

An Efficient and Green Synthesis of 1,4-Dihydropyridine Derivatives through Multi-Component Reaction in Ionic Liquid

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ABSTRACT: *Through multi-component condensation of aldehydes, 1,3-dione, Meldrum's acid, and ammonium acetate in an ionic liquid ([bmim][BF₄]), a series of 1,4-dihydropyridine derivatives were prepared in excellent yields in the absence of any additional catalysts. In addition, [bmim][BF₄] can be recovered and reused effectively for at least six times without obvious decrease of its efficiency. Advantages of this novel protocol include simple operational process, environmental benignancy, and high efficiency.* © 2006 Wiley Periodicals, Inc. *Heteroatom Chem* 17:382–388, 2006; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20221

INTRODUCTION

Pyridine and their hydrogenated derivatives are among the most important heterocycles commonly found in a wide variety of naturally occurring substances possessing a multiplicity of biological activities. Among these, 1,4-dihydropyridines (DHPs)

have been widely studied as a class of organic calcium channel modulators and as potential candidates for the treatment of cardiovascular diseases since their introduction into clinical medicine in the year of 1975 [1]. It has also been further revealed that DHP heterocyclic ring is a common feature of various bioactive compounds such as vasodilator, bronchodilator, antiatherosclerotic, antitumor, and antidiabetic agents [2]. Due to their important pharmacological activities mentioned above, many methods for the synthesis of DHPs have been reported [3]. However, although these methods have successfully led to a large library of DHPs for screening as drug candidates, many of these still suffer from drawbacks such as unsatisfactory yields, long-reaction time, and pollution to the environment due to the use of organic solvent and/or acidic or basic promoters. Therefore, the development of more efficient and greener methods for the preparation of this kind of compounds is still an active ongoing research area and there is scope for further improvement toward milder reaction conditions and improved yields with a greener nature.

Multi-component reactions (MCRs) are special types of synthetically useful organic reactions in which three or more starting materials react to give a product. Compared with classical reactions, MCRs have such advantages as one-pot reaction, giving products with a minute amount of work and leading to complex products by reacting structurally simple

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starting materials. These merits make MCRs very popular in areas like drug discovery process in the pharmaceutical industry and related areas where many different compounds are to be synthesized and screened [4]. On the other hand, the replacement of current chemical process with more environmentally benign alternatives is an increasingly attractive goal in organic synthesis [5]. In this field, room temperature ionic liquids have emerged and attracted much attention as novel media for catalytic process during the last decades and several important organic transformations have been carried out successfully in them [6]. In view of the rapidly increasing importance of imidazolium-based ionic liquids as novel reaction media, we have been working to explore the use of 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF₄]) as recyclable solvent system and promoter for greener organic synthesis [7]. As continuation of our research in this regard, herein we would like to report an efficient procedure for the preparation of 1,4-dihydropyridine derivatives through a four-component reaction including aldehydes **1**, 1,3-dione **2**, Meldrum's acid **3**, and ammonium acetate **4** in [bmim][BF₄] (Scheme 1).

RESULTS AND DISCUSSION

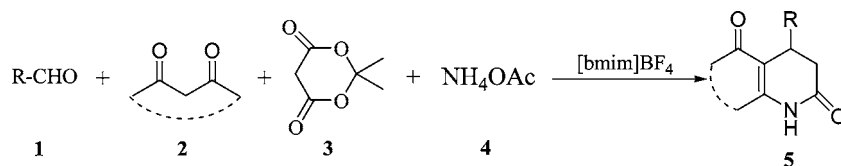
Initially, the reaction of *m*-nitrobenzaldehyde **1a** (0.5 mmol) with 5,5-dimethyl-1,3-cyclohexanedione **2a** (0.5 mmol), ammonium acetate **4** (0.8 mmol), and Meldrum's acid **3** (0.5 mmol) was examined (Scheme 2). For the first run, unfortunately, after the mixture of these four components in 0.5 mL [bmim][BF₄] being stirred for several hours at room temperature, no reaction was observed according to TLC analysis. It was then found out that even with an increased temperature (80°C), the desired product was still reluctant to be formed. Then, an alternative manipulation in terms of the substrates' addition sequence was tried. Thus, **2a** (0.5 mmol) and **4** (0.8 mmol) were first treated with 0.5 mL [bmim][BF₄] and the mixture was stirred at 80°C until the disappearance of **2** (in about 1 h, monitored by TLC). Then, **1a** (0.5 mmol) and **3** (0.5 mmol) were added. After being stirred at 80°C for another 3 h, the

mixture was found to afford product **5a** in high yield (Table 1, entry 4). Further investigations showed that with similar procedure, either higher (Table 1, entries 5 and 6) or lower (Table 1, entries 1–3) reaction temperature than 80°C would more or less reduce the yield of **5a**.

