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An efficient, metal-free, room temperature aromatization of Hantzsch-1,4-dihydropyridines with urea–hydrogen peroxide adduct, catalyzed by molecular iodine

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ABSTRACT

A mild, highly efficient and metal-free synthetic method for aromatization of 1,4-dihydropyridines employing urea–hydrogen peroxide adduct as oxidant catalyzed by 20 mol % of molecular iodine was developed. The reaction was carried out in ethyl acetate at room temperature and the products were isolated in high to excellent yields. A plausible free-radical mechanism is proposed based on results obtained with derivatives having alkyl and aryl substituents in the 1,4-dihydropyridine ring.

1. Introduction

1,4-Dihydropyridines (1,4-DHPs) belong to a class of nitrogen-containing heterocycles having a six-membered ring. Much attention has been devoted to explore their pharmacological activities. On the molecular level, 1,4-DHP compounds cause vasorelaxation by blocking voltage-operated calcium channels in smooth muscle cells and also by increasing NO release from intact endothelium.[1] Among other types of heterocyclic compounds having similar pharmacological activity (verapamil and diltiazem), 1,4-DHPs are the most potent calcium antagonists or calcium channel blockers.[2] They are found to be of use in the treatment of atherosclerosis and other coronary deseases.[3] Recently, their other pharmacological activities have been reported such as: antitumour,[4] bronchodilating,[5] antidiabetic,[6] antiviral,[7] antianginal,[8] amongst others.[9] Some commercial representatives such as amlodipine (**1**), felodipine (**2**), nifedipine (**3**) and nicardipine (**4**) are among the best selling drugs used in the treatment of cardiovascular diseases (Fig. 1).

The oxidation (aromatization) of 1,4-DHPs into the corresponding pyridines is one of the main metabolic pathways of these drugs. This process is catalyzed by the cytochrome P450 (CYP) 3A4 isoform.[10,11] Notably, the 1,4-DHP motif present in coenzymes NADH and NADPH mediates hydrogen-transfer reactions in biological systems.[12] In order to understand these biological processes, as well as to develop a useful synthetic approach to polysubstituted pyridines, the oxidative aromatization of 1,4-DHP derivatives has received considerable attention from synthetic chemists.

Numerous oxidants were studied in the aromatization of 1,4-DHPs such as nitric acid,[10,13] nitrous acid in situ formed by action of acids to $NaNO_2$,[14] nitrogen oxides,[15] metallic nitrates,[16]

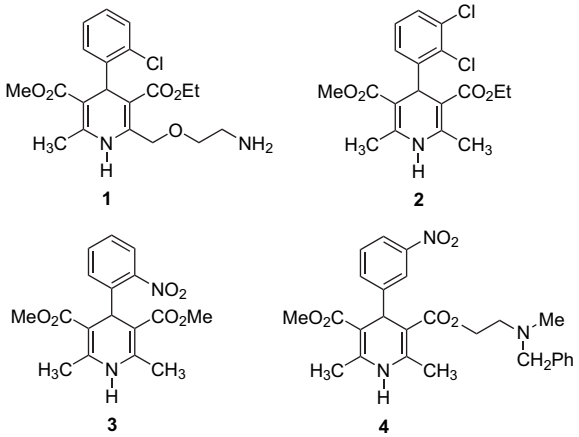

Figure 1.

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chromium(VI) oxidants,[17] CrO_2,[18] manganesse and iron (III) salts,[19] mercury(II) and Tl(III) salts,[20] $SnCl_4$,[21] $Pb(OAc)_4$,[22] $K_2S_2O_8$,[23] S_8,[24] O_2,[25] I_2,[26] and hyper-valentiodine reagents,[24b,27] non-metallic oxidants,[28] amongst others.[29] Some catalytical methods employing oxygen, hydrogen peroxide or other oxidants in stoichiometric amount have been developed such as $RuCl_3/O_2$,[30] $Fe(ClO_4)_3/O_2$,[31] Pd/C,[19c,32] activated charcoal/O_2,[33] Co(II)naphthenate/O_2,[34] $Co(OAc)_2/H_2O_2$[35] and others.[36] Additionally, metalic salts under influence of microwave irradiation have been used more efficiently compared to conventional heating.[37]

Despite the plethora of reagents used for aromatization of 1,4-DHPs, only a few of them are capable of performing the reaction at room temperature.[16c,d,19f,22] This is especially the case with catalytic methods. Most of the methods suffer from low selectivity and cumbersome work-up, which is often connected with production of a large amount of toxic water waste. Therefore, the development of new, facile and 'green' methods, particularly catalytic ones for the aromatization of 1,4-DHP are still demanding.

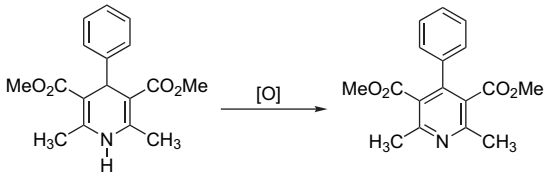
2. Results and discussion

The catalytic methods employing molecular oxygen, hydrogen peroxide or organic hydroperoxides for the aromatization of 1,4-DHP have advantages over the non-catalytic methods as they employ stoichiometric amount of oxidant. From the literature, metallic salts are mostly used as a catalyst to perform the reaction in mild conditions.[30,31,34,35] However, due to environmental issues, non-metallic catalysts would be a much better alternative. In the last decade, molecular iodine has attracted considerable attention in organic synthesis due to low toxicity and lowest reactivity of all halogen elements. Recently, we have utilized molecular iodine as an effective catalyst in a new method for acetoxylation of the 1,4-benzodiazepine ring and applied it for a kilogramme-scale production of lorazepam and oxazepam.[38] In a basic media or under ultrasonic irradiation, molecular iodine selectively oxidizes 1,4-DHPs at elevated temperatures.[26] However, its high molecular weight as well as harsh reaction conditions make this method rather unattractive. Additionally, hydrogen peroxide is a valuable oxidant for a wide variety of transformation in organic synthesis but its relatively low stability prevents its usage in water-immiscible solvents. A good alternative of 'anhydrous' H_2O_2 is a complex with urea (Urea–Hydrogen Peroxide adduct, UHP), which has found application in many oxidation reactions. Similarly to a solution of H_2O_2 in water, an adduct with urea has been utilized for aromatization of 1,4-DHP, but only in ionic liquids as solvent.[28d] The main drawback of all these methods is the inability to regenerate homogeneous catalysts as well as a tedious work-up.

