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FULL-LENGTH PAPER

VCl_3 catalyzed imine-based multicomponent reactions for the facile access of functionalized tetrahydropyridines and β-amino carbonyls

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Abstract A simple, mild, and highly efficient method has been developed for the preparation of functionalized tetrahydropyridines and β-amino carbonyls from the multicomponent reactions involving in situ imines and vanadium (III) chloride as a Lewis acid. The multicomponent reaction of two equivalents of aromatic aldehyde, two equivalents of amine, and one equivalent β-keto ester in the presence of catalytic amount of VCl_3 provides highly atom economic five-component tetrahydropyridines in very good yields. The same catalyst was found useful for the efficient synthesis of a wide variety of β-amino ketones using direct-type Mannich reaction of aromatic aldehyde, amine, and aromatic ketones. The notable advantages of this method are simple procedure, short reaction time and good yields, and applicable to broad range of substrates.

Keywords VCl_3 · Multicomponent reactions · MCRs · Tetrahydropyridines · β-Amino carbonyls

Introduction

Multicomponent reactions (MCRs) are one of the most preferred ways to generate multiple molecular scaffolds to increase structural as well as skeletal diversity from simple and easily available starting materials [1–3]. In recent times, MCRs have gained considerable attention among synthetic community for their efficiency in terms of pot, atom, and step economy (PASE) [4,5]. Imines are one of the versatile reactive intermediate/substrate in multicomponent reactions for the access of diverse heterocycles and acyclic molecules having various pharmacological properties [6–8]. The recent efforts toward the exploration of imines for the access of various N-heterocycles include synthesis of functionalized pyrroles from the multicomponent reaction of 1,3-dicarbonyl compounds, amines, aldehydes, and nitroalkanes [9], imidazolinium salts and imidazolines from the reaction of imines, acid chlorides, and carbon monoxide [10], etc. The sudden rise of the popularity of MCRs involving in situ imines is believed to be due to the substrate-dependent reactivity of imines, which gives different products depending on the specific conditions and structure of the other reacting partners [11]. In this article, we report a versatile method for the easy access of various tetrahydropyridines and β-amino carbonyls employing imine-based multicomponent reactions in presence of catalytic amount of vanadium (III) chloride.

Functionalized tetrahydropyridines represent an important class of organic molecules that attract the interest of both synthetic and medicinal chemists [12–14]. The tetrahydropyridine skeleton is present in numerous natural products as well as synthetic pharmaceuticals. Due to their broad spectrum of pharmacological and biological activities, such as antiviral activity [15], antidepressant effects [16], and antimalarial activity [17] development of general methods for the efficient synthesis of functionalized tetrahydropyridines have gained considerable interest. For example, Tsukamoto and Kondo [18] have reported a interesting Pd(0) catalyzed multicomponent reaction of alkynyl or allenyl amine with formaldehyde and boronic acid derivatives for the synthesis of 1,4-disubstituted 1,2,3,6-tetrahydropyridines. Similarly, substituted tetrahydropyridines can be synthesized from the two-component reaction of *N*-(*p*-methoxyphenyl) aldimines

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and tetrahydro-2H-pyran-2,6-diol [19], by radical cyclization from Baylis–Hillman adducts [20], organocatalyzed domino process involving aza-Morita–Baylis–Hillman reaction [21], etc. In addition to these, $InCl_3$ [22], bromodimethyl sulfonium bromide (BDMS) [23], L-proline/TFA [17], tetrabutyl ammonium tribromide (TBATB) [24], I_2 [25], CAN [26], and $ZrOCl_2 \cdot 8H_2O$ [27] have been reported as catalyst for the synthesis of highly substituted tetrahydropyridines using multicomponent reaction of aldehyde, amine, and β-keto esters. Most of the existing methods suffer from a drawback such as long reaction time, expansive and high catalyst loading, strong acidic condition or the catalyst has to be prepared before use, etc.

Therefore, development of a new and efficient method for the synthesis of functionalized tetrahydropyridines using readily available catalyst is a significant challenge. Vanadium (III) chloride (VCl_3) is a relatively less explored mild Lewis acid catalyst in organic synthesis [28–30].

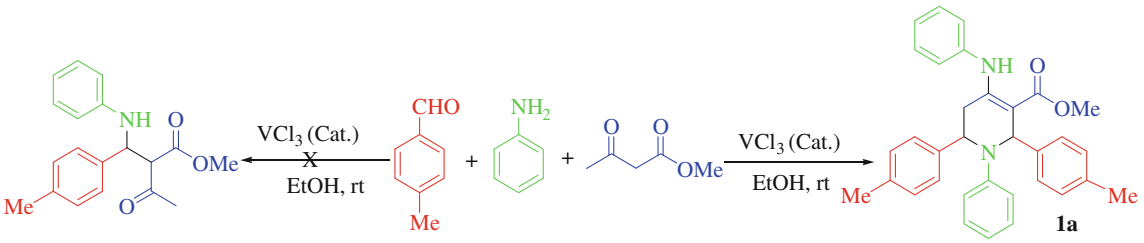
In continuation of our endeavor to develop new synthetic methodologies for the synthesis of diverse heterocycles using multicomponent reactions, we explored the role of VCl_3 as a useful catalyst.

Results and discussion

Initially, the reaction of methyl acetoacetate (1 mmol), 4-methylbenzaldehyde (1 mmol), and aniline (1 mmol) in ethanol was tested in presence of 5 mol% VCl_3. Interestingly, we did not observe any three-component Mannich-type product, instead we ended with a five-component product **1a** in 21% yield (Scheme 1). Product **1a** was fully characterized by spectroscopic techniques and its structure was confirmed by comparing with literature data. Due to the presence of the enamine and ester functionality in the tetrahydropyridine moiety, these molecules have room for further functionalization. Encouraged by this result, we shifted our attention to the optimization of this method. To assess the role of the catalyst VCl_3, a control experiment in the absence of a catalyst was run using same set of reactants in ethanol where only trace amount of product **1a** was isolated after 12 h of reaction time. The same model reaction was performed in various stoichiometric ratios in presence of VCl_3 as catalyst. The combination of 1:2:2 (methyl acetoacetate: 4-methylbenzaldehyde:aniline) in EtOH in the presence of 10 mol% VCl_3 at room temperature was found the most suitable optimum condition with 81% yield within 8 h. Next, various solvents such as THF, DMF, acetonitrile, and CH_2Cl_2 were also screened for the same reaction keeping constant the substrate ratio and VCl_3 amount. Among all these solvents, EtOH was found to be the best solvent for this transformation in terms of yield obtained and reaction time. To verify the generality and explore the scope of this methodology, a wide variety of aromatic aldehydes, aniline derivatives, and β-keto esters were treated under the optimum reaction condition and the corresponding five-component products were isolated in good yields (Table 1, entries 1–12). Reactions worked well in case of aromatic aldehydes tethered with various groups such as Cl, Br, Me, and OMe. We also tried this multicomponent reaction using aliphatic aldehydes such as cyclohexyl carboxaldehyde, phenyl acetaldehyde, heptanal, and butyraldehyde in combination with aniline and methylacetoacetate. Unfortunately, we found that the present protocol is not suitable for these aliphatic aldehydes. These reactions give mixtures of inseparable compounds similar as mentioned by $ZrOCl_2 \cdot 8H_2O$ [27] method, which may be due to the instability of in situ aliphatic imines in presence of Lewis acid as they can undergo various side reactions such as for the aliphatic imines, and if there is an α-hydrogen, the imines can be isomerized to enamines. As in this multicomponent reaction, we believe mechanistically imine plays great role; therefore, less stable imines obtained from aliphatic aldehydes are not suitable for this multicomponent reactions.

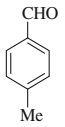
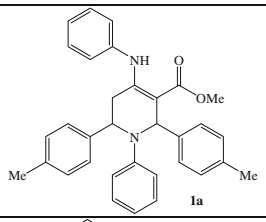
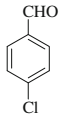
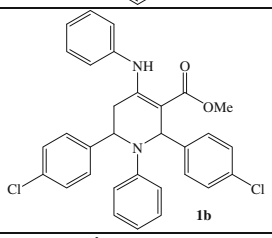
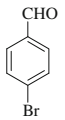
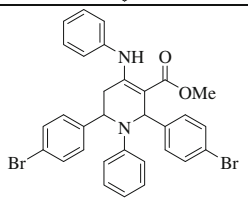
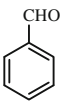
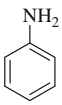
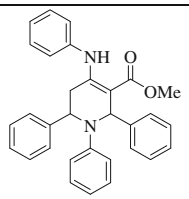
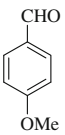
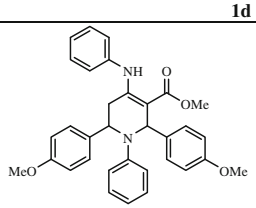
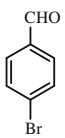
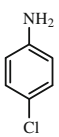
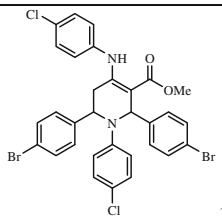
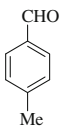
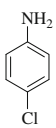
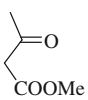
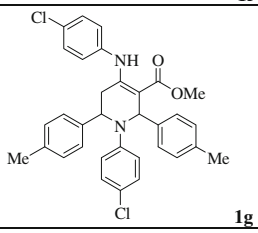
A wide variety of aromatic amines underwent multicomponent reaction under the similar reaction conditions leading to the corresponding functionalized tetrahydropyridines in good yields. Benzyl amine and butyl amine were also found suitable for this multicomponent reaction although the corresponding yields were lesser as compared with the aniline derivatives (Table 1, entries 13 and 14). It is evident from these results that the present protocol is highly variable as all the three starting materials can be varied independently and bond-forming efficiency, i.e., total number of new bond formed in one pot is five for this MCR.

