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Reaction of β-Enaminones and Acetylene Dicarboxylates: Synthesis of Substituted 1,2-Dihydropyridinones†

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Synthesis of substituted 1,2-dihydropyridinones is described in one pot reaction of β-enaminones and acetylene dicarboxylates where new C-C and C-N bonds were formed. The title compounds were obtained in moderate to good yields.

Introduction

Among various heterocyclic molecules, nitrogen heterocyclic molecules have proven as potential compounds[1] in crop protection chemicals, functional materials and medicinal chemistry.[2] Different methods were developed for synthesis of nitrogen heterocyclic molecules[3] via metal catalysed[4] and organocatalysed reactions.[5]

Nitrogen heterocyclic molecules, in particular synthesis[6] of 2-pyridinones[7] have received much attention because of their potential applications in various fields (Figure 1).[8] For example amrinone and milrinone were used as cardiotonics.[9] Perampanel is identified as an important molecule for the treatment of Parkinson's disease.[10] 2-Pyridinone derivatives were showing properties like antihypertensive,[11] antitumor,[12] antibiotic,[13] antiviral,[14] antibacterial,[15] thrombin inhibition,[16] tissue factor VIIa inhibition,[17] human chymase inhibition[18] and human leukocyte elastase inhibition.[19] Some of the 2-pyridinone derivatives have been used as dyes.[20] Significant number of natural products are having 2-pyridinone core unit in their chemical structure.[21] Most of these molecules are exhibiting interesting biological and pharmacological properties.[22] Substituted enaminones have been useful for the synthesis of several nitrogen-containing heterocycles.[23]

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Synthesis of nitrogen heterocyclic molecules by exploiting the chemical reactivity of β-enaminones is of our current interest.

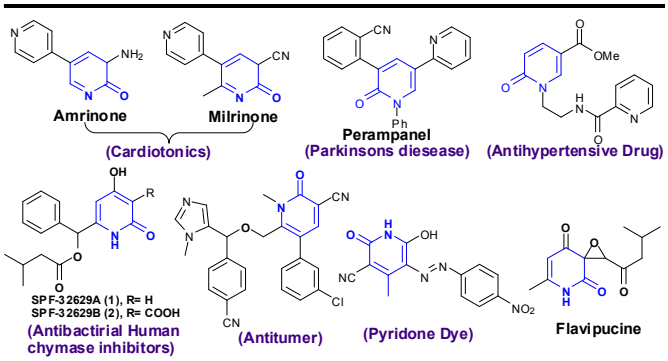


Figure 1 Selected examples of important molecules containing 2-pyridinone core skeletons and their applications.

Results and discussion

Very recently, we have developed two different synthetic methods by exploitation of substituted β-enaminones.[24] Azabicyclo[4.1.0]hepta-2,4-dienes were efficiently synthesized in a reaction of *N*-propargylic β-enaminones with acetylene dicarboxylates by a novel and exceptionally catalyst free conditions.[25a] Synthesis of 3-methylene-3,4-dihydro-2*H*-pyrrolines were achieved by reaction of *N*-propargylic β-enaminones with arynes via gold-catalysis.[25b] In continuation to our efforts towards the exploration of enaminone reactivity, we became interested to test the reactivity of β-enaminones towards activated alkynes.

Liang *et al.*, reported that the reaction of dialkyl acetylene dicarboxylates and β-enaminone derivatives in the presence of copper catalyst to give polysubstituted pyrroles (Figure-2 Scheme-a).[26a] It was reported that tandem reaction of primary

amines and acetylene esters gave 2-pyridones featuring carboxylates as substitutents.[26b]

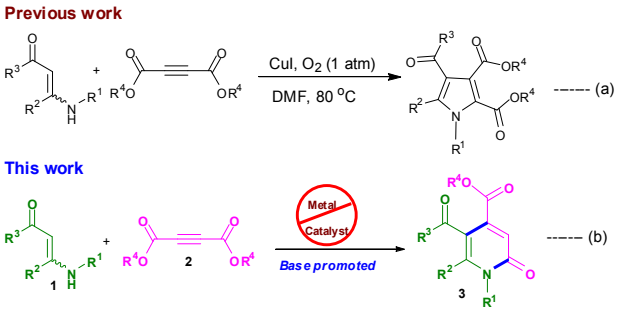
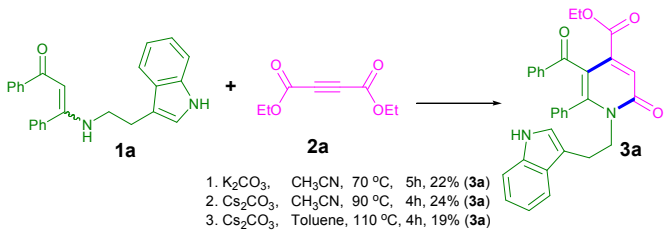


Figure 2 Transformations of *β*-enaminone to nitrogen heterocycles.

Herein, we describe reactivity of substituted *β*-enaminones **1** on dialkyl acetylene dicarboxylates **2** in the presence of base to accesses 1,2-dihydropyridinones **3** (Figure 2, Scheme-b). This reaction offers the synthesis of 2-pyridinones with significant molecular complexity where new C-C and C-N bonds were formed without using transition metals.

In an initial experiment, *β*-enaminone **1a** (1 equiv.) reacted with diethyl acetylene dicarboxylate **2a** (1 equiv.) in the presence of potassium carbonate (1.5 equiv.) in acetonitrile solvent at 70 °C for 5 h, it was observed that the starting materials were fully consumed, very interestingly 22% yields of 1,2-dihydropyridinone **3a** was isolated (Scheme 1).

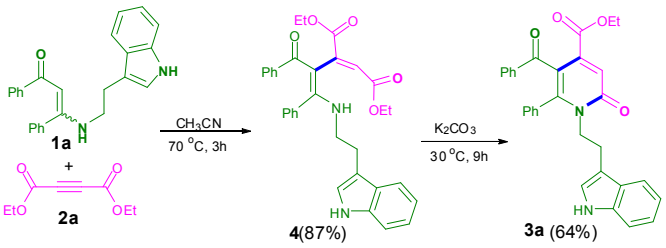


Scheme 1 Synthesis of 2-pyridinone **3a** by reaction of **1a** and **2a**.

We have conducted experiments to improve the yield of this transformation by utilizing **1a** and **2a** in the presence of Cs_2CO_3 in acetonitrile solvent at 90 °C for 4 h. The starting material **1a** was disappeared (monitored by TLC) but the yield of the product **3a** was not improved (24%). In an another experiment, toluene was used as a solvent the above reaction was performed at 110 °C, the starting material **1a** was disappeared (monitored by TLC) but the yield (19%) of the product **3a** was poor.

Based on these observations we have conducted one more experiment by taking *β*-enaminone **1a** (1 equiv.) and diethyl acetylene dicarboxylate **2a** (1 equiv.) in CH_3CN solvent at 70 °C for 3 h. It was observed that the both the starting materials were consumed. However, the pyridone **3a** was not formed in this reaction. It was observed that the addition product **4** was formed in this reaction in 87% yield (Scheme 2). We have further conducted a reaction by taking **4** (1 equiv.) in the presence of K_2CO_3 (1.5 equiv.) to check the formation of **3a**. Very interestingly, we have isolated 64% yield of pyridinone derivative **3a** as a product (Scheme 2).

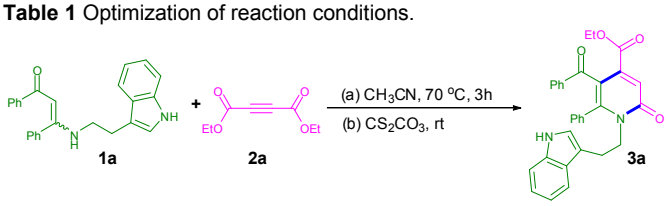
Later we thought of conducting this experiment in one pot to obtain the desired pyridone **3a**. Accordingly, the substrates **1a** and **2a** were heated at 70 °C for 3 h followed by the addition of K_2CO_3 at 30 °C and continued the reaction for 16 h. As expected the desired pyridone **3a** was formed in good yields (Table 1, entry 1).



Scheme 2 Synthesis of 2-pyridinone (**3a**) via intermediate **4**.

Experiments were conducted using *β*-enaminone **1a** (1 equiv.) with **2a** (1 equiv.) in the presence of different bases (1 equiv.) such as Et_3N, pyridine, piperidine, *N,N*-diethylamine, and *N,N*-diisopropylethylamine in acetonitrile. These conditions did not yield product **3a** (Table 1, entries 2-6). When the reaction was performed by using **1a** with **2a** in the presence of *N,N*-diisopropylamine (1 equiv.) and DABCO in acetonitrile solvent for 24 hours the product **3a** was isolated in lower yields (Table 1, entry 7-8). Without using any base, this reaction did not yield product **3a** (Table 1, entry 9).

Table 1 Optimization of reaction conditions.



