An Efficient Microwave-Assisted Synthesis of 3,5-Unsubstituted 4-Substituted-6-aryl-3,4-dihydropyridin-2(1*H*)-ones Derivatives

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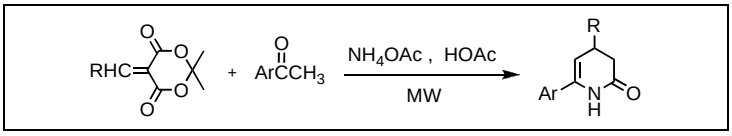

Small libraries of 3,5-unsubstituted 4-substituted-6-aryl-3,4-dihydropyridin-2(1*H*)-ones derivatives were synthesized from the condensation-products of aldehydes with Meldrum's acid, aromatic ketones and ammonium acetate using acetic acid as energy transferring-agent under microwave irradiation without catalyst. This method has the advantages of excellent yields (65–90%), short reaction time (5–10 min) and being environmentally friendly. It aimed to provide new series of potential biologically active compounds for biomedical screening.

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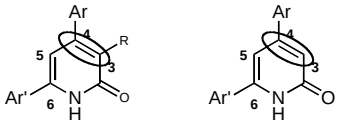
INTRODUCTION

2-Pyridones play an important theoretical and practical role in heterocyclic chemistry [1]. The nucleus of 2-pyridone occurs widely in the structures of biologically important natural alkaloids [2]. Recently, some functionalized 2-pyridone derivatives are even found to exhibit interesting bioactivity and served as versatile synthetic intermediates in pharmaceutical and agrochemical research [3]. Because of their importance, the synthesis of these molecules containing 2(1*H*)-pyridone unit has attracted considerable attention [4].

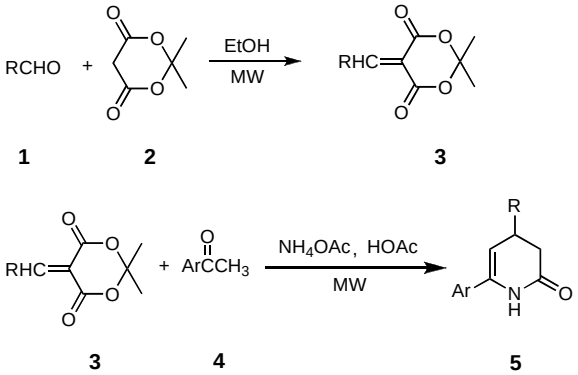
As a member of the 2-pyridone family 4,6-diaryl-2-pyridones are recognized as potent LTB_4 antagonists [5]. Numerous methods for the preparation of the 4,6-diaryl-2-pyridone template have been reported many times in the literature, such as the synthesis of 3-substituted-2-pyridone [6-8] derivatives (**A**) which are functionalized at the 3 and 4 position. In addition, slight modification of the 4,6-diaryl-2-pyridone nucleus was reported to afford a series of 3-unsubstituted 2-pyridone derivatives [5,9-11] (**B**) which provide new series of biologically active compounds.



A **B**

Substituted six-membered lactams, 2-pyridones, and their 3,4-dihydro derivatives have also attracted considerable attention from synthetic organic chemists since these scaffolds are found in a wide variety of naturally occurring alkaloids [12] and compounds with these structural motifs have been shown to exhibit significant pharmacological properties [13], for example dihydro-2-pyridones have been applied as scaffolds to the construction of constrained amino acid [14]. However, little attention has been paid to the synthesis of 3,4-dihydro-4,6-diaryl-2-pyridones which are unsubstituted on the 3- and 5-positions. And up to now, to the best of our knowledge, there are no reports on the synthesis of them. For the aim of offering a new series of candidates for bioactivity screening, herein we carried out the research on the synthesis of this new type of 2-pyridone through an efficient three-component reaction assisted by microwave irradiation (Scheme I).

Scheme I



RESULTS AND DISCUSSION

Initially, we explored the synthesis of **5b** (see Table 1) which was prepared from the condensation-product **3b** [15] (2 mmol), 3-nitroacetophenone (2 mmol) and ammonium acetate (1.0 g) with acetic acid (1.4 mL) as solvent by mechanical stirring. The reaction was performed at 100 °C under conventional heating by 7.5 h,

monitered by TLC, which gave the target product in 55% yield. However, under microwave irradiation at this condition (200 W) for 6 min, the yield was enhanced to 88%. The efficiency of microwave irradiation (MWI) in promoting the above reaction triggered us to apply it to accelerate the reaction and improve the reaction yields.

In this reaction, we use two kinds of representative arones: one contains electron-withdrawing group such as 3-nitroacetophenone, 2-chloroacetophenone and 2,4-dichloro-acetophenone, the other comprises electron-contributing group such as 4-methoxyacetophenone. Table 1 showed that the electrophilic arone could react with a wide range of condensation-products of Meldrum's acid **2** with various aldehydes **1** (including aromatic, aliphatic and hetero cyclic aldehydes) with higher yields (70–90%) in shorter reaction time (5–9 min). when the arone with electron-donating group was used, the yields were relatively lower (65–80%) and the reaction time was longer (7–10 min). The results demonstrated that the electronic nature of arone has significant influence on the reaction.

We supposed the mechanism of this reaction, which includes Michael addition, cyclization and the loss of acetone and carbon dioxide (Scheme II).

It is well known that the Michael addition is strongly affected by solvent and acid-base property besides the nature of reactant [16]. Therefore, we explored the reaction condition by changing the mass ratio of ammonium acetate and acetic acid. When the reaction was processed without acetic acid, the compound **6** [17] of 2,4,6-triarylpyridine derivative was obtained instead of compound **5** (Scheme III). So, the solvents play crucial role in this reaction. The initial results are summarized in Table 2.