Herein, we report a new, environmentally benign and effective catalytic method for aromatization of 1,4-DHPs employing UHP as a stoichiometric oxidant and molecular iodine as a catalyst. We began our studies on simple model 1,4-DHP **5** employing different environmentally friendly oxidants such as sodium perborate, sodium percarbonate, potassium iodate and UHP in acidic and neutral solvents. The results presented in Table 1 show excellent conversion in short reaction times, if sodium perborate and potassium iodate are used as oxidants (entries 1, 2 and 4) in acidic solvents. The method employing potassium iodate in 25% solution of trifluoroacetic acid in 96% ethanol as solvent is also of practical importance due to the fact that the reaction proceeds smoothly even at room temperature (rt).

The active oxidant in this reaction is actually iodic acid (HIO_3) released from its salt by action of strong trifluoroacetic acid. Sodium percarbonate (entry 3), due to rapid decomposition (foaming during addition of oxidant), reached only 50% conversion even after prolonged stirring. Next, we wanted to test UHP as oxidant at room temperature. In ethyl acetate, no reaction was observed even after

Table 1
Aromatization of 1,4-DHP **5** by different methods at rt



5 **6**

Entry	Oxidant	Solvent	*t* (h)	Conversion (%)
1	$NaBO_3 \cdot 4H_2O$[a]	AcOH	1	95
2	$NaBO_3 \cdot 4H_2O$[b]	AcOH	0.5	100 (97)[c]
3	$Na_2CO_3 \cdot 1.5H_2O_2$	AcOH	72	50
4	KIO_3	Mixture[d]	2	100 (95)[c]
5	$H_2O_2 \cdot CO(NH_2)_2$	AcOEt	72	0
6	$H_2O_2 \cdot CO(NH_2)_2/I_2$[e]	AcOEt	1	100 (98)[c]

[a] Reaction temperature (80–90 °C).
[b] Reflux temperature (118 °C).
[c] Yield after isolation.
[d] CF_3COOH (25%) in EtOH (96%).
[e] of I_2 (50 mol %).

72 h. To our surprise, the addition of 50 mol % of molecular iodine to reaction mixture initiated the reaction and complete conversion was reached within 1 h after carrying out the reaction at room temperature. Skulski and co-workers[39] have used a combination of UHP and molecular iodine for iodination of activated aromatics, but only in the presence of concentrated sulfuric acid as catalyst. Our preliminary results showed that aromatization of **5** occurred with 50 mol % of molecular iodine without any acid-catalyst. Encouraged by these results we decided to find the optimal reaction conditions for this reaction. As well as ethyl acetate, the reaction was tested in other solvents of different polarity.

The acidic solvents such as trifluoroacetic acid and acetic acid (Table 2, entries 2 and 4) were superior compared to non-polar solvents, but the selectivity was not as high as in ethyl acetate. In acetonitrile (entry 1), even traces of product were not found neither at room temperature nor at reflux temperature probably due to reaction of oxidant with solvent (formation of acetonitrile-*N*-oxide). Moreover, due to a poor solubility of UHP in dichloromethane the reaction reached only 50% conversion after 48 h of stirring at room temperature. These results led to the conclusion that ethyl acetate is the solvent of choice for the tested reaction. Although the reaction in trifluoroacetic acid is completed in shorter time, a tedious work-up including complete neutralization makes this solvent unacceptable.

Next, we decided to find the optimal amount of catalyst (I_2) to reach complete conversion at room temperature. The results presented in Table 3 show that even 1 mol % of I_2 (entry 2) efficiently catalyzes the reaction compared to the non-catalytic one (entry 1) but higher conversion was not observed even after several days. The incremental amount of catalyst drastically accelerates the reaction with the same level of selectivity. Thus the reaction with 50 mol % of catalyst was completed within 1 h, more efficient

Table 2
Aromatization of model 1,4-DHP **5** with UHP (2 equiv) catalyzed by molecular iodine (50 mol %) in different solvents at room temperature

Entry	Solvent	*t* (h)	Conversion (%)
1	CH_3CN	72	0[a]
2	CF_3COOH	2.5	100
3	AcOEt	3.5	100
4	AcOH	1.1	100[b]
5	CH_2Cl_2	48	50

[a] No conversion even at reflux temperature.
[b] According to TLC analysis about 10% of less polar side product is formed.

Table 3
Influence of the amount of catalyst (I_2) on aromatization of **5** at different period of time

Entry[a]	I_2 (mol %)	Conversion (%)					
		1 h	2 h	3.5 h	6.5 h	24 h	48 h
1	0	0	0	0	0	0	0
2	1	10	20	30	35	40	50
3	5	40	60	70	90	100	—
4	10	50	60	80	100	—	—
5	20	80	100	—	—	—	—
6	50	100	—	—	—	—	—

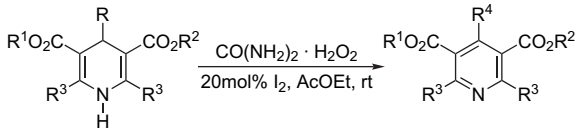
[a] UHP (2 equiv) in ethyl acetate at room temperature.

compared to the literature method employing stoichiometric amount of I_2 as oxidant.[26b] From the results outlined in Table 3, the amount of 20 mol % I_2 was chosen for further experiments due to the fact that the reaction time is similar to 50 mol % compared to lower amounts (entries 3 and 4) that required much longer reaction times.

To explore the scope and limitations of this new catalytic method employing molecular iodine, we decided to test it on a series of substituted 1,4-DHPs having a variety of substituents on all positions in the 1,4-DHP ring. The results presented in Table 4 indicate the generality of the method and high efficacy of this new oxidation system. The main characteristics of the reaction are excellent selectivity, yields and purity of the crude products. The reaction is complete between 30 min and 12 h, except for compound **32**, which is completely oxidized within 24 h. The yield of crude products is between 73–99%. Both electron-withdrawing (Table 4, entries 10–13) and electron-donating substituents (Table 4, entries 14–20) on the aromatic ring are well tolerated and have no considerable influence on the reaction rate. However, compound **26** (Table 4, entry 21) was an exception, and was oxidized three times faster compared to bromothienyl analogue **27** (Table 4, entry 22). Surprisingly, more lipophyllic alkyl substituents on the ester moiety were slowly oxidized (Table 4, entries 25–27) compared to methyl analogues. This could be explained by steric hindrance of the alkyl group rather than electron-donating ability. The most interesting result has been obtained with compound **33** (Table 4, entry 28) having *n*-propyl substituents in positions 2 and 6 of the 1,4-DHP ring. The reaction was complete within 30 min and the product was isolated in almost quantitative yield. This result shows that the electronic nature of the substituents on positions 2 and 6 of 1,4-DHP ring accelerate the reaction.