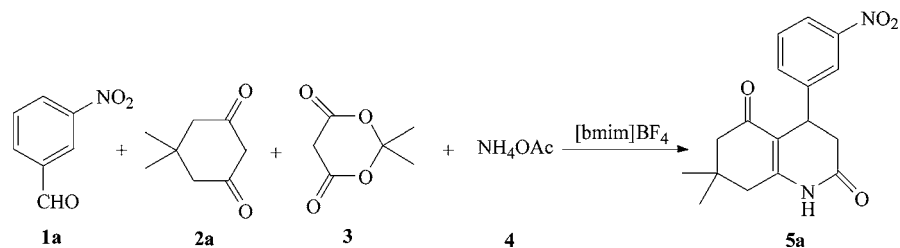
Next, reactions involving several other aldehydes **1** (Scheme 3) and another 1,3-dione, namely 1,3-cyclohexanedione **2b** (Scheme 3), were also investigated. The results are summarized in Table 2. In all cases, the corresponding products were obtained in good to excellent yields. It is worthy to be noted that even comparatively unreactive aldehydes such as heterocyclic and aliphatic aldehydes could undergo similar reaction and give 1,4-dihydropyridines in good yields (Table 2, entries 9–11). On the other hand, when 1,3-cyclohexanedione **2b** (Scheme 3) was used in place of 5,5-dimethyl-1,3-cyclohexanedione **2a**, this condensation process could be realized equally well (Table 2, entries 12–15).

In order to further broaden the scope of this protocol, an acyclic 1,3-dione, pentane-2,4-dione **2c** (Scheme 4), was also tried. It turned out that like its cyclic counterparts **2a** and **2b**, **2c** was also found to undergo the above reaction and afford the corresponding DHP derivative **5p** in moderate yield (42%, Scheme 4). Though the yield is relatively low, it is still remarkable given the fact that it is the first example, as far as we know, in which an acyclic 1,3-dione was successfully employed in this four-component condensation process.

On the other hand, it has been reported in many cases that compared with classical organic solvents, ionic liquids not only possess a green nature, but also demonstrate the advantages of actually accelerating the reaction rate and increasing the yields. Not unexpectedly, these merits of ionic liquids were also confirmed in this protocol. By running the same reaction of **1a**, **2a**, **3**, and **4** in [bmim][BF₄] and in two classical solvents, namely acetic acid and anhydrous ethanol respectively, we were able to come to the conclusion that compared with acetic acid and anhydrous ethanol, reaction run in [bmim][BF₄] gave the corresponding product in much higher yield with much shorter reaction time (Table 3).



SCHEME 1



SCHEME 2

TABLE 1 Studies on the Effect of Reaction Temperature on the Yield of **5a**

Entry	Reaction temperature (°C)	Reaction time (h)	Isolated yield (%)
1	25	48	23
2	40	32	40
3	60	12	81
4	80	4	93
5	100	4	77
6	120	4	67

The recovery and reuse of solvent and/or catalyst are highly preferable in terms of green synthetic process. Therefore, with the success of the above reactions, we continued our research by studying the reuse of [bmim][BF₄]. It turned out that the recovery and reuse of [bmim][BF₄] is very convenient and highly efficient. Thus, at completion of the condensation process, precipitated products were collected by suction and rinsed with cold ethanol, and [bmim][BF₄] could be recovered easily by concentrating the filtrate under reduced pressure and then drying at 100°C for several hours. Studies by using **1a** and **2a** as model substrates showed that the recovered [bmim][BF₄] could be successively recycled in subsequent reactions without almost any decrease in its efficiency (Table 4). It should be noted that even in the sixth round, reuse of [bmim][BF₄] recovered from the fifth round still produced the corresponding product with fairly good yield (Table 4, round 6).

