Synthesis of Hantzsch 1,4-Dihydropyridines under Solvent-free Condition using Zn[(L)proline]$_2$ as Lewis Acid Catalyst

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The present short communication describes a Lewis acid (Zn[(L)proline]$_2$) catalysed one pot synthesis of Hantzsch 1,4-dihydropyridine (DHP) derivatives under solvent-free condition by conventional heating and microwave irradiation. The Lewis acid catalyst Zn[(L)proline]$_2$ used in this reaction afford moderate to good yield. The catalyst is reusable upto five cycles without appreciable loss of its catalytic activity.

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Introduction.

Organic synthesis under solvent free conditions is of great relevance because of emerging environmental issues [1]. The solvent free technique not only eliminates the use of toxic solvents but also provides simplicity in process and easy separation of the products [2]. Microwave accelerated organic synthesis (MAOS) is an effective and non-conventional alternative route proposed during the last decade due to drastic reduction in the reaction time and to minimize cumbersome work-up [3,4].

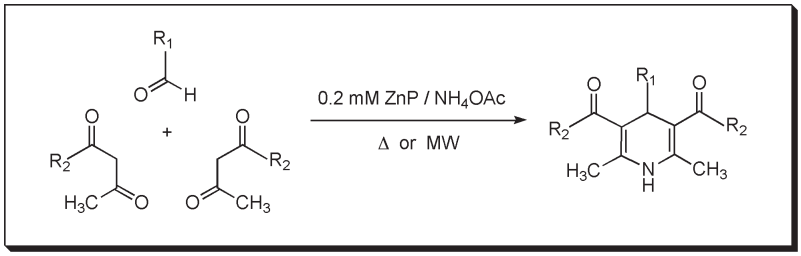
Dihydropyridine (DHP) derivatives are an important class of organic compounds in view of its application in pharmaceuticals and hence their synthesis under solvent-free condition is an interesting approach. 1,4-DHPs are widely known as Ca^{2+} channel blockers and they are emerged as one of the most substantial classes of drugs for the treatment of cardiovascular diseases [5]. The 1,4-DHP heterocyclic ring is an essential nucleus in various bioactive compounds such as vasodilator, bronchodilator, anti-tumor, geroprotective, hepatoprotective and anti-diabetic agents [6a,b].

Conventionally 1,4-DHPs were prepared by one-pot three component condensation of an aryl/alkyl aldehyde, a β-dicarbonyl compound and ammonia in the presence of an acid catalyst under reflux conditions [7]. However the yield of 1,4-DHPs was generally low. The classical Hantzsch 1,4-DHPs synthesis and other modified methods developed until recently were reviewed [8,9]. Although numerous methods under improved conditions have been reported many of them are suffering from serious drawbacks such as lower catalyst life cycle, occurrence of side reactions, unsatisfactory yields, high temperatures and longer reaction times [10-27]. Hence the development of an efficient and versatile method for the preparation of Hantzsch 1,4-DHPs is an important approach. Some of the earlier studies reported on the synthesis of Hantzsch pyridine derivatives assisted with microwave (MW) irradiation but these methods are seriously affected by requirement of high MW power, catalyst recyclability, separation of catalyst, occurrence of side reactions and low yield [18,24,28-33]. Our research group has recently reported the synthesis of novel heterocyclics, 1,5-benzodiazepine derivatives using Zn[(L)proline]$_2$ as new catalyst under solvent-free MW irradiation [34]. We report herein a mild and efficient synthesis of Hantzsch 1,4-dihydropyridine derivatives by adopting Hantzsch procedure using Zn[(L)proline]$_2$ as an inexpensive and recyclable Lewis acid catalyst under solvent-free conditions.

Results and Discussion.

Zn[(L)proline]$_2$ complex was synthesised by stirring 10 mmol of (L)proline and 5 mmol of zinc nitrate solution at room temperature according to our reported procedure [34]. In the present investigation nitro, chloro, methoxy and hydroxy substituted aryl aldehydes and heterocyclic aldehydes such as 2-furfuraldehyde and indole-3-carboxyaldehyde were used for the study. In all the reactions 5 mmol of aldehyde, 11 mmol of active methylene compound and 10 mmol of ammonium acetate were condensed in the presence of 0.2 mmol of catalyst under solvent-free condition (Scheme 1). In order to ascertain the catalytic activity of the catalyst the reactions were carried out by conventional heating and microwave irradiation. The

Scheme 1



microwave irradiated reactions afforded more yield than the conventional heating. The results are listed in Table I.