Interestingly, 2-naphthylamine also afforded corresponding five-component tetrahydropyridine **1o** under the optimum reaction condition with 57% yield. We did not observe



Scheme 1 VCl_3 catalyzed preferential five-component reaction over the Mannich-type reaction

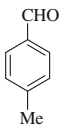
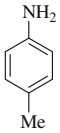
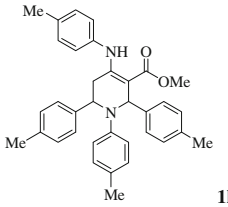
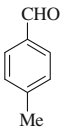
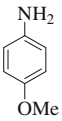
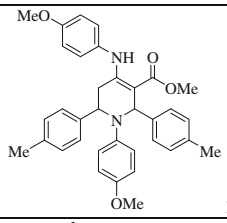
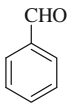
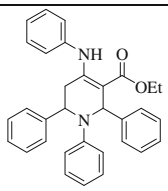
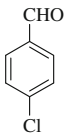
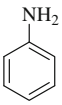
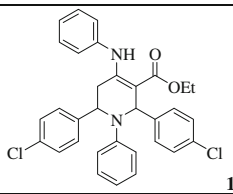
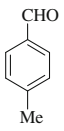
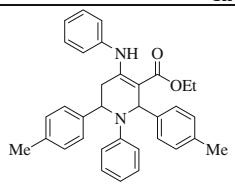
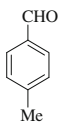
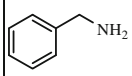
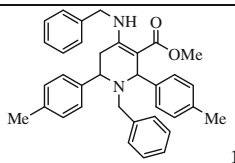
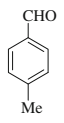
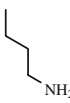
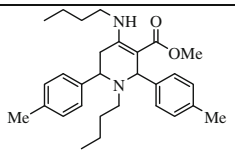
Table 1 VCl_3 catalyzed five-component reactions for the synthesis of functionalized tetrahydro pyridines (**1a–1n**)

Entry	Aromatic aldehydes	Amines	β-ketoesters	Product	Reaction time/h	Yield (%)
1				 **1a**	8	81
2				 **1b**	7	75
3				 **1c**	7	72
4				 **1d**	8	71
5				 **1e**	7.5	73
6				 **1f**	8	71
7				 **1g**	5	71

any three-component benzo[f]quinoline derivative as mentioned by Wang et al. [31] from the combination of 2-naphthylamine, benzaldehyde, and methylacetoacetate (Scheme 2) even under refluxing conditions.

Mechanistically, we believe that one equivalent of amine reacts with β-keto ester to form enamine which further reacts with one equivalent of aldehyde to form an intermediate **B** and another equivalent of amine reacts with one equivalent

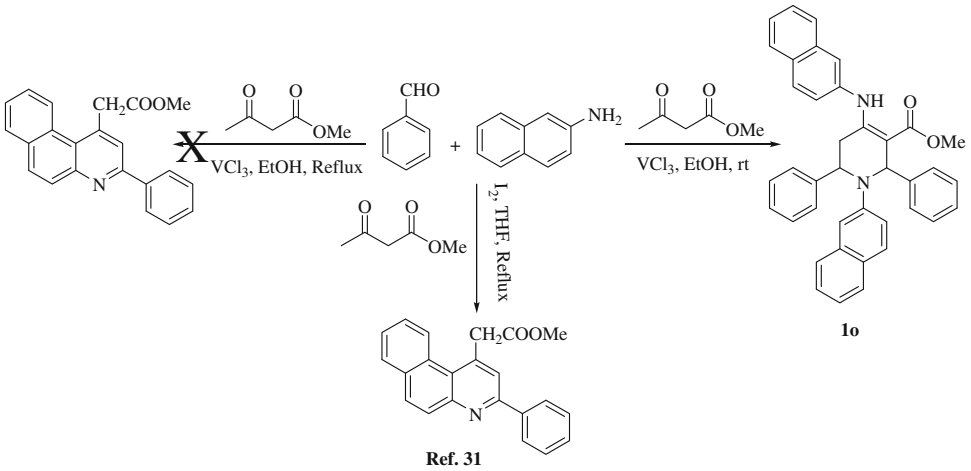
Table 1 continued

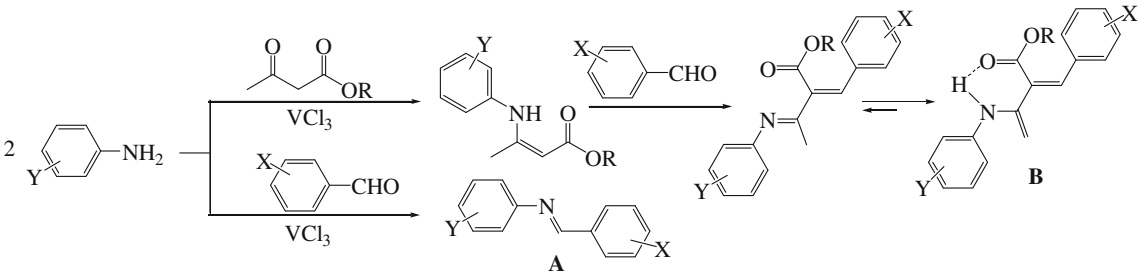
Entry	Aromatic aldehydes	Amines	β-ketoesters	Product	Reaction time/h	Yield (%)
8				 **1h**	6.5	75
9				 **1i**	8	73
10				 **1j**	7.5	73
11				 **1k**	7.5	74
12				 **1l**	8	72
13				 **1m**	10	45
14				 **1n**	12	60

of aldehyde to form corresponding aldemine (**A**). Finally, this reaction undergoes a 4+2 type addition of aldemine (**A**) with the in situ diene (**B**) to generate a highly functionalized tetrahydropyridines (Scheme 3).

To further understand the mechanistic insight and to access diverse tetrahydropyridines, we performed the following reaction. Initially, we wanted to know whether is it possible to synthesize a highly substituted tetrahydropyridine where two different aldehydes can be incorporated by this MCR. For this, aniline was treated with one equivalent of methylacetoacetate in ethanol in the presence of catalytic amount of VCl_3 and the corresponding enamine was generated in situ at room temperature. To this solution, one equivalent of 4-methoxybenzaldehyde was added followed by one equivalent of in situ imine prepared separately in another reaction flask from aniline and 4-methylbenzaldehyde. Interestingly, we identified three products (**1a**, **1e**, and **1p** in 15, 24, and 25% yield, respectively) instead of single product **1p** as shown in

Scheme 2 VCl_3 catalyzed preferential five-component reaction over three component