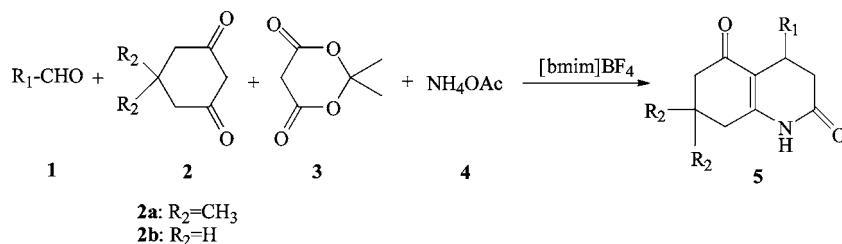
In conclusion, an efficient and environmental friendly procedure for the preparation of hydrogenated pyridine derivatives is described in this paper. The method presented here has the advantages of high efficiency, green nature, simple operational procedure, high versatility and ease of recovery and reuse of the reaction medium. All these merits may make this method attractive for the scale-up preparation of DHP derivatives.

EXPERIMENTAL

Melting points were measured by a Kofler micro melting point apparatus and were uncorrected. Infrared spectra were recorded on a Bruker Vector 22 spectrometer in KBr with absorption in cm⁻¹. ¹H NMR spectra were determined on a Bruker AC 400 spectrometer as DMSO solutions. Chemical shifts (δ) were expressed in ppm downfield from the internal standard tetramethylsilane and coupling constants *J* were given in Hz. Mass spectra were obtained by a HP-5989B mass spectrometer. Elemental analyses were performed on an EA-1110 instrument.

Typical Procedure for the Preparation of Compound **5a**

5,5-Dimethyl-1,3-cyclohexanedione **2a** (0.5 mmol) and ammonium acetate **4** (0.8 mmol) were added to a 10 mL round bottom flask containing 0.5 mL [bmim][BF₄]. The mixture was then stirred at 80°C for about 1 h to give a complete conversion of **2a**



SCHEME 3

TABLE 2 Preparation of DHPs in [bmim][BF₄]

Entry	Products	R ₁	R ₂	2	Reaction time (h)	Isolated yield (%)
1	5a	<i>m</i> -NO ₂ C ₆ H ₄	CH ₃	2a	4	93
2	5b	<i>p</i> -ClC ₆ H ₄	CH ₃	2a	5	85
3	5c	<i>p</i> -OH, <i>m</i> -OCH ₃ C ₆ H ₃	CH ₃	2a	5	89
4	5d	C ₆ H ₅	CH ₃	2a	4	89
5	5e	<i>p</i> -CH ₃ C ₆ H ₄	CH ₃	2a	5	85
6	5f	<i>o</i> -ClC ₆ H ₄	CH ₃	2a	5	83
7	5g	<i>o</i> -BrC ₆ H ₄	CH ₃	2a	5	91
8	5h	<i>p</i> -BrC ₆ H ₄	CH ₃	2a	4	92
9	5i		CH ₃	2a	8	78
10	5j	CH ₃ CH ₂ CH ₂ CH ₂ —	CH ₃	2a	8	71
11	5k	CH ₃ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ —	CH ₃	2a	9	58
12	5l	<i>p</i> -NO ₂ C ₆ H ₄	H	2b	4	86
13	5m	<i>o</i> -NO ₂ C ₆ H ₄	H	2b	4	85
14	5n	<i>p</i> -ClC ₆ H ₄	H	2b	4	81
15	5o	<i>m</i> -NO ₂ C ₆ H ₄	H	2b	4	87