All the reactions (Table I) employing MW irradiation with microwave power supply of 200 W were completed within 2-4 min. This is one of the major advantages and the catalyst exhibits its ability to work with low MW power supply and utilized very low MW power compare other earlier reports [18,24,28-30]. It is noticed that the presence of very low amount (0.2 mmol) of Zn-proline complex effectively catalyses the reaction assisted with low MW power to obtain good yield of the expected product [24,29,30]. The crude products were obtained with acceptable purity after separation from the catalyst and reduces cumbersome workup compare other earlier reports.

In order to evaluate the activity of catalyst, recycling studies have been carried out with 5 mmol of 2-furfuraldehyde, 11 mmol of acetylacetone and 10 mmol of ammonium acetate in the presence of 0.2 mmol of catalyst as a model reaction. The results are shown in Table II. The studies reveal that the catalyst is reusable upto five cycles without appreciable loss of its catalytic activity and no marginal difference in the yield of the product. The reduction of yield in the sixth cycle is due to removal of Zn-proline complex on washing and decomposition of complex due to heating. The decomposition of catalyst and leaching out from the supported material was confirmed by atomic absorption spectroscopy (AAS) analysis. The amount of metal-complex present in the supported catalyst is measured by AAS from each recycling step. The results revealed that from 1 to 5 cycles the amount of Zn^{2+} ion was marginally decreased and drastically decrease in the 6^{th} cycle. Table II shows the amount of Zn^{2+} ion present in the catalyst obtained from AAS analysis.

In order to evaluate the efficiency of our present investigation a comparative study was carried out with earlier reports. The reaction of nitrobenzaldehyde, ethyl acetoacetate and ammonium acetate have been taken as model reaction. The results are listed Table III. It is observed that

Table I

Synthesis of 1,4-Dihydropyridine Derivatives

Entry	R_1	R_2	Conventional Heating Time [a] (h)	Microwave Irradiation Yield [b,c] (%)	Time [a] (min)	Yield [b,c] (%)
1	C_6H_5	OC_2H_5	1	80	2	88
2	4-NO_2-C_6H_4	OC_2H_5	1	80	2	90
3	3-NO_2-C_6H_4	OC_2H_5	2	75	3	83
4	2-NO_2-C_6H_4	OC_2H_5	2.5	70	3	80
5	3-Cl-C_6H_4	OC_2H_5	1.5	81	2	90
6	3-OH-C_6H_4	OC_2H_5	2	83	2	90
7	4-OH 3-CH_3O C_6H_3	OC_2H_5	1.5	85	2	92
8	3,4-$(CH_3O)_2C_6H_3$	OC_2H_5	1.5	85	2	96
9	2-Furyl	OC_2H_5	1	88	2.5	93
10	3-Indolyl	OC_2H_5	1.5	85	3	95
11	C_6H_5	CH_3	2	83	3	90
12	4-NO_2-C_6H_4	CH_3	2	80	3	87
13	3-NO_2-C_6H_4	CH_3	2.5	78	4	83
14	2-NO_2-C_6H_4	CH_3	3	75	4	80
15	3-Cl-C_6H_4	CH_3	2.5	80	2	87
16	3-OH-C_6H_4	CH_3	2	80	2	90
17	4-OH 3-CH_3O C_6H_3	CH_3	1.5	85	2	90
18	3,4-$(CH_3O)_2C_6H_3$	CH_3	1	83	2	93
19	2-Furyl	CH_3	1	85	2.5	95
20	3-Indolyl	CH_3	1.5	88	3	93
21	C_6H_5	OCH_3	2.5	83	3	90
22	4-NO_2-C_6H_4	OCH_3	2	80	3	93
23	3-NO_2-C_6H_4	OCH_3	3	78	4	85
24	2-NO_2-C_6H_4	OCH_3	3.5	75	4	85
25	3-Cl-C_6H_4	OCH_3	3	80	3	85
26	3-OH-C_6H_4	OCH_3	4	75	4	90
27	4-OH 3-CH_3O-C_6H_3	OCH_3	2	84	3	95
28	3,4-$(CH_3O)_2C_6H_3$	OCH_3	1.5	83	2.5	95
29	2-Furyl	OCH_3	1	85	3	93
30	3-Indolyl	OCH_3	1.5	85	4	90

