Glycine-Catalyzed Easy and Efficient One-Pot Synthesis of Polyhydroquinolines Through Hantzsch Multicomponent Condensation under Controlled Microwave

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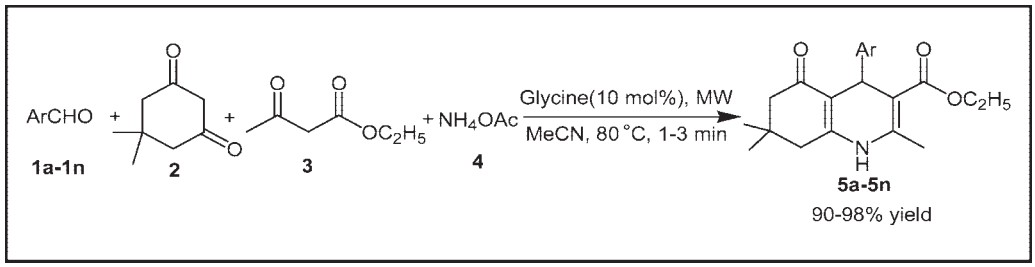
Received September 19, 2009
DOI 10.1002/jhet.308
Published online 8 January 2010 in Wiley InterScience (www.interscience.wiley.com).



Glycine, a novel heterogeneous organocatalyst, is found to be highly effective for the synthesis of polyhydroquinoline derivatives in a one-pot multicomponent reaction *via* Hantzsch condensation under controlled microwave (MW) irradiation. The combination of glycine and MW has promising features for the reaction response, such as the shortest reaction time, excellent product yields, and simple work-up of the products.

J. Heterocyclic Chem., **47**, 194 (2010).

INTRODUCTION

Microwave (MW) irradiation has evolved as a powerful method to perform organic synthesis with great success, particularly in the light of the current paradigm shift to ''green chemistry.'' It provides chemical processes with special attributes, such as enhanced reaction rates, higher yields of pure products, better selectivity, improved ease of manipulation, rapid optimization of reactions, and several eco-friendly advantages [1]. An important way to improve synthetic efficiency and to give access to a multitude of diversified molecules from simple building blocks is the development of multicomponent synthesis. Multicomponent reactions (MCRs) have recently taken a new dimension in organic synthesis, as they comply well with the requirements for ideal organic syntheses [2,3]. According to the current synthetic and environmental requirements, MCRs using MW methodology are of great interest.

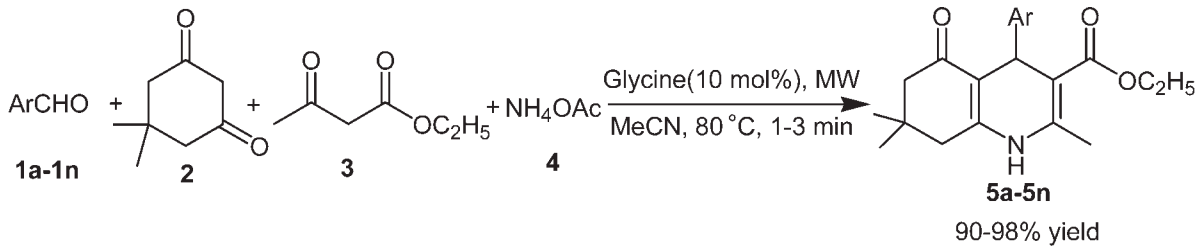
Polyhydroquinoline derivatives have a great deal of importance because of their diverse medicinal applications, which include calcium channel activity, vasodilators, bronchodilators, antiatherosclerotics, hepatoprotective, antidiabetic, antihypertensive, neuroprotectant, platelet antiaggregatory activity, cerebral antischemic activity, and chemosensitizer activity [4–10]. Owing to the remarkable potential of these compounds as a source of valuable drugs, various methods have been reported using conditions such as conventional heating [11], solar thermal energy [12], ionic liquid [13], TMSCl-NaI [14], metal triflates [15], grinding [16], Hy-Zeolite [17], montmorillonite K-10 [18], cerium(IV) ammonium nitrate [19], iron(III) trifluoroacetate [20], $HClO_4$-SiO_2 [21], heteropoly acid [22], molecular iodine [23], PTSA [24], L-proline and derivatives [25], nickel [26], polymers [27], and Baker's yeast [28]. Most of these processes, however, suffer from one or other drawbacks such as longer reaction time, lower product yield, harsh conditions, high costs, and use of hazardous catalysts. As a result, an eco-safe and efficient alternative method for the preparation of polyhydroquinoline is highly desirable. As there is no report on the use of glycine as an organocatalyst in the Hantzsch condensation, we wish to demonstrate the catalytic activity of this organocatalyst in the synthesis of polyhydroquinolines.