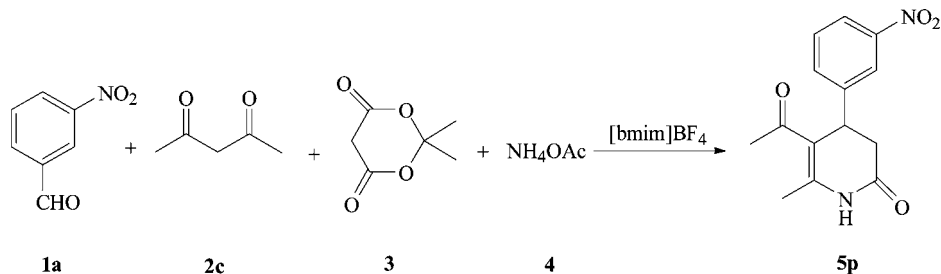
(monitored by TLC). Then, *m*-nitrobenzaldehyde **1a** (0.5 mmol) and Meldrum's acid **3** (0.5 mmol) were added to the reaction mixture and it was stirred for about another 3 h at 80°C. At completion, the reaction mixture was added with 2 mL water and the precipitate was collected by suction and rinsed with cold ethanol to give product **5a** with high purity. The filtrate was concentrated under reduced pressure and dried at 100°C to recover the ionic liquid for subsequent use.

Other products were obtained in a similar manner. The melting point and the spectral data (IR, ¹H NMR) of the known compounds were recorded and were found to be in accordance with what have been reported previously. All the new compounds were fully characterized by IR, ¹H NMR, and elemental analysis.

7,7-Dimethyl-4-(3'-nitrophenyl)-2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline 5a. White solid, mp 193–194°C (Lit. [3f] 192–193°C); ¹H NMR (DMSO-*d*₆,

400 MHz) δ : 0.98 (s, 3H, CH₃), 1.05 (s, 3H, CH₃), 2.15 (d, *J* = 16.0 Hz, 1H, ⁶CH), 2.25 (d, *J* = 16.0 Hz, 1H, ⁶CH), 2.40 (d, *J* = 16.0 Hz, 1H, ⁸CH), 2.48 (d, *J* = 16.0 Hz, 1H, ⁸CH), 2.51 (d, *J* = 16.4 Hz, 1H, ³CH), 3.01 (dd, *J* = 16.4, 8.0 Hz, 1H, ³CH), 4.29 (d, *J* = 8.0 Hz, 1H, ⁴CH), 7.61 (m, 2H, Ar-H), 7.96 (s, 1H, Ar-H), 8.05 (m, 1H, Ar-H), 10.23 (br s, 1H, NH); IR (KBr): 3221 (NH), 1710 (C=O), 1609 (N—C=O) cm⁻¹.

7,7-Dimethyl-4-(4'-chlorophenyl)-2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline 5b. White solid, mp 187–188°C (Lit. [3g] 188–190°C); ¹H NMR (DMSO-*d*₆, 400 MHz) δ : 0.96 (s, 3H, CH₃), 1.04 (s, 3H, CH₃), 2.13 (d, *J* = 16.0 Hz, 1H, ⁶CH), 2.22 (d, *J* = 16.0 Hz, 1H, ⁶CH), 2.37 (d, *J* = 16.0 Hz, 1H, ⁸CH), 2.41–2.43 (m, 2H, ⁸CH, ³CH), 2.93 (dd, *J* = 16.4, 8.4 Hz, 1H, ³CH), 4.12 (d, *J* = 8.4 Hz, 1H, ⁴CH), 7.13 (d, *J* = 8.8 Hz, 2H, Ar-H), 7.32 (d, *J* = 8.8 Hz, 2H, Ar-H), 10.12 (br s, 1H, NH); IR (KBr): 3220 (NH), 1718 (C=O), 1612 (N—C=O) cm⁻¹.



(42%)

SCHEME 4

TABLE 3 Comparison Between Organic Solvents and [bmim][BF₄] in the Synthesis of **5a**

Entry	Solvents	Reaction temperature (°C)	Reaction time (h)	Isolated yields (%)
1	[bmim][BF ₄]	80	4	93
2	Acetic acid	Re ux	16	65
3	Acetic acid	80	16	63
4	Ethanol	Re ux	16	30