It may be generated by a series of addition, elimination, and then cyclization, dehydration and aromatization procedure (Scheme IV). While a small quantity of acetic acid was added as solvent, the mixture of **5** and **6** was

Table 1

Synthesis of 3,4-Dihydropyridine-2(1*H*)-ones Derivatives **5**

Compound	Ar	R	Time (min)	Yield (%)	Mp (°C)
5a	3-$NO_2C_6H_4$	4-ClC_6H_4	5	90	295.6–296.9
5b	3-$NO_2C_6H_4$	4-BrC_6H_4	6	88	205.0–206.0
5c	3-$NO_2C_6H_4$	2-ClC_6H_4	8	85	182.6–183.8
5d	3-$NO_2C_6H_4$	2,4-$Cl_2C_6H_3$	5	80	222.3–223.4
5e	3-$NO_2C_6H_4$	3,4-$Cl_2C_6H_3$	6	82	256.3–257.0
5f	3-$NO_2C_6H_4$	4-FC_6H_4	5	90	232.2–233.2
5g	3-$NO_2C_6H_4$	3-$NO_2C_6H_4$	7	82	279.2–280.0
5h	3-$NO_2C_6H_4$	3,4-$(OCH_3)_2C_6H_3$	9	80	231.2–232.5
5i	3-$NO_2C_6H_4$	4-$CH_3C_6H_4$	9	75	183.0–184.0
5j	3-$NO_2C_6H_4$	3,4-$OCH_2OC_6H_3$	7	85	204.5–205.2
5k	3-$NO_2C_6H_4$	$CH_3(CH_2)_3$	9	70	122.3–124.1
5l	3-$NO_2C_6H_4$	thiophen-2-yl	9	80	142.0–144.0
5m	4-$CH_3OC_6H_4$	4-ClC_6H_4	7	80	164.5–165.9
5n	4-$CH_3OC_6H_4$	4-BrC_6H_4	8	75	173.6–174.8
5o	4-$CH_3OC_6H_4$	2,4-$Cl_2C_6H_3$	9	70	219.0–220.0
5p	4-$CH_3OC_6H_4$	3,4-$Cl_2C_6H_3$	7	68	153.4–154.5
5q	4-$CH_3OC_6H_4$	3,4-$OCH_2OC_6H_3$	10	65	183.9–184.7
5r	4-$NO_2C_6H_4$	4-BrC_6H_4	6	81	214.8–215.5
5s	4-$NO_2C_6H_4$	4-ClC_6H_4	7	82	199.9–201.2
5t	2,4-$Cl_2C_6H_3$	4-ClC_6H_4	9	79	178.0–179.0
5u	2-ClC_6H_4	4-BrC_6H_4	8	80	>300

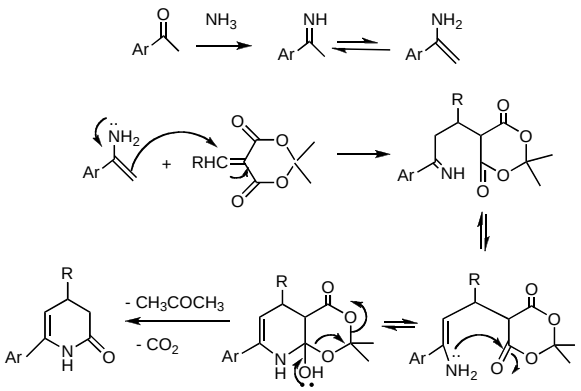
Note: All reactions were performed in 1.4 mL acetic acid

Table 2

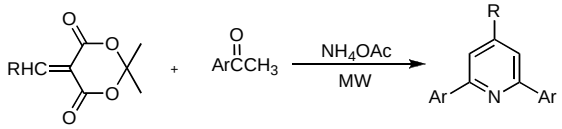
The Reaction of **3** and **4** without Acetic Acid

Compound	Ar	R	Time (min)	Yield (%)	Mp (°C) (lit.)
6a	3-$NO_2C_6H_4$	2-ClC_6H_4	4	89	225.0–226.1
6b	3-$NO_2C_6H_4$	4-$CH_3C_6H_4$	5	86	258.7–263.4
6c	4-$CH_3OC_6H_4$	4-BrC_6H_4	3	91	164.1–165.3 (163.9–165.0)[18]
6d	2,4-$Cl_2C_6H_3$	2,4-$Cl_2C_6H_3$	6	90	202.9–204.7 (203.9–204.8)[18]

Scheme II



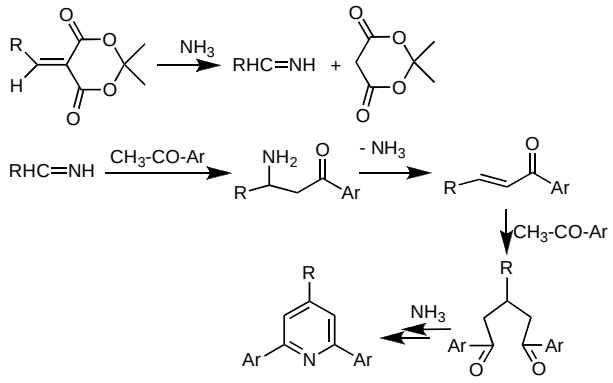
Scheme III



3 **4** **6**

obtained. In order to improve the yields of **5**, we tested various ratios and found when the mass ratio of ammonium acetate and acetic acid is 3:4 the reaction gave the best result.

Scheme IV



All the products were characterized by IR and ^{1}H NMR analysis. And the elemental analyses of these compounds are in agreement with their structures. The structure of **5f** was also confirmed by X-ray diffraction study [18] (Figure 1).