[a] Reaction progress monitored by TLC; [b] Isolated yield after column chromatography; [c] All the products were confirmed by FTIR, MS and elemental analysis with reported literature.

Table II

The Catalyst Recycling Studies [a]

Catalyst recycle	Conventional		Microwave irradiation	
	Time [b] (h)	Yield [c] (%)	Time [b] (min)	Yield [c] (%)
I	1	80	3	90 (0.056)*
II	1	80	3	85(0.053)
III	1	78	3	80(0.050)
IV	1	75	3	80(0.048)
V	1	75	3	80(0.048)
VI	1	60	3	68(0.035)

[a] Model reaction: 5 mmol of 2-furfuraldehyde, 11 mmol of acetyl acetone and 10 mmol of ammonium acetate in the presence of 0.2 mmol of catalyst; [b] Reaction progress monitored by TLC analysis; cIsolated yield; *Values in the paranthesis indicates amount of Zn^{2+} ions measured by AAS (in mmoles).

Table III

A Comparative Study of Present Methodology with Other Reports

Catalyst	MW power (W)	Time (min)	Yield (%)	Reference
$Zn[(L)proline]_2$	200	2	90	Present work
-	700a	4	32	28
50% aqueous solution of NaBGMS*	700	5	65	29
AcOH	400	4	60	30
Bentonite/HNO3	600	5	85	24
-	600 [a]	4	90	18
-	600 [a]	4	88	32

*Sodium butylmonoglycolsulphate; [a] Reactions carried out in ethanol medium

earlier reports utilized high MW power with low yield of 1,4-DHPs. Some of the reported methodology required a high catalyst amount, longer reaction time and low recycling ability. The present methodology exhibits great advantages and eliminates the problems associated with earlier reports.

Conclusions.

The present investigation concludes that $Zn[(L)proline]_2$ complex is found to be a novel catalyst for the preparation of Hantzsch 1,4-dihydropyridine derivatives under solvent-free condition with excellent yields. This catalyst can be used to synthesis 1,4-DHPs employing a wide range of aldehydes including heterocyclic aldehydes and β-dicarbonyl compounds. Microwave-irradiated reactions in the presence of this catalyst afford moderate to good yield in short reaction periods. The catalyst exhibits good catalytic activity even in low MW power (≈ 200 w) when compare with earlier studies and eliminates the problems associated with previous reports. The catalyst is reusable up to five cycles without appreciable loss of its catalytic activity.

EXPERIMENTAL

The FTIR spectra of the products were recorded on a Nicolet 360 FTIR using KBr pellet technique. The elemental analyses were carried out in a Heraeus CHNO-rapid analyser. The mass spectra were recorded on a Finnigan Mat 8230MS spectrometer. The amount of Zn^{2+} ions was measured by GBC 932 plus atomic absorption spectrometer.

a) Synthesis of Bis[(L)proline]Zn Complex.

(L)proline (20 mmol) was dissolved in absolute ethanol (50 mL) containing potassium hydroxide (20 mmol) and stirred well for 15 min. In order to maintain the metal to ligand ratio of 1:2, 10 mmol of $Zn(NO_3)_2.6H_2O$ was dissolved in a small quantity of double distilled water and this solution was added in drops to the (L)proline solution. The contents were vigorously stirred at room temperature for 6 h. $Zn[(L)proline]_2$ complex was obtained as a white solid. It was collected by filtration and dried at 70 °C in vacuum for 6 h. Yield: 94%. FT IR (ν cm^{-1}): 3206, 2995, 1605, 1516, 1403, 1239, 825 and 533.