7,7-Dimethyl-4-(4'-hydroxyl-3'-methoxyphenyl)-2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline 5c. Pale yellow solid, mp 238–240°C; ¹H NMR (DMSO-d₆, 400 MHz) δ: 0.97 (s, 3H, CH₃), 1.03 (s, 3H, CH₃), 2.11 (d, *J* = 16.0 Hz, 1H, ⁶CH), 2.21 (d, *J* = 16.0 Hz, 1H, ⁶CH), 2.33 (d, *J* = 16.8 Hz, 1H, ⁸CH), 2.40–2.42 (m, 2H, ⁸CH, ³CH), 2.82 (dd, *J* = 16.0, 7.6 Hz, 1H, ³CH), 3.78 (s, 3H, OCH₃), 4.01 (d, *J* = 7.6 Hz, 1H, ⁴CH), 6.44 (d, *J* = 8.0 Hz, 1H, Ar-H), 6.60 (d, *J* = 8.0 Hz, 1H, Ar-H), 6.67 (s, 1H, Ar-H), 8.77 (s, 1H, OH), 10.02 (s, 1H, NH); IR (KBr): 3369 (OH), 3222 (NH), 1697 (C=O), 1617 (N–C=O) cm⁻¹. Anal. Calcd for C₁₈H₂₁NO₄: C 68.55, H 6.71, N 4.44; Found C 68.49, H 6.76, N 4.38.

7,7-Dimethyl-4-phenyl-2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline 5d. White solid, mp 217–219°C (Lit. [3f] 211–213°C); ¹H NMR (DMSO-d₆, 400 MHz) δ: 1.00 (s, 3H, CH₃), 1.07 (s, 3H, CH₃), 2.16 (d, *J* = 16.0 Hz, 1H, ⁶CH), 2.24 (d, *J* = 16.0 Hz, 1H, ⁶CH), 2.40 (d, *J* = 16.8 Hz, 1H, ⁸CH), 2.45–2.47 (m, 2H, ⁸CH, ³CH), 2.93 (dd, *J* = 16.0, 8.0 Hz, 1H, ³CH), 4.15 (d, *J* = 8.0 Hz, 1H, ⁴CH), 7.15 (t, *J* = 7.2 Hz, 1H, Ar-H), 7.19 (d, *J* = 7.2 Hz, 2H, Ar-H), 7.27 (t, *J* = 7.2 Hz, 2H, Ar-H), 10.02 (br s, 1H, NH); IR (KBr): 3210 (NH), 1712 (C=O), 1610 (N–C=O) cm⁻¹.

7,7-Dimethyl-4-(4'-methylphenyl)-2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline 5e. White solid, mp 199–201°C; ¹H NMR (DMSO-d₆, 400 MHz) δ: 0.99 (s, 3H, CH₃), 1.07 (s, 3H, CH₃), 2.14 (d, *J* = 16.0 Hz, 1H, ⁶CH), 2.23 (d, *J* = 16.0 Hz, 1H, ⁶CH), 2.24 (s, 3H, CH₃), 2.39 (d, *J* = 16.8 Hz, 1H, ⁸CH), 2.43 (d,

J = 16.8 Hz, 1H, ⁸CH), 2.53 (d, *J* = 16.0 Hz, ³CH), 2.90 (dd, *J* = 16.0, 8.0 Hz, 1H, ³CH), 4.10 (d, *J* = 8.0 Hz, 1H, ⁴CH), 7.02 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.07 (d, *J* = 8.0 Hz, 2H, Ar-H), 9.99 (s, 1H, NH); IR (KBr): 3209 (NH), 1716 (C=O), 1610 (N–C=O) cm⁻¹. Anal. Calcd for C₁₈H₂₁NO₂: C 76.29, H 7.47, N 4.94; Found C 76.18, H 7.50, N 4.91.

7,7-Dimethyl-4-(2'-chlorophenyl)-2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline 5f. White solid, mp 248–250°C (Lit. [3f] 252–254°C); ¹H NMR (DMSO-d₆, 400 MHz) δ: 1.02 (s, 3H, CH₃), 1.04 (s, 3H, CH₃), 2.15 (d, *J* = 16.0 Hz, 1H, ⁶CH), 2.21 (d, *J* = 16.0 Hz, 1H, ⁶CH), 2.29 (d, *J* = 16.4 Hz, 1H, ³CH), 2.43 (d, *J* = 16.8 Hz, 1H, ⁸CH), 2.51 (d, *J* = 16.8 Hz, 1H, ⁸CH), 2.99 (dd, *J* = 16.4, 8.4 Hz, 1H, ³CH), 4.45 (d, *J* = 8.4 Hz, 1H, ⁴CH), 6.93–6.96 (m, 1H, Ar-H), 7.21–7.24 (m, 2H, Ar-H), 7.42–7.25 (m, 1H, Ar-H), 10.19 (s, 1H, NH); IR (KBr): 3219 (NH), 1713 (C=O), 1611 (N–C=O) cm⁻¹.