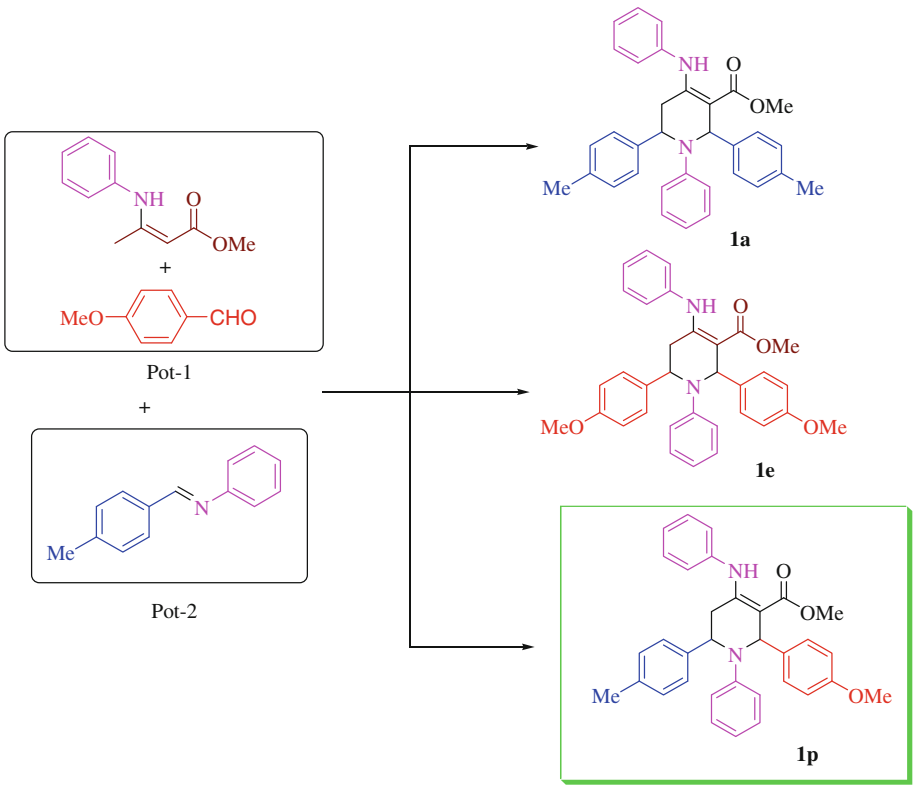




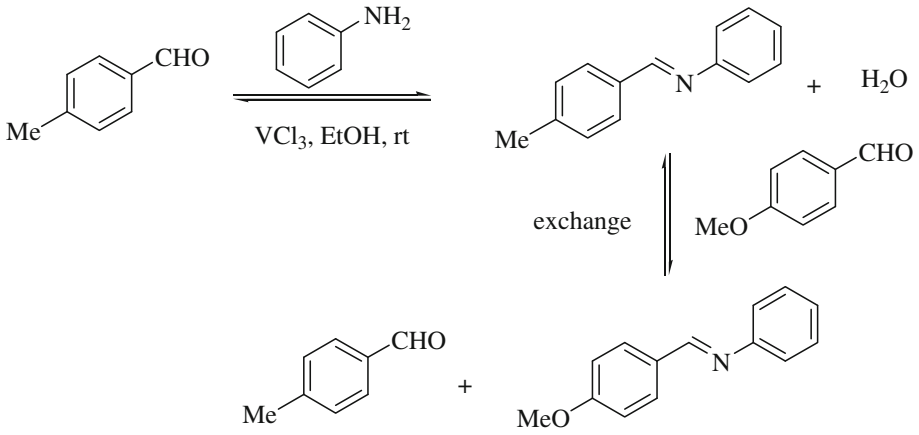
A + B —Aza -Diels Alder→ **Five component product**

Scheme 3 Proposed mechanism for the formation of functionalized tetrahydropyridines

Scheme 4 Sequential reaction for the synthesis of tetrahydopyridines using two different aldehydes



Scheme 5 Exchange reaction between imine and aldehyde

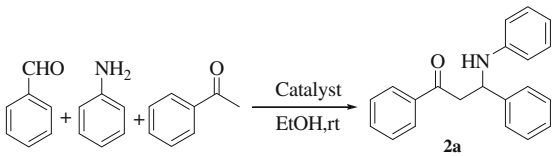


Scheme 4. The formation of three products from this test reaction indicates that in the reaction medium two types of imines exist: one is from the aniline with *p*-methylbenzaldehyde and the other one is from aniline with *p*-methoxybenzaldehyde, and both the two aldehydes were also available for the formation of these product. This observation may be due to two factors: (i) the reaction of enamine and *p*-methoxybenzaldehyde is a reversible process which exists in equilibrium with the proposed diene as a result free *p*-methoxy benzaldehyde will be available in the reaction mixture to participate in the other side reactions, (ii) exchange reaction of imine which takes place during the course of the reaction with the free *p*-methoxy benzaldehyde as shown in Scheme 5.

In an another attempt, the reaction of an electron deficient amine and *p*-tolyl sulfonamide with methyl acetoacetate and benzaldehyde was also tested in the presence of VCl_3 under the optimum reaction conditions failing to provide the corresponding five-component tetrahydropyridine. This indicates that the nature of the amine participating in this multicomponent reaction is also important.

Inspired from this efficient catalytic activity of VCl_3 for the synthesis of tetrahydropyridines by multicomponent approach, we explored its catalytic activity for the three-component reaction of aldehyde, amine, and enolizable ketones, i.e., Mannich-type reactions. The Mannich-type reaction is a useful carbon–carbon bond-forming reaction in organic synthesis [32–35]. β-amino carbonyls obtained from the Mannich-type reactions are very useful as synthetic intermediates of bioactive molecules and natural products [36,37].Very recently, Du et al. [38] revealed that aromatic β-amino-ketone derivatives are novel selective non-steroidal progesterone receptor antagonists. β-amino-ketone derivatives can be synthesized using various catalyst. Among them protic acids [39,40], bromodimethyl sulfonium bromide[41], Lewis Acids such as $Bi(OTf)_3$ [42,43], $NbCl_5$[44], $Zn(BF_4)_2$[45], heteropoly acid [46], $Yb(OPf)_3$ [47], $ZrOCl_2 \cdot 8H_2O$ [48], $BiCl_3$ [49], etc. are notable. Although a good number of methods are available still most of the existing methods suffer from some limitations such as long reaction time, costly catalysts or requirement of special effort for catalyst preparation, etc. To determine the versatility of VCl_3 as catalyst, the Mannich-type reaction of benzaldehyde (1 mmol), aniline (1 mmol), and acetophenone (1 mmol) was chosen as a model reaction using ethanol as solvent. Interestingly, we found that 10 mol% catalyst is efficient enough to get 91% yield of the corresponding Mannich-type product within very short reaction time. Encouraged by this result, the same reaction was tried with various solvent systems for optimization of this protocol. Among CH_2Cl_2, DMSO, CH_3CN, $CHCl_3$, dioxane, and EtOH, ethanol was found the most suitable in terms of yields obtained and reaction time. Lowering the catalyst loading up to 5 mol% under the similar reaction condition, the reaction took longer time and provided lower yields. The virtue of this catalyst can be realized from the comparison Table 2.

Table 2 Comparison of catalytic activity of VCl_3 with other Lewis acid catalysts for the direct-type Mannich reaction of benzaldehyde, aniline, and acetophenone.



2a

Entry	Catalyst (10 mol%)	Reaction time (h)	% Yield
1	No catalyst	48	NR
2	$ZnCl_2$	20	NR [44]
3	$CuCl_2$	20	NR [44]
4	$FeCl_3$	20	NR [49]
5	$LaCl_3$	20	NR [49]
6	$AlCl_3$	24	NR [44]
7	$InCl_3$	20	56 [49]
8	$NbCl_5$	12	95 [44]
9	$BiCl_3$	11	79 [49]
10	VCl_3	1	91[a]

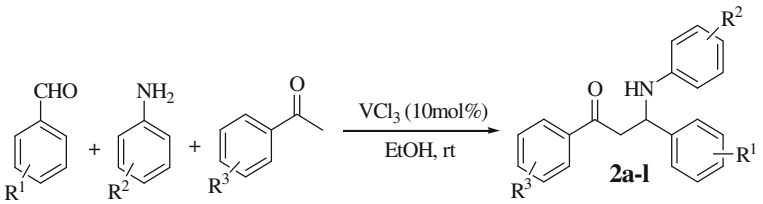
[a] Reaction conditions: benzaldehyde (1 mmol), aniline (1 mmol), acetophenone (1 mmol), ethanol (3 ml), VCl_3 (10 mol%)

Using optimized reaction condition, the scope of the reaction was tested finding excellent results for the different combinations of aldehydes, amines, and acetophenone or its derivatives. The generality of this protocol can be realized from the results summarized in Table 3. A wide variety of structurally divergent aldehydes, amines, and acetophenones underwent Mannich-type reaction within 1–2.5 h time with good to excellent yields. It is evident from these results that the present protocol is advantageous in terms of yield obtained, simple procedure, and short reaction time.

To generalize this method, we studied the reaction of in situ imines with various enolizable C-nucleophiles under the optimum reaction condition. The results of this study are summarized in Table 4. Similar to acetopheone, aliphatic cyclic ketone, cyclohexanone underwent Mannich-type product **3a** in good yield within 1 h. Compound **3a** was isolated as a mixture of diastereomer having 5:95 ratio of *syn: anti* product as determined from the crude ^{1}H NMR. Next, various active methylene compounds were tested with in situ imines in the presence of 10 mol% VCl_3. Diethylmalonate provided its corresponding expected β-amino carbonyl **3b**. Interestingly, ethyl cyanoacetate reacted with in situ imine in the presence of VCl_3 and provided unexpected two-component Knovenagel-type condensation product **3c** instead of corresponding three-component Mannich-type product (Entry 3, Table 4). This result encouraged us to see the reaction of malononitrile with in situ imines under similar reaction condition. Malononitrile also provided two-component condensation product **3d** similar to ethyl cyanoacetate. These two results indicate that the outcome of imine-based MCRs vary depending upon the structure and reactivity pattern of the third reaction partner. We believe the formation of unexpected two-component product is due to (i) reversible nature of the imine which exists in equilibrium with the starting materials, i.e., aldehyde and amine (ii) relatively more electrophilic nature of the free aldehyde in the reaction medium than the imine, as well as (iii) may be the two-component condensation product is more thermodynamically stable than the three-component Mannich-type product. In addition, free amine acts as a base to deprotonate active methylene compounds and promote condensation over the nucleophilic addition. The exact mechanism for this observation is not clear yet.