In summary, we have disclosed a new method to synthesize 4-substituted-6-aryl-3,4-dihydropyridin-2(1*H*)-ones by multi-components of commercially available reagents under microwave irradiation. This method has the advantages of shorter reaction time, higher yields, easy work-up procedure and being environmentally friendly. Most importantly, a series of new compounds synthesized on the basis of 4,6-diaryl-3,4-dihydropyridine-2(1*H*)-one skeleton may lead to new candidates for medicinal application through bioactivity screening and this work is in progress in our laboratory.

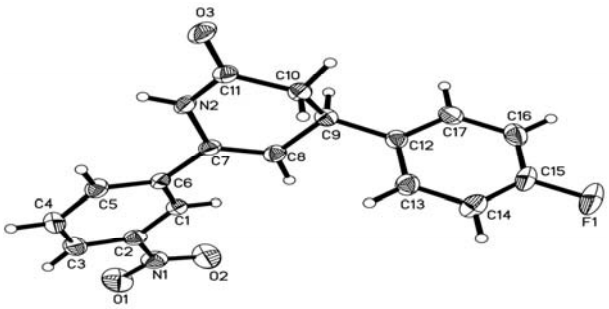


Figure 1. The structure of **5f**.

EXPERIMENTAL

General Procedure for the Reaction of 5-arylidene-2,2-dimethyl-1,3-dioxane-4,6-dione (3). All reactions were performed in a monomodal Emrys™ Creator from Personal Chemistry, Uppsala, Sweden. Typically, in a 10-mL Emrys™ reaction vial, the appropriate aldehyde **1** (5.0 mmol) and the little excessive Meldrum's acid (6.0 mmol) in ethanol (2.0 mL) were mixed and then capped. The mixture was irradiated at 150 W at 80 °C for 3–7 min (the reaction was monitored by TLC). The reaction mixture was cooled to room temperature and filtered to afford the crude products. The crude products were purified by recrystallization from ethanol.

General Procedure for the Reaction of 4-Substituted-6-aryl-3,4-dihydropyridin-2(1*H*)-ones (5). All reactions were performed in a monomodal Emrys™ Creator from Personal Chemistry, Uppsala, Sweden. Typically, in a 10–mL Emrys™ reaction vial, starting-material **3** (2 mmol), aromatic ketone **4** (2 mmol) and ammonium acetate (1.0 g) in acetic acid (1.4 mL) were mixed and then capped. The mixture was irradiated at 200 W at 100 °C for a given time (the reaction was monitored by TLC). The reaction mixture was cooled to room temperature and poured into 50 mL water, filtered to give the crude product, which was further purified by recrystallization from DMF.

4-(4-Chlorophenyl)-6-(3-nitrophenyl)-3,4-dihydropyridin-2 (1*H*)-one (5a). This compound was obtained according to above general procedure; ir (potassium bromide): 3232, 3123, 1677, 1626, 1528, 1469, 1406, 1350, 1088, 1011, 823, 800, 780 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 9.94 (s, 1H, NH), 8.37 (s, 1H, ArH), 8.22 (d, 1H, *J* = 8.4 Hz, ArH), 8.04 (d, 1H, *J* = 7.6 Hz, ArH), 7.69 (t, 1H, *J* = 8.0 Hz, ArH), 7.40 (d, 2H, *J* = 8.4 Hz, ArH), 7.37 (d, 2H, *J* = 8.4 Hz, ArH), 5.80 (d, 1H, *J* = 4.4 Hz, ^{5}CH), 4.03–3.98 (m, 1H, ^{4}CH), 2.77 (dd, 1H, J_1 = 16.0, J_2 = 6.8 Hz, ^{3}CH$_2$), 2.56 (dd, 1H, J_1 = 16.0 Hz, J_2 = 8.0 Hz, ^{3}CH$_2$). *Anal.* Calcd. for $C_{17}H_{13}ClN_2O_3$: C, 62.11; H, 3.99; N, 8.52. Found: C, 62.25; H, 3.86; N, 8.47.

4-(4-Bromophenyl)-6-(3-nitrophenyl)-3,4-dihydropyridin-2 (1*H*)-one (5b). ir (potassium bromide): 3195, 3093, 1668, 1628, 1572, 1522, 1401, 1346, 1166, 1009, 825, 803, 790 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 9.96 (s, 1H, NH), 7.32 (s, 1H, ArH), 8.22 (d, 1H, *J* = 8.0 Hz, ArH), 8.04 (d, 1H, *J* = 8.4 Hz, ArH), 7.70 (t, 1H, *J* = 8.0 Hz, ArH), 7.55 (d, 2H, *J* = 8.4 Hz, ArH), 7.31 (d, 2H, *J* = 8.4

Hz, ArH), 5.82 (d, 1H, *J* = 4.4 Hz, ^{5}CH), 4.01–3.96 (m, 1H, ^{4}CH), 2.76 (dd, 1H, J_1 = 16.0, J_2 = 6.4 Hz, ^{3}CH$_2$), 2.51 (dd, 1H, J_1 = 16.0 Hz, J_2 = 8.0 Hz, ^{3}CH$_2$). *Anal.* Calcd. for $C_{17}H_{13}BrN_2O_3$: C, 54.71; H, 3.51; N, 7.51. Found: C, 54.62; H, 3.43; N, 7.41.