7,7-Dimethyl-4-(2'-bromophenyl)-2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline 5g. White solid, mp 227–228°C; ¹H NMR (DMSO-d₆, 400 MHz) δ: 1.01 (s, 3H, CH₃), 1.04 (s, 3H, CH₃), 2.14 (d, *J* = 16.0 Hz, 1H, ⁶CH), 2.20 (d, *J* = 16.0 Hz, 1H, ⁶CH), 2.29 (d, *J* = 16.4 Hz, 1H, ³CH), 2.43 (d, *J* = 17.6 Hz, 1H, ⁸CH), 2.51 (d, *J* = 17.6 Hz, 1H, ⁸CH), 2.98 (dd, *J* = 16.4, 8.8 Hz, 1H, ³CH), 4.41 (d, *J* = 8.4 Hz, 1H, ⁴CH), 6.93 (d, *J* = 7.6 Hz, 1H, Ar-H), 7.13 (t, *J* = 7.6 Hz, 1H, Ar-H), 7.25 (t, *J* = 7.6 Hz, 1H, Ar-H), 7.61 (d, *J* = 7.6 Hz, 1H, Ar-H), 10.20 (s, 1H, NH); IR (KBr): 3219 (NH), 1713 (C=O), 1611 (N–C=O) cm⁻¹. Anal. Calcd for C₁₇H₁₈BrNO₂: C 58.63, H 5.21, N 4.02; Found C 58.68, H 5.17, N 3.94.

7,7-Dimethyl-4-(4'-bromophenyl)-2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline 5h. White solid, mp 196–198°C (Lit. [2] 196–197°C); ¹H NMR (DMSO-d₆, 400 MHz) δ: 0.94 (s, 3H, CH₃), 1.02 (s, 3H, CH₃), 2.12 (d, *J* = 16.0 Hz, 1H, ⁶CH), 2.20 (d, *J* = 16.0 Hz, 1H, ⁶CH), 2.35 (d, *J* = 17.6 Hz, 1H, ⁸CH), 2.40 (d, *J* = 17.6 Hz, 1H, ⁸CH), 2.40 (d, *J* = 16.0 Hz, 1H, ³CH), 2.91 (dd, *J* = 16.0, 8.0 Hz, 1H, ³CH), 4.09 (d, *J* = 8.0 Hz, 1H, ⁴CH), 7.05 (d, *J* = 8.4 Hz, 2H, Ar-H),

TABLE 4 Studies on the Reuse of Ionic Liquid (IL) in the Preparation of **5a**

Round	Yield (%)	Ionic liquid recovered (%) ^a
1	93	99
2	92	99
3	91	99
4	92	98
5	92	98
6	91	97

^aRecovery yield (%) = mass of the IL recovered/mass of the IL used.

7.44 (d, $J = 8.4$ Hz, 2H, Ar-H), 10.11 (s, 1H, NH); IR (KBr): 3220 (NH), 1716 (C=O), 1610 (N–C=O) cm^{-1} .

7,7-Dimethyl-4-(2-furanyl)-2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline 5i. Light yellow solid, mp 174–176°C; ^1H NMR (DMSO- d_6 , 400 MHz) δ : 0.97 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 2.17 (d, $J = 16.0$ Hz, 1H, ^6CH), 2.24 (d, $J = 16.0$ Hz, 1H, ^6CH), 2.31 (d, $J = 17.2$ Hz, 1H, ^8CH), 2.41 (d, $J = 17.2$ Hz, 1H, ^8CH), 2.56 (d, $J = 16.4$ Hz, 1H, ^3CH), 2.84 (dd, $J = 16.4$, 7.6 Hz, 1H, ^3CH), 4.18 (d, $J = 7.6$ Hz, 1H, ^4CH), 5.94 (s, 1H), 6.31 (s, 1H), 7.51 (s, 1H), 10.09 (s, 1H, NH); IR (KBr): 3229 (NH), 1716 (C=O), 1613 (N–C=O) cm^{-1} . Anal. Calcd for $\text{C}_{15}\text{H}_{17}\text{NO}_3$: C 69.48, H 6.61, N 5.40; Found C 69.40, H 6.69, N 5.42.