Finally, we have tested the reaction of dimedone, 4-chlorobenzaldehyde, and 4-cyanoaniline in ethanol at room temperature using 10 mol% VCl_3 as catalyst. However, even after 12 h of reaction at room temperature, we could not isolate any Mannich-type product and only trace amounts of four-component product **3e** was obtained. This reaction was then optimized by changing the ratio of substrates (2:1:1; dime-

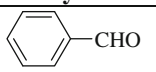
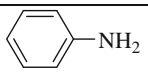
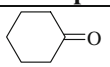
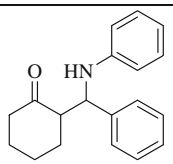
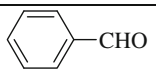
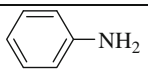
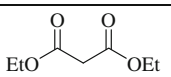
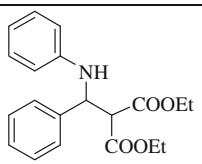
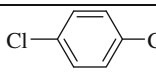
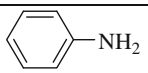
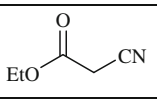
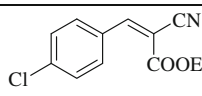
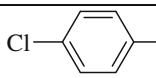
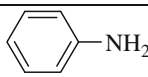
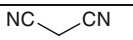
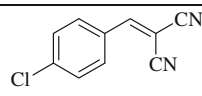
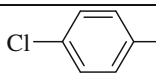
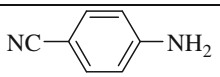
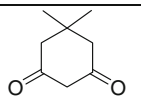
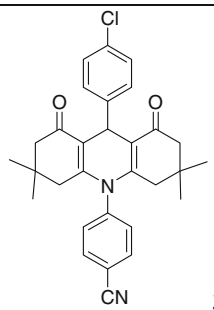
Table 3 VCl_3catalyzed direct-type Mannich reaction of various aromatic aldehydes, amines, and acetophenones



Entry	R^1	R^2	R^3	Product	Reaction time /h	Yield[a] (%)
1	H	H	H	**2a**	01	91
2	4-Me	H	H	**2b**	1.5	90
3	4-OMe	H	H	**2c**	1.5	88
4	4-OMe	4-Cl	H	**2d**	02	87
5	H	4-NO_2	H	**2e**	01	87
6	H	4-Cl	H	**2f**	01	84
7	H	4-Me	H	**2g**	01	87
8	H	4-CN	H	**2h**	02	81
9	4-Cl	4-NO_2	H	**2i**	02	79
10	H	4-Cl	4-Br	**2j**	01	82
11	H	H	4-Br	**2k**	01	90
12	4-Cl	4-NO_2	4-Br	**2l**	2.5	75

Reaction conditions: aromatic aldehyde (1 mmol), aromatic amine (1 mmol), acetophenone (1 mmol), ethanol (3 mL), VCl_3 (10 mol%) at rt
[a] Isolated yields

Table 4 Reaction of in situ imines with various enolizable C-nucleophiles in presence of VCl_3 as catalyst

Entry	Aromatic aldehyde	Amine	Enolizable nucleophile	Product	Reaction Time /h	Yield (%)
1				 **3a**	1	82
2				 **3b**	1	87
3				 **3c**	1	75
4				 **3d**	1	82
5				 **3e**	6	81[a]

[a] Reaction was performed in 1:1:2 ratio of aldehyde, amine, and dimedone under refluxing conditions

done:4-chlorobenzaldehyde:4-cyanoaniline) under refluxing conditions, and the reaction underwent smoothly within 6 h with 81% yield.

From this study, we have realized that the β-ketoesters such as methyl acetoacetate or its derivatives reacts with in situ imines in presence of catalytic amount of VCl_3 leading to the five-component tetrahydropyridine, whereas aromatic enolizable ketones, cyclohexanone, and compounds like diethylmalonate reacts with in situ imines in presence of VCl_3 to provide the corresponding Mannich-type three-component products. Active methylene compounds such as ethyl cyanoactate, malononitrile preferred two-component condensation product leading to electron deficient alkenes. 1,3-diketone such as dimedone provides four component instead of Mannich-type product.

In conclusion, we have explored the catalytic activity of VCl_3 and developed a simple and efficient method for the diversity oriented synthesis of various functionalized tetrahydropyridines and β-amino ketones, electron deficient alkenes, etc. using imine-based multicomponent reactions. The noteworthy features of this procedure are mild reaction conditions, economical steps, high yields, and operational simplicity, and generation of molecular diversity.

Experimental

General

All reagents purchased from commercial sources and used without further purification. IR spectra were recorded on a Shimadzu FTIR spectrophotometer. ^{1}H NMR spectra and ^{13}C NMR spectra were recorded on a Jeol 500 Varian 400 and Bruker 500/400 MHz spectrometer in $CDCl_3$ using TMS as internal reference. Elemental analyses were carried out in a Perkin Elmer 2400 automatic carbon, hydrogen, nitrogen, and sulfur analyzer or Elementer Vario EL III. All compounds were characterized by recording melting point, ^{1}H and ^{13}C NMR and elemental analysis.

General procedure for the synthesis of functionalized tetrahydropyridines (**1a–o**)

In a round-bottom flask, a mixture of aromatic amine (2.0 mmol), methyl acetoacetate (1.0 mmol), and VCl_3 (0.1 mmol) in 5mL ethanol was stirred at room temperature. Subsequently, aromatic aldehyde (2.0 mmol) was added to the mixture. The resulting mixture was stirred until the reaction was completed as indicated by TLC. The resulting precipitate was collected by filtration and washed with ethanol. The crude solid was purified via recrystalization from ethanol to get pure product.

*Methyl 1-phenyl-4-(phenylamino)-2,6-di-p-tolyl-1,2,5,6-tetrahydropyridine-3-carboxylate (***1a***)*

81%. mp: 211–213 °C. IR (KBr): 1658, 1590 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 10.22 (s,1H), 7.16 (d, J = 8.0 Hz, 2H), 6.97–7.06 (m, 11H), 6.57 (t, J = 7.2 Hz, 1H), 6.50 (d, J = 8.4 Hz, 2H), 6.36 (s, 1H), 6.27–6.29 (m, 2H), 5.08–5.09 (m, 1H), 3.89 (s, 3H), 2.82 (dd, J = 15.2, 5.6 Hz, 1H), 2.75 (dd, J = 15.2, 2.4 Hz, 1H), 2.32 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8,156.5, 147.2, 141.1, 139.8, 138.1, 136.8, 136.0, 129.4, 129.1, 129.0, 128.9, 126.7, 126.5, 126.0, 125.8, 116.2, 113.1, 98.3, 58.1, 55.1, 51.2, 33.8, 21.3, 21.2. Elemental analysis calc. for $C_{33}H_{32}N_2O_2$ (488.62): C, 81.12; H, 6.60; N, 5.73. Found: C, 81.02; H, 6.53; N, 5.85.

*Methyl 2,6-bis(4-chlorophenyl)-1-phenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (***1b***)*

75%. mp: 223–225 °C. IR (KBr): 1655, 1595 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 10.25 (s,1H), 7.21–7.26 (m, 7H), 7.13–7.19 (m, 2H), 7.03–7.08 (m, 4H), 6.64 (t, J = 7.2 Hz, 1H), 6.46 (d, J = 8.4 Hz, 2H), 6.41 (d, J = 6.8 Hz, 2H), 6.35 (s,1H), 5.08–5.09 (m, 1H), 3.92 (s, 3H), 2.83 (dd, J = 15.2, 5.6 Hz, 1H), 2.75 (dd, J = 15.2, 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.5, 156.2, 146.6, 142.5, 141.0, 137.7, 133.0, 132.3, 129.2, 128.9, 128.6, 128.2, 127.9, 126.2, 125.9, 116.9, 113.1, 97.6, 57.5, 54.8, 51.3, 33.8. Elemental analysis calc. for $C_{31}H_{26}Cl_2N_2O_2$ (529.46): C, 70.32; H, 4.95; N, 5.29. Found: C, 70.21; H, 4.89; N, 5.41.

Methyl 2,6-bis(4-bromophenyl)-1-phenyl-4-(phenyl amino)-1,2,5,6-tetrahydropyridine-3-carboxylate **(1c)**

72%. mp: 246–248 °C. IR (KBr): 1661, 1589 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 10.22 (s,1H), 7.38 (d, J = 8.2 Hz, 2H), 7.36 (d, J = 8.8 Hz, 2H), 7.12–7.17 (m, 5H), 7.07 (t, J = 7.3 Hz, 2H), 6.98 (d, J = 7.6 Hz, 2H), 6.65 (t, J = 6.7 Hz, 1H), 6.44 (d, J = 7.0 Hz, 2H), 6.39 (d, J = 7.3 Hz, 2H), 6.32 (s, 1H), 5.05–5.06 (m, 1H), 3.91 (s, 3H), 2.81 (dd, J = 14.9, 5.2 Hz, 1H), 2.74 (dd, J = 14.9, 2.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.4, 156.1, 146.5, 142.9, 141.5, 137.6, 131.8, 131.4, 129.8, 129.1, 128.5, 128.2, 126.2, 125.8, 121.0, 120.3, 116.9, 113.0, 97.5, 57.5, 54.8, 51.3, 33.7. Elemental analysis calc. for $C_{31}H_{26}Br_2N_2O_2$ (618.36): C, 60.21; H, 4.24; N, 4.53. Found: C, 60.32; H, 4.31; N, 4.66.

*Methyl 1,2,6-triphenyl-4-(phenylamino)-1,2,5,6-tetra hydropyridine-3-carboxylate (***1d***)*

71%. mp: 195–196 °C. IR (KBr): 1663, 1592 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 10.24 (s,1H), 7.24–7.32 (m, 8H), 7.15 (d, J = 6.4 Hz, 2H), 7.04–7.09 (m, 5H), 6.60 (t, J = 7.3 Hz, 1H), 6.51(d, J = 8.2 Hz, 2H), 6.44 (s, 1H), 6.27 (d, J = 7.6 Hz, 2H), 5.13–5.14 (m, 1H), 3.93 (s, 3H), 2.87 (dd, J = 15.0, 5.8 Hz, 1H), 2.76 (dd, J = 15.0, 2.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.7, 156.4, 147.0, 144.0, 142.5, 137.0, 129.0, 128.9, 128.7, 128.4, 127.3, 126.8, 126.6, 126.0, 125.9, 116.3, 113.0, 98.0, 58.3, 55.2, 51.1, 33.8. Elemental analysis calc. for $C_{31}H_{28}N_2O_2$ (460.57): C, 80.84; H, 6.13; N, 6.08. Found: C, 80.93; H, 6.19; N, 6.21.