4-(2-Chlorophenyl)-6-(3-nitrophenyl)-3,4-dihydropyridin-2 (1*H*)-one (5c). ir (potassium bromide): 3188, 3072, 2921, 1695, 1618, 1577, 1528, 1474, 1411, 1349, 1258, 1162, 1041, 809, 790, 740 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 10.01 (s, 1H, NH), 8.38 (s, 1H, ArH), 8.23 (d, 1H, *J* = 8.0 Hz, ArH), 8.04 (d, 1H, *J* = 8.0 Hz, ArH), 7.70 (t, 1H, *J* = 8.0 Hz, ArH), 7.51 (d, 1H, *J* = 7.8 Hz, ArH), 7.41–7.30 (m, 3H, ArH), 5.79 (d, 1H, *J* = 4.8 Hz, ^{5}CH), 4.33–4.28 (m, 1H, ^{4}CH), 2.84 (dd, 1H, J_1 = 16.0, J_2 = 7.2 Hz, ^{3}CH$_2$), 2.54 (dd, 1H, J_1 = 15.6 Hz, J_2 = 6.4 Hz, ^{3}CH$_2$). *Anal.* Calcd. for $C_{17}H_{13}ClN_2O_3$: C, 62.11; H, 3.99; N, 8.52. Found: C, 62.24; H, 4.02; N, 8.56.

4-(2,4-Dichlorophenyl)-6-(3-nitrophenyl)-3,4-dihydropyridin-2(1*H*)-one (5d). ir (potassium bromide): 3228, 3107, 1682, 1625, 1530, 1463, 1342, 1254, 1094, 1041, 897, 805, 784, 696 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 10.06 (s, 1H, NH), 8.38 (s, 1H, ArH), 8.24 (d, 1H, *J* = 8.0 Hz, ArH), 8.06 (d, 1H, *J* = 8.4 Hz, ArH), 8.39 (t, 1H, *J* = 8.0 Hz, ArH), 8.05 (d, 1H, *J* = 8.0 Hz, ArH), 7.57–7.39 (m, 2H, ArH), 5.82 (d, 1H, *J* = 4.4 Hz, ^{5}CH), 4.33–4.28 (m, 1H, ^{4}CH), 2.82 (dd, 1H, J_1 = 16.0, J_2 = 7.2 Hz, ^{3}CH$_2$), 2.58 (dd, 1H, J_1 = 15.8 Hz, J_2 = 8.0 Hz, ^{3}CH$_2$). *Anal.* Calcd. for $C_{17}H_{12}Cl_2N_2O_3$: C, 56.22; H, 3.33; N, 7.71. Found: C, 56.33; H, 3.18; N, 7.78.

4-(3,4-Dichlorophenyl)-6-(3-nitrophenyl)-3,4-dihydropyridin-2(1*H*)-one (5e). ir (potassium bromide): 3231, 3099, 1695, 1630, 1521, 1465, 1353, 1285, 1138, 1030, 971, 927, 810, 787 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 9.96 (s, 1H, NH), 8.37 (s, 1H, ArH), 8.22 (dd, 1H, J_1 = 8.4 Hz, J_2 = 1.2 Hz, ArH), 8.04 (d, 1H, *J* = 8.4 Hz, ArH), 7.69 (t, 1H, *J* = 8.0 Hz, ArH), 7.63 (s, 1H, ArH), 7.61 (d, 1H, *J* = 8.0 Hz, ArH), 7.35 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.0 Hz, ArH), 5.81 (d, 1H, *J* = 4.0 Hz, ^{5}CH), 4.06–4.01 (m, 1H, ^{4}CH), 2.77 (dd, 1H, J_1 = 16.6 Hz, J_2 = 7.4 Hz, ^{3}CH$_2$), 2.60 (dd, 1H, J_1 = 15.8 Hz, J_2 = 8.8 Hz, ^{3}CH$_2$). *Anal.* Calcd. for $C_{17}H_{12}Cl_2N_2O_3$: C, 56.22; H, 3.33; N, 7.71. Found: C, 56.26; H, 3.36; N, 7.76.

4-(4-Flurophenyl)-6-(3-nitrophenyl)-3,4-dihydropyridin-2(1*H*)-one (5f). ir (potassium bromide): 3233, 3124, 1685, 1648, 1530, 1469, 1352, 1218, 1162, 827, 775, 693 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 9.94 (s, 1H, NH), 8.37 (s, 1H, ArH), 8.22 (d, 1H, *J* = 8.0 Hz, ArH), 8.04 (d, 1H, *J* = 7.2 Hz, ArH), 7.69 (t, 1H, *J* = 7.8 Hz, ArH), 7.39–7.35 (m, 2H, ArH), 7.21–7.16 (m, 2H, ArH), 5.81 (d, 1H, *J* = 4.4 Hz, ^{5}CH), 4.02–3.98 (m, 1H, ^{4}CH), 2.76 (dd, 1H, J_1 = 15.6, J_2 = 6.8 Hz, ^{3}CH$_2$), 2.56 (dd, 1H, J_1 = 15.6 Hz, J_2 = 8.4 Hz, ^{3}CH$_2$). *Anal.* Calcd. for $C_{17}H_{13}FN_2O_3$: C, 65.38; H, 4.20; N, 8.97. Found: C, 65.45; H, 4.32; N, 8.78.

4-(3-Nitrophenyl)-6-(3-nitrophenyl)-3,4-dihydropyridin-2(1*H*)-one (5g). ir (potassium bromide): 3230, 3081, 1686, 1643, 1577, 1521, 1352, 1102, 805, 790 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 10.03 (s, 1H, NH), 8.39 (s, 1H, ArH), 8.23 (dd, 1H, J_1 = 8.0 Hz, J_2 = 1.6 Hz, ArH), 8.20 (s, 1H, ArH), 8.14 (dd, 1H, J_1 = 8.0 Hz, J_2 = 1.6 Hz, ArH), 8.05 (d, 1H, *J* = 8.0 Hz, ArH), 7.84 (d, 1H, *J* = 7.6 Hz, ArH), 7.73–7.65 (m, 2H, ArH), 5.87 (d, 1H, *J* = 3.6 Hz, ^{5}CH), 4.22–4.19 (m, 1H, ^{4}CH), 2.83 (dd, 1H, J_1 = 16.0 Hz, J_2 = 6.8 Hz, ^{3}CH$_2$), 2.66 (dd, 1H, J_1 = 15.8 Hz, J_2 = 8.8 Hz, ^{3}CH$_2$). *Anal.* Calcd. for $C_{17}H_{13}N_3O_5$: C, 60.18; H, 3.86; N, 12.38. Found: C, 60.34; H, 3.79; N, 12.45.