7,7-Dimethyl-4-butyl-2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline 5j. Light yellow solid, mp 120–122°C; ^1H NMR (DMSO- d_6 , 400 MHz) δ : 0.82 (t, $J = 6.4$ Hz, 3H, CH_3), 0.96 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 1.15–1.29 (m, 6H, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$), 2.11 (d, $J = 16.0$ Hz, 1H, ^6CH), 2.20 (d, $J = 16.0$ Hz, 1H, ^6CH), 2.22 (d, $J = 17.2$ Hz, 1H, ^8CH), 2.28 (d, $J = 16.4$ Hz, 1H, ^3CH), 2.36 (d, $J = 17.2$ Hz, 1H, ^8CH), 2.55 (dd, $J = 16.4$, 7.2 Hz, 1H, ^3CH), 2.85 (d, $J = 7.2$ Hz, 1H, ^4CH), 9.91 (s, 1H, NH); IR (KBr): 3234 (NH), 1711 (C=O), 1599 (N–C=O) cm^{-1} . Anal. Calcd for $\text{C}_{15}\text{H}_{23}\text{NO}_2$: C 72.25, H 9.30, N 5.62; Found C 72.19, H 9.36, N 5.57.

7,7-Dimethyl-4-hexyl-2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline 5k. Light yellow solid, mp 97–99°C; ^1H NMR (DMSO- d_6 , 400 MHz) δ : 0.84 (t, $J = 6.4$ Hz, 3H, CH_3), 0.96 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 1.18–1.27 (m, 10H, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-$), 2.10 (d, $J = 16.0$ Hz, 1H, ^6CH), 2.20 (d, $J = 16.0$ Hz, 1H, ^6CH), 2.21 (d, $J = 17.6$ Hz, 1H, ^8CH), 2.27 (d, $J = 16.4$ Hz, 1H, ^3CH), 2.36 (d, $J = 17.6$ Hz, 1H, ^8CH), 2.55 (dd, $J = 16.4$, 7.2 Hz, 1H, ^3CH), 2.85 (d, $J = 7.2$ Hz, 1H, ^4CH), 9.91 (s, 1H, NH); IR (KBr): 3226 (NH), 1695 (C=O), 1635 (N–C=O) cm^{-1} . MS m/z : 277 (M^+ , 10%), 192 (100%), 136 (10%). Anal. Calcd for $\text{C}_{17}\text{H}_{27}\text{NO}_2$: C 73.61, H 9.81, N 5.05; Found C 73.65, H 9.78, N 5.00.

4-(4'-Nitrophenyl)-2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline 5l. Yellow solid, mp 222–224°C; ^1H NMR (DMSO- d_6 , 400 MHz) δ : 1.97–2.01 (m, 2H, CH_2), 2.31 (t, $J = 8.0$ Hz, 2H, CH_2), 2.50 (d, $J = 16.0$ Hz, 1H, ^3CH), 2.56 (t, $J = 8.0$ Hz, 2H, CH_2), 3.01 (dd, $J = 16.0$, 8.0 Hz, 1H, ^3CH), 4.30 (d, $J = 8.0$ Hz, 1H, ^4CH), 7.42 (d, $J = 8.0$ Hz, 2H, Ar-H), 8.15 (d, $J = 8.0$ Hz, 2H, Ar-H), 10.25 (s, 1H, NH); MS m/z : 286 (M^+ , 100%), 269 (45%), 257 (33%), 239 (15%),

164 (15%), 28 (17%). Anal. Calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_4$: C 62.93, H 4.93, N 9.79; Found C 62.95, H 4.87, N 9.82.