The aromatization of 4-ethyl and 4-*n*-propyl 1,4-DHPs (Table 4, entries 4 and 5) afforded the expected pyridines **35** and **36** in 80 and 91% yield, respectively. An interesting result was obtained with the corresponding 4-*i*-Pr and 4-$PhCH_2$–1,4-DHPs (Table 4, entries 2 and 3). According to HPLC analysis the reaction stopped at about 40% conversion accompanied with decolouration of the reaction mixture. No improvement was observed with additional equivalents of oxidant but incremental amount of catalyst (40 and 50 mol %) put forward the conversion to 80% and 100%, respectively. The isolated products showed complete dealkylation affording **34** in almost quantitative yield. The purification of the product obtained from aromatization of 4-benzyl-1,4-DHP **9** required chromatographic separation allowing isolation of benzyl-iodide (**59**; *CAUTION*: strong lachrymator) as a side product in the reaction which additionally proved dealkylation (Scheme 1). Even traces of **60** were not observed in this reaction.

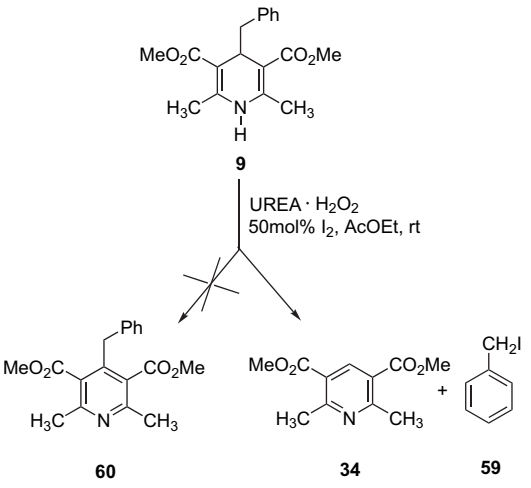
Table 4
Aromatization of substituted 1,4-DHPs with UHP (2 equiv) catalyzed by molecular iodine (20 mol %) at room temperature



5, 7-33 **6, 34-58**

Entry	1,4-DHP	R	R^1; R^2; R^3	Product	R^4	*t* (h)	Yield (%)
1	**7**	H	Me; Me; Me	**34**	H	0.75	99
2	**8**	*i*-Pr	Me; Me; Me	**34**	H	1[a]	99
3	**9**	CH_2Ph	Me; Me; Me	**34**	H	5[a]	99
4	**10**	Et	Me; Me; Me	**35**	Et	8	80
5	**11**	*n*-Pr	Me; Me; Me	**36**	*n*-Pr	3	91
6	**5**	Ph	Me; Me; Me	**6**	Ph	2	98
7	**12**	*o*-ClC_6H_4	Me; Me; Me	**37**	*o*-ClC_6H_4	1.5	95
8	**13**	*m*-ClC_6H_4	Me; Me; Me	**38**	*m*-ClC_6H_4	1.5	96
9	**14**	*p*-ClC_6H_4	Me; Me; Me	**39**	*p*-ClC_6H_4	1.5	96
10	**15**	*o*-$NO_2C_6H_4$	Me; Me; Me	**40**	*o*-$NO_2C_6H_4$	3	87
11	**16**	*m*-$NO_2C_6H_4$	Me; Me; Me	**41**	*m*-$NO_2C_6H_4$	1.25	89
12	**17**	*p*-$NO_2C_6H_4$	Me; Me; Me	**42**	*p*-$NO_2C_6H_4$	2	99
13	**18**	*m*-$NO_2C_6H_4$	Me; Et; Me	**43**	*m*-$NO_2C_6H_4$	1.55	95
14	**19**	*o*-$CH_3C_6H_4$	Me; Me; Me	**44**	*o*-$CH_3C_6H_4$	4.5; 0.42[b]	88
15	**20**	*m*-$CH_3C_6H_4$	Me; Me; Me	**45**	*m*-$CH_3C_6H_4$	2.5	93
16	**21**	*p*-$CH_3C_6H_4$	Me; Me; Me	**46**	*p*-$CH_3C_6H_4$	3	86
17	**22**	2,4-$(CH_3)_2C_6H_3$	Me; Me; Me	**47**	2,4-$(CH_3)_2C_6H_3$	1	89
18	**23**	*o*-$CH_3OC_6H_4$	Me; Me; Me	**48**	*o*-$CH_3OC_6H_4$	0.83	80
19	**24**	*m*-$CH_3OC_6H_4$	Me; Me; Me	**49**	*m*-$CH_3OC_6H_4$	2	97
20	**25**	*p*-$CH_3OC_6H_4$	Me; Me; Me	**50**	*p*-$CH_3OC_6H_4$	2.25	94
21	**26**	2-Thienyl	Me; Me; Me	**51**	2-Thienyl	4	88
22	**27**	2-(5-Br-thienyl)	Me; Me; Me	**52**	2-(5-Br-thienyl)	12	88
23	**28**	2-Furyl	Me; Me; Me	**53**	2-Furyl	6	73
24	**29**	*p*-Ph–C_6H_4	Me; Me; Me	**54**	*p*-Ph–C_6H_4	6	93
25	**30**	Ph	Et; Et; Me	**55**	Ph	12	89
26	**31**	Ph	*i*-Pr; *i*-Pr; Me	**56**	Ph	3	93
27	**32**	Ph	*t*-Bu; *t*-Bu; Me	**57**	Ph	24	83
28	**33**	Ph	Et; Et; *n*-Pr	**58**	Ph	0.5	99

[a] Reaction with 50 mol % I_2.
[b] At reflux temperature.