4-(3,4-Dimethoxyphenyl)-6-(3-nitrophenyl)-3,4-dihydropyridin-2(1*H*)-one (5h). ir (potassium bromide): 3250, 3099, 2935, 2835, 1683, 1609, 1593, 1523, 1416, 1352, 1262, 1138, 1031, 916, 800, 787, 698 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 9.87 (s, 1H, NH), 8.35 (s, 1H, ArH), 8.21 (dd, 1H, J_1 = 8.0 Hz, J_2 = 1.4 Hz, ArH), 8.03 (d, 1H, *J* = 8.4 Hz, ArH), 7.69 (t, 1H, *J* = 8.0 Hz, ArH), 6.95-6.91 (m, 1H, ArH), 6.90 (s, 1H, ArH), 6.83 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.0 Hz, ArH), 5.79 (d, 1H, *J* = 4.4 Hz, ^{5}CH), 3.96–3.87 (m, 1H, ^{4}CH), 3.75 (s, 3H, OCH$_3$), 3.73 (s, 3H, OCH$_3$), 2.72 (dd, 1H, J_1 = 15.8 Hz, J_2 = 7.0 Hz, ^{3}CH$_2$), 2.58 (dd, 1H, J_1 = 15.8 Hz, J_2 = 8.8 Hz, ^{3}CH$_2$). *Anal.* Calcd. for $C_{19}H_{18}N_2O_5$: C, 64.40; H, 5.12; N, 7.91. Found: C, 64.51; H, 5.09; N, 7.85.

4-(4-Methylphenyl)-6-(3-nitrophenyl)-3,4-dihydropyridin-2(1*H*)-one (5i). ir (potassium bromide): 3234, 3125, 1682, 1651, 1611, 1530, 1471, 1349, 810, 781 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 9.88 (s, 1H, NH), 8.35 (s, 1H, ArH), 8.21 (d, 1H, *J* = 8.4 Hz, ArH), 8.03 (d, 1H, *J* = 8.0 Hz, ArH), 7.68 (t, 1H, *J* = 7.6 Hz, ArH), 7.21 (d, 2H, *J* = 7.2 Hz, ArH), 7.15 (d, 2H, *J* = 7.2 Hz, ArH), 5.79 (d, 1H, *J* = 4.4 Hz, ^{5}CH), 3.93–3.88 (m, 1H, ^{4}CH), 2.74 (dd, 1H, J_1 = 16.0 Hz, J_2 = 5.4 Hz, ^{3}CH$_2$), 2.53 (dd, 1H, J_1 = 16.0 Hz, J_2 = 6.4 Hz, ^{3}CH$_2$), 2.28 (s, 3H, CH$_3$). *Anal.* Calcd. for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09. Found: C, 70.26; H, 5.14; N, 9.01.

4-(3,4-Methylenedioxylphenyl)-6-(3-nitrophenyl)-3,4-dihydropyridin-2(1*H*)-one (5j). ir (potassium bromide): 3199, 3095, 2890, 1668, 1608, 1520, 1440, 1344, 1242, 1039, 937, 806, 792 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 9.87 (s, 1H, NH), 8.35 (s, 1H, ArH), 8.21 (d, 1H, *J* = 8.4 Hz, ArH), 8.02 (d, 1H, *J* = 8.0 Hz, ArH), 7.71 (t, 1H, *J* = 8.0 Hz, ArH), 6.92–6.86 (m, 2H, ArH), 6.78 (d, 1H, *J* = 8.0 Hz, ArH), 5.98 (s, 2H, OCH$_2$O), 5.78 (d, 1H, *J* = 4.8 Hz, ^{5}CH), 3.94–3.86 (m, 1H, ^{4}CH), 2.68 (dd, 1H, J_1 = 16.0 Hz, J_2 = 6.8 Hz, ^{3}CH$_2$), 2.51 (dd, 1H, J_1 = 15.8 Hz, J_2 = 8.0 Hz, ^{3}CH$_2$). *Anal.* Calcd. for $C_{18}H_{14}N_2O_5$: C, 63.90; H, 4.17; N, 8.28. Found: C, 64.01; H, 4.12; N, 8.33.

4-Butyl-6-(3-nitrophenyl)-3,4-dihydropyridin-2(1*H*)-one (5k). ir (potassium bromide): 3231, 3098, 2950, 2892, 1681, 1625, 1522, 1467, 1352, 1105, 812, 791, 709 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 9.70 (s, 1H, NH), 8.29 (s, 1H, ArH), 8.18 (d, 1H, *J* = 8.0 Hz, ArH), 7.97 (d, 1H, *J* = 8.0 Hz, ArH), 7.67 (t, 1H, *J* = 8.0 Hz, ArH), 5.64 (d, 1H, *J* = 3.6 Hz, ^{5}CH), 2.59–2.55 (m, 1H, ^{4}CH), 2.48 (dd, 1H, J_1 = 17.0 Hz, J_2 = 7.4 Hz, ^{3}CH$_2$), 2.21 (dd, 1H, J_1 = 15.6 Hz, J_2 = 9.2 Hz, ^{3}CH$_2$), 1.46–1.33 (m, 6H, 3 × CH$_2$), 0.91 (t, 3H, *J* = 7.0 Hz, CH$_3$). *Anal.* Calcd. for $C_{15}H_{18}N_2O_3$: C, 65.68; H, 6.61; N, 10.21. Found: C, 65.79; H, 6.52; N, 10.13.

