, CH_2), 2.53 (s, 2 H, CH_2), 3.96 (s, 2 H, CH_2), 7.39 (t, *J* = 1.0 Hz, 1 H, ArH), 7.43–7.48 (m, 3 H, ArH), 7.67 (d, *J* = 8.0 Hz, 1 H, ArH), 7.72 (s, 1 H, ArH), 7.86–7.88 (m, 2 H, ArH), 7.92 (s, 1 H, ArH), 8.07–8.15 (m, 1 H, ArH), 8.16 (s, 1 H, ArH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.3 (2 C), 33.0, 36.5, 41.4, 50.1, 114.0, 115.9, 121.8, 124.0, 126.3 (2 C), 128.9 (2 C), 129.0, 129.4, 129.7, 133.4, 134.7, 135.6, 140.5, 148.4, 153.7, 154.2, 156.4, 163.2, 194.0.

MS (ESI): *m*/*z* (%) = 484 (100) [M^+ – 1].

Anal. Calcd for $C_{27}H_{23}N_3O_4S$: C, 66.79; H, 4.77; N, 8.65. Found: C, 66.54; H, 4.86; N, 8.67.

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