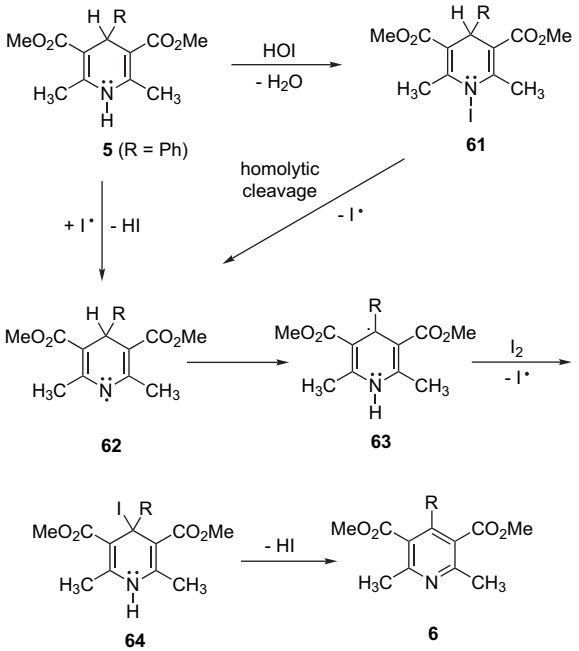


Scheme 1.

In a similar way to **9**, the corresponding 4-isopropyl-1,4-DHP **8** afforded isopropyliodide as a side product but it is probably removed in vacuo (bp 88–90 °C) during the work-up procedure. A possible mechanism of the iodine-catalyzed aromatization of 1,4-DHPs with UHP is outlined in Scheme 2 using the reaction with model 1,4-DHP **5** as a representative.

The aromatization of 1,4-DHPs with stoichiometric amount of molecular iodine takes place in the presence of base or elevated temperature. Similarly, 1,4-DHPs do not react with H_2O_2 at room temperature without a catalyst except, in ionic liquids, which serve as solvent and catalyst. Therefore, the combination of UHP and molecular iodine produces an active species, which is capable of reacting with 1,4-DHPs to give product, a substituted pyridine. Skulski and co-workers[39] have shown that electrophyllic iodination of aromatic compounds takes place smoothly by action of I^+ and I^{3+} species formed by oxidation of molecular iodine in acidic media. However, in neutral media the formation of such a reactive species is unlikely. Therefore, we have proposed that equilibrium amount of hypoiodous acid (HOI) is formed according the equation:

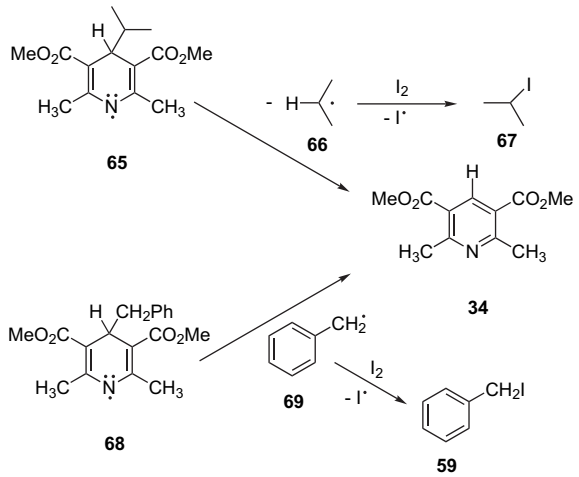
$$H_2O_2 + I_2 \leftrightharpoons 2HOI$$



Scheme 2.

Thus, the formed HOI is rapidly captured by nitrogen from the 1,4-DHP ring to form *N*-iodo derivative **61** with elimination of water.[40] The reaction is similar to N-nitrosation of 1,4-DHPs according to the work of Zhu and co-workers.[15b] If NO is used as oxidant, the formation of an aminyl radical is observed in contrast to reaction with *N*-methyl-*N*-nitrosotoluene-*p*-sulfonamide (MNTS) when the respective *N*-nitroso derivatives are formed as a sole product. This is explained by high electrophilicity of NO nitrogen bounded in MNTS. Similarly, iodine from HOI is also highly electrophillic and easily captured by nitrogen from the 1,4-DHP ring. *N*-Iodo intermediate **61** upon homolytic cleavage gives aminyl radical **62** and iodine atom. The reaction is conceptually similar to photolysis or thermolysis of hypoiodites, *N*-iodoamides and sulfenates.[41] Iodine atoms formed in the homolytic cleavage of **61** easily recombine to give molecular iodine[41a] and thus regenerate the catalyst. However, it cannot be excluded that iodine atoms react directly with 1,4-DHP **5** to form an aminyl radical **62** and HI, which is instantly oxidized with H_2O_2 to form water and I_2. Moreover, *N*-iodo-1,4-DHP **61** could rearrange directly to substituted tertiary iodide **64** via Kharasch-type iodine transfer. This one-step process is only possible at the beginning of the reaction when the concentration of **61** is still high.[41a] However, a two-step process including hydrogen transfer of **62** to give a more stable benzyllic radical **63**, followed by quenching with I_2 affording **61** is probably a major pathway due to the fact that I_2 is used as a catalyst. Finally, **64** upon elimination of HI gives substituted pyridine **6**. The difference in reactivities of **26** and **27** could be explained by the first step of the mechanism, by formation of *N*-iodo-1,4-DHP **61** or by the last step, by elimination of HI from **64**. These two steps are slightly sensitive to the electronic nature of the substituents present on aromatic ring. Thus, the presented mechanism is characteristic for 4-aryl-sustituted 1,4-DHPs as well as for 1,4-DHPs having primary aliphatic substituents such as ethyl and *n*-propyl (**10** and **11**). The dealkylation of 4-isopropyl-1,4-DHP **8** and 4-benzyl-1,4-DHP **9** can be easily explained by the mechanism presented in Scheme 3.

The aminyl radicals **65** and **68**, formed by homolytic cleavage of the corresponding *N*-iodo intermediates upon hydrogen transfer, give the same product of dealkylation **34** with elimination of isopropylic (**66**) and benzylic (**69**) radicals. The irreversible reaction with I_2 gives the corresponding isopropyliodide (**67**) and benzyliodide (**59**), which leads to complete consumption of the catalyst. Therefore, a stoichiometric amount of I_2 is required to reach 100% conversion of the starting 1,4-DHPs. It is worth mentioning that during aromatization of compounds **31** and **32**, having isopropyl and *tert*-butyl ester moieties, a small amount (<1%) of less polar unstable side-products were formed. It was proposed that



Scheme 3.

iodination of side-chain esters took place by hydrogen transfer from the isopropyl and *tert*-butyl groups to the aminyl radical. The investigation of this reaction is in progress and the results will be published in due course.

