Tetrahedron 66 (2010) 7762–7772

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Iodine catalyzed one-pot five-component reactions for direct synthesis of densely functionalized piperidines

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ARTICLE INFO

Article history:
Received 11 April 2010
Received in revised form 22 July 2010
Accepted 24 July 2010
Available online 3 August 2010

Keywords:
Heterocycles
Piperidines
Iodine
1,3-Dicarbonyl compounds
Amines
Aldehydes

ABSTRACT

A simple and convenient one-pot multicomponent reaction (MCR) has been developed for the synthesis of highly functionalized piperidines catalyzed by molecular iodine. This strategy demonstrated five-component reactions of 1,3-dicarbonyl compounds, amines and aromatic aldehydes in methanol using 10 mol % of iodine at room temperature. This methodology provides an alternative approach for easy access of highly and fully substituted piperidines in moderate to good yields using three readily available starting materials. Notably, this method is mild, cheap, straight forward, applicable to broad range of substrates and environmentally friendly as compared to the existing methods. Synthetic and mechanistic studies are presented here.

1. Introduction

The piperidine and its analogues are widely distributed in many natural products, biologically active molecules and organic fine chemicals.[1] Some of them also act as therapeutic agents.[2] Compounds containing piperidine structural motif exhibit anti-hypertensive,[3] anti-bacterial,[4] anti-convulsant and anti-inflammatory activities.[5] Recently, Tripathi et al. reported that some of the substituted piperidines also display antimalarial activity.[6] As a result, a considerable efforts have been made from all over the world towards the synthesis of this important class of compounds due to their medicinal properties.[7] Some of the synthetic strategies for their preparation are imino-Diels-Alder reactions,[8] aza-Prins-cyclizations,[9] intramolecular Michael reactions[10] and intramolecular Mannich reaction onto iminium ions.[11] An alternative strategy for the synthesis of functionalized piperidines is using multicomponent reactions (MCRs). Recently, MCRs have emerged as a powerful synthetic tool in organic synthesis due to their advantages over the conventional multi-step synthesis.[12,13] In addition, MCRs are eco-friendly, superior atom economic as well as they avoid costly purification processes and protection-deprotection steps with minimum synthetic effort and time.[14] Therefore, MCRs satisfy some of the tenets of 'Green Chemistry'. Literature reveals only a few methods to synthesis highly functionalized piperidine derivatives via MCRs using catalysts, such as a combination of L-proline/TFA,[6] bromodimethylsulfonium bromide (BDMS),[15a] tetrabutylammonium tribromide (TBATB)[15b] and $InCl_3$.[16] The aforesaid methods have some of the disadvantages such as use of expensive and excess amount of catalysts and failure in some of the cases to obtain the desired product. Therefore, there is a need for simple and greener methods, which are applicable to a broad range of substrates to access these compounds.

Molecular iodine has emerged as an inexpensive, non-toxic, non-metallic, readily available and environmentally benign catalyst for various organic transformations, which has been reviewed recently.[17] The current literature reveals that molecular iodine can be used as an efficient catalyst for a diverse range of multicomponent reactions[18a–d] as well as synthesis of various heterocycles.[18e–h] We conceived that molecular iodine is to be an ideal Lewis acid for one-pot synthesis of highly substituted piperidine derivatives from aromatic aldehydes, amines and β-keto esters. Herein, we disclose the synthesis and mechanistic aspects of densely functionalized piperidine derivatives (**1**) using MCRs (Scheme 1).

2. Results and discussion

Initially, the mixture of 4-methylbenzaldehyde (1 mmol), aniline (1 mmol) and methyl acetoacetate (1 mmol) in acetonitrile (5 mL) was treated with 10 mol % of iodine at room temperature. We obtained a highly functionalized piperidine **1a** in 36% yield

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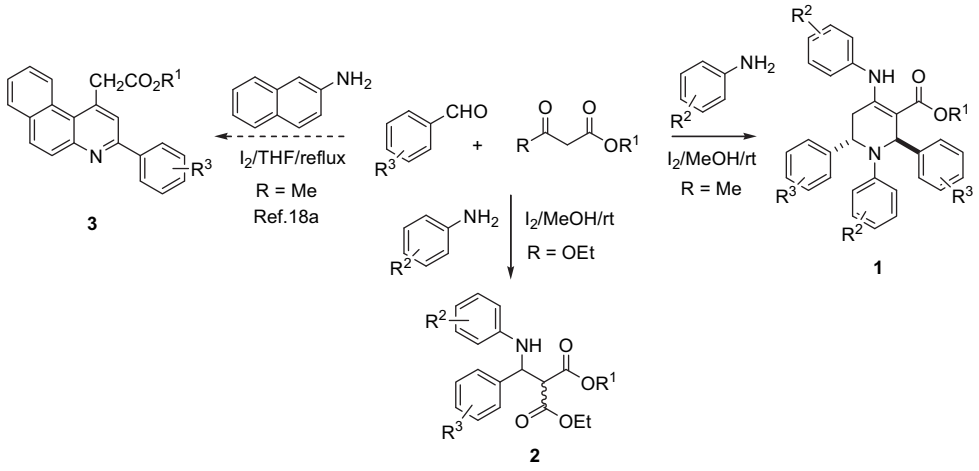
doi:10.1016/j.tet.2010.07.075



Scheme 1. Direction of product formation in iodine catalyzed MCRs.

along with unreacted methyl acetoacetate and the product was characterized from ^{1}H NMR, ^{13}C NMR spectra, HRMS and by elemental analysis. It is quite clear that the product **1a** was obtained via five-component reactions.

For optimization of the amount of catalyst and choosing the suitable solvent, various trial reactions were investigated with a combination of 4-methylbenzaldehyde, aniline and methyl acetoacetate to obtain the best yield of **1a**, which is summarized in Table 1. We have noted that 10 mol % of the catalyst gives the best result for the formation of product. It has also been observed that methanol is the best solvents for the present reaction among various other solvents, such as acetonitrile, dichloromethane, ethanol and ethyl acetate. For this transformation, ethanol can be a second choice of solvent. Under solvent-free conditions, the product was obtained in a moderate yield (48%) that may be due to lack of effective interaction of reactants with the catalyst in the absence of solvent.

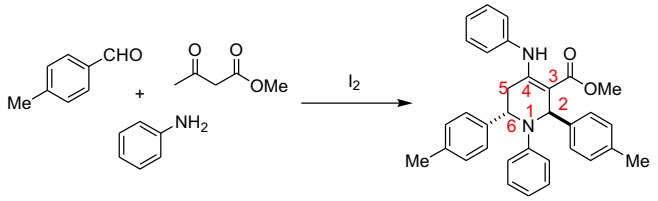
Having established the optimal reaction conditions, the mixture of 4-methylbenzaldehyde, aniline and ethyl acetoacetate in methanol was treated with 10 mol % iodine to obtain the desired piperidine derivative **1b** as shown in Table 2. Similarly, various other β-keto esters like *tert*-butyl acetoacetate and allyl acetoacetate also provided the corresponding piperidine derivatives **1c** and **1d** in good yields (Table 2, entries 3 and 4). From these observations, we may conclude that the alkoxy (−OR) moiety present in the β-keto ester does not have any significant role in determining the course of the reaction. However, in case of diethylmalonate (Table 2, entry 5), yielded the corresponding β-amino carbonyl compound (**2**) under identical reaction conditions. This can be attributed to the lack of enolizable alkyl group in the β-position.

In addition, the effect of an alkyl group was also studied by varying the substitutents at the β-position of the β-keto esters. The reaction of ethyl propionylacetate with 4-chlorobenzaldehyde and aniline afforded fully substituted piperidine **1e** in 42% yield in the presence of 10 mol % molecular iodine (Table 2, entry 6). Similarly, the reaction of ethyl butyrylacetate with 4-chlorobenzaldehyde and aniline also provided the desired piperidine **1f** in 36% yield under similar reaction conditions (Table 2, entry 7). The fully substituted piperidine derivatives were derivatives not reported earlier.[6,15a,16] From these observations, it is clear that methyl and ethyl group can be introduced easily at the 5-position of the piperidine ring by choosing a suitable β-keto ester. Next, we wanted to incorporate a phenyl group at the 5-position in the piperidine ring. For this purpose, the required β-keto ester (ethyl 3-oxo-4-phenylbutanoate) was prepared by following the literature procedure.[19] Then it was subjected with 4-chlorobenzaldehyde and aniline in presence of 10 mol % catalyst under identical reaction conditions (Table 2, entry 8). Unfortunately, we did not get the desired piperidine derivative after 48 h of stirring. These investigations suggest that not only methyl group but any enolizable alkyl group present in the β position of β-keto esters, is a necessary and sufficient condition for the formation of highly substituted piperidines using MCRs (Table 2).

We proceeded further to investigate the reaction of various aromatic aldehydes having substituents, such as OMe, Cl, Br, F and NO_2 with aniline and methyl acetoacetate under the same reaction conditions (Table 3, entries 1–8). The reaction time and yield of the products **1g**–**n** are shown in Table 3. The low yields obtained in case of entries **7** and **8** is caused by: (i) formation of more stable imine due to extra conjugation in the presence of nitro group, which is less reactive and (ii) partial or less solubility in methanol. Unfortunately, some of the aldehydes, such as β-naphthaldehyde and *n*-butanal, did not give the corresponding functionalized piperidines.

We have noted, in some cases, such as benzaldehyde, 4-chlorobenzaldehyde and 4-nitrobenzaldehyde, a small quantity of

Table 1
Optimization of reaction conditions for the synthesis of functionalized piperidine **1a**[a]

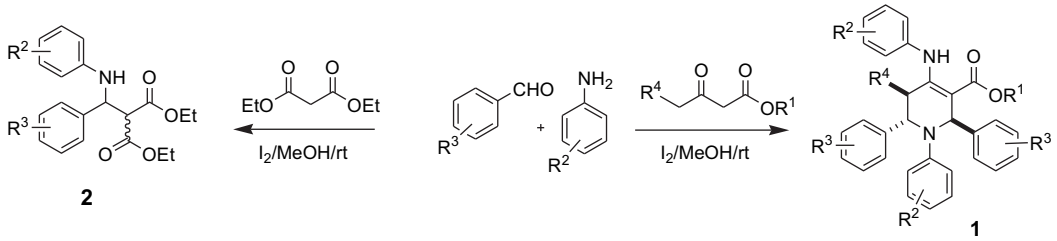


1a

Entry	Solvent	Catalyst (mol %)	Time (h)	Yield[b] (%)
1	CH_3CN	No catalyst	12	0
2	CH_3CN	5	12	52
3	CH_3CN	10	12	72
4	CH_3CN	20	12	69
5	CH_2Cl_2	10	12	60
6	C_2H_5OH	10	10	78
7	CH_3OH	10	8	84
8	EtOAc	10	12	62
9	Neat	10	12	48

[a] Reaction conditions: 4-Methylbenzaldehyde, aniline and methyl acetoacetate were taken in 2:2:1 ratio at rt.
[b] Isolated yields.