Anal. Calcd for $C_{10}H_{16}N_2O_4Zn$. C, 40.91; H, 5.49; N, 9.54. Found: C, 40.74; H, 5.60; N, 9.30.

b) Synthesis of 1,4-Dihydropyridines.

Conventional Method.

4-Nitrobenzaldehyde (5 mmol), ethyl acetoacetate (11 mmol) and ammonium acetate (10 mmol) were thoroughly mixed with 0.2 mmol of catalyst and adsorbed on neutral alumina. The alumina supported mixture was taken in a 15 ml clean stainless steel autoclave and thermostated at 70 °C up to the time indicated in Table I. After completion of reaction, the mixture was diluted with dichloromethane and the product was seperated by simple filtration. The alumina supported catalyst was regenerated for reuse in the next reaction. The excess solvent in the product was removed by evaporation and purified by column chromatography (silicagel 100-200 mesh, *n*-hexane to ethyl acetate ratio = 80:20, v/v). The product was obtained as a yellow crystalline solid. The same procedure was adopted for other reactions. The reaction time and yield for all the reactions are presented in Table I.

Microwave Irradiation Method.

2-Furfuraldehyde (5 mmol), acetylacetone (11 mmol) and ammonium acetate (10 mmol) were thoroughly mixed with 0.2 mmol of catalyst and adsorbed on 5 g of neutral alumina. The alumina supported mixture was taken in an open Erlenmeyer flask and irradiated using a household microwave oven (model: IFB 17PM 1S) with a power range of 200w and a pulse of 15 seconds. The progress of the reaction was monitered by TLC (silica gel precoated plate, eluent: *n*-hexane to ethyl acetate ratio = 80 : 20, v/v). After completion of the reaction, the mixture was diluted with dichloromethane and the product was seperated by simple filtration. The excess solvent was removed by distillation and the crude product was purified by column chromatography (*n*-hexane to ethyl acetate ratio = 80:20). The above mentioned procedure was followed for all the reactions. The reaction time and yield for all the reactions are as in Table I.

Recycling Studies.

2-Furfuraldehyde (5 mmol), acetylacetone (11 mmol) and ammonium acetate (10 mmol) were thoroughly mixed with catalyst (0.2 mmol) and adsorbed on neutral alumina (5 g) was taken

as model reaction. The progress of reaction was monitored by TLC analysis. The alumina supported catalyst recovered after completion of the reaction was thoroughly washed with dichloromethane until complete removal of the organic components. Further, the catalyst was washed with small portions of methanol and dried in vaccum at 70 °C for 6 h. The dried catalyst was used for next cycle and the same procedure was adopted for all the recycling studies. The reaction time and yield for different cycles are presented in Table II.

Diethyl 4-Phenyl 2,6-dimethyl-1,4-dihydropyridine 3,5-Dicarboxylate (**1**).

This compound has FTIR (KBr): 3313(N-H str), 3035 (Ar C-H str), 2985 (Ali C-H str), 1675 (C=O str). MS(EI): m/z: 329 (M, 85 %).

Anal. Calcd. for $C_{19}H_{23}NO_4$ (329.16): C, 69.28; H, 7.04; N, 4.25; O, 19.43. Found: C, 69.15; H, 7.10; N, 4.15; O, 19.40.

Diethyl 4 (4-Nitro phenyl) 2,6-dimethyl-1,4-dihydropyridine 3,5-Dicarboxylate (**2**).

This compound has FTIR (KBr): 3329 (N-H str), 3088 (Ar C-H str), 2975 (Ali. C-H str), 1690 (C=O str). MS (EI) m/z: 374 (M, 90 %), 375 (10 %).

Anal. Calcd. for $C_{19}H_{22}N_2O_6$ (374.15): C, 60.95; H, 5.92; N, 7.48; O, 25.64. Found: C, 60.90; H, 5.85; N, 7.40; O, 25.60.

Diethyl 4 (3-Chloro phenyl)-2,6-dimethyl-1,4-dihydropyridine 3,5-Dicarboxylate (**5**).

This compound has FTIR (KBr): 3339 (N-H str), 3075 (Ar C-H str), 2970 (Ali. C-H str), 1684 (C=O str). MS (EI) m/z: 363 (M, 85 %), 365 (15.0%).