3. Conclusions

Molecular iodine acts as an efficient catalyst for the aromatization of 1,4-DHPs employing the urea–hydrogen peroxide adduct as an environmentally benign stoichiometric oxidant. The reaction proceeds smoothly at room temperature in neutral conditions and products of high purity were isolated after a simple work-up procedure in good-to-high yields. The proposed reaction mechanism initially includes the formation of *N*-iodo derivatives, which upon homolytic cleavage give the corresponding aminyl radical. In the next step, by hydrogen transfer, the more stable benzylic radical is formed and captured by molecular iodine to give the unstable tertiary iodide, which upon elimination of HI gives the product, substituted pyridine. The catalyst (I_2) is regenerated either by recombination of iodine atoms or oxidation of HI by H_2O_2.

4. Experimental section

4.1. General

All IR spectra were recorded on a Perkin–Elmer Spectrum One spectrometer. ^{1}H NMR and ^{13}C NMR were recorded on a Bruker 600 for $CDCl_3$ solutions, shifts are given in parts per million downfield from TMS as an internal standard. HPLC analyses were performed with a Thermo Separation Products (San Jose, USA) instrument equipped with vacuum degasser SCM 1000, quaternary gradient pump P 4000, autosampler AS 3000, scanning UV/VIS detector UV 3000 HR and ChromQuest 251 software. TLC analyses were performed on Merck's (Darmstadt, Germany) DC-alufolien with Kieselgel 60_{254}. Melting points were determined using a Büchi B540 instrument. Elemental analyses were done in Central Analytical Service (CAS) at Ruđer Bošković Institute. Gram-scale samples of 1,4-DHPs **5**, **10**–**12**, **19**–**21** and **24**–**32** were prepared by modified Hantzsch method employing 2 equiv of corresponding aminocrotonate esters[42] and aliphatic or aromatic aldehyde.[43] Compounds **13** and **14** were efficiently prepared by a method developed in our laboratory employing tetraethyl orthosilicate as a water scavenging agent,[44] whilst 1,4-DHPs (**7**–**9**, **15**–**18**, **22**, **23** and **33**) by modification of classical literature methods.[22,43a,45] The literature known products were characterized by a comparison with authentic samples (melting point) and their NMR (^{1}H, ^{13}C) and IR spectra.[17f,19e,22,26a,28d]

4.2. General procedure for the Hantzsch condensation of aromatic and aliphatic aldehydes with 2 equiv of methyl-3-aminocrotonate

To a solution of corresponding aromatic or aliphatic aldehydes (0.05 mol) in 2-PrOH (25 mL) methyl-3-aminocrotonate (11.51 g, 0.1 mol) was added at once. The reaction mixture was heated at reflux temperature until the disappearance of starting aldehyde (TLC control). After cooling to room temperature, the reaction mixture was allowed to stand in a refrigerator for 48 h. Thus obtained crystals were removed by filtration, washed with cold 2-PrOH (2×20 mL) and dried in vacuum to constant weight. 1,4-DHPs **19** and **21** crystallized upon addition of diisopropyl ether (50 mL) to crude reaction mixtures. After cooling in a refrigerator for 48 h, obtained crystals were removed by filtration, washed with cold diisopropyl ether (2×20 mL) and dried in vacuum to a constant weight.

*4.2.1. 2,6-Dimethyl-3,5-dimethoxycarbonyl-4-(2-methylphenyl)-1,4-dihydropyridine (**19**)*

Yellow crystals; yield: 1.5 g (9.5%); R_f (CH_2Cl_2/EtOAc, 9:1)=0.42; mp 160.0–163.5 °C; IR (KBr): ν=3383, 2951, 2925, 1690, 1651, 1622, 1484, 1460, 1434, 1378, 1337, 1312, 1298, 1252, 1213, 1184, 1145, 1118, 1095, 1050, 1021 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=2.30 (s, 6H, Me), 2.54 (s, 2H, Me), 3.61 (s, 6H, OMe), 5.14 (s, 1H, CH), 5.83 (s, 1H, NH), 6.97–7.07 (m, 3H), 7.30 (d, 1H, J=7.4 Hz); ^{13}C NMR ($CDCl_3$): δ=18.9, 19.3, 35.3, 50.6, 104.6, 125.8, 126.0, 129.1, 129.6, 134.9, 143.9, 147.5, 168.1; Anal. Calcd for $C_{18}H_{21}NO_4$: C 68.55, H 6.71, N 4.44; found: C 68.5, H 6.7, N 4.4.

*4.2.2. 2,6-Dimethyl-3,5-dimethoxycarbonyl-4-(3-methylphenyl)-1,4-dihydropyridine (**20**)*

Pale yellow crystals; yield: 4.61 g (29%); R_f (CH_2Cl_2/EtOAc, 9:1)=0.60; mp 189.5–191.0 °C; IR (KBr): ν=3354, 3247, 3096, 3030, 3008, 2989, 2948, 2847, 2780, 1703, 1652, 1626, 1603, 1586, 1489, 1459, 1437, 1424, 1381, 1343, 1315, 1298, 1266, 1247, 1217, 1187, 1139, 1160, 1123, 1098, 1052, 1017 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=2.27 (s, 3H, Me), 2.29 (s, 6H, Me), 3.64 (s, 6H, OMe), 4.98 (s, 1H, CH), 6.19 (s, 1H, NH), 6.94 (d, 1H, J=7.0 Hz), 7.05–7.12 (m, 3H); ^{13}C NMR ($CDCl_3$): δ=19.2, 21.4, 38.9, 50.8, 103.4, 124.5, 126.9, 127.7, 128.1, 137.2, 144.4, 147.2, 168.1; Anal. Calcd for $C_{18}H_{21}NO_4$: C 68.55, H 6.71, N 4.44; found: C 68.4, H 6.6, N 4.4.