Table 2
Scope of β-keto esters in the formation of product with aromatic aldehydes and amines using iodine as catalyst[a]



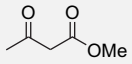
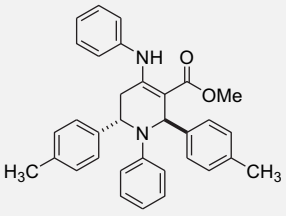
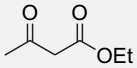
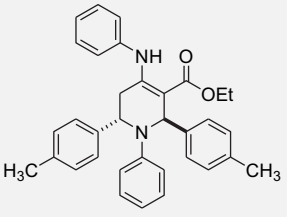
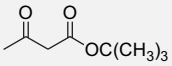
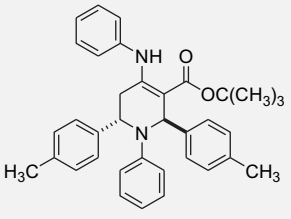
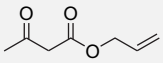
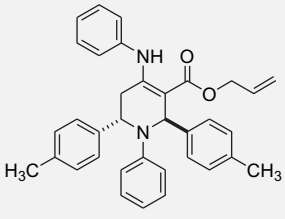
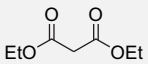
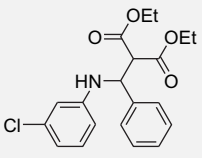
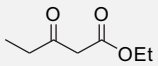
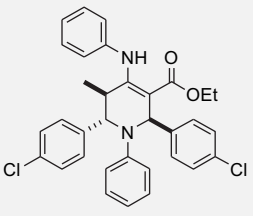
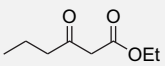
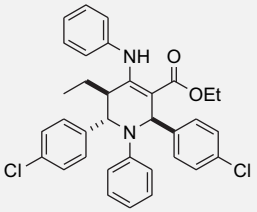
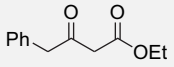
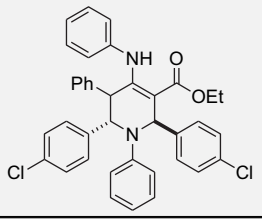
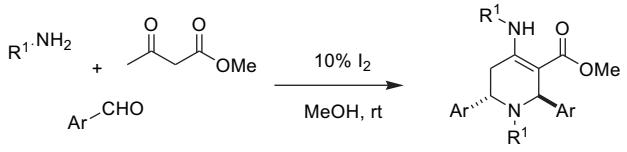
Entry	β-Keto esters	Time (h)	Product	Yield[b] (%)
1		8	 **1a**	84
2		8	 **1b**	78
3		10	 **1c**	68
4		10	 **1d**	66
5		8	 **2**	88[c]
6		48	 **1e**	42

Table 2 (*continued*)

Entry	β-Keto esters	Time (h)	Product	Yield[b] (%)
7		48	 **1f**	36
8		48		00[d]

[a] Reactions were performed in the ratio of 2:2:1 (aldehydes: amines: β-keto esters) in presence of 10 mol % iodine in 5 mL methanol at rt.
[b] Isolated yields.
[c] Unreacted imine (0.150 g) was recovered from the reaction.
[d] Determined by crude ^{1}H NMR.

Table 3
Scope for one-pot five-component reactions of methyl acetoacetate with aromatic aldehydes and amines[a]



1g-1u

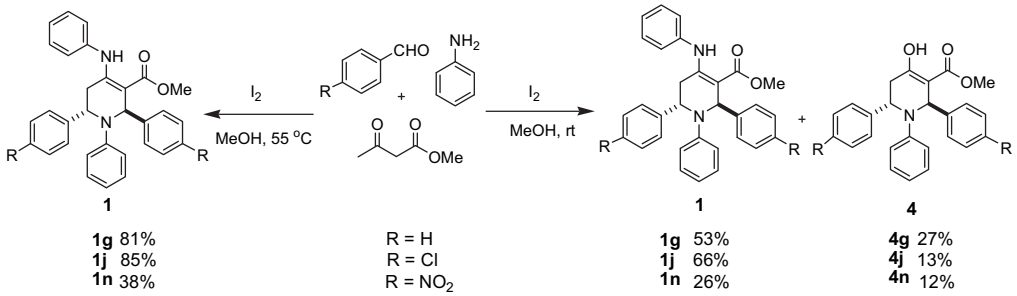
Entry	Ar	R^1	Time (h)	Product	Yield[b] (%)
1	Ph	Ph	8	**1g**	81[c]
2	4-$CH_3OC_6H_4$	Ph	8	**1h**	74
3	3,4,5-$(CH_3O)_3C_6H_2$	Ph	18	**1i**	68
4	4-ClC_6H_4	Ph	6	**1j**	85[c]
5	4-BrC_6H_4	Ph	6	**1k**	81
6	4-FC_6H_4	Ph	8	**1l**	74
7	3-$NO_2C_6H_4$	Ph	6	**1m**	36
8	4-$NO_2C_6H_4$	Ph	6	**1n**	38[c]
9	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	8	**1o**	68
10	4-$CH_3C_6H_4$	4-$C_2H_5C_6H_4$	10	**1p**	65
11	4-$CH_3C_6H_4$	4-$CH_3OC_6H_4$	8	**1q**	74
12	4-$CH_3C_6H_4$	4-BrC_6H_4	8	**1r**	68
13	4-$CH_3C_6H_4$	4-$NO_2C_6H_4$	38	**1s**	57
14	4-$CH_3C_6H_4$	*n*-C_4H_9	48	**1t**	48
15	4-$CH_3C_6H_4$	$C_6H_5CH_2$	48	**1u**	55

[a] Aldehyde, amine and methyl acetoacetate were taken in 2:2:1 ratio in presence of 10 mol % iodine at rt.
[b] Isolated yields.
[c] Reaction was carried out at 55 °C.

enol-piperidines were formed along with the desired piperidines as shown in Scheme 2. For example, the reaction of benzaldehyde with aniline and methyl acetoacetate in presence of iodine at room temperature provided, a mixture of desired piperidine **1g** and enol-piperidine **4g** in 53% and 27%, respectively.

It is speculated that the formation of **4** may be due to either hydrolysis of the enamine-piperidines **1** or through a four-component reaction. If the product **4** is forming from hydrolysis of **1**, then we expected the enol-piperidine derivative **4** should have obtained in more quantities at elevated temperature. To investigate this, the reaction was carried out at 55 °C and surprisingly, we isolated the piperidine **1g** exclusively in 81% yield not enol-piperidine after 5 h. Further, we did not obtain the hydrolysed product **4g** from **1g** even upon hydrolysis under both acidic and basic reaction conditions. From these observations, we may conclude that the enol-piperidine **4g** is obtained exclusively through a four-component reaction rather from hydrolysis of **1**.

To find the generality and scope of this MCR, various amines were also examined. A wide variety of anilines tethered with substituents, such as Me, Et, OMe, Br, NO_2 were treated with 4-methylbenzaldehyde and methyl acetoacetate under similar reaction conditions. All the reactions underwent smoothly to provide the corresponding piperidine derivative **1o**–**s**, in moderate to good yields (Table 3, entries 9–13). Likewise, aliphatic amines viz. *n*-butylamine and benzylamine also afforded the corresponding piperidines **1t** and **1u**, respectively, in moderate yields. It is worthwhile to mention that

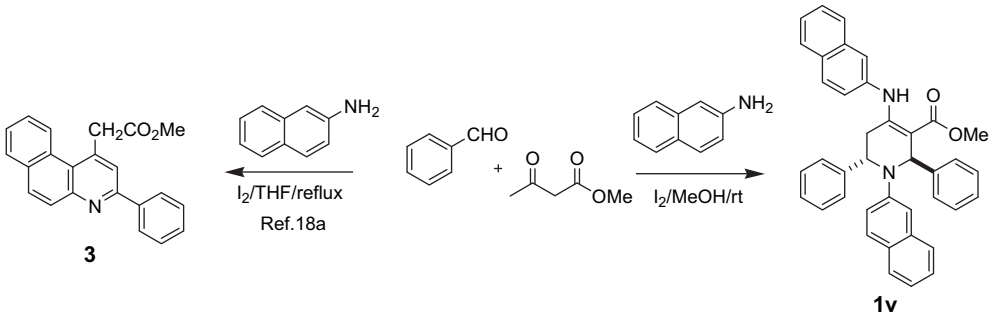


Scheme 2. Formation of product at different reaction conditions.

4-nitroaniline and aliphatic amines did not give the corresponding piperidine derivatives by using $InCl_3$.[15]

It is interesting to point out here, in our experimental conditions when 2-naphthylamine was treated with methyl acetoacetate and aldehydes, such as benzaldehyde and 4-methylbenzaldehyde to give the desired piperidine derivatives **1v** and **1w** in 53% and 51%, respectively. However, Wang et al. recently reported[18a] that same combination of 2-naphthylamine and benzaldehyde with methyl acetoacetate catalyzed by molecular iodine in THF at reflux temperature provided 3-aryl-1-substituted benzo[*f*]quinoline derivative **3** in good yield (Scheme 3). Unfortunately, 1-naphthylamine did not give the expected piperidine derivative under similar reaction conditions. This may be due to the steric hindrance of the bulky naphthyl group.

undergoes Diels-Alder reaction with imine **6** to give the desired product. To prove this mechanism, we had tried to trap the intermediate diene with other reactive dienophiles such as maleic anhydride, dihydropyran and dimethyl acetylenedicarboxylate. Unfortunately, we did not get any desired cycloaddition products. However, in the case of diethylmalonate on reaction with imine **6** furnished the Mannich-type product **2** (Table 2, entry 5). Therefore, we would like to propose an alternate plausible mechanism in which the product formed via double Mannich-type reactions. The enamine **4** and imine **5** were formed initially in the presence of iodine (Scheme 4). It is well known that enamine **5** would be a better nucleophile as compared to diethylmalonate. So, it is quite obvious that the nucleophilic attack by enamine **5** will take place preferentially on the iodine-activated imine **6** to give Mannich-



Scheme 3. Role of reaction condition towards different product formation.