Entry	Base	Solvent	Time (h)	Yield(%)
1	K_2CO_3	CH_3CN	16	61
2	Et_3N	CH_3CN	24	pno
3	Pyridine	CH_3CN	42	pno
4	Piperidine	CH_3CN	42	pno
5	Diethylamine	CH_3CN	42	pno
6	*N,N*-Diisopropyl ethylamine	CH_3CN	42	pno
7	*N,N*-Diisopropyl amine	CH_3CN	24	23
8	DABCO	CH_3CN	24	31
9	No base	CH_3CN	42	pno
10	Cs_2CO_3	CH_3CN	9	73
11	Na_2CO_3	CH_3CN	16	31
12	NaOH	CH_3CN	13	33
13	KOH	CH_3CN	13	28
14	Cs_2CO_3	H_2O	24	cm
15	Cs_2CO_3	MeOH	16	27
16	Cs_2CO_3	DMF	16	21
17	Cs_2CO_3	THF	18	61
18	Cs_2CO_3	1,4-dioxane	16	62
19	Cs_2CO_3	$CHCl_3$	16	66
20	Cs_2CO_3	Toluene	18	64

Reaction conditions: **1a** (0.273 mmol), **2a** (0.273 mmol), solvent (3 mL), All reactions initially conducted at 70 °C for 3 h then base was added at room temperature; Base (0.409 mmol); pno: product not observed. cm: complex mixture; Yields are for isolated products.

Further experiments were conducted by utilizing **1a** and **2a** in acetonitrile solvent in the presence of Cs_2CO_3, the product **3a** yield (73%) was improved (Table 1, entry 10). Reaction of **1a** with **2a** by utilizing bases such as Na_2CO_3, NaOH and KOH in acetonitrile solvent, these conditions gave product **3a** in lower yields (Table 1, entries 11-13). Having these results in hand, we

have further screened for solvent choice. Reaction of **1a** and **2a** in the presence of Cs_2CO_3 different solvents were used to get better yields of product **3a**. In the presence of water this reaction did not yield the desired product **3a** (Table 1, entry 14). Two reactions were performed by using **1a** and **2a** in the presence of Cs_2CO_3 in polar solvents like methanol and DMF, the product **3a** was isolated in poor yields (Table 1, entries 15-16). We have next performed the reaction of **1a** with **2a** in the presence of Cs_2CO_3 in THF, 1,4-dioxane, toluene and chloroform, good yields of the product **3a** was observed (Table 1, entries 17-20).

Based on the best optimized reaction conditions (Table 1, entry 10), various substituted *β*-enaminones **1a-u** and substituted acetylenedicarboxylates **2a** and **2b** were employed. The results are summarized in Table 2. When substituted *β*-enaminone **1b** reacted with diethyl acetylenedicoaroxylate **2a** gave **3b** in 76% yield (Table 2, entry 2). Substrate **1c** which is having electron donating group (*4-OMe*-C_6H_4) in the R^3 position reacted with **2a** gave 63% yield of **3c** (Table 2, entry 3). Electron withdrawing substrate like *4-F*-C_6H_4 at R^3 position **1d** reacted with **2a** gave 74% yield of **3d** (Table 2, entry 4). *β*-Enaminone substrate that contain both electron donating (R^2:*4-Me*-C_6H_4) group and withdrawing (R^3:*4-NO_2*-C_6H_4) group like **1e** reacted with **2a** to give 71% yield of **3e** (Table 2, entry 5). In the case of **1f** reaction with **2a**, the corresponding pyridone **3f** was isolated in 75% yield (Table 2, entry 6). The structure of the product **3f** was further confirmed by single crystal X-ray analysis (Figure 3).

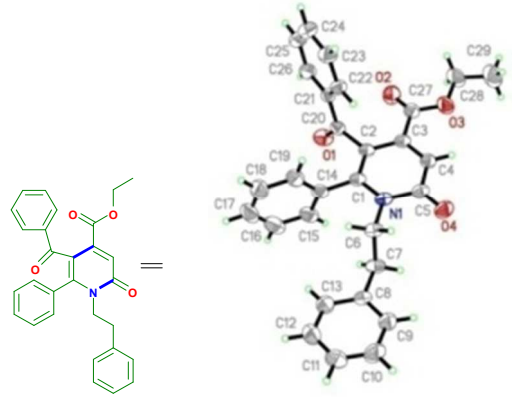
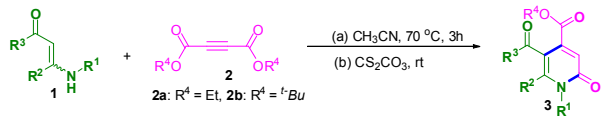


Figure 3 ORTEP representation of 1,2-dihydropyridinones (**3f**: CCDC 1004429)

Substrates which are having electron withdrawing groups like **1g** (R^3:*4-F*-C_6H_4) and **1h** (R^3:*4-NO_2*-C_6H_4) reacted with **2a** gave 70% and 65% yields of **3g** and **3h**, respectively (Table 2, entries 7-8). Cyclohexyl substituted *β*-enaminone **1i** reaction with **2a** gave 73% yield of product **3i** (Table 2, entry 9). *β*-Enaminone **1j** reacted with **2a** gave 63% yield of **3j** (Table 2, entry 10). Electron donating functional groups at R^2 (R^2:*4-Me*-C_6H_4) and R^3 (R^3:*4-OMe*-C_6H_4) positions derived *β*-enaminone like **1k** reacted with **2a** gave 64% yield of **3k** (Table 2, entry 11). Reaction of **1l** with **2a** gave 72% yield of **3l** (Table 2, entry 12). The substituted *β*-enaminone having *n*-propane at R^1 position and withdrawing group at R^3 (R^3:*4-F*-C_6H_4) position like **1m** reacted with **2a** gave 67% yield of product **3m** (Table 2, entry 13). *β*-Enaminone derivative containing withdrawing groups at R^2 (R^2:*4-F*-C_6H_4) and R^3 (R^3:*4-CF_3*-C_6H_4) positions like **1n** reacted with **2a** gave 75% yield of product **3n** (Table 2, entry no. 14).

Table 2 Scope of the synthesis of 1,2-dihydropyridinones.



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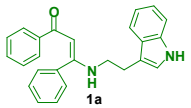
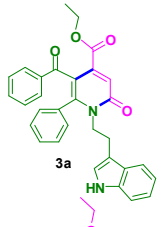
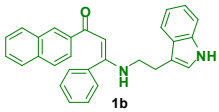
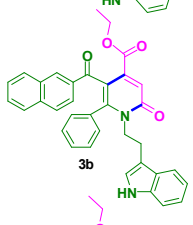
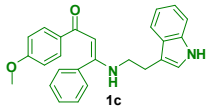
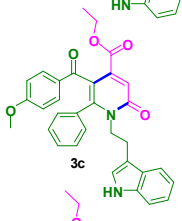
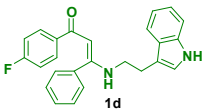
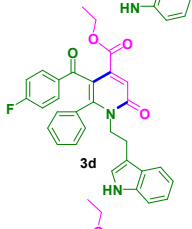
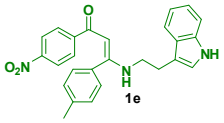
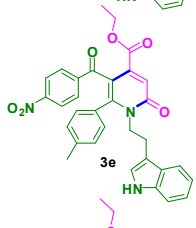
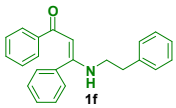
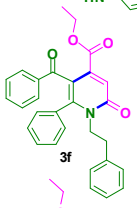
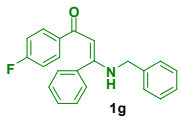
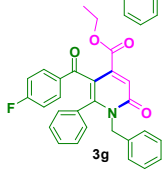
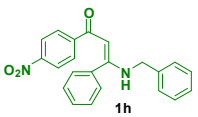
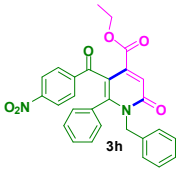
1		2a		73
2		2a		76
3		2a		63
4		2a		74
5		2a		71
6		2a		75
7		2a		70
8		2a		65

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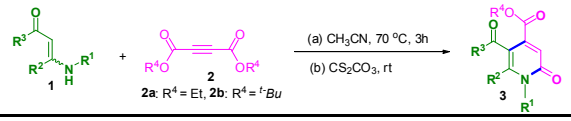