RESULTS AND DISCUSSION

We report herein a benign, rapid, and efficient four-component, one-pot synthesis of polyhydroquinolines in excellent yields using aromatic aldehydes, dimedone, ethyl acetoacetate, and ammonium acetate in the presence of catalytic amount of glycine (10 mol %) in acetonitrile under monomode MW irradiation (Scheme 1).

To optimize the synthesis, a typical four-component reaction of benzaldehyde **1a**, dimedone **2**, ethyl acetoacetate **3**, and ammonium acetate **4** was undertaken using

Scheme 1



a catalytic amount of different amino acids such as L-alanine, L-valine, and glycine in different solvents such as acetonitrile, ethanol, and water under varying reaction conditions to obtain the corresponding polyhydroquinoline derivative **5a** (Table 1). Consistent with Table 1, the optimum yield (95%) of product **5a** was obtained in the presence of catalytic amount of glycine (10 mol %) in solvent acetonitrile (entry 6) in 1 min under single-mode MW heating (180 W, 80°C). Decreasing the catalyst levels, MW power or temperature reduced the product yield considerably (Table 1; Entries 13, 16, and 17). An increase in the molar proportion of catalyst, MW power, and temperature did not bring about any further increase in the product yield, rather, a bit diminution was observed (Table 1; entries 14, 15, 18, and 19). It is assumed that the acidic hydrogen of carboxylic function and the small size of glycine play a key role in the catalysis of the reaction. Under the optimized set of reaction conditions (entry 6), a number of aromatic aldehydes **1** were allowed to undergo MCR with **2**, **3**, and **4** in a molar ratio of 1:1:1:1.2 in the presence of glycine (10 mol %) in acetonitrile under MW (180 W, 80°C) heating. The results are given in Table 2. All the electron-rich and electron-deficient aldehydes worked well leading to excellent yields of products.

After completion of the reaction, the resulting precipitate was filtered and recrystallized from methanol to yield pure substituted polyhydroquinolines **5a–5n**. All the products were crystalline and fully characterized on the basis of their melting points, elemental analyses, and spectral data (IR, ^{1}H-NMR, and ^{13}C-NMR).

Table 1

Optimization of reaction conditions for the multicomponent synthesis of **4a**.

			Reaction conditions					
			Room temperature		Reflux		Microwave[b]	
Entry	Catalyst[a]	Solvent	Time (h)	Yield (%)	Time (min)	Yield (%)	Time (min)	Yield (%)
1	–	Water	3.0	14	60	28	5	46
2	–	Ethanol	3.0	15	60	29	5	50
3	–	MeCN	3.0	15	60	32	5	54
4	Glycine	Water	1.0	54	30	61	1	75
5	Glycine	Ethanol	1.0	57	20	68	1	84
6	Glycine	MeCN	1.0	64	20	86	1	95
7	L-Alanine	Water	1.0	42	20	51	1	63
8	L-Alanine	Ethanol	1.0	46	20	58	1	72
9	L-Alanine	MeCN	1.0	52	20	66	1	78
10	L-Valine	Water	1.0	46	20	57	1	70
11	L-Valine	Ethanol	1.0	50	20	61	1	78
12	L-Valine	MeCN	1.0	56	20	72	1	86
13	Glycine	MeCN	1.0	57	30	79	3	87
14	Glycine	MeCN	1.0	64	30	84	2	95
15	Glycine	MeCN	1.0	63	30	80	2	93
16	Glycine	MeCN	–	–	–	–	3	89
17	Glycine	MeCN	–	–	–	–	3	88
18	Glycine	MeCN	–	–	–	–	2	93
19	Glycine	MeCN	–	–	–	–	2	95

[a] Catalyst concentration 10 mol % except for entries 13 (5 mol %), 14 (15 mol %), and 15 (20 mol %).
[b] Microwave heating performed on 180 W power and 80°C temperature except for entries 16 (120 W, 80°C), 17 (180 W, 50°C), 18 (250 W, 80°C), and 19 (180 W, 100°C).