The products were characterized by IR, ^1H NMR and ^{13}C NMR spectra, HRMS and by elemental analysis. The assignment of the piperidine ring protons and carbons were made by using $^1H-^1H$-COSY and $^1H-^{13}C$-COSY spectra. And finally, the structures as well as the relative stereochemistry of piperidine **1f** (Fig. 1) and **1k** (Fig. S1) were confirmed by X-ray crystallographic analysis. From the structures, it was found that the piperidine ring adopted a boat conformation in case of compound **1f** in which flag pole positions 2 and 5 of the piperidine ring, as well as the CO group of the ester and the −NH are on the same side of the plane and having intramolecular hydrogen bonding, as shown in Figure 1.

type intermediate **7** like diethylmalonate. Then the intermediate **7** reacts with aldehyde to give **8** by elimination of water molecule. Further, there will be a spontaneous tendency in the presence of iodine for tautomerization to give the intramolecular hydrogen bonded species either **9** or **10**. However, the tautomer **9** immediately undergoes intramolecular Mannich-type reaction to form intermediate **11**. The tautomer **10** would have given a four-membered ring product **12**, which is unfavourable. Finally, the intermediate **11** tautomerizes to give the final piperidine derivative **1** due to conjugation with the ester group. However, the exact explanation is not yet clear and under investigation.

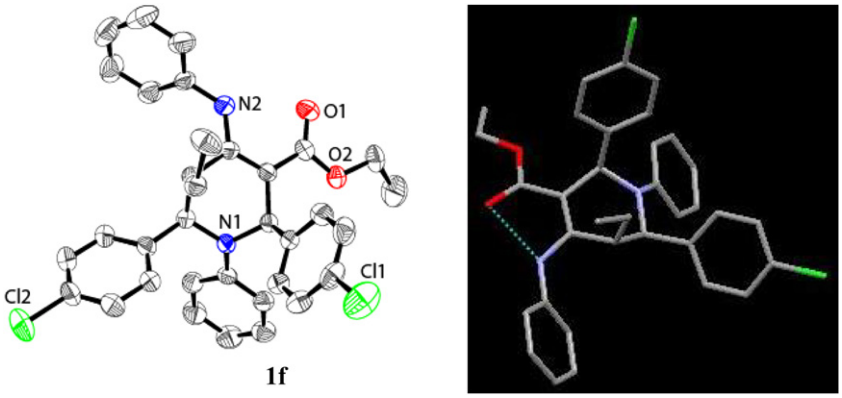
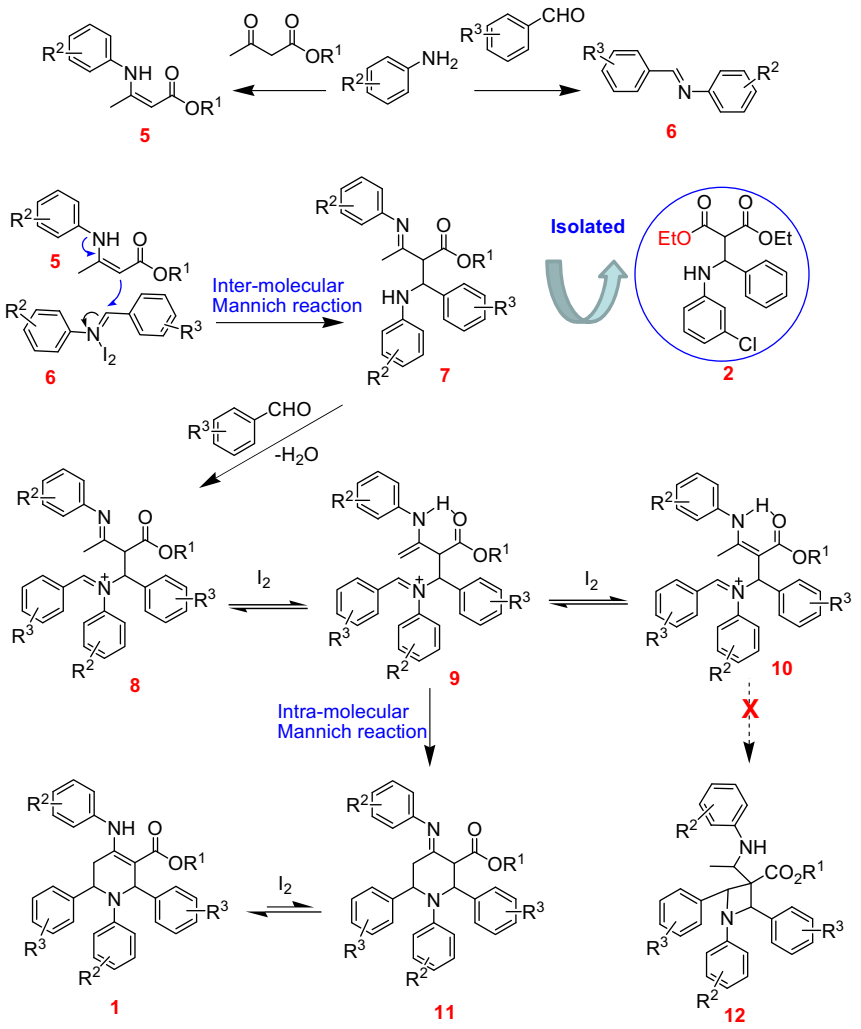


Figure 1. Crystal structures of **1f** (CCDC no. 756203).

Finally, we turned our attention towards mechanistic studies for this transformation. Earlier, reported papers[6,15a,16] proposed that the formation of piperidine is going through [4+2] aza-Diels-Alder reaction. It was expected that β-keto ester reacts with amine to give enamine **5** and it reacts with aldehyde to provide Knoevenagel type product, which acts as the reactive diene. Finally, it

The formation of four-component product in a few cases discussed earlier (Scheme 3) may be explained as follows: the enol form of methyl acetoacetate reacts with imine **6** instead of enamine **5** to form a Mannich-type intermediate, which is analogue to **7**. The remaining steps may be similar as depicted in Scheme 4.



Scheme 4. A plausible mechanism for the formation of highly substituted piperidine in the presence of iodine.

3. Conclusions

In summary, a general methodology is reported for the formation of highly as well as fully functionalized piperidines in presence of iodine as catalyst via one-pot five-component reaction from common available starting materials. The salient features of this protocol are good yields, mild reaction conditions, environmentally benign, superior atom economy, the readily accessibility of the catalyst and its cost effectiveness. In addition, we propose the possibility for the formation of piperidines via double Mannich-type intermediates and mechanism is under investigation.

4. Experimental section

4.1. General

Melting points were determined on a Büchi melting point apparatus and are uncorrected. IR spectra were recorded on Perkin–Elmer 281 IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on Varian 400 spectrometer TMS as an internal reference; chemical shifts (δ scale) are reported in parts per million (ppm). ^{1}H NMR Spectra are reported in the order: no of protons, multiplicity and coupling constant (J value) in hertz (Hz); signals were characterized as s (singlet), d (doublet), t (triplet), m (multiplet), br s (broad singlet), dq (doublet of quartet) and ddt (doublet of doublet of triplet). HRMS spectra were recorded using WATERS MS system, Q-TOF premier and data analyzed using Mass Lynx 4.1. Elemental analyses were carried out using Perkin–Elmer 2400 Series II CHNS/O analyzer at the Department of Chemistry, Indian Institute of Technology, Guwahati. Crystal data were collected with Bruker Smart Apex-II CCD diffractometer using graphite monochromated Mo Kα radiation (λ=0.71073 Å) at 298 K.

4.2. General procedure for the synthesis of highly functionalized piperidines 1

To a solution of amine (2 mmol) and methyl acetoacetate (1 mmol) in 5 mL of methanol was added iodine (0.1 mmol) and stirred at room temperature. After 20 min, aromatic aldehyde (2 mmol) was added to the reaction mixture and stirring was continued for completion. The reaction time of individual cases is indicated in Tables 2 and 3. The thick precipitate was filtered off and washed with ethanol to give pure products.

*4.2.1. Methyl 2,6-bis(4-methylphenyl)-1-phenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1a**).* White solid (0.410 g, 84%); [found: C, 80.96; H, 6.55; N, 5.80. $C_{33}H_{32}N_2O_2$ requires C, 81.12; H, 6.60; N, 5.73%]; mp 215–217 °C; R_f (5% ethyl acetate/hexane) 0.46; ν_{max} (KBr) 1657 (C=O), 1591 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.25 (1H, s, NH), 7.19 (2H, d, J 8.0 Hz, ArH), 7.10–7.02 (11H, m, ArH), 6.59 (1H, t, J 7.2 Hz, ArH), 6.52 (2H, d, J 8.0 Hz, ArH), 6.39 (1H, s, H-2), 6.30 (2H, d, J 8.0 Hz, ArH), 5.11 (1H, d,

J 3.2 Hz, H-6), 3.92 (3H, s, OMe), 2.86 (1H, dd, *J* 15.2, 5.6 Hz, H-5′), 2.75 (1H, dd, *J* 15.2, 2.4 Hz, H-5″), 2.33 (3H, s, Me), 2.32 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 168.8 (C=O), 156.5 (C-4), 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, 116.1, 113.0, 98.2 (C-3), 58.1 (C-6), 55.0 (C-2), 51.2, 33.8 (C-5), 21.3, 21.2; HRMS (ESI): MH^+, found 489.2556. $C_{33}H_{32}N_2O_2$ requires 489.2542.