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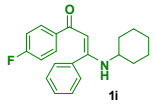
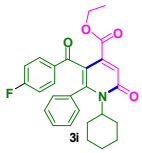
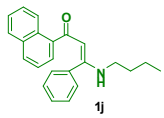
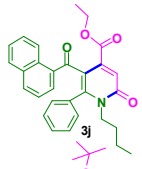
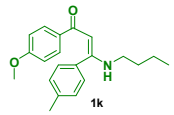
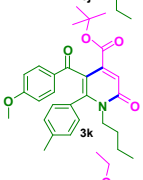
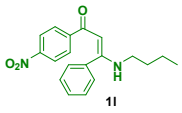
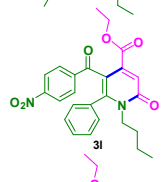
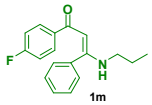
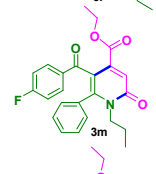
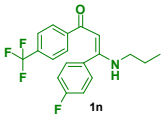
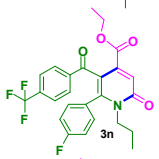
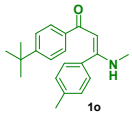
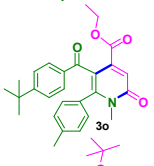
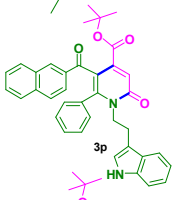
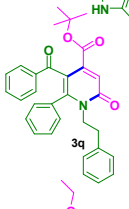
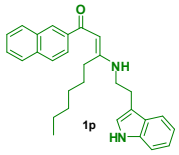
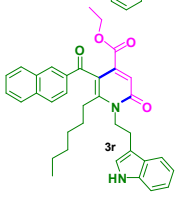
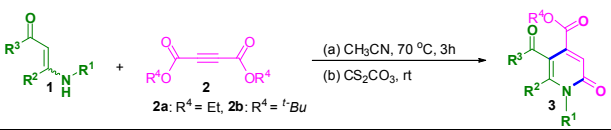
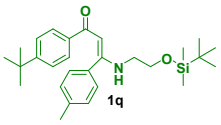
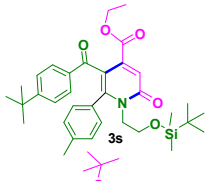
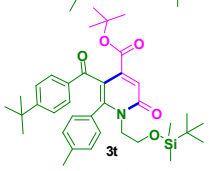
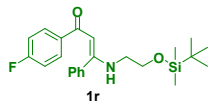
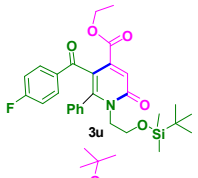
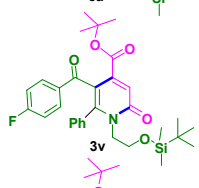
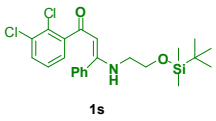
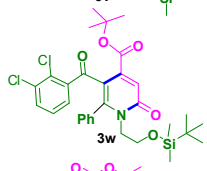
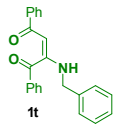
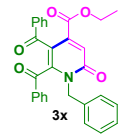
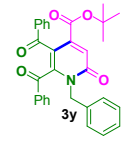
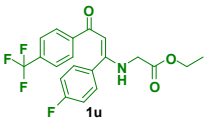
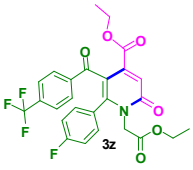
9		2a		73
10		2a		63
11		2b		64
12		2a		72
13		2a		67
14		2a		75
15		2a		70
16	1b	2b		74
17	1f	2b		72
18		2a		73

(**Table 2** *Contd.*)



Entry	Substrate (1)	Substrate (2)	Product	Yield (%)
19		2a		68
20	1q	2b		72
21		2a		78
22	1r	2b		75
23		2b		69
24		2a		65
25	1t	2b		68
26		2a		71

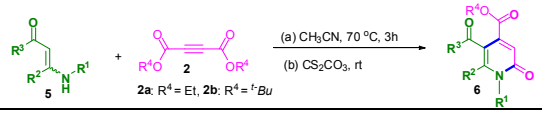
Reaction conditions: **1a** (0.273 mmol), **2a** (0.273 mmol) CH_3CN (3 mL); All reactions initially conducted at 70 °C for 3 h then base was added at room temperature; Cs_2CO_3 (0.409 mmol); Yields are for isolated products.

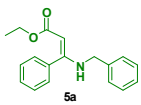
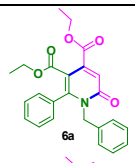
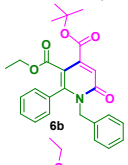
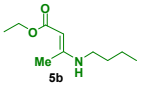
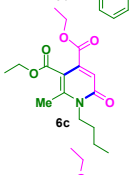
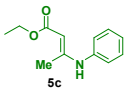
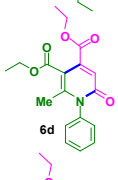
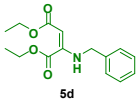
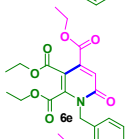
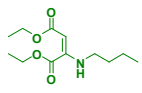
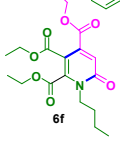
β-Enaminone substituted at R^2 (R^2:*4-Me*-C_6H_4) and R^3 (*4-*^{t}*Bu*-C_6H_4) positions like **1o** reaction with **2a** gave 70% yields of product **3o** (Table 2, entry 15). In case of *β*-enaminone **1b** reaction with diterterybutyl acetylene dicarboxylate **2b** gave 74% yield of **3p** (Table 2, entry 16). *β*-Enaminone **1f** reacted with **2b** gave 72% yield of **3q** (Table 2, entry 17). *β*-Enaminone derivative containing *n*-alkyl group at R^2 (R^2:C_6H_{13}) position like **1p** reaction with **2a** gave 73% yield of **3r** (Table 2, entry 18). The substrate *β*-Enaminone which is having substitutions

at R^1 position (*tert*-butyl(ethoxy)dimethylsilane), R^2 position (*4-Me*-C_6H_4) and R^3 position (*4-CMe*$_3$-C_6H_4) like **1q** reacted with **2a** and **2b** gave highly functionalised 2-pyridinones **3s** and **3t** in 68% and 72% yields, respectively (Table 2, entries 19-20). *β*-Enaminone derivative **1r** that contain *tert*-butyl(ethoxy)dimethylsilane at R^1 position and electron withdrawing group at R^2 (R^2:*4-F*-C_6H_4) position reacted with **2a** and **2b** gave 78% and 75% yields of products **3u** and **3v**, respectively (Table 2, entries 21-22). *β*-Enaminone **1s**, containing electron withdrawing substitutions at R^3 (R^3:2,3-di Cl-C_6H_3) position, reacted with **2b** gave 69% yield of product **3w** (Table 2, entry 23). *β*-Enamine derived from 1,4-diketone like **1t** reacted with **2a** and **2b** gave the products **3x** and **3y** in 65% and 68% yields, respectively (Table 2, entries 24-25). *β*-Enaminone derivative that contain acetate substitution at R^1 (R^1 = -CH_2-COOEt) position like **1u** reacted with **2a** gave product **3z** in 71% yield (Table 2, entry 26).

We have further tested the scope of this transformation using *β*-enamino esters instead of *β*-enaminones. *β*-Enamino ester **5a** reacted with **2a** and **2b** gave products **6a** and **6b** in 63% and 65% yields, respectively (Table 3, entries 1-2).

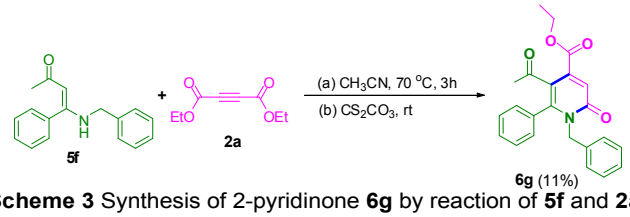
Table 3 Scope of the synthesis of 1, 2-dihydropyridinones.



Entry	Substrate (1)	Substrate (2)	Product	Yield (%)
1	 5a	2a	 6a	63
2	5a	2b	 6b	65
3	 5b	2a	 6c	40
4	 5c	2a	 6d	47
5	 5d	2a	 6e	45
6	 5e	2a	 6f	48

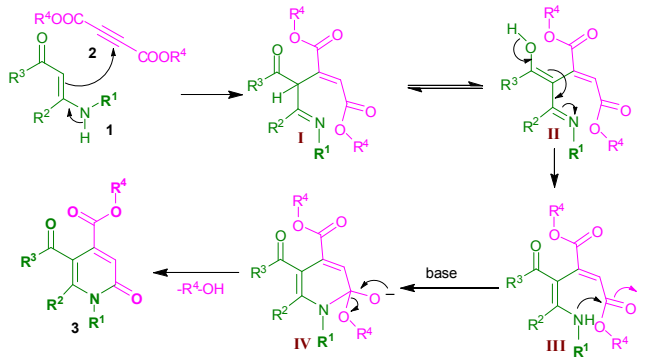
Reaction conditions: **5** (0.355 mmol), **2** (0.355 mmol) CH_3CN (3 mL); All reactions initially conducted at 70 °C for 3 h then base was added at room temperature; Cs_2CO_3 (0.533 mmol); Yields are for isolated products.

β-Enamino ester derivative having alkyl substitutions at R^1 and R^2 positions and like **5b** reacted with **2a** gave moderate yield of product **6c** (Table 3, entry 3). Reaction of **5c** with **2a** gave 47% yield of product **6d** (Table 3, entry 4). Enamines derived from acetylene diesters like **5d** and **5e** reacted with **2a** gave 45% and 48% yields of highly functionalised 2-pyridones **6e** and **6f**, respectively (Table 3, entries 5-6). β-Enaminone derivative having alkyl substitution at R^3 position and aromatic group at R^2 position like **5f** reacted with **2a** gave very poor yield of product **6g** (Scheme 3). This reaction clearly indicate that the *β*-enaminone derivative containing alkyl substitution at R^3 position leads to produce very poor yield of 2-pyridinone (**6g**).



Scheme 3 Synthesis of 2-pyridinone **6g** by reaction of **5f** and **2a**.