*4.2.3. 2,6-Dimethyl-3,5-dimethoxycarbonyl-4-(4-methylphenyl)-1,4-dihydropyridine (**21**)*

Yellow crystals; yield: 0.85 g (5.5%); R_f (CH_2Cl_2/EtOAc, 9:1)=0.60; mp 168.5–171.0 °C; IR (KBr): ν=3315, 3250, 3049, 3023, 2943, 2842, 1698, 1655, 1496, 1435, 1381, 1341, 1316, 1305, 1243, 1216, 1188, 1141, 1122, 1096, 1048, 1020 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=2.27 (s, 3H, Me), 2.30 (s, 6H, Me), 3.64 (s, 6H, OMe), 4.97 (s, 1H, CH), 6.01 (s, 1H, NH), 7.02 (d, 2H, J=7.9 Hz), 7.15 (d, 2H, J=7.9 Hz); ^{13}C NMR ($CDCl_3$): δ=15.3, 20.9, 38.6, 50.8, 103.7, 127.3, 128.6, 135.5, 144.2, 144.4, 168.0; Anal. Calcd for $C_{18}H_{21}NO_4$: C 68.55, H 6.71, N 4.44; found: C 68.4, H 6.6, N 4.3.

*4.2.4. 2,6-Dimethyl-3,5-dimethoxycarbonyl-4-(5′-bromo-2-thienyl)-1,4-dihydropyridine (**27**)*

Pale yellow crystals; 5.59 g (29%); R_f (CH_2Cl_2/EtOAc, 9:1)=0.57; mp 195.5–197.5 °C; IR (KBr): ν=3348, 3090, 2993, 2947, 2835, 1698, 1684, 1644, 1619, 1530, 1486, 1429, 1380, 1342, 1308, 1282, 1265, 1213, 1186, 1159, 1114, 1095, 1053, 1019 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=2.33 (s, 6H, Me), 3.72 (s, 6H, OMe), 5.24 (s, 1H, CH), 6.08 (s, 1H, NH), 6.52 (d, 1H, J=3.7 Hz), 6.78 (d, 1H, J=3.7 Hz); ^{13}C NMR ($CDCl_3$): δ=19.3, 34.6, 51.1, 102.5, 109.5, 123.1, 129.1, 145.1, 152.6, 167.4; Anal. Calcd for $C_{15}H_{16}BrNO_4S$: C 46.64, H 4.18, Br 20.69, N 3.63, S 8.30; found: C 46.6, H 4.1, Br 20.5, N 3.6, S 8.2.

*4.2.5. 2,6-Dimethyl-3,5-dimethoxycarbonyl-4-(4′-biphenyl)-1,4-dihydropyridine (**29**)*

Pale yellow crystals; 9.43 g (50%); R_f (CH_2Cl_2/EtOAc, 9:1)=0.56; mp 226.0–227.5 °C; IR (KBr): ν=3347, 3244, 3082, 3025, 2947, 2842, 1701, 1652, 1626, 1489, 1449, 1431, 1375, 1344, 1301, 1263, 1219, 1180, 1144, 1122, 1098, 1053, 1017, 1008 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=2.32 (s, 6H, Me), 3.66 (s, 6H, OMe), 5.06 (s, 1H, CH), 6.01 (s, 1H, NH), 7.24–7.28 (m, 1H), 7.32 (d, 2H, J=8.3 Hz), 7.37 (d, 2H, J=7.7 Hz), 7.41–7.45 (m, 2H), 7.53 (d, 2H, J=7.3 Hz); ^{13}C NMR ($CDCl_3$): δ=19.3, 38.8, 50.9, 103.5, 126.7, 126.8, 126.8, 127.8, 128.5, 138.9, 141.0, 144.4, 146.4, 168.0; Anal. Calcd for $C_{23}H_{23}NO_4$: C 73.19, H 6.14, N 3.71; found: C 73.1, H 6.1, N 3.7.

*4.2.6. 2,6-Dimethyl-3,5-dimethoxycarbonyl-4-(2,4-dimethylphenyl)-1,4-dihydropyridine (**22**)*

A solution of 2,4-dimethylbenzaldehyde (10.0 g, 74.5 mmol), methyl acetoacetate (17.3 g, 149 mmol) and ammonium acetate (6.36 g, 82.5 mmol) in 2-PrOH (50 mL) was heated at reflux

temperature during 23 h, cooled to rt and evaporated to dryness. To the residue, chloroform (50 mL) and water (50 mL) were added and pH was adjusted to 8 with solid $NaHCO_3$ (foaming). After separation, organic layer was dried over anhydrous sodium sulfate, filtered and evaporated to dryness. The residue was dissolved in hot diisopropyl ether (150 mL) and the resultant solution was cooled to rt. The product was filtered, washed with diisopropyl ether (3×30 mL) and dried in vacuum to give **22** as yellow crystals; yield: 8.52 g (17%); R_f (CH_2Cl_2/EtOAc, 9:1)=0.46; mp 191.5–193.5 °C; IR (KBr): ν=3371, 2990, 2947, 1688, 1655, 1655, 1625, 1486, 1458, 1436, 1377, 1338, 1313, 1298, 1255, 1213, 1184, 1148, 1121, 1096, 1051, 1020 cm^{-1}; ^1H NMR ($CDCl_3$): δ=2.22 (s, 3H, Me), 2.25 (s, 6H, Me), 2.51 (s, 3H, Me), 3.61 (s, 6H, OMe), 5.10 (s, 1H, CH), 6.19 (s, 1H, NH), 6.85 (s, 1H), 6.87 (s, 1H), 7.19 (d, 1H, J=7.7 Hz); ^{13}C NMR ($CDCl_3$): δ=18.8, 19.2, 19.3, 34.9, 50.6, 104.6, 126.8, 128.9, 130.3, 134.6, 135.1, 143.8, 144.6, 168.1; Anal. Calcd for $C_{19}H_{23}NO_4$: C 69.28, H 7.04, N 4.25; found: C 69.3, H 7.0, N 4.2.

4.2.7. 2,6-Dimethyl-3,5-diisopropoxycarbonyl-4-phenyl-1,4-dihydropyridine (*31*)