*4.2.2. Ethyl 2,6-bis(4-methylphenyl)-1-phenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1b**).* White solid (0.392 g, 78%); [found C, 81.13; H, 6.76; N, 5.69. $C_{34}H_{34}N_2O_2$ requires C, 81.24; H, 6.82; N, 5.57%]; mp 228–231 °C; R_f (5% ethyl acetate/hexane) 0.48; ν_{max} (KBr) 1649 (C=O), 1592 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.29 (1H, s, NH), 7.22 (2H, d, *J* 8.0 Hz, ArH), 7.10–7.02 (11H, m, ArH), 6.59 (1H, t, *J* 7.2 Hz, ArH), 6.53 (2H, d, *J* 8.8 Hz, ArH), 6.40 (1H, s, H-2), 6.30 (2H, d, *J* 7.6 Hz, ArH), 5.11 (1H, d, *J* 2.4 Hz, H-6), 4.51–4.40 (1H, m, OCH_aH_b), 4.36–4.26 (1H, m, OCH_aH_b), 2.86 (1H, dd, *J* 15.2, 5.6 Hz, H-5′), 2.76 (1H, dd, *J* 15.2, 2.4 Hz, H-5″), 2.33 (3H, s, Me), 2.32 (3H, s, Me), 1.46 (3H, t, *J* 7.2 Hz, OCH_2CH_3); δ_C (100 MHz, $CDCl_3$) 168.4 (C=O), 156.2 (C-4), 147.2, 141.2, 139.9, 138.2, 136.8, 135.9, 129.4, 129.1, 129.0, 128.9, 126.7, 126.5, 125.9, 125.7, 116.1, 113.1, 98.5 (C-3), 59.8, 58.1 (C-6), 55.0 (C-2), 33.8 (C-5), 21.3, 21.2, 15.0; HRMS (ESI): MH^+, found: 503.2683. $C_{34}H_{34}N_2O_2$ requires 503.2699.

*4.2.3. tert-Butyl 2,6-bis(4-methylphenyl)-1-phenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1c**).* Light yellow solid (0.361 g, 68%); [found C, 81.32; H, 7.31; N, 5.37. $C_{36}H_{38}N_2O_2$ requires C, 81.47; H, 7.22; N, 5.28%]; mp 171–173 °C; R_f (5% ethyl acetate/hexane) 0.64; ν_{max} (KBr) 3447 (N–H), 1648 (C=O), 1592 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.25 (1H, s, NH), 7.23 (2H, d, *J* 8.0 Hz, ArH), 7.09–7.03 (11H, m, ArH), 6.58 (1H, t, *J* 7.2 Hz, ArH), 6.51 (2H, d, *J* 8.4 Hz, ArH), 6.35 (1H, s, H-2), 6.29 (2H, d, *J* 7.2 Hz, ArH), 5.08 (1H, d, *J* 3.2 Hz, H-6), 2.82 (1H, dd, *J* 15.2, 5.6 Hz, H-5′), 2.74 (1H, dd, *J* 15.2, 2.8 Hz, H-5″), 1.64 (9H, s, CMe_3), 2.31 (3H, s, Me), 2.33 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 168.4 (C=O), 155.3 (C-4), 147.4, 141.5, 140.0, 138.5, 136.7, 135.8, 129.4, 129.1, 128.9, 126.7, 126.6, 125.7, 125.4, 116.1, 113.1, 100.2 (C-3), 80.1, 58.2 (C-6), 55.4 (C-2), 33.8 (C-5), 29.0, 21.3, 21.2; HRMS (ESI): MH^+, found: 531.3013. $C_{36}H_{38}N_2O_2$ requires 531.3012.

*4.2.4. Allyl 2,6-bis(4-methylphenyl)-1-phenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1d**).* Light yellow solid (0.339 g, 66%); [found C, 81.56; H, 6.57; N, 5.51. $C_{35}H_{34}N_2O_2$ requires C, 81.68; H, 6.66; N, 5.44%]; mp 186–188 °C; R_f (5% ethyl acetate/hexane) 0.49; ν_{max} (KBr) 3242 (N–H), 1658 (C=O), 1591 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.26 (1H, s, NH), 7.21 (2H, d, *J* 8.0 Hz, ArH), 7.15–7.02 (11H, m, ArH), 6.58 (1H, t, *J* 7.2 Hz, ArH), 6.52 (2H, d, *J* 8.4 Hz, ArH), 6.43 (1H, s, H-2), 6.30 (2H, dd, *J* 8.0, 2.4 Hz, ArH), 6.15–6.06 (1H, m, =*CH*), 5.45 (1H, dq, *J* 17.2, 1.2 Hz, $=CH_aH_b$), 5.31 (1H, dq, *J* 10.4, 1.2 Hz, $=CH_aH_b$), 5.10 (1H, d, *J* 3.6 Hz, H-6), 4.87 (1H, ddt, *J* 13.6, 5.6, 1.6 Hz, CH_aH_b), 4.80 (1H, ddt, *J* 13.6, 5.5, 1.6 Hz, CH_aH_b), 2.86 (1H, dd, *J* 15.2, 5.6 Hz, H-5′), 2.76 (1H, dd, *J* 15.2, 2.4 Hz, H-5″), 2.32 (3H, s, Me), 2.31 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 168.0 (C=O), 156.8 (C-4), 147.2, 141.2, 139.8, 138.1, 136.8, 136.0, 133.3, 129.4, 129.1, 129.04, 128.98, 126.8, 126.5, 126.0, 125.8, 117.8, 116.2, 113.1, 98.2 (C-3), 64.5, 58.1 (C-6), 55.1 (C-2), 33.9 (C-5), 21.3, 21.2; HRMS (ESI): MH^+, found: 515.2697. $C_{35}H_{34}N_2O_2$ requires 515.2699.

*4.2.5. Ethyl 2,6-bis(4-chlorophenyl)-5-methyl-1-phenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1e**).* White solid (0.234 g, 42%); [found: C, 71.01; H, 5.33; N, 5.12. $C_{33}H_{30}N_2O_2Cl_2$ requires C, 71.09; H, 5.42; N, 5.02%]; mp 198–199 °C; R_f (5% ethyl acetate/hexane) 0.45; ν_{max} (KBr) 1651 (C=O), 1594 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.38 (1H, s, NH), 7.27–7.18 (9H, m, ArH), 7.09 (2H, t, *J* 7.6 Hz, ArH), 7.00 (2H, d, *J* 8.4 Hz, ArH), 6.68 (1H, t, *J* 7.2 Hz, ArH), 6.57 (2H, d, *J* 8.4 Hz, ArH), 6.52–6.50 (2H, m, ArH), 6.20 (1H, s, H-2), 4.87 (1H, s, H-6), 4.43–4.35 (1H, m, CH_aH_b), 4.32–4.24 (1H, m, CH_aH_b), 3.01 (1H, dq, *J* 7.2 Hz, 1.6 Hz, H-5), 1.37 (3H, t, *J* 7.2 Hz, Me), 1.04 (3H, d, *J* 7.2 Hz, Me); δ_C (100 MHz, $CDCl_3$) 169.0 (C=O), 159.8 (C-4), 147.4, 142.8, 141.8, 138.2, 132.8, 132.2, 129.4, 129.3, 129.0, 128.7, 128.8, 128.1, 127.1, 126.7, 117.9, 115.5, 96.1 (C-3), 64.0 (C-6), 60.1 (C-2), 55.7, 38.7 (C-5), 19.2, 14.8.

*4.2.6. Ethyl 2,6-bis(4-chlorophenyl)-5-ethyl-1-phenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1f**).* White solid (0.206 g, 36%); [found: C, 71.34; H, 5.53; N, 5.02. $C_{34}H_{32}N_2O_2Cl_2$ requires C, 71.45; H, 5.64; N, 4.90%]; mp 239–241 °C; R_f (5% ethyl acetate/hexane) 0.47; ν_{max} (KBr) 1655 (C=O), 1594 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.78 (1H, s, NH), 7.43–7.38 (4H, m, ArH), 7.34 (2H, d, *J* 8.4 Hz, ArH), 7.25–7.12 (10H, m, ArH), 6.78 (2H, d, *J* 8.0 Hz, ArH), 5.99 (1H, s, H-2), 4.86 (1H, d, *J* 4.0 Hz, H-6), 4.33–4.25 (1H, m, CH_aH_b), 4.15–4.07 (1H, m, CH_aH_b), 3.05–3.04 (1H, m, H-5), 1.22 (3H, t, *J* 7.2 Hz, Me), 0.85–0.77 (1H, m, CH_aH_b), 0.76–0.67 (1H, m, CH_aH_b), 0.18 (3H, t, *J* 7.2 Hz, Me); δ_C (100 MHz, $CDCl_3$) 169.2 (C=O), 161.8 (C-4), 151.2, 145.8, 139.9, 139.1, 132.7, 132.4, 129.6, 129.0, 128.9, 128.5, 128.4, 126.6, 126.3, 119.2, 116.8, 95.6 (C-3), 63.8 (C-6), 61.7 (C-2), 60.0, 43.1 (C-5), 22.2, 14.6, 12.1.

*4.2.7. Methyl 1,2,6-triphenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1g**).* To a solution of amine (2 mmol) and methyl acetoacetate (1 mmol) in 5 mL of methanol was added iodine (0.1 mmol) and stirred at 55 °C. After 10 min, benzaldehyde (2 mmol) was added to the reaction mixture and stirring was continued for completion at the same temperature. The reaction mixture was cooled to room temperature. The thick precipitate was filtered off and washed with ethanol to give pure products as white solid (0.373 g, 81%); [found: C, 80.72; H, 6.07; N, 6.09. $C_{31}H_{28}N_2O_2$ requires C, 80.84; H, 6.13; N, 6.08%]; mp 185–186 °C; R_f (5% ethyl acetate/hexane) 0.38; ν_{max} (KBr) 3444 (N–H), 1661 (C=O), 1591 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.24 (1H, s, NH), 7.32–7.24 (8H, m, ArH), 7.16 (2H, d, *J* 8.0 Hz, ArH), 7.10–7.03 (5H, m, ArH), 6.59 (1H, t, *J* 7.2 Hz, ArH), 6.51 (2H, d, *J* 8.8 Hz, ArH), 6.44 (1H, s, H-2), 6.27 (2H, d, *J* 8.0 Hz, ArH), 5.14 (1H, d, *J* 4.4 Hz, H-6), 3.93 (3H, s, Me), 2.86 (1H, dd, *J* 15.2, 5.6 Hz, H-5′), 2.75 (1H, dd, *J* 15.2, 2.4 Hz, H-5″), δ_C (100 MHz, $CDCl_3$) 168.7 (C=O), 156.4 (C-4), 147.1, 144.0, 142.9, 137.9, 129.0, 128.9, 128.8, 128.4, 127.3, 126.8, 126.5, 126.0, 125.9, 116.3, 113.0, 98.0 (C-3), 58.3 (C-6), 55.2 (C-2), 51.2, 33.8 (C-5); HRMS (ESI): MH^+, found: 461.2256. $C_{31}H_{28}N_2O_2$ requires 461.2229.