A possible reaction mechanism may be explained for the formation of 1,2-dihydropyridinones (Scheme 3). Initially, nucleophilic addition of *β*-enaminones **1** to the electrophile **2** would take place to give intermediate **I**. The enolate **II** of intermediate **I** would give intermediate **III**. Then the intermediate **III** undergo cyclisation to give pyridinones **3**. We have isolated an analogue of this intermediate **I,** for example compound **4** which was further converted to pyridone **3a** (Scheme 4).



Scheme 4 A possible reaction mechanism.

Conclusions

In conclusion, we have developed a straightforward and efficient method for synthesis of dihydropyridone derivatives having significant molecular complexity with good yields. Importantly, this transformation was achieved in one pot without using transition metals or catalysts. Current research is focused on further exploitation of the reactivity of substituted *β*-enaminone derivatives.

Experimental

General information

All the reactions were carried out in oven dried reaction flasks under nitrogen atmosphere and also solvents and reagents were transferred by oven-dried syringes to ambient temperature. TLC was performed on Merck silica gel aluminium sheets using UV as a visualizing agent and a 0.5% aqueous potassium permanganate solution and heat

as developing agents. Solvents were removed under reduced pressure. Columns were packed as slurry of silica gel in hexane and ethyl acetate solvent mixture. The elution was assisted by applying pressure with an air pump. ^{13}C NMR spectra were recorded on 75 and 125 MHz spectrometers. ^{1}HNMR spectra were recorded on 300 and 500 MHz spectrometers in appropriate solvents using TMS as internal standard. The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, dd = double doublet, t = triplet, m = multiplet. All reactions were performed under nitrogen atmosphere with freshly distilled and dried solvents and solvents were distilled using standard procedures. Unless otherwise noted, reagents were obtained from Aldrich, Alfa Aesar, and TCI used without further purification. Substituted β-enaminones (**1a-u**) were prepared by following the reported procedure.[27]

X-ray Crystallography: X-ray data for the compound was collected at room temperature using a Bruker Smart Apex CCD diffractometer with graphite monochromated MoKα radiation (λ=0.71073Å) with ω-scan method.[28] Preliminary lattice parameters and orientation matrices were obtained from four sets of frames. Unit cell dimensions were determined using 6371 reflections in the range of 2.51□ < θ < 23.79° for **3f**. Integration and scaling of intensity data were accomplished using SAINT program.[28] The structure was solved by direct methods using SHELXS97[29] and refinement was carried out by full-matrix least-squares technique using SHELXL97.[29] Anisotropic displacement parameters were included for all non-hydrogen atoms. H atoms were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å and U_{iso}(H) = 1.2U_{eq}(C) or 1.5U_{eq}(C)]. The crystal was found to be twinned and the exact twin matrix was identified by the integration program as -1.002 0 0.004, 0 -1 0, 0.801 0 1.002. The structure was refined using the hklf 5 routine with all reflections, resulting in a BASF value of 0.178 (2).

General procedure for Synthesis of 1,2-dihydropyridinones (3a)

In a 25 mL round-bottomed two-neck flask compound enaminone **1a** (0.1g, 0.273 mmol, 1 equiv.) was taken then dissolved in acetonitrile (2 mL) to this reaction mixture compound **2a** (0.046g 0.273 mmol, 1 equiv.) was added and allowed to stir at 70 °C for 3 h under nitrogen atmosphere (yellow colour reaction mass was observed in the reaction flask). This reaction mixture was allowed to room temperature. Progress of the reaction was monitored by TLC. Then Cs_2CO_3 (0.133g, 0.409 mmol, 1.5 equiv.) was added portion wise at room temperature to this reaction mixture. Reaction mixture colour was changed from yellow to brown colour. This reaction mixture was allowed to stir at room temperature for 9 h. Progress of the reaction was monitored by TLC. After completion of the reaction, 3 mL of water was added to the reaction mixture. Reaction mass was extracted with ethyl acetate (3 x 5 mL). The combined organic layers were washed with aqueous brine, dried over anhydrous Na_2SO_4, and concentrated under vacuum. The crude residue was purified through a silica gel column using hexane and ethyl acetate as eluent (10/3) to give pure 1,2-dihydropyridine-4-carboxylates **3a**. The similar procedure was followed for the synthesis of all 2-pyridinone derivatives (**3a-z**).

Ethyl 1-(2-(1*H*-indol-3-yl)ethyl)-5-benzoyl-2-oxo-6-phenyl-1,2-dihydropyridine-4-carboxylate (3a)

R_f: 0.3; Hexane: Ethyl acetate mixture (10:3); Yield: 73%; light brown colour solid; Melting Point: 143-145 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (brs, 1H), 7.49-7.45 (m, 2H), 7.43-7.38 (m, 1H), 7.32-7.27 (m. 3H), 7.25-7.23 (brs, 2H), 7.16-7.10 (m, 3H), 6.95-6.86 (m, 4H) ,6.84 (brs, 1H), 4.13-4.06 (m, 4H), 3.06 (t, J = 7.6 Hz, 2H), 1.08 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.0,164.4, 162.0, 148.6, 140.2, 138.1, 136.0, 132.6, 131.5, 129.6, 129.3, 128.7, 128.1, 127.1, 122.3, 121.9, 121.4, 119.2, 118.4, 111.8, 111.0, 62.2, 47.3, 23.9, 13.5; HRMS (ESI): calcd. for $C_{31}H_{27}N_2O_4$ $[M+H]^+$ 491.1965; found 491.1975.

Ethyl 1-(2-(1H-indol-3-yl)ethyl)-5-(2-naphthoyl)-2-oxo-6-phenyl-1,2-dihydropyridine-4-carboxylate (3b)

R_f: 0.3; Hexane: Ethyl acetate mixture (10:3); Yield: 76%; orange colour solid; Melting Point: 190-194 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.04-7.95 (brs, 2H), 7.89-7.77 (m, 2H), 7.74-7.67 (m, 1H), 7.66-7.45 (m, 3H), 7.37-7.16 (m, 3H), 7.16-7.03 (m, 3H), 7.02-6.81 (m, 5H), 4.17-4.00 (m, 4H), 3.07 (t, J = 8.1 Hz, 2H), 1.03 (t, J = 7.1 Hz, 3H), ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.8, 164.4, 162.0, 148.7, 140.2, 135.9, 135.5, 135.3, 132.1, 131.5, 130.7, 129.5, 129.4, 128.4, 128.2, 127.7, 127.1, 126.6, 124.1, 122.2, 121.9, 121.5, 119.3, 118.4, 111.8, 111.0, 62.0, 47.3, 24.0, 13.5; HRMS (ESI): calcd for $C_{35}H_{29}N_2O_4$ $[M+H]^+$ 541.2121; found 541.2131.

Ethyl 1-(2-(1H-indol-3-yl)ethyl)-5-(4-methoxybenzoyl)-2-oxo-6-phenyl-1,2-dihydropyridine-4-carboxylate (3c)

R_f: 0.2; Hexane: Ethyl acetate mixture (10:3); Yield: 63%; pale orange colour semisolid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.13 (brs, 1H), 7.46 (d, J = 8.6 Hz, 2H), 7.30-7.25 (m, 3H), 7.18-7.10 (m, 3H), 6.94-6.86 (m, 4H), 6.82 (d, J = 1.8 Hz, 1H), 6.74 (d, J = 8.8 Hz, 2H), 4.13-4.06 (m, 4H), 3.81 (s, 3H), 3.05 (t, J = 7.7 Hz, 2H), 1.09 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.5,164.4, 163.1, 162.0, 148.3, 140.0, 135.9, 131.6, 131.2, 131.1, 129.5, 129.3, 128.1, 127.1, 122.4, 121.8, 121.3, 119.2, 118.5, 118.4, 113.3, 111.8, 111.0, 62.1, 55.3, 47.3, 23.9, 13.5; HRMS (ESI): calcd. for $C_{32}H_{29}N_2O_5$ $[M+H]^+$ 521.2071; found 521.2065.

Ethyl 1-(2-(1H-indol-3-yl)ethyl)-5-(4-fluorobenzoyl)-2-oxo-6-phenyl-1,2-dihydropyridine-4-carboxylate (3d)

R_f: 0.4; Hexane: Ethyl acetate mixture (10:3); Yield: 74%; orange colour semisolid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.09 (brs,1H), 7.45 (q, J = 5.2 Hz, 2H), 7.28 (q, J = 8.3 Hz, 3H), 7.13 (q, J = 6.7 Hz, 3H) , 6.98-6.79 (m, 7H), 4.19-4.04 (m, 4H), 3.06 (t , J = 8.3 Hz, 2H), 1.12 (t, J = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.6, 166.2, 164.4, 161.9, 148.4, 140.0, 135.9, 134.6, 131.4, 131.3, 131.2, 129.5, 129.4, 128.1, 127.2, 122.4, 122.0, 121.6, 119.3, 118.4, 115.3, 115.1, 111.0, 62.2, 47.4, 23.8, 13.6; HRMS (ESI): calcd for $C_{31}H_{26}FN_2O_4$ $[M+H]^+$ 509.1871; found 509.1885.