*Methyl 2,6-bis(4-methoxyphenyl)-1-phenyl-4-(phenyl amino)-1,2,5,6-tetrahydropyridine-3 carboxylate (***1e***)*

73%. mp: 180–182 °C. IR (KBr): 1657, 1593 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 10.28 (s,1H), 7.22 (d, J = 8.5 Hz, 2H), 7.07–7.13 (m, 7H), 6.81 (d, J = 8.2 Hz, 4H), 6.61 (t, J = 7.3 Hz, 1H), 6.54 (d, J = 8.2 Hz, 2H), 6.36–6.38 (m, 3H), 5.09–5.10 (m, 1H), 3.93 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 2.86 (dd, J = 15.0, 5.2 Hz, 1H), 2.75 (dd, J = 15.0, 2.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.7, 158.8, 158.1, 156.5, 147.1, 138.0, 135.9, 134.7, 128.9, 127.8, 127.5, 125.9, 125.8, 116.1, 114.1, 113.6, 113.0, 98.2, 57.6, 55.4, 54.6, 51.1, 33.8. Elemental analysis calc. for $C_{33}H_{32}N_2O_4$ (520.62):C, 76.13; H, 6.20; N, 5.38. Found: C, 76.03; H, 6.13; N, 5.49.

Methyl 2,6-bis(4-bromophenyl)-1-(4-chlorophenyl)-4-(4-chlorophenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate **(1f)**

71%. mp 159–161 °C. IR (KBr):1655, 1610 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 10.24 (s, 1H), 7.40–7.45 (m, 4H), 7.10–7.27 (m, 4H), 6.99–7.04 (m, 4H), 6.27–6.38 (m, 5H), 5.07 (s, 1H), 3.97 (s, 3H), 2.80 (dd, J = 15.2, 5.6 Hz, 1H), 2.67 (dd, J = 15.2, 2.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.3, 155.4, 145.0, 142.2, 140.9, 136.1, 132.0, 131.9, 131.8, 129.3, 129.0, 128.4, 128.3, 127.0, 122.0, 121.3, 120.6, 114.1, 98.0, 57.6, 55.0, 51.4, 33.6. Elemental analysis calc. for $C_{31}H_{24}Br_2Cl_2N_2O_2$ (687.25): C, 54.18; H, 3.52; N, 4.08. Found: C, 54.28; H, 3.59; N, 4.21

*Methyl 1-(4-chlorophenyl)-4-(4-chlorophenylamino)2,6-di-p-tolyl-1,2,5,6 tetrahydropyridine- 3-carboxylate (***1g***)*

71%. mp:181–183 °C. IR (KBr): 1651, 1603 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$) δ: 10.18 (s, 1H), 7.14 (d, J = 7.9 Hz, 2H), 7.09 (d, J = 7.9 Hz, 2H), 7.07 (d, J = 7.9 Hz, 2H), 7.04 (d, J = 8.2 Hz, 2H), 7.02 (d, J = 7.6 Hz, 2H), 6.98 (d, J = 8.8 Hz, 2H), 6.41 (d, J = 8.8 Hz, 2H), 6.31 (s, 1H), 6.17 (d, J = 8.5 Hz, 2H), 5.05–5.06 (m, 1H), 3.92 (s, 3H), 2.83 (dd, J = 15.3, 5.8 Hz, 1H), 2.68 (dd,J = 15.3, 2.4 Hz, 1H), 2.33 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.6, 155.7, 145.6, 140.2, 139.3, 137.1, 136.5, 136.2, 131.4, 129.5, 129.1, 129.0, 128.8, 127.1, 126.5, 126.3, 121.1, 114.1, 98.7, 58.1, 55.2, 51.2, 33.6, 21.2, 21.1. Elemental analysis calc. for $C_{33}H_{30}Cl_2N_2O_2$ (557.51) : C, 71.09; H, 5.42; N, 5.02. Found: C, 71.15; H, 5.47; N, 5.14.

Methyl 1,2,6-tri-p-tolyl-4-(p-tolylamino)-1,2,5,6-tetra hydropyridine-3-carboxylate **(1h)**

75%. mp: 205–207 °C. IR (KBr): 1656, 1594 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.16 (s,1H), 7.19 (d, J = 8.2 Hz, 2H), 7.06–7.08 (m, 4H), 7.03 (d, J = 7.9 Hz, 2H), 6.88 (d, J = 7.9 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 6.42 (d, J = 8.8 Hz, 2H), 6.34 (s, 1H), 6.16 (d, J = 8.2 Hz, 2H), 5.06–5.07 (m, 1H), 3.90 (s, 3H), 2.81 (dd, J = 15.3, 5.8 Hz, 1H), 2.71 (dd, J = 15.3, 2.4 Hz, 1H), 2.33 (s, 3H), 2.31 (s, 3H), 2.26 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.7, 156.7, 145.0, 141.4, 140.0, 136.6, 135.7, 135.6, 135.3, 129.5, 129.3, 129.0, 126.7, 126.4, 126.0, 124.9, 112.9, 97.6, 58.0, 55.1, 51.0, 33.7, 21.2, 21.1, 21.0, 20.2. Elemental analysis calc. for $C_{35}H_{36}N_2O_2$ (516.67): C, 81.36; H, 7.02; N, 5.42. Found: C, 81.44; H, 7.08; N, 5.56.

*Methyl 1-(4-methoxyphenyl)-4-(4-methoxyphenylamino)-2,6-dip-tolyl-1,2,5,6-tetrahydropyridine-3-carboxy-late (***1i***)*

73%. mp: 223–225 °C. IR (KBr): 1656, 1611 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.09 (s,1H), 7.17 (d, J = 8.2 Hz, 2H), 7.08 (d, J = 7.8 Hz, 2H), 7.05 (d, J = 7.8 Hz, 2H), 7.03 (d, J = 8.2 Hz, 2H), 6.65 (d, J = 9.1 Hz, 2H), 6.61 (d, J = 8.7 Hz, 2H), 6.44 (d, J = 9.1 Hz, 2H), 6.27 (s, 1H), 6.21 (d, J = 8.7 Hz, 2H), 5.00–5.01 (m, 1H), 3.89 (s, 3H), 3.74 (s, 3H), 3.65 (s, 3H), 2.77 (dd, J = 15.1, 5.9 Hz, 1H), 2.63 (dd, J = 15.1, 2.3 Hz, 1H), 2.34 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) : δ = 168.8, 157.9, 157.2, 151.0, 141.9, 141.5, 140.4, 136.7, 135.8, 131.0, 129.4, 129.0, 128.0, 126.9, 126.6, 114.6, 114.2, 114.1, 97.3, 58.1, 55.8, 55.7, 55.6, 51.0, 33.8, 21.3, 21.2. Elemental analysis calc. for $C_{35}H_{36}N_2O_4$ (548.67): C, 76.62; H, 6.61; N, 5.11. Found: C, 76.51; H, 6.68; N, 5.24.

*Ethyl 1,2,6-triphenyl-4-(phenylamino)-1,2,5,6-tetrahydro-pyridine-3-carboxylate (***1j***)*

73%. mp: 172–174 °C. IR (KBr): 1651, 1594 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.30 (s,1H), 7.35 (d, J = 7.6 Hz, 2H), 7.25–7.30 (m, 5H), 7.22 (d, J = 7.0 Hz, 1H), 7.17–7.20 (m, 2H), 7.06–7.12 (m, 5H), 6.61 (t, J = 7.0 Hz, 1H), 6.53 (d, J = 8.5 Hz, 2H), 6.47 (s, 1H), 6.27–6.29 (m, 2H), 5.15–5.16 (m, 1H), 4.40–4.50 (m, 1H), 4.31–4.37 (m, 1H), 2.89 (dd, J = 15.0, 5.8 Hz, 1H), 2.77 (dd, J = 15.0, 2.4 Hz, 1H), 1.48 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.3, 156.2, 147.1, 144.1, 142.8, 138.0, 129.0, 128.9, 128.7, 128.3, 127.2, 126.7, 126.5, 126.4, 125.9, 125.8, 116.2, 113.0, 98.3, 59.8, 58.3, 55.2, 33.7, 14.9. Elemental analysis calc. for $C_{32}H_{30}N_2O_2$ (474.59): C, 80.98; H, 6.37; N, 5.90. Found: C, 80.89; H, 6.43; N, 6.04.