*4.2.8. Methyl 2,6-bis(4-methoxyphenyl)-1-phenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1h**).* White solid (0.385 g, 74%); [found C, 76.01; H, 6.11; N, 5.49. $C_{33}H_{32}N_2O_4$ requires C, 76.13; H, 6.20; N, 5.38%]; mp 186–188 °C; R_f (5% ethyl acetate/hexane) 0.16; ν_{max} (KBr) 1654 (C=O), 1593 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.27 (1H, s, NH), 7.21 (2H, d, *J* 8.8 Hz, ArH), 7.11 (2H, d, *J* 7.2 Hz, ArH), 7.07 (1H, t, *J* 7.2 Hz, ArH), 7.06 (2H, d, *J* 8.8 Hz, ArH), 7.05 (2H, d, *J* 8.4 Hz, ArH), 6.81 (4H, d, *J* 8.8 Hz, ArH), 6.60 (1H, t, *J* 7.2 Hz, ArH), 6.52 (2H, d, *J* 8.0 Hz, ArH), 6.38–6.34 (3H, m, ArH and H-2), 5.07 (1H, d, *J* 3.2 Hz, H-6), 3.92 (3H, s, OMe), 3.79 (3H, s, OMe), 3.78 (3H, s, OMe), 2.85 (1H, dd, *J* 15.2, 5.6 Hz, H-5′), 2.75 (1H, dd, *J* 15.2, 2.4 Hz, H-5″); δ_C (100 MHz, $CDCl_3$) 168.8 (C=O), 158.8, 158.2, 156.5 (C-4), 147.1, 138.1, 136.0, 134.8, 129.0, 127.8, 127.6, 125.9, 125.8, 116.2, 114.1, 113.7, 113.1, 98.2 (C-3), 57.7 (C-6), 55.4, 54.7 (C-2), 51.2, 33.9 (C-5); HRMS (ESI): MH^+, found: 521.2449. $C_{33}H_{32}N_2O_4$ requires 521.2440.

*4.2.9. Methyl 2,6-bis(3,4,5-trimethoxyphenyl)-1-phenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1i**).* Light yellow solid (0.435 g, 68%); [found: C, 69.28; H, 6.24; N, 4.46. $C_{37}H_{40}N_2O_8$ requires C, 69.36; H, 6.29; N, 4.37%]; mp 197–199 °C; R_f (30% ethyl acetate/hexane) 0.22; ν_{max} (KBr) 1655 (C=O), 1594 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.26 (1H, s, NH), 7.15 (2H, d, *J* 7.6 Hz, ArH), 7.12 (1H, t, *J* 7.2 Hz, ArH), 7.09 (2H, d, *J* 8.0 Hz, ArH), 6.65 (1H, t, *J* 7.6 Hz, ArH), 6.57 (2H, d, *J* 8.0 Hz, ArH), 6.53 (2H, s, ArH), 6.39 (2H, d, *J* 7.7 Hz, ArH), 6.35 (2H, s, ArH), 6.34(1H, s, H-2), 5.03 (1H, d, *J* 3.2 Hz, H-6), 3.90 (3H, s, OMe), 3.85 (3H, s, OMe), 3.84 (3H, s, OMe), 3.74

(6H, s, 2×OMe), 3.70 (6H, s, 2×OMe), 2.95 (1H, dd, *J* 15.2, 5.6 Hz, H-5′), 2.77 (1H, dd, *J* 15.2, 2.4 Hz, H-5″); δ_C (100 MHz, $CDCl_3$) 168.5 (C=O), 157.0 (C-4), 153.4, 153.1, 147.0, 139.7, 138.5, 137.8, 137.0, 136.5, 128.9, 126.3, 126.2, 116.6, 113.1, 103.9, 103.2, 97.3 (C-3), 61.0, 58.3 (C-6), 56.0, 55.6 (C-2), 51.1, 33.8 (C-5); HRMS (ESI): MH^+, found: 641.2800. $C_{37}H_{40}N_2O_8$ requires 641.2863.

*4.2.10. Methyl 2,6-bis(4-chlorophenyl)-1-phenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1j**).* To a solution of amine (2 mmol) and methyl acetoacetate (1 mmol) in 5 mL of methanol was added iodine (0.1 mmol) and stirred at 55 °C. After 10 min, 4-chlorobenzaldehyde (2 mmol) was added to the reaction mixture and stirring was continued for completion at the same temperature. The reaction mixture was cooled to room temperature. The thick precipitate was filtered off and washed with ethanol to give pure products as white solid **1i** (0.450 g, 85%) as white solid; [found: C, 70.29; H, 4.83; N, 5.34. $C_{31}H_{26}Cl_2N_2O_2$ requires C, 70.32; H, 4.95; N, 5.29%]; mp 225–227 °C; R_f (5% ethyl acetate/hexane) 0.27; ν_{max} (KBr) 1660 (C=O), 1591 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.25 (1H, s, NH), 7.36–7.24 (5H, m, ArH), 7.15 (2H, d, *J* 7.2 Hz, ArH), 7.10 (2H, t, *J* 7.6 Hz, ArH), 7.07 (2H, d, *J* 8.4 Hz, ArH), 7.05 (2H, d, *J* 8.0 Hz, ArH), 6.64 (1H, t, *J* 7.2 Hz, ArH), 6.45 (2H, d, *J* 8.0 Hz, ArH), 6.40 (2H, d, *J* 8.0 Hz, ArH), 6.35 (1H, s, H-2), 5.09 (1H, d, *J* 2.4 Hz, H-6), 3.92 (3H, s, OMe), 2.82 (1H, dd, *J* 15.2, 5.6 Hz, H-5′), 2.74 (1H, dd, *J* 15.2, 2.4 Hz, H-5″); δ_C (100 MHz, $CDCl_3$) 168.4 (C=O), 156.2 (C-4), 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 (C-3), 57.5 (C-6), 54.8 (C-2), 51.3, 33.8 (C-5); HRMS (ESI): MH^+, found: 529.1445. $C_{31}H_{26}N_2O_2Cl_2$ requires 529.1450.

*4.2.11. Methyl 2,6-bis(4-bromophenyl)-1-phenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1k**).* Light yellow solid (0.500 g, 77%); [found: C, 60.45; H, 4.15; N, 4.97. $C_{31}H_{26}Br_2N_2O_2$ requires C, 60.21; H, 4.24; N, 4.53%]; mp 245–247 °C; R_f (5% ethyl acetate/hexane) 0.27; ν_{max} (KBr) 1661 (C=O), 1590 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.24 (1H, s, NH), 7.40 (2H, d, *J* 8.4 Hz, ArH), 7.39 (2H, d, *J* 8.4 Hz, ArH), 7.18 (2H, d, *J* 8.4 Hz, ArH), 7.16 (2H, d, *J* 8.0 Hz, ArH), 7.15 (1H, t, *J* 7.2 Hz, ArH), 7.08 (2H, t, *J* 7.2 Hz, ArH), 7.00 (2H, d, *J* 8.4 Hz, ArH), 6.65 (1H, t, *J* 7.2 Hz, ArH), 6.45 (2H, d, *J* 8.8 Hz, ArH), 6.40 (2H, d, *J* 7.6 Hz, ArH), 6.34 (1H, s, H-2), 5.08 (1H, d, *J* 3.6 Hz, H-6), 3.93 (3H, s, OMe), 2.82 (1H, dd, *J* 15.2, 5.6 Hz, H-5′), 2.74 (1H, dd, *J* 15.2, 2.4 Hz, H-5″); δ_C (100 MHz, $CDCl_3$) 168.4 (C=O), 156.1 (C-4), 146.5, 143.0, 141.6, 137.7, 131.9, 131.5, 129.2, 129.18, 128.6, 128.3, 126.2, 125.9, 121.1, 120.4, 116.9, 113.0, 97.6 (C-3), 57.5 (C-6), 54.9 (C-2), 51.3, 33.8 (C-5); HRMS (ESI): MH^+, found: 617.0433. $C_{31}H_{26}N_2O_2Br_2$ requires 617.0439.

*4.2.12. Methyl 2,6-bis(4-fluorophenyl)-1-phenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1l**).* White solid (0.367 g, 74%); [found: C, 74.91; H, 5.11; N, 5.84. $C_{31}H_{26}F_2N_2O_2$ requires C, 74.98; H, 5.28; N, 5.64%]; mp 193–195 °C; R_f (5% ethyl acetate/hexane) 0.38; ν_{max} (KBr) 1657 (C=O), 1592 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.23 (1H, s, NH), 7.25 (2H, t, *J* 8.4 Hz, ArH), 7.17–7.06 (7H, m, ArH), 6.96 (4H, t, *J* 8.4 Hz, ArH), 6.64 (1H, t, *J* 7.2 Hz, ArH), 6.47 (2H, d, *J* 8.4 Hz, ArH), 6.39 (2H, d, *J* 8.0 Hz, ArH), 6.37 (1H, s, H-2), 5.11 (1H, d, *J* 2.8 Hz, H-6), 3.93 (3H, s, OMe), 2.83 (1H, dd, *J* 15.2, 5.6 Hz, H-5′), 2.75 (1H, dd, *J* 15.2, 2.4 Hz, H-5″); δ_C (100 MHz, $CDCl_3$) 168.6 (C=O), 163.4, 160.5, 156.3 (C-4), 146.7, 139.5, 138.2, 137.8, 129.2, 128.4, 128.3, 128.1, 128.0, 126.2, 125.9, 116.7, 115.8, 115.6, 115.3, 115.1, 113.1, 97.9 (C-3), 57.5 (C-6), 54.7 (C-2), 51.4, 33.9 (C-5); HRMS (ESI): MH^+, found: 497.2245. $C_{31}H_{26}N_2O_2F_2$ requires 497.2241.