4-(2'-Nitrophenyl)-2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline 5m. Light yellow solid, mp 217–219°C; ^1H NMR (DMSO- d_6 , 400 MHz) δ : 1.99 (m, 2H, CH_2), 2.24 (m, 2H, CH_2), 2.41 (d, $J = 16.8$ Hz, 1H, ^3CH), 2.61 (m, 2H, CH_2), 3.13 (dd, $J = 16.8$, 8.8 Hz, 1H, ^3CH), 4.48 (d, $J = 8.8$ Hz, 1H, ^4CH), 7.22 (d, $J = 8.0$ Hz, 1H, Ar-H), 7.48 (t, $J = 8.0$ Hz, 1H, Ar-H), 7.62 (t, $J = 8.0$ Hz, 1H, Ar-H), 7.91 (d, $J = 8.0$ Hz, 1H, Ar-H), 10.32 (s, 1H, NH); IR (KBr): 3476 (NH), 1694 (C=O), 1637 (N–C=O), 1518 and 1347 (NO_2) cm^{-1} . Anal. Calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_4$: C 62.93, H 4.93, N 9.79; Found C 62.98, H 4.85, N 9.74.

4-(4'-Chlorophenyl)-2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline 5n. White solid, mp 177–179°C; ^1H NMR (DMSO- d_6 , 400 MHz) δ : 1.97 (m, 2H, CH_2), 2.30 (t, $J = 8.0$ Hz, 2H, CH_2), 2.45 (d, $J = 16.4$ Hz, 1H, ^3CH), 2.53 (t, $J = 8.0$ Hz, 2H, CH_2), 2.92 (dd, $J = 16.4$, 8.0 Hz, 1H, ^3CH), 4.16 (d, $J = 8.0$ Hz, 1H, ^4CH), 7.16 (d, $J = 8.0$ Hz, 2H, Ar-H), 7.33 (d, $J = 8.0$ Hz, 2H, Ar-H), 10.16 (s, 1H, NH); IR (KBr): 3454 (NH), 1706 (C=O), 1619 (N–C=O) cm^{-1} . MS m/z : 275 (M^+ , 74%), 240 (29%), 207 (19%), 28 (100%). Anal. Calcd for $\text{C}_{15}\text{H}_{14}\text{ClNO}_2$: C 65.34, H 5.12, N 5.08; Found C 65.30, H 5.14, N 5.05.

4-(3'-Nitrophenyl)-2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline 5o. Light yellow solid, mp 224–226°C; ^1H NMR (DMSO- d_6 , 400 MHz) δ : 2.00 (m, 2H, CH_2), 2.32 (t, $J = 8.0$ Hz, 2H, CH_2), 2.53 (d, $J = 16.0$ Hz, 1H, ^3CH), 2.56 (t, $J = 8.0$ Hz, 2H, CH_2), 3.00 (dd, $J = 16.0$, 8.0 Hz, 1H, ^3CH), 4.34 (d, $J = 8.0$ Hz, 1H, ^4CH), 7.60 (m, 2H, Ar-H), 7.99 (s, 1H, Ar-H), 8.06 (m, 1H, Ar-H), 10.27 (s, 1H, NH); IR (KBr): 3464 (NH), 1710 (C=O), 1613 (N–C=O), 1526 and 1349 (NO_2) cm^{-1} . MS m/z : 286 (M^+ , 38%), 269 (100%), 239 (43%), 207 (19%), 28 (66%). Anal. Calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_4$: C 62.93, H 4.93, N 9.79; Found C 62.84, H 4.99, N 9.85.

5-Acetyl-6-methyl-4-(3'-nitrophenyl)-3,4-dihydropyridin-2(1H)-one 5p. mp 175–178°C; ^1H NMR (DMSO- d_6 , 400 MHz) δ : 2.09 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 2.37 (d, $J = 16.0$ Hz, 1H, ^3CH), 2.99 (dd, $J = 16.0$, 8.0 Hz, 1H, ^3CH), 4.40 (d, $J = 8.0$ Hz, 1H, ^4CH), 7.65 (m, 2H, Ar-H), 8.03 (s, 1H, Ar-H), 8.11 (m, 1H, Ar-H), 9.99 (s, 1H, NH); IR (KBr): 3471 (NH), 1625 (C=O), 1594 (N–C=O) cm^{-1} . MS m/z : 274 (M^+ , 20%), 257 (100%), 227 (24%), 176 (16%), 43 (10%). Anal. Calcd for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_4$: C 61.31, H 5.14, N 10.21; Found C 61.22, H 5.18, N 10.29.

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