4-(2-Thiofuran)-6-(3-nitrophenyl)-3,4-dihydropyridin-2(1*H*)-one (5l). ir (potassium bromide): 3215, 3089, 1697, 1654, 1524, 1471, 1416, 1349, 1282, 1050, 798, 700 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 9.94 (s, 1H, NH), 8.35 (s, 1H, ArH), 8.23 (d, 1H, *J* = 7.6 Hz, ArH), 8.03 (d, 1H, *J* = 8.0 Hz, ArH), 7.70 (t, 1H, *J* = 8.0 Hz, ArH), 7.40 (dd, 1H, J_1 = 5.0 Hz, J_2 = 1.0 Hz, thiophen-2-yl-H), 7.01–6.99 (m, 2H, thiophen-2-yl-H), 5.87 (d, 1H, *J* = 4.8 Hz, ^{5}CH), 4.28–4.21 (m, 1H, ^{4}CH), 2.87 (dd, 1H, J_1 = 16.0 Hz, J_2 = 6.8 Hz, ^{3}CH$_2$), 2.61 (dd, 1H, J_1 = 15.8 Hz, J_2 = 6.8 Hz, ^{3}CH$_2$). *Anal.* Calcd. for $C_{15}H_{12}N_2O_3S$: C, 59.99; H, 4.03; N, 9.33; S, 10.68. Found: C, 60.08; H, 3.96; N, 9.25; S, 10.62.

4-(4-Chlorophenyl)-6-(4-methoxyphenyl)-3,4-dihydropyridin-2(1*H*)-one (5m). ir (potassium bromide): 3220, 3101, 1671, 1652, 1609, 1518, 1472, 1373, 1245, 1190, 819 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 9.60 (s, 1H, NH), 7.49 (d, 1H, *J* = 8.8 Hz, ArH), 7.39 (d, 1H, *J* = 8.4 Hz, ArH), 7.32 (d, 1H, *J* = 8.4 Hz, ArH), 6.93 (d, 1H, *J* = 8.8 Hz, ArH), 5.44 (d, 1H, *J* = 4.4 Hz, ^{5}CH), 3.93–3.88 (m, 1H, ^{4}CH), 3.76 (s, 3H, OCH$_3$), 2.71 (dd, 1H, J_1 = 16.0 Hz, J_2 = 6.8 Hz, ^{3}CH$_2$), 2.48 (dd, 1H, J_1 = 15.2 Hz,

J_2 = 7.2 Hz, $^3CH_2$). *Anal.* Calcd. for $C_{18}H_{16}ClNO_2$: C, 68.90; H, 5.14; N, 4.46. Found: C, 69.02; H, 5.01; N, 4.38.

4-(4-Bromophenyl)-6-(4-methoxyphenyl)-3,4-dihydropyridin-2(1*H*)-one (5n). ir (potassium bromide): 3222, 3103, 1673, 1655, 1609, 1515, 1488, 1372, 1246, 1188, 1010, 824 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 9.59 (s, 1H, NH), 7.53 (d, 2H, *J* = 8.4 Hz, ArH), 7.50 (d, 2H, *J* = 8.8 Hz, ArH), 7.28 (d, 2H, *J* = 8.4 Hz, ArH), 6.94 (d, 2H, *J* = 8.8 Hz, ArH), 5.44 (d, 1H, *J* = 4.4 Hz, ^{5}CH), 3.92–3.87 (m, 1H, ^{4}CH), 3.78 (s, 3H, OCH_3), 2.72 (dd, 1H, J_1 = 15.8 Hz, J_2 = 7.0 Hz, $^3CH_2$), 2.49 (dd, 1H, J_1 = 16.0 Hz, J_2 = 8.0 Hz, $^3CH_2$). *Anal.* Calcd. for $C_{18}H_{16}BrNO_2$: C, 60.35; H, 4.50; N, 3.91. Found: C, 60.34; H, 4.52; N, 3.40.

4-(2,4-Dichlorophenyl)-6-(4-methoxyphenyl)-3,4-dihydropyridin-2(1*H*)-one (5o). ir (potassium bromide): 3230, 3113, 3071, 1684, 1607, 1515, 1455, 1378, 1252, 1179, 1091, 1043, 956, 831 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 9.72 (s, 1H, NH), 7.55-7.50 (m, 3H, ArH), 7.39 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.4 Hz, ArH), 7.33 (s, 1H, ArH), 6.95 (d, 1H, *J* = 8.8 Hz, ArH), 5.46 (d, 1H, *J* = 4.8 Hz, ^{5}CH), 4.22–4.17 (m, 1H, ^{4}CH), 3.81 (s, 3H, OCH_3), 2.81 (dd, 1H, J_1 = 15.8 Hz, J_2 = 7.0 Hz, $^3CH_2$), 2.50 (dd, 1H, J_1 = 16.0 Hz, J_2 = 8.8 Hz, $^3CH_2$). *Anal.* Calcd. for $C_{18}H_{15}Cl_2NO_2$: C, 62.08; H, 4.34; N, 4.02. Found: C, 62.12; H, 4.36; N, 4.12.