*4.2.13. Methyl 2,6-bis(3-nitrophenyl)-1-phenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1m**).* Yellow solid (0.198 g, 36%); [found C, 67.51; H, 4.68; N, 10.29. $C_{31}H_{26}N_4O_6$ requires C, 67.63; H, 4.76; N, 10.18%]; mp 182–183 °C; R_f (15% ethyl acetate/hexane) 0.21; ν_{max} (KBr) 3436 (N–H), 1655 (C=O), 1595 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.30 (1H, s, NH), 8.22 (1H, s, ArH), 8.15–8.10 (2H, m, ArH), 7.94 (s, 1H, ArH), 7.66 (1H, d, *J* 7.6 Hz, ArH), 7.50–7.45 (3H, m, ArH), 7.16–7.14 (3H, m, ArH), 7.10 (2H, t, *J* 7.2 Hz, ArH), 6.70 (1H, t, *J* 7.2 Hz, ArH), 6.48 (1H, s, H-2), 6.44 (2H, d, *J* 8.8 Hz, ArH), 6.41–6.38 (2H, m, ArH), 5.33 (1H, t, *J* 4.0 Hz, H-6), 3.99 (3H, s, OMe), 2.88 (2H, d, *J* 4.0 Hz, CH_2); δ_C (100 MHz, $CDCl_3$) 168.2 (C=O), 155.7 (C-4), 148.8, 148.7, 146.5, 145.9, 144.6, 137.3, 132.7, 129.8, 129.5, 129.3, 126.7, 125.8, 122.6, 122.0, 121.7, 121.5, 117.9, 113.2, 96.9 (C-3), 57.2 (C-6), 55.3 (C-2), 51.6, 33.9 (C-5).

*4.2.14. Methyl 2,6-bis(4-nitrophenyl)-1-phenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1n**).* The reaction was carried out at 55 °C, after completion, the reaction was cool to room temperature. The thick precipitate was filtered off and washed with ethanol to give pure products **1n** (0.209 g, 38%) as light yellow solid; [found C, 67.51; H, 4.69; N, 10.31. $C_{31}H_{26}N_4O_6$ requires C, 67.63; H, 4.76; N, 10.18%]; mp 239–241 °C; R_f (15% ethyl acetate/hexane) 0.21; ν_{max} (KBr) 3356 (N–H), 1660 (C=O), 1593 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.26 (1H, br s, NH), 8.14 (2H, d, *J* 8.8 Hz, ArH), 8.12 (2H, d, *J* 8.8 Hz, ArH), 7.48 (2H, d, *J* 8.4 Hz, ArH), 7.27 (2H, d, *J* 8.8 Hz, ArH), 7.17–7.13 (3H, m, ArH), 7.09 (1H, d, *J* 7.2 Hz, ArH), 7.07 (1H, d, *J* 7.2 Hz, ArH), 6.68 (1H, t, *J* 7.2 Hz, ArH), 6.46 (1H, s, H-2), 6.42–6.37 (4H, m, ArH), 5.25–5.24 (1H, m, H-6), 3.95 (3H, s, OMe), 2.85 (2H, d, *J* 4.0 Hz, CH_2); δ_C (100 MHz, $CDCl_3$) 168.1 (C=O), 155.7 (C-4), 151.8, 149.9, 147.5, 146.9, 145.9, 137.3, 129.5, 129.4, 127.6, 127.5, 126.6, 125.7, 124.1, 123.9, 117.8, 113.1, 96.8 (C-3), 57.5 (C-6), 55.4 (C-2), 51.6, 33.7 (C-5).

*4.2.15. Methyl 2,6-bis(4-methylphenyl)-1-(4-methylphenyl)-4-(4-methylphenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1o**).* Light yellow solid (0.351 g, 68%); [found: C, 81.24; H, 7.01; N, 5.53. $C_{35}H_{36}N_2O_2$ requires C, 81.36; H, 7.02; N, 5.42%]; mp 206–208 °C; R_f (5% ethyl acetate/hexane) 0.48; ν_{max} (KBr) 3249 (N–H), 1655 (C=O), 1594 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.17 (1H, s, NH), 7.20 (2H, d, *J* 8.0 Hz, ArH), 7.09–7.03 (6H, m, ArH), 6.89 (2H, d, *J* 8.0 Hz, ArH), 6.87 (2H, d, *J* 8.8 Hz, ArH), 6.43 (2H, d, *J* 8.0 Hz, ArH), 6.35 (1H, s, H-2), 6.18 (2H, d, *J* 8.0 Hz, ArH), 5.07 (1H, d, *J* 4.0 Hz, H-6), 3.91 (3H, s, OMe), 2.82 (1H, dd, *J* 15.2, 5.6 Hz, H-5′), 2.72 (1H, dd, *J* 15.2, 2.4 Hz, H-5″), 2.34 (3H, s, Me), 2.32 (3H, s, Me), 2.27 (3H, s, Me), 2.15 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 168.8 (C=O), 156.8 (C-4), 145.1, 141.4, 140.1, 136.6, 135.8, 135.6, 135.4, 129.5, 129.4, 129.0, 126.7, 126.5, 126.1, 125.0, 113.0, 97.7 (C-3), 58.0 (C-6), 55.1 (C-2), 51.0, 33.7 (C-5), 21.3, 21.2, 21.0, 20.3; HRMS (ESI): MH^+, found: 517.2847. $C_{35}H_{36}N_2O_2$ requires 517.2855.

*4.2.16. Methyl 2,6-bis(4-methylphenyl)-1-(4-ethylphenyl)-4-(4-ethylphenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1p**).* Light yellow solid (0.354 g, 65%); [found: C, 81.49; H, 7.07; N, 5.24. $C_{37}H_{40}N_2O_2$ requires C, 81.58; H, 7.40; N, 5.14%]; mp 177–178 °C; R_f (5% ethyl acetate/hexane) 0.48; ν_{max} (KBr) 3264 (N–H), 1653 (C=O), 1593 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.17 (1H, s, NH), 7.19 (2H, d, *J* 8.4 Hz, ArH), 7.09–7.03 (6H, m, ArH), 6.91 (2H, d, *J* 8.4 Hz, ArH), 6.88 (2H, d, *J* 8.8 Hz, ArH), 6.44 (2H, d, *J* 8.8 Hz, ArH), 6.35 (1H, s, H-2), 6.19 (2H, d, *J* 8.4 Hz, ArH), 5.07 (1H, d, *J* 3.6 Hz, H-6), 3.90 (3H, s, OMe), 2.82 (1H, dd, *J* 15.2, 5.6 Hz, H-5′), 2.73 (1H, dd, *J* 15.2, 2.4 Hz, H-5″), 2.56 (2H, q, *J* 7.6 Hz, CH_2CH_3), 2.45 (2H, q, *J* 7.6 Hz, CH_2CH_3), 2.31(3H, s, Me), 2.34 (3H, s, Me), 1.18 (3H, t, *J* 7.6 Hz, Me), 1.11 (3H, t, *J* 7.6 Hz, Me); δ_C (100 MHz, $CDCl_3$) 168.8 (C=O), 156.8 (C-4), 145.3, 142.0, 141.5, 140.2, 136.7, 135.8, 135.6, 131.5, 129.4, 129.1, 128.3, 126.8, 126.6, 126.2, 113.0, 97.8 (C-3), 58.2 (C-6), 55.2 (C-2), 51.1, 33.8 (C-5), 28.4, 27.8, 21.3, 21.2, 15.9, 15.7; HRMS (ESI): MH^+, found: 545.3151. $C_{37}H_{40}N_2O_2$ requires 545.3168.

*4.2.17. Methyl 2,6-bis(4-methylphenyl)-1-(4-methoxyphenyl)-4-(4-methoxyphenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1q**).* White solid (0.406 g, 74%); [found: C, 76.56; H, 6.55; N, 5.26.

$C_{35}H_{36}N_2O_4$ requires C, 76.62; H, 6.61; N, 5.11%]; mp 230–231 °C; R_f (5% ethyl acetate/hexane) 0.20; ν_{max} (KBr) 3442 (N–H), 1657 (C=O), 1611 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.08 (1H, s, NH), 7.16 (2H, d, *J* 8.0 Hz, ArH), 7.09–7.02 (6H, m, ArH), 6.64 (2H, d, *J* 9.2 Hz, ArH), 6.60 (2H, d, *J* 9.2 Hz, ArH), 6.43 (2H, d, *J* 9.2 Hz, ArH), 6.26 (1H, s, H-2), 6.21 (2H, d, *J* 9.2 Hz, ArH), 5.00 (1H, d, *J* 2.8 Hz, H-6), 3.89 (3H, s, OMe), 3.74 (3H, s, OMe), 3.65 (3H, s, OMe), 2.77 (1H, dd, *J* 15.2, 5.6 Hz, H-5′), 2.62 (1H, dd, *J* 15.2, 2.8 Hz, H-5″), 2.33 (3H, s, Me), 2.31 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 168.9 (C=O), 157.9, 157.2, 151.0 (C-4), 141.9, 141.5, 140.4, 136.7, 135.9, 131.0, 129.4, 129.0, 128.0, 126.9, 126.6, 114.7, 114.3, 114.2, 114.1, 97.3 (C-3), 58.1 (C-6), 55.8 (C-2), 55.7, 55.6, 51.0, 33.8 (C-5), 21.3, 21.2; HRMS (ESI): MH^+, found: 549.2753. $C_{35}H_{36}N_2O_4$ requires 549.2753.