Ethyl 1-(2-(1H-indol-3-yl)ethyl)-5-(4-nitrobenzoyl)-2-oxo-6-p-tolyl-1,2-dihydropyridine-4-carboxylate (3e)

R_f: 0.3; Hexane: Ethyl acetate mixture (10:3); Yield: 71%; light brown colour solid; Melting Point: 150-154 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10-8.01 (m, 3H), 7.5 (d, J = 9.0 Hz, 2H), 7.36-7.29 (m, 2H), 7.16 (t, J = 7.5 Hz, 1H), 6.97-6.82 (m, 5H), 6.61 (d, J = 8.3 Hz, 2H), 4.22-4.05 (m, 4H), 3.07 (t, J = 7.5 Hz, 2H), 2.26 (s, 3H), 1.18 (t, J = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.7, 164.3, 162.0, 149.6, 149.1, 142.7, 140.0, 139.8, 136.0, 129.4, 128.9, 128.0, 127.2, 123.2, 122.5, 121.9, 121.6, 119.2, 118.3, 117.5, 111.8, 111.1, 62.4, 47.3, 23.6, 21.1, 13.7; HRMS (ESI): calcd. for $C_{32}H_{27}N_2O_6Na$ $[M+Na]^+$ 572.1792; found 572.1795.

Ethyl 5-benzoyl-2-oxo-1-phenethyl-6-phenyl-1,2-dihydropyridine-4-carboxylate (3f)

R_f: 0.3; Hexane: Ethyl acetate mixture (10:3); Yield: 75%; light orange colour solid; Melting Point: 140-144 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ 7.54 (d, J = 6.7 Hz, 2H), 7.47-7.38 (m, 1H), 7.34-7.23 (m, 4H), 7.23-7.12 (m, 5H), 6.91 (d, J = 7.5 Hz, 2H), 6.87-6.80 (m, 2H), 4.10 (q, J = 6.7 Hz, 2H), 3.98 (t, J = 7.5 Hz, 2H), 2.88 (t, J = 7.5 Hz, 2H), 1.08 (t, J = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.8, 164.3, 161.7, 148.4, 140.1, 138.0, 137.6, 132.7, 131.3, 129.5, 129.4, 128.7, 128.4, 128.2, 128.1, 126.5, 121.4, 118.4, 62.2, 47.9, 34.1, 13.5; HRMS (ESI): calcd. for $C_{29}H_{25}NO_4Na$ $[M+Na]^+$ 474.1675; found; 474.1673.

Crystal data for 3f: $C_{29}H_{25}NO_4$, M = 451.50, colorless block, 0.21 x 0.17 x 0.09 mm^3, monoclinic, space group $P2_1/c$ (No. 14), a = 8.1432(16), b = 15.506(3), c = 19.315(4) Å, β = 99.992(3)°, V = 2401.8(8) $Å^3$, Z = 4, D_c = 1.249 g/cm^3, F_{000} = 952, Bruker SMART APEX CCD area-detector, MoKα radiation, λ = 0.71073 Å, T = 294(2)K, $2\theta_{max}$ = 50.0º, 21908 reflections collected, 21908 unique (R_{int} = 0.0000). Final *GooF* = 1.051, *R1* = 0.0604, *wR2* = 0.1685, *R* indices based on 15095 reflections with I>2σ(I) (refinement on F^2), 309 parameters, 0 restraints, μ = 0.083 mm^{-1}. CCDC 1004429 contains supplementary Crystallographic data for the structure. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk.

Ethyl 1-benzyl-5-(4-fluorobenzoyl)-2-oxo-6-phenyl-1,2-dihydropyridine-4-carboxylate (3g)

R_f: 0.3; Hexane: Ethyl acetate mixture (10:3); Yield: 70%; brown liquid; ^1H NMR (500 MHz, $CDCl_3$): δ 7.58-7.54 (m, 2H), 7.31 (s, 1H), 7.22-7.15 (m, 4H), 7.07 (t, J = 7.6 Hz, 2H), 6.95-6.90 (m , 2H), 6.85-6.80 (m, 4H), 5.11 (brs, 2H), 4.15 (q, J = 7.1 Hz, 2H), 1.13 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.4, 166.2, 164.3, 162.1, 148.6, 140.4, 136.0, 134.5, 131.3, 131.2, 131.1, 129.5, 128.3, 127.9, 127.4, 126.8, 121.8, 118.4, 115.3, 115.1, 62.3, 48.9, 13.6; HRMS (ESI): calcd for $C_{28}H_{22}FNO_4$ $[M+H]^+$ 456.1605; Found 456.1611.

Ethyl 1-benzyl-5-(4-nitrobenzoyl)-2-oxo-6-phenyl-1,2-dihydropyridine-4-carboxylate (3h)

R_f: 0.4; Hexane: Ethyl acetate mixture (10:3); Yield: 65%; brown colour liquid; ^1H NMR (300 MHz, $CDCl_3$): δ 8.08 (d, J = 9.0 Hz, 2H), 7.65 (d, J = 9.0 Hz, 2H), 7.33 (s, 1H), 7.24-7.14 (m, 4H), 7.06 (t, J = 7.5 Hz, 2H), 6.84-6.77 (m, 4H), 5.11 (s, 2H), 4.19 (q, J = 7.5 Hz, 2H), 1.18 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.6, 164.2, 162.1, 149.6, 148.9, 142.6, 140.2, 135.8, 130.7, 129.9, 129.6, 129.3, 128.4, 128.1, 127.5, 126.8, 123.2, 122.0, 117.8, 62.5, 48.9, 13.7; HRMS (ESI): calcd. for $C_{28}H_{22}N_2O_6Na$ $[M+Na]^+$ 505.1370; found 505.1375.

Ethyl 1-cyclohexyl-5-(4-fluorobenzoyl)-2-oxo-6-phenyl-1,2-dihydropyridine-4-carboxylate (3i)

R_f: 0.4; Hexane: Ethyl acetate mixture (10:3); Yield: 73%; yellow colour solid; Melting Point: 170-174 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ 7.70-7.65 (m, 2H), 7.27 (m, 3H), 7.21-7.17 (m, 2H), 6.93-6.88 (m, 2H), 6.7 (s, 1H), 3.91 (q, J = 7.1 Hz, 2H), 3.31 (m, 1H), 2.36-2.18 (m, 2H), 1.80-1.48 (m, 8H), 1.02 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$)**:** δ 189.5, 168.1, 166.1, 165.1, 156.3, 137.3, 134.7, 131.4, 131.3, 130.3, 128.6, 128.5, 121.2, 115.2, 115.0, 60.9, 55.2, 29.7, 25.9, 24.8, 13.7; HRMS (ESI): calcd. for $C_{27}H_{27}FNO_4$ $[M+H]^+$ 448.1918; found 448.1927.

Ethyl 5-(1-naphthoyl)-1-butyl-2-oxo-6-phenyl-1,2-dihydropyridine-4-carboxylate (3j)

R_f: 0.4; Hexane: Ethyl acetate mixture (10:3); Yield: 63%; orange colour solid; Melting Point: 98-101 ^oC; ^1H NMR (300 MHz, $CDCl_3$); δ 8.42-8.34 (m, 1H), 7.83 (d, J = 8.3 Hz, 1H), 7.78-7.68 (m, 1H), 7.63 (d, J = 6.7 Hz, 1H), 7.48-7.39 (m, 2H), 7.33 (t, J = 7.5 Hz, 1H), 7.10 (s, 1H), 7.03-6.87 (m, 5H), 4.07 (q, J = 7.5 Hz, 2H), 3.72 (t, J = 7.5 Hz, 2H), 1.56-1.41 (m, 2H), 1.40-1.13 (m, 2H), 1.10-1.00 (m, 3H), 0.66 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.3,165.3, 161.7,149.6, 141.7, 135.8, 133.3, 132.9, 131.5, 130.2, 129.0, 128.7, 127.9, 127.8, 127.4, 126.1,125.5, 123.7, 120.5, 62.1, 45.9, 30.3, 19.7, 13.5, 13.1; HRMS (ESI): calcd. for $C_{29}H_{28}NO_4$ $[M+H]^+$ 454.2012; found 454.2015.

Tert-butyl 1-butyl-5-(4-methoxybenzoyl)-2-oxo-6-p-tolyl-1,2-dihydropyridine-4-carboxylate (3k)

R_f: 0.2; Hexane: Ethyl acetate mixture (10:3); Yield: 64%; pale orange semisolid; ^1H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, J = 8.6 Hz, 2H), 7.41 (s, 1H), 7.21-7.10 (m, 4H), 6.94 (d, J = 8.6 Hz, 2H), 3.96 (s, 3H), 3.89 (t, J = 7.9 Hz, 2H), 2.42 (s, 3H), 1.73-1.60 (m, 2H), 1.36 (s, 9H), 1.25 (q, J = 7.3 Hz, 2H), 0.86 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 192.2, 163.5, 163.2, 162.0, 148.4, 141.5, 139.3, 131.2, 129.1, 128.7, 126.0, 120.6, 118.3, 113.3, 83.5, 55.3, 46.0, 30.4, 27.3, 21.2, 19.8, 13.3; HRMS (ESI): calcd for $C_{29}H_{34}NO_5$ $[M+H]^+$ 476.2431; found 476.2433.