To a suspension of ammonium carbamate (15.61 g, 0.2 mol) in MeOH (100 mL), isopropyl-acetoacetate (28.83 g, 0.14 mol) was added at once with stirring. The reaction mixture was stirred at rt during 22 h and then evaporated to dryness. Thus obtained crude isopropyl-3-aminocrotonate (quantitative yield) was dissolved in *i*-PrOH (50 mL) and to the resulting solution, benzaldehyde (7.43 g, 0.07 mol) was added. The reaction mixture was heated at reflux temperature during 40 h, cooled to rt and then evaporated to dryness. The residue was dissolved in hot diisopropyl ether (50 mL) and then *n*-hexane (100 mL) was added dropwise at about 60 °C. After that, the reaction mixture was slowly cooled to −18 °C with stirring. The product is filtered, washed with cold *n*-hexane (3×20 mL), and dried in vacuum to give **31** as yellow crystals; yield: 7.57 g (31%); R_f (CH_2Cl_2/EtOAc, 9:1)=0.59; mp 127.5–129.5 °C; IR (KBr): ν=3356, 3085, 3027, 2982, 2935, 1690, 1654, 1561, 1482, 1452, 1374, 1362, 1337, 1310, 1298, 1247, 1213, 1180, 1143, 1108, 1090, 1014 cm^{-1}; ^1H NMR ($CDCl_3$): δ=1.11 (d, 6H, CH_3CHCH_3, J=6.3 Hz), 1.24 (d, 6H, CH_3CHCH_3, J=6.2 Hz), 2.29 (s, 6H, Me), 4.88–5.03 (m, 2H, CHMe), 4.96 (s, 1H, CH), 5.98 (s, 1H, NH), 7.07–7.12 (m, 1H), 7.16–7.21 (m, 2H), 7.25–7.29 (m, 2H); ^{13}C NMR ($CDCl_3$): δ=19.2, 21.6, 21.9, 39.6, 66.8, 104.1, 125.8, 127.5, 128.0, 143.6, 147.8, 167.1; Anal. Calcd for $C_{21}H_{27}NO_4$: C 70.56, H 7.61, N 3.92; found: C 70.5, H 7.6, N 3.9.

4.2.8. 2,6-Dimethyl-3,5-di-(tert-butoxycarbonyl)-4-phenyl-1,4-dihydropyridine (*32*)

To a solution of ammonium carbamate (15.61 g, 0.2 mol) in MeOH (100 mL), *tert*-butyl-acetoacetate (31.64 g, 0.2 mol) was added at once with stirring. The reaction mixture was stirred at rt during 22 h and then evaporated to dryness. Thus obtained crude *tert*-butyl-3-aminocrotonate (quantitative yield) was dissolved in 2-PrOH (50 mL) and to the resulting solution benzaldehyde (10.61 g, 0.1 mol) was added. The reaction mixture was heated at reflux temperature during 43 h, cooled to rt and evaporated to dryness. The residue was dissolved in hot diethyl ether (50 mL) and then *n*-hexane (100 mL) was added dropwise. After that reaction mixture was slowly cooled to −18 °C with stirring. The product is filtered, washed with cold diethyl ether (3×20 mL) and dried in vacuum to give **32** as yellow crystals; yield: 12.11 g (40%); R_f (CH_2Cl_2/EtOAc, 9:1)=0.69; mp 168.0–171.5 °C; IR (KBr): ν=3480, 3325, 3251, 3106, 3083, 3028, 3003, 2975, 2930, 2893, 2828, 1698, 1644, 1611, 1538, 1493, 1454, 1436, 1389, 1366, 1356, 1340, 1304, 1269, 1255, 1228, 1163, 1144, 1115, 1100, 1073, 1046, 1014 cm^{-1}; ^1H NMR ($CDCl_3$): δ=1.39 (s, 18H, CMe_3), 2.28 (s, 6H, Me), 4.92 (s, 1H, CH), 5.45 (s, 1H, NH), 7.08–7.13 (m, 1H), 7.17–7.22 (m, 2H), 7.27–7.31 (m, 2H); ^{13}C NMR ($CDCl_3$): δ=19.3, 28.2, 40.1, 79.5, 105.2, 125.8, 126.5, 127.6, 127.9, 128.4, 124.7, 147.8, 167.0; Anal. Calcd for $C_{23}H_{31}NO_4$: C 71.66, H 8.11, N 3.63; found: C 71.5, H 8.0, N 3.6.

4.2.9. 2,6-Di-n-propyl-3,5-diethoxycarbonyl-4-phenyl-1,4-dihydropyridine (*33*)

To a suspension of ammonium acetate (1.54 g, 0.02 mol) in 2-PrOH (100 mL), ethyl butyrylacetate (6.33 g, 6.39 mL, 0.04 mol) and benzaldehyde (2.12 g, 2.02 mL, 0.02 mmol) were added dropwise (5 min). The reaction mixture was heated at reflux temperature during 43 h. After cooling to rt, reaction mixture was left at −18 °C for 20 days. Obtained crystals were filtered, washed with cold 2-PrOH (2×5 mL) and dried in vacuum to give **33** as white crystals; yield: 0.28 g (3.6%); R_f (CH_2Cl_2/EtOAc, 9:1)=0.76; mp 112.0–113.0 °C; IR (KBr): ν=3313, 3090, 2961, 2934, 2903, 2874, 1693, 1669, 1640, 1615, 1493, 1450, 1433, 1368, 1284, 1250, 1198, 1121, 1103, 1074, 1057 cm^{-1}; ^1H NMR ($CDCl_3$): δ=1.00 (t, 6H, $CH_2CH_2CH_3$, J=7.3 Hz), 1.24 (t, 6H, CH_2CH_3, J=7.1 Hz), 1.55–1.74 (m, 2H, $CH_2CH_2CH_3$), 2.57–2.69 (m, 2H, $CH_2CH_2CH_3$), 2.74–2.83 (m, 2H, $CH_2CH_2CH_3$), 4.02–4.18 (m, 4H, CH_2CH_3), 5.03 (s, 1H, CH), 5.75 (s, 1H, NH), 7.10–7.19 (m, 1H), 7.21–7.24 (m, 2H), 7.28–7.32 (m, 2H, arom.); ^{13}C NMR ($CDCl_3$): δ=13.8, 14.1, 21.8, 34.4, 39.6, 59.5, 103.6, 125.9, 127.7, 127.8, 147.8, 148.1, 167.2; Anal. Calcd for $C_{23}H_{31}NO_4$: C 71.66, H 8.11, N 3.63; found: C 71.6, H 8.0, N 3.6.

4.3. General procedure for the aromatization of 1,4-DHPs with UHP catalyzed by molecular iodine

To a solution of corresponding 1,4-DHPs (1.0 mmol) in EtOAc (10 mL), molecular iodine (51 mg, 0.2 mmol, 20 mol %) and UHP (0.19 g, 2.0 mmol) were added. The reaction mixture was stirred at rt for the time indicated in Table 4. The progress of the reactions was monitored by TLC. After that to the reaction mixtures, water (10 mL) and solid $Na_2S_2O_5$ in small portions were added to complete decolouration. The phases were separated and the aqueous phase was additionally extracted with EtOAc (10 mL). The combined organic layers were dried over Na_2SO_4, filtered and evaporated to dryness. The crude products were recrystallized from diisopropyl ether to give products of purity >99%.