*4.2.18. Methyl 2,6-bis(4-methylphenyl)-1-(4-bromophenyl)-4-(4-bromophenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1r**).* Light yellow solid (0.440 g, 68%); [found C, 61.23; H, 4.57; N, 4.46. $C_{33}H_{30}Br_2N_2O_2$ requires C, 61.32; H, 4.68; N, 4.33%]; mp 230–232 °C; R_f (5% ethyl acetate/hexane) 0.42; ν_{max} (KBr) 3446 (N–H), 1650 (C=O), 1605 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.17 (1H, s, NH), 7.20 (2H, d, *J* 8.4 Hz, ArH), 7.15–7.07 (8H, m, ArH), 7.02 (2H, d, *J* 8.0 Hz, ArH), 6.38 (2H, d, *J* 9.2 Hz, ArH), 6.31 (1H, s, H-2), 6.13 (2H, d, *J* 8.4 Hz, ArH), 5.06 (1H, d, *J* 3.6 Hz, H-6), 3.93 (3H, s, OMe), 2.84 (1H, dd, *J* 15.2, 5.6 Hz, H-5′), 2.70 (1H, dd, *J* 15.2, 2.4 Hz, H-5″), 2.34 (3H, s, Me), 2.32 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 168.6 (C=O), 155.6 (C-4), 146.1, 140.2, 139.2, 137.2, 137.1, 136.3, 132.1, 131.7, 129.6, 129.2, 127.4, 126.6, 126.4, 119.2, 114.7, 108.4, 98.9 (C-3), 58.1 (C-6), 55.2 (C-2), 51.3, 33.6 (C-5), 21.3, 21.2; HRMS (ESI): MH^+, found: 645.0753. $C_{33}H_{30}N_2O_2Br_2$ requires 645.0752.

*4.2.19. Methyl 2,6-bis(4-methylphenyl)-1-(4-nitrophenyl)-4-(4-nitrophenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1s**).* Yellow solid (0.330 g, 57%); [found: C, 68.39; H, 5.14; N, 9.88. $C_{33}H_{30}N_4O_6$ requires C, 68.50; H, 5.23; N, 9.68%]; mp 253–255 °C; R_f (15% ethyl acetate/hexane) 0.20; ν_{max} (KBr) 1658 (C=O), 1587 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.55 (1H, s, NH), 8.00 (2H, d, *J* 9.2 Hz, ArH), 7.97 (2H, d, *J* 9.6 Hz, ArH), 7.13 (6H, s, ArH), 7.02 (2H, d, *J* 8.0 Hz, ArH), 6.54 (2H, d, *J* 9.6 Hz, ArH), 6.48 (1H, s, H-2), 6.43 (2H, d, *J* 9.2 Hz, ArH), 5.27 (1H, d, *J* 3.2 Hz, H-6), 3.99 (3H, s, OMe), 3.06 (1H, dd, *J* 15.2, 5.6 Hz, H-5′), 2.94 (1H, dd, *J* 15.2, 2.4 Hz, H-5″), 2.34 (6H, s, 2×Me); δ_C (100 MHz, $CDCl_3$) 168.3 (C=O), 153.3 (C-4), 151.9, 144.1, 138.3, 138.1, 137.9, 137.5, 137.2, 130.0, 129.7, 126.2, 126.1, 125.9, 125.1, 123.1, 112.3, 102.0 (C-3), 58.5 (C-6), 55.8 (C-2), 52.0, 33.8 (C-5), 21.3, 21.2; HRMS (ESI): MH^+, found: 579.2244. $C_{33}H_{30}N_4O_6$ requires 579.2244.

*4.2.20. Methyl 2,6-bis(4-methylphenyl)-1-butyl-4-(butylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1t**).* Light yellow solid (0.215 g, 48%); [found C, 77.51; H, 8.91; N, 6.37. $C_{29}H_{40}N_2O_2$ requires C, 77.64; H, 8.99; N, 6.24%]; mp 158–160 °C; R_f (5% ethyl acetate/hexane) 0.46; ν_{max} (KBr) 3428 (N–H), 1649 (C=O), 1597 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 9.22 (1H, t, *J* 4.8 Hz, NH), 7.31 (2H, d, *J* 8.0 Hz, ArH), 7.17 (2H, *J* 8.0 Hz, ArH), 7.08 (4H, t, *J* 7.6 Hz, ArH), 4.92 (1H, s, H-2), 3.85 (1H, dd, *J* 11.6, 5.2 Hz, H-6), 3.55 (3H, s, OMe), 3.38–3.24 (2H, m, CH_2), 2.60 (1H, dd, *J* 17.2, 11.2 Hz, H-5′), 2.51 (1H, dd, *J* 17.2, 5.2 Hz, H-5″), 2.32 (3H, s, Me), 2.30 (3H, s, Me), 2.15–2.08 (2H, m, CH_2), 1.68–1.60 (2H, m, CH_2), 1.52–1.43 (2H, m, CH_2), 1.36–1.26 (2H, m, CH_2), 1.23–1.10 (2H, m, CH_2), 0.98 (3H, t, *J* 7.2 Hz, CH_3), 0.79 (3H, t, *J* 7.2 Hz, CH_3); δ_C (100 MHz, $CDCl_3$) 171.4 (C=O), 159.7 (C-4), 142.4, 139.3, 136.4, 135.6, 128.9, 128.8, 128.4, 127.3, 87.9 (C-3), 58.6 (C-6), 52.5 (C-2), 50.6, 44.7, 42.1, 32.5 (C-5), 31.1, 25.6, 21.3, 20.6, 20.5, 14.3, 14.1; HRMS (ESI): MH^+, found: 449.3160. $C_{29}H_{40}N_2O_2$ requires 449.3168.

*4.2.21. Methyl 2,6-bis(4-methylphenyl)-1-benzyl-4-(benzylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1u**).* Light yellow solid (0.284 g, 55%); [found C, 81.22; H, 7.07; N, 5.57. $C_{35}H_{36}N_2O_2$ requires C, 81.36; H, 7.02; N, 5.42%]; mp 172–173 °C; R_f (5% ethyl acetate/hexane) 0.32; ν_{max} (KBr) 3272 (N–H), 1650 (C=O), 1594 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 9.67 (1H, t, *J* 6.0 Hz, NH), 7.40–7.37 (6H, m, ArH), 7.32 (4H, t, *J* 8.0 Hz, ArH), 7.24 (2H, d, *J* 8.4 Hz, ArH), 7.20 (2H, d, *J* 8.4 Hz, ArH), 7.08 (4H, t, *J* 8.0 Hz, ArH), 4.73 (1H, s, H-2), 4.63 (1H, dd, *J* 15.6, 6.4 Hz, H-6), 4.57 (1H, dd, *J* 15.6, 6.0 Hz, CH_aH_b), 4.02 (1H, dd, *J* 11.2, 5.2 Hz, CH_aH_b), 3.37 (1H, d, *J* 13.6 Hz, CH_aH_b), 3.46 (3H, s, OMe), 3.32 (1H, d, *J* 13.6 Hz, CH_aH_b), 2.73 (1H, dd, *J* 17.2, 11.6 Hz, H-5′), 2.62 (1H, dd, *J* 17.2, 5.2 Hz, H-5″), 2.28 (3H, s, Me), 2.30 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 171.3, 159.0 (C-4), 141.9, 140.5, 139.1, 138.7, 136.7, 135.8, 129.1, 129.0, 128.8, 128.4, 128.3, 127.6, 127.4, 127.0, 126.9, 89.3, 58.1, 52.2, 50.6, 49.7, 46.3, 25.5, 21.3; HRMS (ESI): MH^+, found: 517.2872. $C_{35}H_{36}N_2O_2$ requires 517.2855.

*4.2.22. Diethyl 2-(phenyl(3-chlorophenylamino)methyl)malonate (**2**).* White solid (0.295 g, 88%); [found: C, 63.73; H, 5.79; N, 3.63. $C_{20}H_{22}ClNO_4$ requires C, 63.91; H, 5.90; N, 3.73%]; mp 112–114 °C; R_f (5% ethyl acetate/hexane) 0.2; ν_{max} (KBr) 3369 (N–H), 1752 (C=O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.35–7.32 (5H, m, ArH), 6.99 (1H, t, *J* 8.0 Hz, ArH), 6.61 (1H, d, *J* 8.0 Hz, ArH), 6.58 (1H, s), 6.46 (1H, d, *J* 8.4 Hz, ArH), 5.49 (1H, d, *J* 6.0 Hz), 5.18 (1H, br s), 4.17–4.07 (4H, m), 3.88 (1H, d, *J* 5.2 Hz), 1.17 (3H, t, *J* 7.2 Hz), 1.13 (3H, t, *J* 7.2 Hz); δ_C (100 MHz, $CDCl_3$) 168.2, 167.3, 148.0, 139.3, 135.0, 130.3, 128.9, 128.0, 126.8, 117.9, 113.6, 112.1, 62.1, 61.8, 58.1, 57.0, 14.1, 14.0.

*4.2.23. Methyl 4-hydroxy-1,2,6-triphenyl-1,2,5,6-tetrahydropyridine-3-carboxylate (**4g**).* To a solution of amine (2 mmol) and methyl acetoacetate (1 mmol) in 5 mL of methanol was added iodine (0.1 mmol) and stirred at room temperature. After 20 min, benzaldehyde (2 mmol) was added to the reaction mixture and stirring was continued for completion. The thick precipitate was filtered off and washed with ethanol to give mixture of two products of R_f (5% ethyl acetate/hexane) 0.38 and 0.49, respectively. Products were purified by column chromatography using ethyl acetate/hexane (98:2) furnished **4g** (0.124 g, 29%) as white solid; [found: C, 77.78; H, 5.91; N, 3.45. $C_{25}H_{23}NO_3$ requires C, 77.90; H, 6.01; N, 3.63%]; mp 166–168 °C; R_f (5% ethyl acetate/hexane) 0.49; ν_{max} (KBr) 1658 (C=C), 1595 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 11.94 (1H, br s, OH), 7.28–7.16 (10H, m, ArH), 7.03 (2H, t, *J* 7.2 Hz, ArH), 6.67 (1H, t, *J* 7.6 Hz, ArH), 6.55 (2H, d, *J* 8.4 Hz, ArH), 5.99 (1H, s, H-2), 5.12 (1H, t, *J* 5.2 Hz, H-6), 3.87 (3H, s, OMe), 3.08 (1H, dd, *J* 16.2, 5.6 Hz, H-5′), 2.73 (1H, dd, *J* 16.4, 4.8 Hz, H-5″); δ_C (100 MHz, $CDCl_3$) 170.8, 170.5, 142.7, 142.3, 128.9, 128.8, 128.5, 127.3, 127.1, 127.0, 126.6, 118.3, 116.5, 102.2, 57.6, 56.9, 52.2, 36.8.