Anal. Calcd. for $C_{19}H_{22}ClNO_4$ (363.12): C, 62.72; H, 6.09; N, 3.85; O, 17.59. Found: C, 62.68; H, 6.03; N, 3.75; O, 17.65.

Diethyl 4 (3-Hydroxy phenyl)-2,6-dimethyl-1,4-dihydropyridine 3,5-Dicarboxylate (**6**).

This compound has FTIR (KBr): 3405 (O-H str), 3345 (N-H str), 3080 (Ar C-H str), 2993 (Ali. C-H str), 1687 (C=O str). MS (EI) m/z: 345 (M, 90 %), 346 (13 %).

Anal. Calcd for $C_{19}H_{23}NO_5$ (345.16): C, 66.07; H, 6.71; N, 4.06; O, 23.16. Found: C, 66.16; H, 6.65; N, 4.13; O, 23.20.

Diethyl 4-(4-Hydroxy–3-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine 3,5-Dicarboxylate (**7**).

This compound has FTIR (KBr): 3415 (O-H str), 3340 (N-H str), 3073 (Ar C-H str), 2980 (Ali. C-H str). 1701 (C=O str). MS (EI) m/z: 375 (M, 84 %), 376 (10 %).

Anal. Calcd. for $C_{20}H_{25}NO_6$ (375.17): C, 63.99; H, 6.71; N, 3.73; O, 25.57. Found: C, 63.80; H, 6.65; N, 3.78; O, 25.60.

Diethyl 4-(3,4-Dimethoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine 3,5-Dicarboxylate (**8**).

This compound has FTIR (KBr): 3355 (N-H str), 3075 (Ar C-H str), 2994 (Ali. C-H str), 1696 (C=O str). MS (EI) m/z: 389 (M, 100 %), 390 (15 %).

Anal. Calcd. for $C_{21}H_{27}NO_6$ (389.18): C, 64.77; H, 6.99; N, 3.60; O, 24.65. Found: C, 64.69; H, 6.91; N, 3.54; O, 24.70.

Diethyl 4(2-Furyl)-2,6-dimethyl-1,4-dihydropyridine 3,5-Dicarboxylate (**9**).

This compound has FTIR (KBr): 3360 (N-H str), 3010 (C-H str), 1705 (C=O str). MS (EI) m/z: 319 (M, 90 %), 320 (10 %).

Anal. Calcd. for $C_{17}H_{21}NO_5$ (319.14): C, 63.94; H, 6.63; N, 4.39; O, 25.05. Found: C, 63.85; H, 6.50; N, 4.45; O, 25.15.

Diethyl 4-(3–Indolyl) 2,6-dimethyl-1,4-Dihydropyridine 3,5-Dicarboxylate (**10**).

This compound has FTIR (KBr): 3360 (N-H str), 3083 (Ar C-H str), 2980 (Ali. C-H str), 1702 (C=O str). MS (EI) m/z: 368 (100.0%), 369 (10.1%).

Anal. Cacld. for $C_{21}H_{24}N_2O_4$ (368.17): C, 68.46; H, 6.57; N, 7.60; O, 17.37. Found: C, 68.50; H, 6.65; N, 7.54; O, 17.30.

3,5-Diacyl-4-phenyl-2,6-dimethyl-1,4-dihydropyridine (**11**).

This compound has FTIR (KBr): 3365 (N-H str), 3075 (Ar C-H str), 2976 (Ali. C-H str), 1725 (C=O str). MS (EI) m/z: 269 (M, 100 %).

Anal. Calcd. for $C_{17}H_{19}NO_2$ (269.14): C, 75.81; H, 7.11; N, 5.20; O, 11.88. Found: C, 75.74; H, 7.05; N, 5.10; O, 11.75.

3,5-Diacyl-4-(4-nitro phenyl)-2,6-dimethyl-1,4-dihydropyridine (**12**).

This compound has FTIR (KBr): 3370 (N-H str), 3070 (Ar C-H str), 2983 (Ali. C-H str), 1723 (C=O str). MS (EI) m/z: 314 (M, 100 %), 315 (8 %).