*Ethyl 2,6-bis(4-chlorophenyl)-1-phenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (***1k***)*

74%. mp: 206–208 °C. IR (KBr): 1652, 1597 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$) δ: 10.27 (s, 1H), 7.21–7.25 (m, 8H), 7.03–7.16 (m, 5H), 6.64 (t, J = 6.8 Hz, 1H), 6.45 (d, J = 8.2 Hz, 2H), 6.39 (d, J = 7.3 Hz, 2H), 6.35 (s, 1H), 5.07–5.08 (m, 1H), 4.42–4.45 (m, 1H), 4.31–4.33 (m, 1H), 2.80 (dd, J = 15.1, 6.0 Hz, 1H), 2.75 (dd, J = 15.1, 2.4 Hz, 1H), 1.44 (t, J = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ:168.1, 155.9, 146.6, 142.5, 141.0, 137.7, 132.9, 132.2, 129.1, 129.0, 128.9, 128.5, 128.1, 127.9, 126.0, 125.8, 116.8, 113.0, 97.8, 59.9, 57.5, 54.8, 33.8, 14.8. Elemental analysis calc. for $C_{32}H_{28}Cl_2N_2O_2$ (543.49) : C, 70.72; H, 5.19; N, 5.15. Found: C, 70.79; H, 5.12; N, 5.27.

*Ethyl1-phenyl-4-(phenylamino)-2,6-di-p-tolyl-1,2,5,6-tetra hydropyridine-3-carboxylate (***1l***)*

72%. mp: 229–230 °C. IR (KBr): 1650, 1592 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.28 (s,1H), 7.21 (d, J = 7.8 Hz, 2H), 7.04–7.07 (m, 11H), 6.58 (t, J = 7.3 Hz, 1H), 6.52 (d, J = 8.2 Hz, 2H), 6.40 (s, 1H), 6.29 (d, J = 6.8 Hz, 2H), 5.09–5.10 (m, 1H), 4.42–4.44 (m, 1H), 4.29–4.33 (m, 1H), 2.86 (dd, J = 15.1, 5.5 Hz, 1H), 2.75 (dd, J = 15.1, 2.4 Hz, 1H), 2.33 (s, 3H), 2.31 (s, 3H), 1.45 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.4, 156.2, 147.2, 141.2, 139.9, 138.2, 136.7, 135.9, 129.4, 129.1, 129.0, 128.9, 126.7, 126.5, 125.9, 125.7, 116.1, 113.1, 98.6, 59.8, 58.1, 55.0, 33.8, 21.3, 21.2, 15.0. Elemental analysis calc. for $C_{34}H_{34}N_2O_2$ (502.65): C, 81.24; H, 6.82; N, 5.57. Found: C, 81.34; H, 6.90; N, 5.71.

Methyl 1-benzyl-4-(benzylamino)-2,6-dip-tolyl-1,2,5,6-tetrahydropyridine-3-carboxylate **(1m)**

45%. mp: 171–173 °C. IR (KBr) : 1649, 1597 cm^{-1}.^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.66 (t, J = 5.6 Hz, 1H), 7.35–7.38 (m, 6H), 7.31 (t, J = 7.2 Hz, 3H), 7.17–7.24 (m, 5H), 7.07 (t, J = 8.4 Hz, 4H), 4.73 (s, 1H), 4.62 (dd, J = 15.6, 6.0 Hz, 1H), 4.54 (dd, J = 15.6, 6.0 Hz, 1H), 4.01 (dd, J = 11.6, 5.2 Hz, 1H), 3.45 (s, 3H), 3.33 (d, J = 13.6 Hz, 1H), 3.31 (d, J = 13.6 Hz, 1H), 2.70 (dd, J = 17.2,11.6 Hz, 1H), 2.61 (dd, J = 17.2, 5.2 Hz, 1H), 2.30 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.3, 159.0, 141.9, 140.5, 139.2, 138.8, 136.8, 135.8, 129.2, 129.1, 128.8, 128.5, 128.3, 127.6, 127.4, 127.0, 126.9, 89.5, 58.2, 52.3, 50.6, 49.8, 46.4, 33.1, 25.7, 21.3. Elemental analysis calc. for $C_{35}H_{36}N_2O_2$ (516.67): C, 81.36; H, 7.02; N, 5.42. Found: C, 81.47; H, 7.09; N, 5.30.

*Methyl 1-butyl-4-(butylamino)-2,6-dip-tolyl-1,2,5,6-tetra hydropyridine-3-carboxylate (***1n***)*

60%. mp:153–155 °C. IR (KBr) : 1645, 1597 cm^{-1}.^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.20 (m, 1H), 7.31 (d, J = 7.6 Hz, 2H), 7.17 (d, J = 7.6 Hz, 2H), 7.06 (d, J = 7.6 Hz, 2H), 7.04 (d, J = 7.6 Hz, 2H), 4.92 (s, 1H), 3.82 (dd, J = 11.2, 5.2 Hz, 1H), 3.53 (s, 3H), 3.25–3.34 (m, 2H), 2.59 (dd, J = 17.2, 11.2 Hz, 1H), 2.48 (dd, J = 17.2, 5.2 Hz, 1H), 2.32 (s, 3H), 2.27 (s, 3H), 2.07-2.15 (m, 2H), 1.56-1.67 (m, 2H), 1.41–1.51 (m, 2H), 1.25–1.34 (m, 2H), 1.08–1.20 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H), 0.78 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.4, 159.7, 142.5, 139.3, 136.4, 135.6, 128.9, 128.8, 128.4, 127.4, 88.0, 58.5, 52.5, 50.6, 44.8, 42.1, 32.6, 31.1, 25.6, 21.3, 20.6, 20.5, 14.3, 14.1. Elemental analysis calc. for $C_{29}H_{40}N_2O_2$ (448.64): C, 77.64; H, 8.99; N, 6.24. Found: C, 77.75; H, 8.91; N, 6.37.

*Methyl 1-(naphthalen-2-yl)-4-(naphthalen-2-ylamino)-2,6-diphenyl-1,2,5,6-tetrahydropyridine-3-carboxylate (***1o***)*

57%. mp: 197–199 °C. IR (KBr): 3442, 1666, 1598 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.45 (s,1H), 7.75 (d, J = 7.4 Hz, 1H), 7.59 (t, J = 8.6 Hz, 2H), 7.52–7.55 (m, 2H), 7.40–7.45 (m, 3H), 7.32–7.35 (m, 4H), 7.20–7.31 (m, 7H), 7.11 (t, J = 8.0 Hz, 1H), 6.97 (dd, J = 9.2, 2.6 Hz, 1H), 6.76 (d, J = 2.3 Hz, 1H), 6.65 (s, 1H), 6.58 (s, 1H), 6.54 (dd, J = 8.6, 2.3 Hz, 1H), 5.29 (s, 1H), 3.98 (s, 3H), 2.91–2.95 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8, 156.4, 145.1, 144.0, 143.1, 135.5, 135.0, 133.5, 131.6, 129.1, 128.8, 128.5, 127.8, 127.7, 127.5, 127.4, 126.9, 126.7, 126.5, 126.2, 125.9, 125.0, 123.3, 122.0, 116.2, 107.2, 98.4, 58.6, 55.5, 51.3, 33.8. Elemental analysis calc. for $C_{39}H_{32}N_2O_2$ (560.68): C, 83.54; H, 5.75; N, 5.00. Found: C, 83.42; H, 5.82; N, 5.14.

Procedure for the preparation of **1p:**

In a round-bottom flask, a mixture of aniline (1.0 mmol) and methyl acetoacetate (1.0 mmol) was stirred in the presence of 10 mol% VCl_3. After 1 h, to this solution 1.0 mmol 4-methoxy benzaldehyde was added under stirring. Subsequently, to this mixture in situ imine prepared in a separate reaction flask from the 1.0 mmol aniline and 1.0 mmol 4-methybenzaldehyde was added and stirred for 6 h. After completion of the reaction, the solvent was removed using a rotavapor and the product was purified by silica gel column chromatography.

*Methyl 2-(4-methoxyphenyl)-1-phenyl-4-(phenylamino)-6-p-tolyl-1,2,5,6- tetrahydropyridine-3-carboxylate (***1p***)*

25%. mp: 160–162 °C. IR (KBr): 3454, 1655, 1594 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.27 (s,1H), 7.20 (d, J = 8.2 Hz, 2H), 7.03–7.12 (m, 9H), 6.82 (d, J = 8.6 Hz, 2H), 6.60 (t, J = 7.3 Hz, 1H), 6.53 (d, J = 8.2 Hz, 2H), 6.30–6.39 (m, 3H), 5.10–5.11 (m, 1H), 3.92 (s, 3H), 3.78 (s, 3H), 2.86 (dd, J = 15.3, 5.5 Hz, 1H), 2.75 (dd, J = 15.3, 2.4 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.7, 158.8, 156.4, 147.1, 140.9, 138.0, 135.9, 134.8, 129.3, 128.9, 127.8, 127.5, 126.4, 125.8, 116.1, 114.1, 113.6, 113.0, 98.1, 57.9, 55.3, 54.7, 51.0, 33.8, 21.2. Elemental analysis calc. for $C_{33}H_{32}N_2O_3$ (504.62): C, 78.55; H, 6.39; N, 5.55. Found: C, 76.66; H, 6.47; N, 5.68.

General procedure for the preparation of β-amino ketones (**2a–l**)

In a round-bottom flask, a mixture of aromatic aldehyde (1.0 mmol), aromatic amine (1.0 mmol), aromatic ketone (1.0 mmol), and VCl_3 (0.1mmol) in 3 mL ethanol was stirred at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction, the crude solid was filtered off and washed with ethanol. The crude solid was purified by recrystallization from ethanol to afford pure product.