Table 2

Glycine-catalyzed Hantzsch condensation to polyhydroquinoline derivatives.[a]

Product	Ar	Time (min)	Yield[b] (%)	Mp (°C) Obs	Mp (°C) Lit
5a	C_6H_5	1	95	203–205	202–204 [15(a)]
5b	4-$CH_3C_6H_4$	1	96	259–260	260–261 [15(a)]
5c	4-$CH_3OC_6H_4$	1	98	256–257	257–259 [15(a)]
5d	4-ClC_6H_4	2	97	246–248	245–246 [21]
5e	3-ClC_6H_4	2	94	192–193	–
5f	4-BrC_6H_4	2	96	254–256	253–255 [15(a)]
5g	3-BrC_6H_4	2	93	235–237	234–236 [16]
5h	4-FC_6H_4	2	95	184–186	184–186 [15(a)]
5i	4-$NO_2C_6H_4$	3	93	243–245	243–244 [21]
5j	3-$NO_2C_6H_4$	3	91	176–177	178–179 [21]
5k	4-OH-3-$CH_3OC_6H_3$	2	94	211–213	211–212 [21]
5l	4-$(CH_3)_2NC_6H_4$	2	95	232–233	229–231 [15(a)]
5m	2-Furyl	2	90	247–249	246–248 [15(a)]
5n	2,4-$Cl_2C_6H_3$	2	94	243–245	242–244 [21]

[a] Microwave heating performed on 180 W power and 80°C temperature.
[b] Isolated yield.

CONCLUSIONS

In conclusion, the present MW irradiation procedure provides an easy and efficient access to polyhydroquinolines *via* Hantzsch condensation using glycine as an organocatalyst. The mildness of the conversion, experimental simplicity, compatibility with various functional groups, excellent product yield, shorter reaction time, and the easy work-up procedure make this approach more attractive in synthesizing a variety of such derivatives.

EXPERIMENTAL

All the chemicals were procured from Aldrich, USA and E. Merck, Germany and were purified before use. IR spectra were recorded on a JASCO FT/IR-5300 spectrophotometer. NMR spectra were run on a JEOL AL300 FTNMR spectrometer; chemical shifts are given in δ ppm, relative to TMS as an internal standard. Elemental microanalysis was performed on Exeter Analytical Model CE-440 CHN analyzer. Melting points were measured in open capillaries and are uncorrected. The MW irradiation was effected using the CEM's Discover Bench Mate (magnetron frequency 2455 MHz) single-mode MW synthesis system using safe pressure regulation 10-mL pressurized vials with ''snap-on'' cap.

General procedure for the synthesis of polyhydroquinolines 5. A mixture of aldehyde **1** (1 mmol), dimedone **2** (1 mmol), ethyl acetoacetate **3** (1 mmol), ammonium acetate **4** (1.2 mmol), glycine (10 mol %), and acetonitrile (1 mL) was placed in a sealed pressure regulation 10-mL pressurized vial with ''snap-on'' cap and was irradiated in the single-mode MW synthesis system at 180 W power and 80°C temperature for 1–3 min. After completion of reaction (TLC), the mixture was cooled and the resulting product was washed with cold water to remove any unreacted ammonium acetate. The crude product was finally recrystallized from methanol to afford the pure products **5a–5n**.