Ethyl 1-butyl-5-(4-nitrobenzoyl)-2-oxo-6-phenyl-1,2-dihydropyridine-4-carboxylate (3l)

R_f: 0.3; Hexane: Ethyl acetate mixture (10:3); Yield: 72%; brown colour liquid; ^1H NMR (300 MHz, $CDCl_3$): δ 8.12 (d, J = 9.0 Hz, 2 H), 7.68 (d, J = 9.0 Hz, 2H), 7.33-7.18 (m, 4H), 7.07 (d, J = 6.7 Hz, 2H), 4.17 (q, J = 6.7 Hz, 2H) 3.82-3.72 (m, 2H), 1.58-1.45 (m, 2H), 1.21-1.03 (m, 5H), 0.70 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.8, 164.3, 161.7, 149.6, 148.6, 142.7, 139.7, 131.1, 129.9, 129.5, 129.4, 128.3, 123.2, 121.7, 117.5, 62.4, 46.1, 30.3, 19.8, 13.7, 13.2; HRMS (ESI): calcd. for $C_{25}H_{25}N_2O_6$ $[M+H]^+$ 449.1707; found 449.1713.

Ethyl 5-(4-fluorobenzoyl)-2-oxo-6-phenyl-1-propyl-1,2-dihydropyridine-4-carboxylate (3m)

R_f: 0.2; Hexane: Ethyl acetate mixture (10:3); Yield: 67%; brown colour semi solid; ^1H NMR (500 MHz, $CDCl_3$): δ 7.59-7.54 (m, 2H), 7.27 (m, 1H), 7.24-7.20 (m, 3H), 7.09-7.06 (m, 2H), 6.94 (t, J = 8.5 Hz, 2H), 4.12 (q, J = 7.1 Hz, 2H), 3.71 (t, J = 7.7 Hz, 2H), 1.6-1.5 (m, 2H), 1.11 (t, J = 7.1 Hz, 3H), 0.69 (t, J = 7.32 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.6, 166.3, 161.8, 148.3, 139.8, 134.6,131.4, 131.3, 131.2, 129.6, 129.4, 128.2, 121.5, 118.1, 115.3, 115.2, 62.2, 47.8, 21.8, 13.6, 11.0,; HRMS (ESI): calcd. for $C_{24}H_{23}FNO_4$ $[M+H]^+$ 408.1605; found 408.1603.

Ethyl 6-(4-fluorophenyl)-2-oxo-1-propyl-5-(4-(trifluoromethyl)benzoyl)-1,2-dihydropyridine-4-carboxylate (3n)

R_f: 0.3; Hexane: Ethyl acetate mixture (10:3); Yield: 75%; pale yellow semisolid; ^1H NMR (500 MHz, $CDCl_3$): δ 7.67 (d, J = 8.2 Hz, 2H), 7.58 (d, J = 8.2 Hz, 2H),7.29 (s, 1H), 7.11-7.06 (m, 2H),

6.94 (t, J = 8.5 Hz, 2H), 4.14 (q, J = 7.0 Hz, 2H), 3.74-3.69 (m, 2H), 1.61-1.52 (m, 2H), 1.14 (t, J = 7.1 Hz, 3H), 0.73 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.0, 164.6, 164.1, 161.7, 147.4, 140.7, 139.6, 131.5, 131.4, 128.7, 125.3, 125.2, 121.9, 115.7, 115.4, 62.3, 47.8, 21.8, 13.5, 11.0; HRMS (ESI): calcd. for $C_{25}H_{21}F_4NO_4$ $[M+H]^+$ 476.1479; found 476.1466.

Ethyl 5-(4-tert-butylbenzoyl)-1-methyl-2-oxo-6-p-tolyl-1,2-dihydropyridine-4-carboxylate (3o)

R_f: 0.3; Hexane: Ethyl acetate mixture (10:3); Yield: 70%; yellow colour semisolid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50 (d, J = 8.5 Hz, 2H), 7.30 (d, J = 7.3 Hz, 2H),7.19 (s, 1H), 7.04 (d, J = 7.7 Hz, 2H), 6.98 (d, J = 7.9 Hz, 2H), 4.07 (q, J = 7.1 Hz, 2H), 3.29 (s, 3H), 2.26 (s, 3H), 1.28 (s, 9H), 1.04 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.3, 164.4, 162.3, 156.3, 149.0, 140.3, 139.5, 135.4, 129.1, 129.0, 128.7, 128.6, 124.9, 120.2,118.4, 62.0, 34.8, 34.1, 30.8, 21.1, 13.3; HRMS (ESI): calcd. for $C_{27}H_{30}NO_4$ $[M+H]^+$ 432.2169; found 432.2153.

Tert-butyl 1-(2-(1H-indol-3-yl)ethyl)-5-(2-naphthoyl)-2-oxo-6-phenyl-1,2-dihydropyridine-4-carboxylate (3p)

R_f: 0.3; Hexane: Ethyl acetate mixture (10:3); Yield: 74%; pale orange colour solid; Melting Point: 185-188 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.04-7.95 (m, 2H), 7.89-7.77 (m, 2H), 7.72 (d, J = 8.6 Hz, 1H), 7.67-7.47 (m, 3H), 7.31-7.22 (m, 2H), 7.19 (d, J = 7.5 Hz, 1H), 7.15-7.04 (m, 3H), 7.00-6.93 (m, 2H), 6.92-6.82 (m, 3H), 4.11 (t, J = 7.5 Hz, 2H), 3.06 (t, J = 8.1 Hz, 2H), 1.16 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.6, 163.6, 162.1, 148.7, 142.0, 136.0, 135.6, 135.2, 132.1, 131.7, 130.8, 129.5, 129.3, 128.4, 128.1, 127.6, 127.1, 123.6, 124.2, 122.3, 121.9, 121.0, 119.2, 118.4, 118.3, 111.8, 111.0, 83.8, 47.2, 27.3, 24.0; HRMS (ESI): calcd. for $C_{37}H_{33}N_2O_4$ $[M+H]^+$ 569.2434; found; 569.2435.

Tert-butyl 5-benzoyl-2-oxo-1-phenethyl-6-phenyl-1,2-dihydropyridine-4-carboxylate (3q)

R_f: 0.3; Hexane: Ethyl acetate mixture (10:3); Yield: 72%; pale yellow colour solid; Melting Point: 167-170 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59-7.53 (m, 2H), 7.48-7.39 (m, 1H), 7.35-7.24 (m, 3H), 7.24-7.10 (m, 6H), 6.92 (d, J = 6.7 Hz, 2H), 6.88-6.81 (m, 2H), 3.97 (t, J = 7.5 Hz, 2H), 2.86 (t, J = 7.5 Hz, 2H), 1.22 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.5, 163.5, 161.9, 148.4, 141.9, 138.3, 137.7, 132.7, 131.6, 129.4, 128.9, 128.7, 128.4, 128.1, 126.5, 121.0, 118.2, 83.8, 47.8, 34.2, 27.3; HRMS (ESI): calcd. for $C_{31}H_{30}NO_4$ $[M+H]^+$ 480.2169; found; 480.2171.

Ethyl 1-(2-(1H-indol-3-yl)ethyl)-5-(2-naphthoyl)-6-hexyl-2-oxo-1,2-dihydropyridine-4-carboxylate (3r)

R_f: 0.2; Hexane: Ethyl acetate mixture (10:3); Yield: 73%; red colour solid; Melting Point: 140-144 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17-8.07, (m, 2H), 7.93-7.82 (m, 4H), 7.64 (d, J = 7.7 Hz, 1H), 7.61-7.49 (m, 2H), 7.38 (d, J = 7.5 Hz, 1H), 7.25-7.12 (m, 2H), 7.06 (d, J = 2.2 Hz, 1H), 6.64 (s, 1H), 3.9 (t, J = 6.9 Hz, 2H), 3.56 (q, J = 7.1 Hz, 2H), 3.17 (t, J = 7.7 Hz, 2H), 2.25-2.15 (m, 2H), 1.47-1.35 (m, 2H), 1.18-0.97 (m, 6H), 0.82-0.69 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 190.7, 168.5, 165.2, 160.3, 137.4, 136.4, 136.2, 135.3, 132.3, 129.9, 129.4, 128.3, 128.2, 127.6, 127.1, 126.6, 124.5, 122.3, 120.2, 119.7, 118.3, 112.1, 111.5, 111.4, 60.7, 41.7, 31.0, 29.1, 28.5, 25.8, 24.9, 22.3, 13.8, 13.4; HRMS (ESI): calcd. for $C_{35}H_{37}N_2O_4$ $[M+H]^+$ 549.2747; found 549.2753.

Ethyl 5-(4-tert-butylbenzoyl)-1-(2-(tert-butyldimethylsilyloxy)ethyl)-2-oxo-6-p-tolyl-1,2-dihydropyridine-4-carboxylate (3s)

R_f: 0.4; Hexane: Ethyl acetate mixture (10:3); Yield: 68%; pale brown colour semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (d, J = 8.39 Hz, 2H), 7.37 (t, J = 3.20 Hz, 3H), 7.08 (q, J = 7.93 Hz, 4H), 4.18 (q, J = 7.01 Hz, 2H), 4.06 (t, J = 6.25 Hz, 2H), 3.89 (t, J = 6.25 Hz, 2H), 2.34 (s, 3H), 1.38 (s, 12H), 0.92 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.6, 164.5, 162.0, 156.2, 149.5, 139.3, 135.7, 129.8, 128.74, 128.7, 128.6, 128.4, 124.9, 120.7, 118.7, 62.0, 59.4, 47.9, 34.9, 30.9, 25.8, 25.7, 21.1, 13.4, -5.5; HRMS (ESI): calcd. for $C_{34}H_{46}O_5NSi$ $[M+H]^+$ 576.3141; found 576.3141.