Anal. Calcd. for $C_{17}H_{18}N_2O_4$ (314.13): C, 64.96; H, 5.77; N, 8.91; O, 20.36. Found: C, 64.80; H, 5.65; N, 8.83; O, 20.30.

3,5-Diacyl 4 (3-chloro phenyl) 2,6-dimethyl 1,4-dihydropyridine (**15**).

This compound has FTIR (KBr): 3363 (N-H str), 3080 (Ar C-H str), 2985 (Ali. C-H str), 1720 (C=O str). MS (EI) m/z: 303 (M, 95 %).

Anal. Calcd. for $C_{17}H_{18}ClNO_2$ (303): C, 67.21; H, 5.97; N, 4.61; O, 10.53. Found: C, 67.26; H, 5.85; N, 4.55; O, 10.45.

3,5-Diacyl-4-(3-hydroxyphenyl)-2,6-dimethyl-1,4-dihydropyridine (**16**).

This compound has FTIR (KBr): 3415 (O-H str), 3368 (N-H str), 3070 (Ar C-H str), 2982 (Ali. C-H str), 1723 (C=O str). MS (EI) m/z: 285 (M, 100 %), 286 (12 %).

Anal. Calcd. for $C_{17}H_{19}NO_3$ (285.14): C, 71.56; H, 6.71; N, 4.91; O, 16.82. Found: C, 71.45; H, 6.60; N, 4.85; O, 16.90.

3,5-Diacyl-4-(4-hydroxy-3-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine (**17**).

This compound has FTIR (KBr): 3420 (O-H str), 3368 (N-H str), 2990 (Ali. C-H str), 1730 (C=O str). MS (EI) m/z: 315 (M, 100 %).

Anal. Calcd. for $C_{18}H_{21}NO_4$ (315.15): C, 68.55; H, 6.71; N, 4.44; O, 20.29. Found: C, 68.40; H, 6.60; N, 4.35; O, 20.20.

3,5-Diacyl-4-(3,4-dimethoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine (**18**).

This compound has FTIR (KBr): 3370 (N-H str), 3075 (Ar C-H str), 2976 (Ali. C-H str), 1727 (C=O str). MS (EI) m/z: 329 (M, 85 %), 330 (15 %).

Anal. Calcd. for $C_{19}H_{23}NO_4$ (329.16): C, 69.28; H, 7.04; N, 4.25; O, 19.43. Found: C, 69.20; H, 6.95; N, 4.10; O, 19.35.

3,5-Diacyl-4-(2-furyl)-2,6-dimethyl-1,4-dihydropyridine (**19**).

This compound has FTIR (KBr): 3360 (N-H str), 3076 (Ar C-H str), 2984 (Ali. C-H str), 1724 (C=O str). MS (EI) m/z: 259 (M, 100 %), 260 (7 %).

Anal. Calcd. for $C_{15}H_{17}NO_3$ (259.12): C, 69.48; H, 6.61; N, 5.40; O, 18.51. Found: C, 69.40; H, 6.51; N, 5.35; O, 18.39.

3,5-Diacyl-4-(3–indolyl)-2,6-dimethyl-1,4-dihydropyridine (**20**).

This compound has FTIR (KBr): 3363 (N-H str), 3073 (Ar C-H str), 2984 (Ali. C-H str), 1728 (C=O str). MS (EI) m/z: 308 (M, 87 %), 309 (13 %).

Anal. Calcd. for $C_{19}H_{20}N_2O_2$ (308.15): C, 74.00; H, 6.54; N, 9.08; O, 10.38. Found: C, 74.10; H, 6.60; N, 9.15; O, 10.30.

Dimethyl-4-phenyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (**21**).

This compound has FTIR (KBr): 3370 (N-H str), 3075 (Ar C-H str), 2980 (Ali. C-H str), 1708 (C=O str). MS (EI) m/z: 301 (M, 93 %), 302 (10 %).

Anal. Calcd. for $C_{17}H_{19}NO_4$ (301.13): C, 67.76; H, 6.36; N, 4.65; O, 21.24. Found: C, 67.80; H, 6.30; N, 4.63; O, 21.15.