Ethyl 2,7,7-trimethyl-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5a). IR (KBr): 3289, 3080, 2961, 1699, 1612 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.26–7.31 (m, 2H), 7.17–7.22 (m, 2H), 7.07–7.11 (m, 1H), 5.85 (s, 1H), 5.05 (s, 1H), 4.05 (q, *J* = 7.2 Hz, 2H), 2.38 (s, 3H), 2.18–2.31 (m, 4H), 1.19 (t, *J* = 7.2 Hz, 3H), 1.08 (s, 3H), 0.94 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 195.70, 167.47, 148.72, 147.05, 143.67, 127.96, 127.83, 125.98, 111.92, 105.93, 59.78, 50.72, 40.85, 36.55, 32.64, 29.41, 27.08, 19.24, 14.17; Anal. Calcd. for $C_{21}H_{25}NO_3$: C, 74.31; H, 7.42; N, 4.13; Found: C, 74.23; H, 7.48; N, 4.19.

Ethyl 4-(4-methylphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5b). IR (KBr): 3276, 3078, 2960, 1702, 1646 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.16 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.4 Hz, 2H), 5.69 (s, 1H), 5.07 (s, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 2.37 (s, 3H), 2.32 (s, 3H), 2.16–2.29 (m, 4H), 1.23 (t, *J* = 7.2 Hz, 3H), 1.06 (s, 3H), 0.95 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 195.68, 167.39, 148.74, 146.95, 143.71, 127.97, 127.83, 126.07, 112.01, 105.98, 59.83, 50.77, 40.92, 36.59, 32.73, 29.45, 27.06, 19.81, 19.23, 14.16; Anal. Calcd. for $C_{22}H_{27}NO_3$: C, 74.76; H, 7.70; N, 3.96; Found: C, 74.85; H, 7.66; N, 3.90.

Ethyl 4-(4-methoxyphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5c). IR (KBr): 3279, 3079, 2959, 1702, 1646 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.21 (d, *J* = 8.4 Hz, 2H), 6.73 (d, *J* = 8.4 Hz, 2H), 5.75 (s, 1H), 4.99 (s, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 3.74 (s, 3H), 2.37 (s, 3H), 2.17–2.30 (m, 4H), 1.20 (t, *J* = 7.2 Hz, 3H), 1.07 (s, 3H), 0.94 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 195.65, 167.51, 157.72, 148.18, 143.21, 139.60, 128.91, 113.20, 112.21, 106.24, 59.75, 55.08, 50.73, 40.95, 35.67, 32.64, 29.41, 27.13, 19.31, 14.21; Anal. Calcd. for $C_{22}H_{27}NO_4$: C, 71.52; H, 7.37; N, 3.79; Found: C, 71.61; H, 7.40; N, 3.70.

Ethyl 4-(4-chlorophenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5d). IR (KBr): 3274, 3206, 3085, 2938, 1705, 1606 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$):

δ = 7.14–7.23 (m, 2H), 7.05–7.11 (m, 2H), 5.77 (s, 1H), 5.02 (s, 1H), 4.05 (q, *J* = 7.2 Hz, 2H), 2.41 (s, 3H), 2.16–2.37 (m, 4H), 1.19 (t, *J* = 7.2 Hz, 3H), 1.08 (s, 3H), 0.94 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 195.64, 167.31, 149.20, 144.53, 133.55, 129.11, 128.08, 126.23, 111.14, 105.12, 59.79, 50.67, 40.64, 36.58, 32.59, 29.34, 27.01, 19.06, 14.13; Anal. Calcd. for $C_{21}H_{24}ClNO_3$: C, 67.46; H, 6.47; N, 3.75; Found: C, 67.34; H, 6.52; N, 3.78.

Ethyl 4-(3-chlorophenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5e). IR (KBr): 3274, 3202, 3074, 2934, 1704, 1605 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.08–7.24 (m, 4H), 5.78 (s, 1H), 5.03 (s, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 2.43 (s, 3H), 2.19–2.39 (m, 4H), 1.20 (t, *J* = 7.2 Hz, 3H), 1.09 (s, 3H), 0.95 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 195.66, 167.25, 149.28, 144.41, 133.53, 129.10, 128.05, 126.19, 111.11, 105.10, 59.78, 50.64, 40.61, 36.57, 32.55, 29.31, 27.04, 19.05, 14.13; Anal. Calcd. for $C_{21}H_{24}ClNO_3$: C, 67.46; H, 6.47; N, 3.75; Found: C, 67.51; H, 6.44; N, 3.70.