4-(3,4-Dichlorophenyl)-6-(4-methoxyphenyl)-3,4-dihydropyridin-2(1*H*)-one (5p). ir (potassium bromide): 3235, 3112, 2965, 2902, 1685, 1609, 1513, 1459, 1369, 1242, 1180, 1033, 961, 820 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 9.64 (s, 1H, NH), 7.60 (d, 2H, *J* = 8.4 Hz, ArH), 7.49 (d, 1H, *J* = 8.4 Hz, ArH), 7.31 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.0 Hz, ArH), 6.93 (d, 2H, *J* = 8.8 Hz, ArH), 5.45 (d, 1H, *J* = 4.4 Hz, ^{5}CH), 3.96–3.91 (m, 1H, ^{4}CH), 3.76 (s, 3H, OCH_3), 2.72 (dd, 1H, J_1 = 16.0 Hz, J_2 = 6.8 Hz, $^3CH_2$), 2.52 (dd, 1H, J_1 = 16.0 Hz, J_2 = 8.0 Hz, $^3CH_2$). *Anal.* Calcd. for $C_{18}H_{15}Cl_2NO_2$: C, 62.08; H, 4.34; N, 4.02. Found: C, 62.16; H, 4.31; N, 4.00.

4-(3,4-Methylenedioxylphenyl)-6-(4-methoxyphenyl)-3,4-dihydropyridin-2(1*H*)-one (5q). ir (potassium bromide): 3227, 3105, 2887, 2840, 1673, 1609, 1576, 1485, 1368, 1245, 1190, 1038, 932, 822 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 9.51 (s, 1H, NH), 7.50 (d, 2H, *J* = 8.8 Hz, ArH), 6.94 (d, 2H, *J* = 8.8 Hz, ArH), 6.86 (d, 2H, *J* = 8.8 Hz, ArH), 6.77 (d, 1H, *J* = 8.4 Hz, ArH), 5.98 (s, 2H, OCH_2O), 5.42 (d, 1H, *J* = 4.4 Hz, ^{5}CH), 3.84–3.79 (m, 1H, ^{4}CH), 3.78 (s, 3H, OCH_3), 2.68 (dd, 1H, J_1 = 16.0 Hz, J_2 = 6.8 Hz, $^3CH_2$), 2.48 (dd, 1H, J_1 = 16.0 Hz, J_2 = 7.2 Hz, $^3CH_2$). *Anal.* Calcd. for $C_{19}H_{17}NO_4$: C, 70.58; H, 5.30; N, 4.33. Found: C, 70.49; H, 5.42; N, 4.29.

4-(4-Bromophenyl)-6-(4-nitrophenyl)-3,4-dihydropyridin-2(1*H*)-one (5r). ir (potassium bromide): 3237, 3126, 3078, 2902, 1679, 1611, 1598, 1513, 1380, 1226, 1158, 1067, 749 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 9.93 (s, 1H, NH), 8.23 (d, 2H, *J* = 8.8 Hz, ArH), 7.84 (d, 2H, *J* = 8.8 Hz, ArH), 7.55 (d, 2H, *J* = 8.0 Hz, ArH), 7.30 (d, 2H, *J* = 8.0 Hz, ArH), 5.86 (d, 1H, *J* = 4.8 Hz, ^{5}CH), 4.03–3.98 (m, 1H, ^{4}CH), 2.76 (dd, 1H, J_1 = 15.6 Hz, J_2 = 6.8 Hz, $^3CH_2$), 2.55 (dd, 1H, J_1 = 16.0 Hz, J_2 = 8.4 Hz, $^3CH_2$). *Anal.* Calcd. for $C_{17}H_{13}BrN_2O_3$: C, 54.71; H, 3.51; N, 7.51. Found: C, 54.83; H, 3.48; N, 7.55.

4-(4-Chlorophenyl)-6-(4-nitrophenyl)-3,4-dihydropyridin-2(1*H*)-one (5s). ir (potassium bromide): 3228, 3111, 2885, 2837, 1683, 1606, 1598, 1519, 1492, 1346, 1089, 823, 750 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 9.93 (s, 1H, NH), 8.24 (d, 2H, *J* = 8.8 Hz, ArH), 7.85 (d, 2H, *J* = 8.8 Hz, ArH), 7.42 (d, 2H, *J* = .4 Hz, ArH), 7.36 (d, 2H, *J* = 8.4 Hz, ArH), 5.87 (d, 1H, *J* = 4.4 Hz, ^{5}CH), 4.05–3.40 (m, 1H, ^{4}CH), 2.76 (dd, 1H, J_1 = 16.0 Hz, J_2 = 7.2 Hz, $^3CH_2$), 2.56 (dd, 1H, J_1 = 15.6 Hz, J_2 = 8.4 Hz, $^3CH_2$). *Anal.* Calcd. for $C_{17}H_{13}ClN_2O_3$: C, 62.11; H, 3.99; N, 8.52. Found: C, 62.19; H, 4.03; N, 8.57.

4-(4-Chlorophenyl)-6-(2,4-dichlorophenyl)-3,4-dihydropyridin-2(1*H*)-one (5t). ir (potassium bromide): 3185, 3086, 2909, 2846, 1681, 1612, 1587, 1472, 1376, 1298, 1096, 994, 829, 794 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 9.62 (s, 1H, NH), 7.70 (s, 1H, ArH), 7.48–7.46 (m, 2H, ArH), 7.42 (d, 2H, *J* = 8.8 Hz, ArH), 7.37 (d, 2H, *J* = 8.8 Hz, ArH), 5.21 (d, 1H, *J* = 3.6 Hz, ^{5}CH), 3.94–3.90 (m, 1H, ^{4}CH), 2.78 (dd, 1H, J_1 = 16.0 Hz, J_2 = 7.2 Hz, $^3CH_2$), 2.46 (dd, 1H, J_1 = 16.0 Hz, J_2 = 7.2 Hz, $^3CH_2$). *Anal.* Calcd. for $C_{17}H_{12}Cl_3NO$: C, 57.90; H, 3.43; N, 3.97. Found: C, 57.97; H, 3.31; N, 3.88.