*1,3-Diphenyl-3-(phenylamino)propan-1-one (***2a***)*

91%. mp: 171–172 °C. IR (KBr): 3396, 1671 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.89 (d, J = 7.3 Hz, 2H), 7.55 (t, J = 7.3 Hz, 1H), 7.42–7.45 (m, 4H), 7.31 (t, J = 7.3 Hz, 2H), 7.21–7.24 (m, 1H), 7.10 (t, J = 7.3 Hz, 2H), 6.72 (t, J = 7.3 Hz, 1H), 6.63 (d, J = 8.2 Hz, 2H), 5.00–5.02 (m, 1H), 3.58 (dd, J = 16.5, 5.5 Hz, 1H), 3.50 (dd, J = 16.5, 7.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.4, 147.1, 143.1, 136.8, 133.5, 129.2, 128.9, 128.8, 128.3, 127.4, 126.5, 117.9, 113.9, 54.9, 46.4. Elemental analysis calc. for

$C_{21}H_{19}NO$ (301.38): C, 83.69; H, 6.35; N, 4.65. Found: C, 83.60; H, 6.28; N, 4.78.

*1-Phenyl-3-(phenylamino)-3-p-tolylpropan-1-one (**2b**)*

90%. mp: 138–140 °C. IR (KBr): 3385, 1667 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, J = 7.3 Hz, 2H), 7.58 (t, J = 7.3 Hz, 1H), 7.40 (t, J = 7.8 Hz, 2H), 7.35 (d, J = 8.2 Hz, 2H), 7.07–7.16 (m, 4H), 6.72 (t, J = 7.3 Hz, 1H), 6.64 (d, J = 8.0 Hz, 2H), 4.97 (m, 1H), 3.46–3.72 (m, 2H), 2.30 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.5, 147.1, 140.0, 137.0, 136.8, 133.5, 129.6, 129.2, 128.8, 128.3, 126.3, 117.8, 113.9, 54.6, 46.4, 21.2. Elemental analysis calc. for $C_{22}H_{21}NO$ (315.41): C, 83.78; H, 6.71; N, 4.44. Found: C, 83.89; H, 6.76; N, 4.56.

*3-(4-Methoxyphenyl)-1-phenyl-3-(phenylamino)-propan-1-one (**2c**)*

88%. mp: 151–152 °C. IR (KBr): 3377, 1666 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d,J = 7.2 Hz, 2H), 7.56 (t,J = 7.2 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 7.36 (d, J = 8.8 Hz, 2H), 7.11 (t, J = 8.4 Hz, 2H), 6.84 (d, J = 8.4 Hz, 2H), 6.75 (t, J = 7.2 Hz, 1H), 6.64 (d, J = 8.0 Hz, 2H), 4.96 (t, J = 6.4 Hz, 1H), 3.76 (s, 3H), 3.50–3.55 (m,2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.5, 158.8, 147.1, 136.8, 135.0, 133.5, 129.2, 128.8, 128.3, 127.5, 117.8, 114.3, 113.9, 55.3, 54.3, 46.4. Elemental analysis calc. for $C_{22}H_{21}NO_2$ (331.41): C, 79.73; H, 6.39; N, 4.23. Found: C, 79.62; H, 6.45; N, 4.35.

*3-(4-Chlorophenylamino)-3-(4-methoxyphenyl)-1-phenylpropan-1-one (**2d**)*

87%. mp: 151–152 °C. IR (KBr): 3384, 1669 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, J = 8.0 Hz, 2H), 7.55 (t, J = 7.3 Hz, 1H), 7.42 (t, J = 7.8 Hz, 2H), 7.32(d, J = 8.5 Hz, 2H), 7.17 (d, J = 8.8 Hz, 2H), 7.05 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 8.6 Hz, 2H), 4.88 (t, J = 6.4 Hz, 1H), 3.75 (s,3H), 3.58 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.4, 158.9, 145.7, 136.7, 134.5, 133.6, 129.0, 128.8, 128.3, 127.5, 122.4, 115.0, 114.3, 55.4, 54.4, 46.4. Elemental analysis calc. for $C_{22}H_{20}ClNO_2$ (365.85): C, 72.22; H, 5.51; N, 3.83. Found: C, 72.30; H, 5.58; N, 3.96.

*3-(4-Nitrophenylamino)-1,3-diphenylpropan-1-one (**2e**)*

87%. mp: 176–177 °C. IR (KBr): 3361, 1685 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, J = 9.2 Hz, 2H), 7.89 (d, J = 7.2 Hz, 2H), 7.58 (t, J = 7.2 Hz,1H), 7.45 (t, J = 7.6 Hz, 2H), 7.38 (t, J = 7.2 Hz, 3H), 7.34 (d, J = 8.0 Hz, 1H), 7.28 (d, J = 7.2 Hz, 1H), 6.52 (d, J = 9.2 Hz, 2H), 5.10 (t, J = 6.0 Hz, 1H), 3.54 (d, J = 6.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.0, 152.2, 141.2, 138.6, 136.4, 133.9, 129.2, 128.9, 128.2, 128.0, 126.3, 126.2, 112.3, 54.4, 45.6. Elemental analysis calc. for $C_{21}H_{18}N_2O_3$ (346.38): C, 72.82; H, 5.24; N, 8.09. Found: C, 72.92; H, 5.32; N, 8.22.

*3-(4-Chlorophenylamino)-1,3-diphenylpropan-1-one (**2f**)*

84%. mp: 171–172 °C. IR (KBr): 3373, 1665 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, J = 7.6 Hz, 2H), 7.57 (t, J = 7.6 Hz, 1H), 7.40–7.45 (m, 4H), 7.32 (t, J = 8.0 Hz, 2H), 7.22 (t, J = 7.6 Hz, 1H), 7.02 (d, J = 8.8 Hz, 2H), 6.47 (d, J = 8.0 Hz, 2H), 4.95 (m, 1H), 4.62 (s, 1H), 3.50 (dd, J = 16.0, 4.8 Hz, 1H), 3.42 (dd, J = 16.0, 7.6 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.3, 145.6, 142.6, 136.6, 133.7, 129.0, 128.8, 128.3, 127.6, 126.4, 122.5, 115.0, 54.9, 46.3. Elemental analysis calc. for $C_{21}H_{18}ClNO$ (335.83): C, 75.11; H, 5.40; N, 4.17. Found: C, 75.01; H, 5.46; N, 4.29.

*1,3-Diphenyl-3-(p-tolylamino)propan-1-one (**2g**)*

87%. mp: 170–171 °C. IR (KBr): 3396, 1684 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.90 (d, J = 7.3 Hz, 2H), 7.55 (t, J = 7.3 Hz, 1H), 7.42–7.45 (m, 4H), 7.31 (t, J = 7.3 Hz, 2H), 7.23 (t, J = 7.8 Hz, 1H), 6.90 (d, J = 7.8 Hz, 2H), 6.51 (d, J = 8.2 Hz, 2H), 4.96–4.99 (m,1H), 3.53 (dd, J = 16.5, 5.5 Hz, 1H), 3.45 (dd, J = 16.5, 7.8 Hz, 1H), 2.18 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.4, 144.7, 143.2, 136.7, 133.5, 129.7, 128.9, 128.8, 128.3, 127.4, 127.1, 126.5, 114.0, 55.1, 46.5, 20.5. Elemental analysis calc. for $C_{22}H_{21}NO$ (315.41): C, 83.78; H, 6.71; N, 4.44. Found: C, 83.66; H, 6.78; N, 4.57.

*4-(3-Oxo-1,3-diphenylpropylamino)benzonitrile (**2h**)*

81%. mp: 151–152 °C. IR (KBr): 3386, 2223, 1671 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.88 (d, J = 7.0 Hz, 2H), 7.57 (t, J = 7.3 Hz, 1H), 7.44 (t, J = 7.9 Hz, 2H), 7.38 (d, J = 7.3 Hz, 2H), 7.31–7.34 (m, 4H), 7.57 (t, J = 7.3 Hz, 1H), 7.25 (t, J = 7.6 Hz, 1H), 6.54 (d, J = 8.6 Hz, 2H), 5.01–5.04 (m, 1H), 3.48–3.53 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.0, 150.3, 141.6, 136.8, 133.8, 133.7, 129.2, 128.9, 128.3, 127.9, 126.2, 120.4, 113.4, 99.5, 54.3, 45.8. Elemental analysis calc. for $C_{22}H_{18}N_2O$ (326.39):C, 80.96; H, 5.56; N, 8.58. Found: C, 80.84; H, 5.63; N, 8.71.

*3-(4-Chlorophenyl)-3-(4-nitrophenylamino)-1-phenylpropan-1-one (**2i**)*

79%. mp: 152–153 °C. IR (KBr): 3373, 1685, 1597, 1300 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.99 (d, J = 8.1 Hz, 2H), 7.87 (d, J = 7.3 Hz, 2H), 7.58 (t, J = 7.3 Hz, 1H), 7.45 (t, J = 7.8 Hz, 2H), 7.33 (d, J = 8.7 Hz, 2H), 7.30 (d, J = 8.7 Hz, 2H), 6.50 (d, J = 9.1 Hz, 2H), 5.58 (d,J = 6.4

Hz, 1H), 5.08 (q, J = 6.0 Hz, 1H), 3.54 (dd, J = 16.5, 6.4 Hz, 1H), 3.49 (dd, J = 16.5, 5.5 Hz, 1H).^{13}C NMR (125 MHz, $CDCl_3$): δ = 197.6, 152.1, 139.8, 138.6, 136.3, 134.0, 133.7, 129.4, 129.0, 128.2, 127.7, 126.3, 112.3, 53.7, 45.4. Elemental analysis calc. for $C_{21}H_{17}ClN_2O_3$ (380.82): C, 66.23; H, 4.50; N, 7.36. Found: C, 66.34; H, 4.44; N, 7.49.