Ethyl 4-(4-bromophenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5f). IR (KBr): 3274, 3205, 3072, 2955, 1702, 1604 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.18–7.23 (m, 2H), 7.02–7.08 (m, 2H), 6.56 (s, 1H), 5.03 (s, 1H), 4.02–4.11 (m, 2H), 2.34 (s, 3H), 2.12–2.28 (m, 4H), 1.22 (t, *J* = 7.2 Hz, 3H), 1.08 (s, 3H), 0.95 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 195.38, 167.76, 148.87, 145.69, 143.71, 131.03, 129.73, 111.14, 106.05, 59.79, 50.67, 40.64, 36.28, 32.59, 29.34, 27.01, 19.16, 14.15; Anal. Calcd. for $C_{21}H_{24}BrNO_3$: C, 60.29; H, 5.78; N, 3.35; Found: C, 60.42; H, 5.71; N, 3.29.

Ethyl 4-(3-bromophenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5g). IR (KBr): 3275, 3204, 3074, 2957, 1703, 1605 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.40 (s, 1H), 7.21–7.26 (m, 2H), 7.04–7.09 (m, 1H), 6.60 (s, 1H), 5.02 (s, 1H), 4.02–4.12 (m, 2H), 2.35 (s, 3H), 2.13–2.29 (m, 4H), 1.21 (t, *J* = 7.2 Hz, 3H), 1.07 (s, 3H), 0.95 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 195.56, 167.16, 149.08, 144.00, 131.04, 129.25, 126.87, 122.02, 111.42, 105.43, 59.90, 50.67, 40.89, 36.63, 32.69, 29.36, 27.13, 19.31, 14.17; Anal. Calcd. for $C_{21}H_{24}BrNO_3$: C, 60.29; H, 5.78; N, 3.35; Found: C, 60.20; H, 5.83; N, 3.42.

Ethyl 4-(4-fluorophenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5h). IR (KBr): 3287, 3209, 2960, 1697, 1615 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.21–7.26 (m, 2H), 6.89–7.03 (m, 2H), 5.69 (s, 1H), 5.11 (s, 1H), 4.07 (q, *J* = 7.2 Hz, 2H), 2.35 (s, 3H), 2.14–2.28 (m, 4H), 1.20 (t, *J* = 7.2 Hz, 3H), 1.08 (s, 3H), 0.94 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 195.65, 167.55, 153.72, 149.27, 144.60, 138.63, 129.51, 112.17, 106.25, 59.84, 50.78, 40.97, 36.12, 32.71, 29.42, 27.15, 19.31, 14.22; Anal. Calcd. for $C_{21}H_{24}FNO_3$: C, 70.57; H, 6.77; N, 3.92; Found: C, 70.46; H, 6.74; N, 3.88.

Ethyl 4-(4-nitrophenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5i). IR (KBr): 3285, 3203, 3078, 2964, 1676, 1605, 1515 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 5.75 (s, 1H), 5.15 (s, 1H), 4.04 (q, *J* = 7.2 Hz, 2H), 2.42 (s, 3H), 2.11–2.35 (m, 4H), 1.17 (t, *J* = 7.2 Hz, 3H), 1.09 (s, 3H), 0.91 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 195.38, 166.82, 154.50, 148.88, 146.16, 144.48, 128.92, 123.28, 110.99, 104.83, 60.04, 50.57, 40.93, 37.18, 32.67, 29.32, 27.01, 19.37, 14.15; Anal. Calcd. for $C_{21}H_{24}N_2O_5$: C, 65.61; H, 6.29; N, 7.29; Found: C, 65.56; H, 6.33; N, 7.37.

Ethyl 4-(3-nitrophenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5j). IR (KBr): 3283, 3210, 3079, 2958, 1705, 1608, 1532 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.10 (s, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 7.8 Hz, 1H), 5.88 (s, 1H), 5.15 (s, 1H), 4.06 (q, *J* = 6.9 Hz, 2H), 2.41 (s, 3H), 2.12–2.36 (m, 4H), 1.19 (t, *J* = 6.9 Hz, 3H), 1.10 (s, 3H), 0.94 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 195.52, 166.90, 149.15, 148.20, 144.52, 134.73, 128.54, 122.81, 121.23, 111.09, 104.99, 60.02, 50.54, 40.84, 36.95, 32.70, 29.32, 27.02, 19.33, 14.13; Anal. Calcd. for $C_{21}H_{24}N_2O_5$: C, 65.61; H, 6.29; N, 7.29; Found: C, 65.70; H, 6.34; N, 7.20.