4-(4-Bromophenyl)-6-(2-chlorophenyl)-3,4-dihydropyridin-2(1*H*)-one (5u). ir (potassium bromide): 3199, 3064, 2880, 2839, 1763, 1729, 1668, 1590, 1489, 1357, 1294, 1074, 1011, 932, 827 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 10.04 (s, 1H, NH), 7.62 (d, 2H, *J* = 8.4 Hz, ArH), 7.53 (d, 1H, *J* = 8.4 Hz, ArH), 7.32 (dd, 1H, J_1 = 8.6 Hz, J_2 = 2.2 Hz ArH), 7.25 (d, 1H, *J* = 8.4 Hz, ArH), 7.07 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.0 Hz ArH), 7.01–6.98 (m, 2H, ArH), 5.12 (d, 1H, *J* = 4.4 Hz, ^{5}CH), 3.63–3.35 (m, 1H, ^{4}CH), 2.32 (dd, 1H, J_1 = 16.0 Hz, J_2 = 6.8 Hz, $^3CH_2$), 2.19 (dd, 1H, J_1 = 16.0 Hz, J_2 = 7.2 Hz, $^3CH_2$). *Anal.* Calcd. for $C_{17}H_{13}BrClNO$: C, 56.30; H, 3.61; N, 3.86. Found: C, 56.43; H, 3.52; N, 3.77.

General Procedure for the Reaction of 2,4,6-triaryl pyridine (6). All reactions were performed in a monomodal Emrys™ Creator from Personal Chemistry, Uppsala, Sweden. Typically, in a 10-mL Emrys™ reaction vial, the appropriate the starting-materials **3** (2 mmol), aromatic ketone (2 mmol), ammonium acetate (1.0 g) were mixed and then capped. The mixture was irradiated at 200 W at 100 °C for 3–6 min (the reaction was monitored by TLC). The reaction mixture was cooled to room temperature and filtered to afford the crude products. The crude products were purified by recrystallization from ethanol.

4-(2-Chlorophenyl)-2,6-bis(3-nitrophenyl)pyridine (6a). ir (potassium bromide): 3085, 1699, 1603, 1524, 1488, 1437, 1351, 884, 807, 750, 733 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 9.10 (s, 2H, Pyridyl-H), 8.76 (d, 2H, *J* = 8.0 Hz, ArH), 8.37 (dd, 2H, J_1 = 8.0 Hz, J_2 = 1.6 Hz, ArH), 8.34 (s, 2H, ArH), 7.88 (t, 2H, *J* = 8.0 Hz, ArH), 7.75–7.70 (m, 2H, ArH), 7.58–7.56 (m, 2H, ArH). *Anal.* Calcd. for $C_{23}H_{14}ClN_3O_4$: C, 63.97; H, 3.27; N, 9.73. Found: C, 64.03; H, 3.22; N, 9.65.

4-(4-Methylphenyl)-2,6-bis(3-nitrophenyl)pyridine (6b). ir (potassium bromide): 3090, 1602, 1529, 1445, 1345, 880, 823, 804, 709 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 9.14 (s, 2H, Pyridyl-H), 8.82 (d, 2H, *J* = 8.0 Hz, ArH), 8.48 (s, 2H, ArH), 8.36 (d, 2H, *J* = 8.4 Hz, ArH), 8.08 (d, 2H, *J* = 8.0 Hz, ArH), 7.88 (t, 2H, *J* = 8.0 Hz, ArH), 7.42 (d, 2H, *J* = 7.6 Hz, ArH), 2.43 (s, 3H, CH_3). *Anal.* Calcd. for $C_{24}H_{17}N_3O_4$: C, 70.07; H, 4.16; N, 10.21. Found: C, 71.06; H, 4.08; N, 10.18.

4-(4-Bromophenyl)-2,6-bis(4-methoxyphenyl)pyridine (6c). ir (potassium bromide): 3082, 1605, 1577, 1540, 1490, 1459, 1423, 1384, 1361, 819 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 8.27 (d, 2H, *J* = 8.0Hz, ArH), 8.06 (s, 2H, Pyridyl-H), 8.00 (d, 2H, *J* = 8.0Hz, ArH), 7.75 (d, 2H, *J* = 8.0Hz, ArH), 7.08 (d, 2H, *J* = 8.0Hz, ArH), 3.85 (s, 6H, 2 × OCH_3). *Anal.* Calcd. for $C_{25}H_{20}BrNO_2$: C, 67.27; H, 4.52; N, 3.14. Found: C, 67.35; H, 4.48; N, 3.16.

4-(2,4-Dichlorophenyl)-2,6-bis(2,4-dichlorophenyl)pyridine (6d). ir (potassium bromide): 3080, 1596, 1554, 1536, 1471, 1414, 1363, 1052, 869, 816 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 7.88 (s,

2H, Pyridyl-H), 7.76–7.84 (m, 4H, ArH), 7.72–7.50 (m, 1H, ArH), 7.70–7.66 (m, 1H, ArH), 7.52–7.63 (m, 3H, ArH). *Anal*. Calcd. for $C_{23}H_{11}Cl_6N$: C, 53.74; H, 2.16; N, 2.72. Found: C, 53.88; H, 2.08; N, 2.75.

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[18] Crystal data for 5f: Empirical formula $C_{17}H_{13}FN_2O_3$, Mr = 312.29, T = 294(2) K, Monoclinic, space group P2(1)/c, a = 13.960(3) Å, b = 8.5633(18) Å, c = 12.523(3) Å, α = 90°, β = 103.789(4)°, γ = 90°, V = 1453.9(5) Å^3, Z = 4, Dc = 1.427 Mg/cm^3, λ(MoK α) = 0.71073 Å, μ = 0.108 mm^{-1}, F(000) = 648, 1.50°< θ<26.39°, R = 0.0443, wR_2 = 0.0970, S = 0.989, Largest diff. Peak and hole: 0.160 and -0.189 e/Å^3.