Tert-butyl 5-(4-tert-butylbenzoyl)-1-(2-(tert-butyldimethylsilyloxy)ethyl)-2-oxo-6-p-tolyl-1,2-dihydropyridine-4-Carboxylate (3t)

R_f: 0.4; Hexane: Ethyl acetate mixture (10:3); Yield: 72%; pale brown colour semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (d, J = 8.24 Hz, 2H), 7.49-7.44 (m, 2H), 7.24 (s, 1H), 7.20-7.13 (m, 4H), 4.11 (t, J = 6.25 Hz, 2H), 3.93 (t, J = 6.25 Hz, 2H), 2.41 (s, 3H), 1.44 (s, 9H), 1.34 (s, 9H), 0.98 (s, 9H), 0.12 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.0, 163.6, 162.0, 156.3, 149.4, 142.1, 139.2, 135.7, 129.5, 128.8, 128.7, 128.5, 124.9, 120.1, 118.3, 83.4, 59.4, 47.7, 34.8, 30.8, 27.1, 25.7, 21.0, 18.1, -5.6; HRMS (ESI): calcd for $C_{36}H_{50}O_5NSi$ $[M+H]^+$ 604.3452; found 604.3455.

Ethyl 1-(2-(tert-butyldimethylsilyloxy)ethyl)-5-(4-fluorobenzoyl)-2-oxo-6-phenyl-1,2-dihydropyridine-4-carboxylate (3u)

R_f: 0.4; Hexane: Ethyl acetate mixture (10:3); Yield: 78%; pale brown colour semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63-7.58 (m, 2H), 7.31-7.28 (m, 1H), 7.27-7.22 (m, 3H), 7.19-7.15 (m, 2H), 6.97 (t, J = 8.54 Hz, 2H), 4.19 (q, J = 7.17 Hz, 2H), 4.00 (t, J = 6.2 Hz, 2H), 3.86 (t, J = 6.2 Hz, 2H), 1.17 (t, J = 7.1 Hz, 3H), 0.87 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.7, 166.2, 164.4, 161.9, 149.0, 140.2, 134.6, 131.2, 130.0, 129.5, 128.0, 121.3, 118.2, 115.2, 115.1, 62.2, 59.3, 48.1, 29.6, 25.8, 13.5, -5.4. HRMS (ESI): calcd for $C_{29}H_{35}O_5NFSi$ $[M+H]^+$ 524.2260; found 524.2260.

Tert-butyl 1-(2-(tert-butyldimethylsilyloxy)ethyl)-5-(4-fluorobenzoyl)-2-oxo-6-phenyl-1,2-dihydropyridine-4-carboxylate (3v)

R_f: 0.4; Hexane: Ethyl acetate mixture(10:3); Yield: 75%; pale brown colour semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57-7.51 (m, 2H), 7.25-7.20 (m,1H), 7.18 (t, J = 7.93 Hz, 2H), 7.12 (s, 1H), 7.08 (d, J = 8.24 Hz, 2H), 6.92 (t, J = 8.24 Hz, 2H), 3.92 (t, J = 6.1 Hz, 2H), 3.77 (t, J = 6.1 Hz, 2H), 1.24 (s, 9H), 0.80 (s, 9H), 0.06 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.3, 166.2, 163.4, 161.9, 148.9, 141.9, 134.7, 131.5, 131.3, 129.9, 129.4, 128.0, 120.8, 118.0, 115.2, 83.7, 59.4, 47.9, 27.3, 25.8, 18.2, -5.4. HRMS (ESI): calcd for $C_{31}H_{39}O_5NFSi$ $[M+H]^+$ 552.2548; found 552.2550.

Tert-butyl 1-(2-(tert-butyldimethylsilyloxy)ethyl)-5-(2,3-dichlorobenzoyl)-2-oxo-6-phenyl-1,2-dihydropyridine-4-carboxylate (3w)

R_f: 0.4; Hexane: Ethyl acetate mixture (10:3); Yield: 69%; pale brown colour semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34-7.31 (m, 1H), 7.22-7.16 (m, 2H), 7.15-7.10 (m, 2H), 7.06 (d, J = 7.17 Hz, 2H), 7.01-6.96 (m, 2H), 3.85 (t, J = 6.25 Hz, 2H), 3.75 (t, J = 6.25 Hz, 2H), 1.43 (s, 9H), 0.79 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 191.6, 164.4, 162.0, 149.8, 143.7, 139.5, 133.9,

132.4, 131.3, 130.8, 129.5, 129.2, 128.2, 126.4, 120.4, 83.6, 59.4, 47.8, 31.8, 27.7, 25.8, 14.0, -5.4. HRMS (ESI): calcd for $C_{31}H_{38}O_5NCl_2Si$ $[M+H]^+$ 602.1914; found 602.1890.

Ethyl 5,6-dibenzoyl-1-benzyl-2-oxo-1,2-dihydropyridine-4-carboxylate (3x)

R_f: 0.4; Hexane: Ethyl acetate mixture (10:3); Yield: 65%; pale brown colour semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58-7.37 (m, 6H), 7.32 (t, J = 7.5 Hz, 2H), 7.24-7.14 (m, 3H), 7.07 (s, 5H), 5.23 (brs, 2H), 3.91 (q, J = 7.1 Hz, 2H), 1.00 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 191.9, 189.3, 164.2, 161.3, 147.6, 141.5, 137.3, 135.2, 134.8, 134.4, 133.2, 129.4, 128.8, 128.4, 128.3, 128.1, 127.8, 122.3, 116.7, 62.4, 48.6, 13.4; HRMS (ESI): calcd for $C_{29}H_{24}O_5N$ $[M+H]^+$ 466.1624; found 466.1624.

Tert-butyl 5,6-dibenzoyl-1-benzyl-2-oxo-1,2-dihydropyridine-4-carboxylate (3y)

R_f: 0.4; Hexane: Ethyl acetate mixture (10:3); Yield: 68%; pale brown colour semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54-7.45 (m, 2H), 7.44-7.31 (m, 3H), 7.31-7.21 (m,3 H), 7.15-7.05 (m, 3H), 7.00 (s, 5H), 5.15 (brs, 2H), 1.08 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 191.7, 189.4, 163.2, 161.4, 147.3, 142.9, 137.4, 135.2, 134.9, 134.4, 133.2, 129.4, 128.9, 128.4, 128.3, 128.1, 127.7, 122.1, 116.7, 84.1, 48.5, 27.1; HRMS (ESI): calcd for $C_{31}H_{28}O_5N$ $[M+H]^+$ 494.1934; found 494.1934.

Ethyl 1-(2-ethoxy-2-oxoethyl)-6-(4-fluorophenyl)-2-oxo-5-(4-(trifluoromethyl)benzoyl)-1,2-dihydropyridine-4-carboxylate (3z)

R_f: 0.4; Hexane: Ethyl acetate mixture (10:3); Yield: 71%; pale brown colour semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, J = 7.9 Hz, 2H), 7.58 (d, J = 8.0 Hz, 2H), 7.30 (s, 1H), 7.15-7.08 (m, 2H), 6.92 (t, J = 8.2 Hz, 2H), 4.46 (s, 2H), 4.22-4.13 (m, 4H), 1.23 (t, J = 7.0 Hz, 3H), 1.14 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ, 192.6, 167.3, 163.9, 161.5, 161.4, 147.2, 140.4, 131.5, 131.4, 128.8, 126.7, 125.3, 121.9, 118.1, 116.0, 115.8, 62.5, 61.9, 47.4, 13.9, 13.5; HRMS (ESI): calcd for $C_{26}H_{22}O_6NF_4$ $[M+H]^+$ 520.1405; found 520.1377.

General procedure for Synthesis of intermediate (4)

In a 25 mL round-bottomed two-neck flask compound **1a** (0.1g, 0.273 mmol, 1equiv.) was taken then dissolved in acetonitrile (2 mL) after that compound **2a** (0.046gm 0.273 mmol, 1 equiv.) was added and allowed to stir the reaction mixture at 70 °C for 3 h. Progress of the reaction was monitored by TLC. After completion of the reaction, acetonitrile solvent was removed in vacuum. The crude residue was purified through a silica gel column using hexane and ethyl acetate as eluent (10/2) to give (87%) pure addition product **4**.