*4.2.24. Methyl 4-hydroxy-2,6-bis(4-nitrophenyl)-1-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate (**4n**).* Purification was performed by column chromatography using ethyl acetate/hexane (95:5) to furnished **4n** (0.057 g, 12%) as light yellow solid; [found: C, 63.02; H, 4.31; N, 8.71. $C_{25}H_{21}N_3O_7$ requires C, 63.15; H, 4.45; N, 8.84%]; mp 173–175 °C; R_f (15% ethyl acetate/hexane) 0.26; ν_{max} (KBr) 1638 (C=O), 1595 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 11.99 (1H, br s, OH), 8.11 (4H, t, *J* 7.2 Hz, ArH), 7.36 (2H, d, *J* 8.4 Hz, ArH), 7.33 (2H, d, *J* 8.4 Hz, ArH), 7.04 (2H, t, *J* 7.6 Hz, ArH), 6.76 (1H, t, *J* 7.2 Hz, ArH), 6.46 (2H, d, *J* 8.0 Hz, ArH), 5.95 (1H, s, H-2), 5.13 (1H, t, *J* 5.2 Hz, H-6), 3.85 (3H, s, OMe), 3.07 (1H, dd, *J* 17.2, 4.8 Hz, H-5′), 2.76 (1H, dd, *J* 17.2, 5.2 Hz, H-5″); δ_C (100 MHz, $CDCl_3$) 170.7, 149.4, 147.5, 129.3, 128.1, 127.8, 124.3, 123.9, 120.7, 118.2, 101.0, 58.4, 56.5, 52.4, 36.9.

*4.2.25. Methyl 1-(2-naphthyl)-4-(2-naphthylamino)-2,6-diphenyl-1,2,5,6-tetrahydropyridine-3-carboxylate (**1v**).* Reaction was carried out with 2-naphthylamine (1 mmol), methyl acetoacetate (0.5 mmol) and benzaldehyde (1 mmol) in methanol (3 mL) in the presence of 10 mol % iodine at room temperature or at 55 °C. After completion of reaction, solid precipitate was filtered and washed with ethanol to give **1v** (0.297 g, 53%) as white solid; [found: C,

83.38; H, 5.63; N, 5.10. $C_{39}H_{32}N_2O_2$ requires C, 83.54; H, 5.75; N, 5.00%]; mp 196–198 °C; R_f (5% ethyl acetate/hexane) 0.30; ν_{max} (KBr) 3421 (N–H), 1657 (C=O), 1594 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.45 (1H, s, NH), 7.75 (1H, dd, *J* 8.0, 2.0 Hz, ArH), 7.59 (2H, t, *J* 8.4 Hz, ArH), 7.56–7.52 (2H, m, ArH), 7.47–7.41 (3H, m, ArH), 7.34–7.33 (4H, m, ArH), 7.31–7.20 (7H, m, ArH), 7.11 (1H, t, *J* 8.0 Hz, ArH), 6.97 (1H, dd, *J* 9.2, *J* 2.4 Hz, ArH), 6.77 (1H, d, *J* 2.4 Hz, ArH), 6.66 (1H, s, ArH), 6.59 (1H, s, H-2), 6.55 (1H, dd, *J* 8.8, 2.4 Hz, ArH), 5.30 (1H, br s, H-6), 3.99 (3H, s, OMe), 2.93 (2H, d, *J* 4.0 Hz, CH_2); δ_C (100 MHz, $CDCl_3$) 168.8 (C=O), 156.4 (C-4), 145.1, 144.0, 143.1, 135.5, 135.0, 133.5, 131.8, 129.1, 128.8, 128.5, 127.8, 127.7, 127.5, 127.4, 126.9, 126.7, 126.6, 126.5, 126.2, 125.9, 125.0, 123.3, 122.0, 116.2, 107.2, 98.4 (C-3), 58.6 (C-6), 55.4 (C-2), 51.4, 33.7 (C-5).

*4.2.26. Methyl 2,6-bis(4-methylphenyl)-1-(2-naphthyl)-4-(2-naphthylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (**1w**).* Reaction carried out with 2-naphthylamine (1 mmol), methyl acetoacetate (0.5 mmol) and methylbenzaldehyde (1 mmol) in methanol (3 mL) in the presence of 10 mol % iodine at room temperature. After completion, solid precipitate formed was filtered and washed with ethanol to give **1w** (0.300 g, 51%) as white solid; [found: C, 83.49; H, 5.91; N, 4.71. $C_{41}H_{36}N_2O_2$ requires C, 83.64; H, 6.16; N, 4.76%]; mp 220–222 °C; R_f (5% ethyl acetate/hexane) 0.33; ν_{max} (KBr) 3445 (N–H), 1656 (C=O), 1593 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.45 (1H, s, NH), 7.75 (2H, d, *J* 7.2 Hz, ArH), 7.60 (2H, t, *J* 8.8 Hz, ArH), 7.54–7.50 (2H, m, ArH), 7.47–7.42 (3H, m, ArH), 7.25–7.23 (3H, m, ArH), 7.14 (4H, s, ArH), 7.09 (2H, t, *J* 8.0 Hz, ArH), 6.98 (1H, dd, *J* 9.2, 2.4 Hz, ArH), 6.77 (1H, d, *J* 2.0 Hz, ArH), 6.60 (1H, s, H-2), 6.59–6.57 (2H, m, ArH), 5.26 (1H, br s, H-6), 3.98 (3H, s, OMe), 2.91 (2H, d, *J* 4.0 Hz, CH_2), 2.39 (3H, s, Me), 2.32 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 168.9 (C=O), 156.4 (C-4), 145.2, 141.0, 140.1, 137.0, 136.1, 135.6, 135.0, 133.6, 131.5, 129.7, 129.2, 129.0, 128.7, 127.8, 127.6, 127.5, 126.8, 126.6, 126.5, 126.4, 126.1, 125.8, 125.0, 123.2, 121.9, 116.2, 107.1, 98.5 (C-3), 58.4 (C-6), 55.2 (C-2), 51.3, 33.7 (C-5), 21.4, 21.2.

4.2.27. Ethyl 3-oxo-4-phenylbutanoate. It was prepared according to the literature procedure[19] from phenylacetyl chloride. To a solution of 2,2-dimethyl-1,3-dioxane-4,6-dione (1.44 g, 10 mmol) in CH_2Cl_2 (6 mL) at 0 °C in 100 mL round-bottomed flask equipped with a dropping funnel was added pyridine (2 mL) over 5 min. To this solution was then added a solution of phenylacetyl chloride (1.33 mL, 10 mmol) in CH_2Cl_2 (14 mL) over 10 min. This resulted in the formation of an orange solution. The reaction was stirred at 0 °C for 30 min and at rt for 1 h. CH_2Cl_2 (20 mL) was added and the solution was washed with water (30 mL×4). The organic phase was dried over $MgSO_4$ and the solvent was removed to give as an orange oil (2.2 g). This was dissolved in EtOH (30 mL) and heated at reflux for 3 h. Evaporation of the solvent afforded crude as an orange oil, which was purified by column chromatography using ethyl acetate/hexane (98:2) furnished (1.65 g, 80%) as a colourless oil; R_f (2% ethyl acetate/hexane) 0.4; ν_{max} (KBr) 1744 (C=O), 1716 (C=O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.36–7.28 (3H, m, ArH), 7.21 (2H, d, *J* 7.2 Hz, ArH), 4.17 (2H, q, *J* 7.2 Hz, OCH_2), 3.83 (3H, s, $PhCH_2$), 3.45 (2H, s, $COCH_2CO$), 1.26 (3H, t, *J* 7.2 Hz, CH_3); δ_C (100 MHz, $CDCl_3$) 200.6, 167.2, 133.4, 129.7, 129.0, 127.5, 61.5, 50.1, 48.4, 14.2.

4.3. Crystallographic description

Crystal data were collected with Bruker Smart Apex-II CCD diffractometer using graphite monochromated Mo Kα radiation (λ=0.71073 Å) at 298 K. Cell parameters were retrieved using SMART[20a] software and refined with SAINT[20a] on all observed reflections. Data reduction was performed with the SAINT software and corrected for Lorentz and polarization effects. Absorption corrections were applied with the program SADABS[20b]. The structure was solved by direct methods implemented in SHELX-97[20c] program and refined by full-matrix least-squares methods on F2. All non-hydrogen atomic positions were located in difference Fourier maps and refined anisotropically. The hydrogen atoms were placed in their geometrically generated positions. Compound **1f** empirical formula $C_{34}H_{32}Cl_2N_2O_2$, colourless prismatic crystal, formula wt 571.52, monoclinic, *P*2(1)/*n*, *a*=11.2764(3), *b*=12.9186(4), *c*=20.6225(6) Å, *V*=2976.78(15) $Å^3$, *Z*=4, *F* (0 0 0)=1200, GOF(S)=0.958. Final indices R_{obs}=0.0545, wR_{obs}=0.1747 with $I>2r(I)$; R_{all}=0.1118, wR_{all}=0.1924 for all data. Compound **1k** empirical formula $C_{31}H_{26}Br_2N_2O_2$, colourless prismatic crystal, formula wt 618.36, triclinic, *P*-1 *a*=10.1710(5), *b*=10.7901(5), *c*=13.9201(6) Å, *V*=1385.53(11) $Å^3$, *Z*=2, *F* (0 0 0)=624, GOF(S)=0.994. Final indices R_{obs}=0.0434, wR_{obs}=0.1026 with $I>2r(I)$; R_{all}=0.1047, wR_{all}=0.1289 for all data.

Complete crystallographic data of **1f** and **1k** for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, as supplementary publication CCDC no. are 756203 and 756204. Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44 1223 336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

Acknowledgements

M.M.K. is thankful to UGC, New Delhi, India for his research fellowship. We acknowledge DST, New Delhi for providing single crystal XRD facility to the Department of Chemistry under FIST programme (S.No.: SR/FST/CSII-007/2003).

Supplementary data

The general experimental procedures, X-ray crystallographic data (CIF file) of **1f** and **1k** as well as copies of ^1H and ^{13}C NMR and HRMS spectra of products. This information can be found in the online version, at doi:10.1016/j.tet.2010.07.075. These data include MOL files and InChIKeys of most important compounds described in this article.

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