Dimethyl 4-(4-Nitrophenyl)-2,6-dimethyl-1,4-dihydropyridine 3,5-Dicarboxylate (**22**).

This compound has FTIR (KBr): 3367 (N-H str), 3095 (Ar C-H str), 2980 (Ali. C-H str), 1697 (C=O str). MS (EI) m/z: 346 (M, 95 %), 347 (8 %).

Anal. Calcd. for $C_{17}H_{18}N_2O_6$ (346.12): C, 58.96; H, 5.24; N, 8.09; O, 27.72. Found: C, 58.80; H, 5.10; N, 8.15; O, 27.65.

Dimethyl 4-(3-Chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine 3,5-Dicarboxylate (**25**).

This compound has FTIR (KBr): 3363 (N-H str), 3065 (Ar C-H str), 2990 (Ali. C-H str), 1704 (C=O str). m/z: 335 (M, 100 %), 337 (20 %).

Anal. Calcd. for $C_{17}H_{18}ClNO_4$ (335.09): C, 60.81; H, 5.40; Cl, 10.56; N, 4.17; O, 19.06. Found: C, 60.79; H, 5.35; N, 4.10; O, 19.10.

Dimethyl 4-(3-Hydroxyphenyl)-2,6-dimethyl-1,4-dihydropyridine 3,5-Dicarboxylate (**26**).

This compound has FTIR (KBr): 3435 (O-H str), 3348 (N-H str), 3095 (Ar C-H str), 2990 (Ali. C-H str), 1710 (C=O str). MS (EI) m/z: 317 (M, 90 %), 318 (14 %).

Anal. Calcd. for $C_{17}H_{19}NO_5$ (317.13): C, 64.34; H, 6.03; N, 4.41; O, 25.21. Found: C, 64.30; H, 6.10; N, 4.35; O, 25.17.

Dimethyl 4-(4-Hydroxy-3-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine 3,5-Dicarboxylate (**27**).

This compound has FTIR (KBr): 3430 (O-H str), 3357 (N-H str), 3081 (Ar C-H str), 2993 (Ali. C-H str), 1697 (C=O str). MS (EI) m/z: 347 (M, 100 %), 348 (10 %).

Anal. Calcd. for $C_{18}H_{21}NO_6$ (347.14): C, 62.24; H, 6.09; N, 4.03; O, 27.64. Found: C, 62.15; H, 6.02; N, 3.93; O, 27.60.

Dimethyl 4 (3,4-Dimethoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine 3,5-Dicarboxylate (**28**).

This compound has FTIR (KBr): 3363 (N-H str), 3065 (Ar C-H str), 2973 (Ali. C-H str), 1704 (C=O str). MS (EI) m/z: 361 (M, 100 %).

Anal. Calcd. for $C_{19}H_{23}NO_6$ (361.15): C, 63.15; H, 6.41; N, 3.88; O, 26.56. Found: C, 63.04; H, 6.35; N, 3.80; O, 26.50.

Dimethyl 4 (2-Furyl)-2,6-dimethyl-1,4-dihydropyridine 3,5-Dicarboxylate (**29**).

This compound has FTIR (KBr): 3355 (N-H str), 3080 (Ar C-H str), 2990 (Ali. C-H str), 1996 (C=O str). MS (EI) m/z: 291 (M, 90 %), 292 (10 %).

Anal. Calcd. for $C_{15}H_{17}NO_5$ (291.11): C, 61.85; H, 5.88; N, 4.81; O, 27.46. Found: C, 61.74; H, 5.75; N, 4.70; O, 27.35.

Dimethyl 4 (3-Indolyl)-2,6-dimethyl-1,4-dihydropyridine 3,5-Dicarboxylate (**30**).

This compound has FTIR (KBr): 3350 (N-H str), 3095 (Ar C-H str), 2980 (Ali. C-H str), 1702 (C=O str). MS (EI) m/z: 340 (M, 90 %), 341 (8 %).

Anal. Calcd. for $C_{19}H_{20}N_2O_4$ (340.14): C, 67.05; H, 5.92; N, 8.23; O, 18.80. Found: C, 67.10; H, 5.85; N, 8.14; O, 18.65.

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