*1-(4-Bromophenyl)-3-(4-chlorophenylamino)-3-phenyl-propan-1-one (***2j***)*

82%. mp: 143–145 °C. IR (KBr): 3362, 1679 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.72 (d, J = 8.6 Hz, 2H), 7.57 (d, J = 8.5 Hz, 2H), 7.38 (d, J = 7.6 Hz, 2H), 7.31 (t, J = 7.6 Hz, 2H), 7.24 (t, J = 7.0 Hz, 1H), 7.03 (d, J = 8.8 Hz, 2H), 6.53 (d, J = 8.6 Hz, 2H), 4.93 (t, J = 6.4 Hz, 1H), 3.47 (d, J = 6.1 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 197.3, 145.5, 142.3, 135.3, 132.1, 129.8, 129.1, 128.9, 128.3, 127.7, 126.3, 122.6, 115.0, 54.8, 46.2. Anal. Calcd for $C_{21}H_{17}BrClNO$ (414.73) : C, 60.82; H, 4.13; N, 3.38. Found: C, 60.75; H, 4.08; N, 3.46.

*1-(4-bromophenyl)-3-phenyl-3-(phenylamino)propan-1-one (***2k***)*

90%. mp: 139–141 °C. IR (KBr): 3378, 1671 cm^{-1}.^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.73 (d, J = 8.4 Hz, 2H), 7.56 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 6.8 Hz, 2H), 7.30 (t, J = 7.6 Hz, 2H), 7.21–7.25 (m, 1H), 7.11 (t, J = 7.2 Hz, 2H), 6.74 (t, J = 7.2 Hz, 1H), 6.65 (d, J = 6.8 Hz, 2H), 4.98–5.01 (m, 1H), 3.51–3.53 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 197.4, 146.9, 142.8, 135.5, 132.1, 129.8, 129.2, 128.9, 128.8, 127.5, 126.4, 118.0, 113.9, 54.8, 46.2. Elemental analysis calc. for $C_{21}H_{18}BrNO$ (380.28): C, 66.33; H, 4.77; N, 3.68. Found: C, 66.27; H, 4.23; N, 3.74.

*1-(4-bromophenyl)-3-(4-chlorophenyl)-3-(4-nitro phenyl amino)propan-1-one (***2l***)*

75%. mp: 138–140 °C. IR (KBr): 3387, 1668 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.01 (d,J = 9.1 Hz, 2H), 7.72 (d, J = 8.2 Hz, 2H), 7.59 (d, J = 8.2 Hz, 2H), 7.31 (s, 4H), 6.49 (d, J = 9.1 Hz, 2H), 5.48 (d, J = 6.0 Hz, 1H), 5.03–5.07 (m, 1H), 3.49 (dd, J = 16.5 and 6.8 Hz, 1H), 3.44 (dd, J = 16.5 and 5.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 196.6, 151.8, 139.5, 138.8, 136.5, 134.1, 132.3, 130.1, 129.7, 129.4, 127.6, 126.2, 112.3, 53.7, 45.2. Elemental analysis calc. for $C_{21}H_{16}BrClN_2O_3$ (459.72): C, 54.86; H, 3.51; N, 6.09. Found: C, 54.89; H, 3.48; N, 6.14.

*2-(Phenyl(phenylamino)methyl)cyclohexanone (***3a***)*

82%. mp: 115–116 °C. IR (KBr): 3381, 1694 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37 (d, J = 7.5 Hz, 2H), 7.29 (t, J = 7.5 Hz, 2H), 7.20 (t, J = 7.2 Hz, 1H), 7.06 (t, J = 7.9 Hz, 2H), 6.64 (t, J = 7.2 Hz, 1H), 6.55 (d, J = 7.9 Hz, 2H), 4.80 (d, J = 4.4 Hz, 1H), 4.61 (d, J = 7.2 Hz, 1H), 2.78–2.81 (m, 1H), 2.31–2.46 (m, 2H), 1.84–1.92 (m, 4H), 1.58–1.68 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 213.0, 147.3, 141.8, 129.1, 128.7, 127.3, 127.2, 117.6, 113.7, 58.0, 57.5, 41.9, 31.4, 28.6, 23.7. Elemental analysis calc. for $C_{19}H_{21}NO$ (279.38): C, 81.68; H, 7.58; N, 5.01. Found: C, 81.80; H, 7.65; N, 5.14.

*Diethyl 2-(phenyl(phenylamino)methyl)malonate (***3b***)*

87%. mp: 92–94 °C. IR (KBr): 3376, 1727, 1731, 1603, 1518, 1295.cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 (d, J = 7.3 Hz, 2H), 7.28 (t, J = 7.3 Hz, 2H), 7.21 (t, J = 7.3 Hz, 1H), 7.08 (t, J = 7.9 Hz, 2H), 6.65 (t, J = 7.3 Hz, 1H), 6.59 (d, J = 7.9 Hz, 2H), 5.29 (m, 1H), 5.21 (d, J = 5.8 Hz, 1H), 4.13 (q, J = 7.0 Hz, 2H), 4.07 (q, J = 7.0 Hz, 2H), 3.89 (d, J = 5.8 Hz, 1H), 1.15 (t, J = 7.0 Hz, 3H), 1.11 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 167.5, 146.5, 139.9, 129.3, 128.8, 127.8, 126.4, 118.0, 113.9, 62.0, 61.7, 58.4, 57.2, 14.1. Elemental analysis calc. for $C_{20}H_{23}NO_4$ (341.40): C, 70.36; H, 6.79; N, 4.10. Found: C, 70.47; H, 6.85; N, 4.23.

Procedure for the synthesis of **3c** and **3d**

A solution of 4-chlorobenzaldehyde (1.0 mmol), aniline (1.0 mmol), and VCl_3 (0.1 mmol) was stirred in 3 mL of ethanol at room temperature. After complete formation of the imine, as indicated by TLC, malononitrile/ethyl cyanoacetate (1.0 mmol) was added to the mixture, and stirring was continued for completion. The product precipitated from the reaction mixture. The precipitate was filtered off, dissolved in hot EtOH to afford pure final material.

*Ethyl 3-(4-chlorophenyl)-2-cyanoacrylate (***3c***)*

75%. mp: 87 °C. IR (KBr): 2242, 1760, 1581 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.17 (s, 1H), 7.91 (d, J = 8.5 Hz, 2H), 7.45 (d, J = 8.5 Hz, 2H), 4.36 (q, J = 7.3 Hz, 2H), 1.38 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.3, 153.4, 139.6, 132.3, 129.9, 129.7, 115.3, 103.6, 62.9, 14.2. Elemental analysis calc. for $C_{12}H_{10}ClNO_2$ (235.66): C, 61.16; H, 4.28; N, 5.94. Found: C, 61.28; H, 4.20; N, 5.81.

*2-(4-Chlorobenzylidene)malononitrile (***3d***)*

82%. mp: 162 °C. IR (KBr): 2227, 1585 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.85 (d, J = 8.2 Hz, 2H), 7.73 (s, 1H), 7.52 (d, J = 8.2 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.4, 141.2, 131.9, 130.2, 129.4, 113.5, 112.4, 83.4.

Elemental analysis calc. for $C_{10}H_5ClN_2$ (188.61) : C, 63.68; H, 2.67; N, 14.85. Found: C, 63.79; H, 2.61; N, 14.72.

Procedure for the synthesis of (**3e**)

In a 25 mL round-bottom flask, dimedone (2.0 mmol), 4-chlorobenzaldehyde (1.0 mmol) and 4-cyanoaniline (1.0 mmol) in ethanol (5 mL) were mixed and stirred under refluxing conditions. To this, VCl_3 (10 mol %) was added. The progress of the reaction mixture was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature. A precipitate was formed, filtered off, and washed with cold EtOH to afford pure product.

*4-(9-(4-chlorophenyl)-3,3,6,6-tetramethyl-1,8-dioxo-1,2,3,4,5,6,7,8-octahydroacridin-10(9H)-yl)benzonitrile (***3e***)*

81%. mp: 242–244 °C. IR (KBr): 2233, 1650, 1583, 1508 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.89$ (d, $J = 8.0$ Hz, 2H), 7.39 (d, $J = 8.0$ Hz, 2H), 7.32 (d, $J = 8.3$ Hz, 2H), 7.20 (d, $J = 8.3$ Hz, 2H), 5.21 (s, 1H), 2.19 (d, $J = 16.3$ Hz, 2H), 2.13 (d, $J = 16.3$ Hz, 2H), 2.02 (d, $J = 17.1$ Hz, 2H), 1.73 (d, $J = 17.4$ Hz, 2H), 0.95 (s, 6H), 0.80 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 195.6, 148.5, 144.3, 143.2, 134.2, 131.9, 131.0, 129.3, 128.4, 117.4, 115.0, 114.0, 50.1, 42.0, 32.7, 32.5, 29.7, 26.9$. Elemental analysis calc. for $C_{30}H_{29}ClN_2O_2$ (485.02): C, 74.29; H, 6.03; N, 5.78. Found: C, 74.18; H, 5.95; N, 5.65.

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