Diethyl 2-(1-(2-(1*H*-indol-3-yl)ethylamino)-3-oxo-1,3-diphenylprop-1-en-2-yl)maleate (4)

R_f: 0.3; Hexane: Ethyl acetate mixture(10:1); Yield: 82%; brown colour semisolid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.26 (brs,1H), 8.15 (brs, 1H), 7.44-7.34 (m, 2H), 7.33-7.10 (m, 10H), 7.08-6.93 (m, 3H), 6.12 (s, 1H), 4.03 (q, J =6.9 Hz, 2H), 3.83 (q, J = 6.9 Hz, 2H), 3.36 (q, J = 6.9 Hz, 2H), 3.01 (t, J = 6.9 Hz, 2H), 1.16 (t, J = 7.1 Hz, 3H), 1.05 (t, J = 7.1 Hz, 3H); ^{13}C NMR (300 MHz, $CDCl_3$): δ 192.5, 166.1, 165.3, 145.2, 142.2, 136.2, 133.0, 129.0, 128.9, 128.6, 128.3, 127.9, 127.4, 127.1, 121.7, 119.1, 118.1, 111.6, 111.2, 101.7, 61.2, 60.2, 45.3, 26.5, 14.0, 13.8; HRMS (ESI): calcd. for $C_{33}H_{33}O_5N_2$ $[M+H]^+$ 537.2378; found 537.2384.

General procedure for Synthesis of 1,2-dihydropyridinones (6a)

In a 25 mL round-bottomed two-neck flask compound carboxylate substituted enaminone **5a** (0.1g, 0.355 mmol, 1 equiv.) was taken then dissolved in acetonitrile (2 mL) to this reaction mixture compound **2a** (0.06g 0.355 mmol, 1 equiv.) was added and allowed to stir at 70 °C for 3 h (yellow colour reaction mass was observed in the reaction flask). This reaction mixture was allowed to room temperature. Progress of the reaction was monitored by TLC. Then Cs_2CO_3 (0.173g, 0.533 mmol, 1.5 equiv.) was added portion wise at room temperature to this reaction mixture. Reaction mixture colour was changed from yellow to brown colour. This reaction mixture was allowed to stir at room temperature for 9 h. Progress of the reaction was monitored by TLC. After completion of the reaction, 3 mL of water was added to the reaction mixture. Reaction mass was extracted with ethyl acetate (3 x 5 mL). The combined organic layers were washed with aqueous brine, dried over anhydrous Na_2SO_4, and concentrated under vacuum. The crude residue was purified through a silica gel column using hexane and ethyl acetate as eluent (10/3) to give pure 1,2-dihydropyridine-4-carboxylates **6a**. The similar procedure was followed for the synthesis of all 2-pyridinone derivatives (**6a-f**).

Diethyl 1-benzyl-6-oxo-2-phenyl-1,6-dihydropyridine-3,4-dicarboxylate (6a)

R_f: 0.4; Hexane: Ethyl acetate mixture (10:3); Yield: 63%; semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 (t, J = 7.3 Hz, 1H), 7.30 (t, J = 7.7 Hz, 2H), 7.22-7.13 (m, 4H), 7.05 (d, J = 7.1 Hz, 2H), 6.84-6.76 (m, 2H), 5.08 (brs, 2H), 4.35 (q, J = 7.1 Hz, 2H), 3.86 (q, J = 7.1 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H); 0.85 (t, J = 7.17 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.6, 164.6, 162.0, 149.9, 140.2, 136.0, 132.0, 129.6, 129.0, 128.3, 128.0, 127.3, 126.7, 120.9, 113.0, 62.2, 61.2, 49.0, 13.9, 13.3; HRMS (ESI): calcd for $C_{24}H_{24}O_5N$ $[M+H]^+$ 406.1652; found 406.1653.

4-Tert-butyl 3-ethyl 1-benzyl-6-oxo-2-phenyl-1,6-dihydropyridine-3,4-dicarboxylate (6b)

R_f: 0.4; Hexane: Ethyl acetate mixture (10:3); Yield: 65%; semi solid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40 (t, J = 7.4 Hz, 1H), 7.30 (t, J = 7.7 Hz, 2H), 7.19-7.15 (m 3H), 7.10 (s, 1H), 7.05 (d, J = 7.1 Hz, 2H), 6.82-6.78 (m, 2H), 5.07 (brs, 2H), 3.86 (q, J = 7.1 Hz, 2H), 1.55 (s, 9H), 0.84 (t, J = 7.1 Hz, 3H);^{13}C NMR (125 MHz, $CDCl_3$): δ 165.8, 163.6, 162.1, 149.5, 141.5, 136.0, 132.0, 129.6, 129.0, 128.3, 128.0, 127.3, 126.7, 120.7, 113.3, 83.4, 61.2, 48.9, 27.7, 13.3; HRMS (ESI): calcd for $C_{26}H_{28}O_5N$ $[M+H]^+$ 434.1943; found 434.1941.

Diethyl 1-butyl-2-methyl-6-oxo-1,6-dihydropyridine-3,4-dicarboxylate (6c)

R_f: 0.3; Hexane: Ethyl acetate mixture (10:3); Yield: 40%; pale brown colour semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.84 (s, 1H), 4.30 (m, 4H), 4.17-4.00 (m, 2H), 2.52 (s, 3H), 1.72-1.59 (m, 2H), 1.50-1.22 (m, 9H), 0.97 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.7, 165.1, 161.8, 147.4, 140.3, 118.6, 111.0, 61.9, 61.6, 44.8, 30.1, 20.1, 17.1, 13.8, 13.5, HRMS (ESI): calcd for $C_{16}H_{24}O_5N$ $[M+H]^+$ 310.1635; found 310.1637.

Diethyl 2-methyl-6-oxo-1-phenyl-1,6-dihydropyridine-3,4-dicarboxylate (6d)

R_f: 0.4; Hexane: Ethyl acetate mixture (10:3); Yield: 47%; solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58-7.52 (m, 2H), 7.51-7.46 (m, 1H), 7.16 (m, 2H), 6.93 (s, 1H), 4.35 (q, J = 7.1 Hz, 2H), 4.30 (q, J = 7.1 Hz, 2H), 2.10 (s, 3H), 1.38 (t, J = 7.1 Hz, 3H), 1.33 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.3, 165.0, 162.2, 148.5, 141.5, 137.7, 129.9, 129.1, 127.4, 119.3, 110.5, 62.0, 61.6, 19.1, 13.8, 13.7; HRMS (ESI): calcd for $C_{18}H_{20}O_5N$ $[M+H]^+$ 330.1340; found 330.1339.

Triethyl 1-benzyl-6-oxo-1,6-dihydropyridine-2,3,4-tricarboxylate (6e)

R_f: 0.3; Hexane: Ethyl acetate mixture (10:3); Yield: 45%; semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40-7.23 (m, 3H), 7.22-7.14 (m, 2H), 6.84 (s, 1H), 5.31 (s, 2H), 4.35 (q, J = 7.1 Hz, 2H), 4.23 (q, J = 7.1 Hz, 2H), 4.15 (q, J = 7.1 Hz, 2H), 1.40-1.24 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.1, 163.3, 161.5, 160.7, 144.5, 142.7, 134.9, 128.5, 127.8, 127.3, 120.8, 63.0, 62.2, 62.0, 48.8, 29.6, 13.9, 13.8, 13.2; HRMS (ESI): calcd for $C_{21}H_{24}O_7N$ $[M+H]^+$ 402.1556; found 402.1556.

Triethyl 1-butyl-6-oxo-1,6-dihydropyridine-2,3,4-tricarboxylate (6f)

R_f: 0.4; Hexane: Ethyl acetate mixture (10:3); Yield: 48%; pale brown colour semi solid ; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.71 (s, 1H), 4.44 (q, J = 7.0 Hz, 2H), 4.34 (q, J = 7.1 Hz, 2H), 4.25 (q, J = 7.1 Hz, 2H), 3.9 (t, J = 7.9 Hz, 2H), 2.73 (t, J = 7.1 Hz, 3H), 1.75-1.66 (m, 2H), 1.44-1.38 (m, 2H), 1.35 (t, J = 7.1 Hz, 3H) 1.30 (t, J = 7.1 Hz, 3H), 0.94 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.4, 163.3, 161.7, 160.4, 145.2, 142.9, 120.1, 106.9, 63.2, 62.2, 62.0, 47.4, 30.6, 20.0, 13.9, 13.8, 13.7, 13.5; HRMS (ESI): calcd for $C_{16}H_{27}O_7NNa$ $[M+H]^+$ 368.1690; found 368.1688.

Ethyl 5-acetyl-1-benzyl-2-oxo-6-phenyl-1,2-dihydropyridine-4-carboxylate (6g)

R_f: 0.4; Hexane: Ethyl acetate mixture (10:3); Yield: 11%; brown colour semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (d, J = 7.78 Hz, 2H), 7.59-7.55 (m, 1H), 7.45 (t, J = 7.78 Hz, 2H), 7.33 (t, J = 7.47 Hz, 2H), 7.30-7.27 (m, 1H), 7.19-7.15 (m, 3H), 5.42 (s, 2H), 4.05 (q, J = 7.17 Hz, 2H), 2.18 (s, 3H), 1.08 (t, J = 7.17 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 194.6, 164.3, 162.5, 146.2, 140.4, 137.7, 135.2, 133.4, 128.9, 128.8, 127.6, 126.3, 119.7, 117.1, 62.1, 47.6, 18.0, 13.5; HRMS (ESI): calcd for $C_{23}H_{22}NO_4$ [M+H]+376.1543; found 376.1542.

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