Ethyl 4-(4-hydroxy-3-methoxyphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5k). IR (KBr): 3399, 3292, 2934, 1698, 1591 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 8.99 (s, 1H), 8.63 (s, 1H), 6.69 (s, 1H), 6.49–6.58 (m, 2H), 4.74 (s, 1H), 4.40 (q, *J* = 6.9 Hz, 2H), 2.50 (s, 3H), 1.95–2.39 (m, 7H), 1.16 (t, *J* = 6.9 Hz, 3H), 1.01 (s, 3H), 0.88 (s, 3H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 194.49, 167.10, 149.39, 146.78, 144.49, 139.10, 119.59, 114.98, 112.03, 110.22, 104.14, 59.05, 55.49, 50.35, 35.07, 32.16, 29.29, 26.42, 18.28, 14.28; Anal. Calcd. for $C_{22}H_{27}NO_5$: C, 68.55; H, 7.06; N, 3.63; Found: C, 68.61; H, 7.11; N, 3.58.

Ethyl 4-(4-dimethylaminophenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5l). IR (KBr): 3280, 3207, 3079, 2954, 1700, 1607 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.15 (d, *J* = 8.4 Hz, 2H), 6.59 (d, *J* = 8.7 Hz, 2H), 5.70 (s, 1H), 4.95 (s, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 2.87 (s, 6H), 2.18–2.36 (m, 7H), 1.22 (t, *J* = 7.2 Hz, 3H), 1.07 (s, 3H), 0.97 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 195.56, 167.65, 148.97, 147.59, 142.75, 135.81, 128.58, 112.47, 106.55, 59.72, 50.76, 40.94, 35.29, 32.70, 29.41, 27.33, 19.42, 14.25; Anal. Calcd. for $C_{23}H_{30}N_2O_3$: C, 72.22; H, 7.91; N, 7.32; Found: C, 72.10; H, 7.95; N, 7.38.

Ethyl 4-(furan-2-yl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5m). IR (KBr): 3287, 3220, 3086, 2932, 1675, 1605 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.18 (s, 1H), 6.20 (s, 1H), 6.00 (s, 1H), 5.89 (s, 1H), 5.25 (s, 1H), 4.12–4.16 (m, 2H), 2.19–2.39 (m, 7H), 1.25 (t, *J* = 6.9 Hz, 3H), 1.10 (s, 3H), 1.02 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 195.57, 167.34, 157.94, 150.61, 144.26, 140.85, 111.13, 105.03, 103.07, 59.83, 50.63, 36.88, 32.48, 29.71, 27.03, 19.08, 14.17; Anal. Calcd. for $C_{19}H_{23}NO_4$: C, 69.28; H, 7.04; N, 4.25; Found: C, 69.17; H, 7.10; N, 4.28.

Ethyl 4-(2,4-dichlorophenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5n). IR (KBr): 3287, 3204, 3088, 2936, 1703, 1607 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.30 (d, 1H), 7.22 (s, 1H), 7.10 (d, 1H), 6.13 (s, 1H), 5.23 (s, 1H), 3.97–4.06 (m, 2H), 2.38 (s, 3H), 2.18–2.36 (m, 4H), 1.18 (t, *J* = 7.2 Hz, 3H), 1.07 (s, 3H), 0.94 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 195.41, 167.23, 149.38, 142.42, 133.67, 132.78, 132.04, 129.13, 126.86, 111.13, 104.59, 60.11, 50.58, 41.07, 32.73, 29.12, 27.37, 19.11, 14.17; Anal. Calcd. for $C_{21}H_{23}Cl_2NO_3$: C, 61.77; H, 5.68; N, 3.43; Found: C, 61.84; H, 5.71; N, 3.39.

Acknowledgments. The authors are thankful to the Department of Biotechnology, New Delhi, for financial assistance.

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