4.3.1. 2,6-Dimethyl-3,5-dimethoxycarbonyl-4-(2-methylphenyl)-pyridine (*44*)

Yellow needles; yield: 0.28 g (88%); R_f (CH_2Cl_2/EtOAc, 9:1)=0.30; mp 71.0–73.5 °C; IR (KBr): ν=2994, 2951, 1727, 1558, 1493, 1441, 1405, 1378, 1302, 1237, 1213, 1166, 1117, 1102 cm^{-1}; ^1H NMR ($CDCl_3$): δ=2.09 (s, 3H, Me), 2.60 (s, 6H, Me), 3.47 (s, 6H, OMe), 7.01–7.03 (m, 1H), 7.12–7.31 (m, 1H); ^{13}C NMR ($CDCl_3$): δ=19.5, 22.7, 51.8, 124.7, 126.7, 128.1, 128.3, 129.3, 135.0, 135.8, 146.2, 155.3, 167.8; Anal. Calcd for $C_{18}H_{19}NO_4$: C 68.99, H 6.11, N 4.47; found: C 68.9, H 6.1, N 4.4.

4.3.2. 2,6-Dimethyl-3,5-dimethoxycarbonyl-4-(3-methylphenyl)-pyridine (*45*)

Yellow crystals; yield: 0.29 g (93%); R_f(CH_2Cl_2/EtOAc, 9:1)=0.31; mp 93.5–95.5 °C; IR (KBr): ν=2959, 2927, 1733, 1606, 1563, 1488, 1454, 1428, 1373, 1289, 1239, 1209, 1106, 1033 cm^{-1}; ^1H NMR ($CDCl_3$): δ=2.35 (s, 3H, Me), 2.59 (s, 6H, Me), 3.55 (s, 6H, OMe), 7.02–7.05 (m, 2H), 7.16–7.18 (m, 1H), 7.23–7.28 (m, 1H); ^{13}C NMR ($CDCl_3$): δ=21.2, 22.8, 52.0, 124.7, 126.6, 128.0, 128.2, 129.2, 136.2, 137.8, 146.2, 155.3, 168.4; Anal. Calcd for $C_{18}H_{19}NO_4$: C 68.99, H 6.11, N 4.47; found: C 68.8, H 5.9, N 4.3.

4.3.3. 2,6-Dimethyl-3,5-dimethoxycarbonyl-4-(4-methylphenyl)-pyridine (*46*)

Pale yellow crystals; yield: 0.27 g (86%); R_f (CH_2Cl_2/EtOAc, 9:1)=0.30; mp 82.5–85.0 °C; IR (KBr): ν=2997, 2952, 1728, 1612,

1554, 1512, 1433, 1396, 1373, 1299, 1234, 1212, 1184, 1105, 1043, 1018 cm^{-1}; ^1H NMR ($CDCl_3$): δ=2.36 (s, 3H, CH_3), 2.58 (s, 6H, CH_3), 3.56 (s, 6H, OMe), 7.13 (d, 2H, J=8.0 Hz), 7.18 (d, 2H, J=8,0 Hz); ^{13}C NMR ($CDCl_3$): δ=21.0, 22.6, 51.9, 127.0, 127.4, 128.7, 133.1, 138.1, 146.0 155.1, 168.3; Anal. Calcd for $C_{18}H_{19}NO_4$: C 68.99, H 6.11, N 4.47; found: C 68.8, H 6.0, N 4.4.

4.3.4. 2,6-Dimethyl-3,5-dimethoxycarbonyl-4-(2,4-dimethyl-phenyl)-pyridine (**46**)

Pale yellow oil; yield: 0.29 g (89%); R_f(CH_2Cl_2/EtOAc, 9:1)=0.32; IR (film): ν=2953, 2924, 1736, 1614, 1561, 1501, 1435, 1403, 1379, 1331, 1294, 1239, 1211, 1193, 1150, 1120, 1103, 1039 cm^{-1}; ^1H NMR ($CDCl_3$): δ=2.05 (s, 3H, Me), 2.32 (s, 3H, Me), 2.59 (s, 6H, Me), 3.51 (s, 6H, OMe), 6.89–6.97 (m, 2H), 7.00 (s, 1H); ^{13}C NMR ($CDCl_3$): δ=19.5, 21.1, 22.9, 51.9, 125.6, 127.0, 128.1, 130.2, 132.1, 135.6, 138.0, 146.5, 155.2, 168.0; Anal. Calcd for $C_{19}H_{21}NO_4$: C 69.71, H 6.47, N 4.28; found: C 69.6, H 6.4, N 4.0.

4.3.5. 2,6-Dimethyl-3,5-dimethoxycarbonyl-4-(5-bromothienyl)-pyridine (**52**)

Pale yellow crystals; yield: 0.34 g (88%); R_f (CH_2Cl_2/EtOAc, 9:1)=0.42; mp 110.0–112.0 °C; IR (KBr): ν=2953, 1732, 1559, 1530, 1433, 1400, 1374, 1337, 1238, 1208, 1125, 1102, 1037 cm^{-1}; ^1H NMR ($CDCl_3$): δ=2.57 (s, 6H, Me), 3.73 (s, 6H, OCH_3), 6.81–6.82 (d, 2H, J=3.8 Hz), 7.01 (d, 2H, J=3.8 Hz); ^{13}C NMR ($CDCl_3$): δ=22.8, 52.5, 114.6, 126.9, 128.8, 130.0, 137.2, 137.5, 155.6, 167.9; Anal. Calcd for $C_{15}H_{14}BrNO_4S$: C 46.89, H 3.67, Br 20.80, N 3.65, S 8.34; found: C 46.7, H 3.5, Br 20.0, N 3.6, S 8.3.

4.3.6. 2,6-Dimethyl-3,5-dimethoxycarbonyl-4-(4′-biphenyl)-pyridine (**54**)

Pale yellow needles; yield: 0.35 g (93%); R_f (CH_2Cl_2/EtOAc, 9:1)=0.23; mp 143.0–145.0 °C; IR (KBr): ν=1727, 1599, 1567, 1519, 1488, 1436, 1401, 1373, 1335, 1298, 1243, 1192, 1157, 1110, 1044, 1008 cm^{-1}; ^1H NMR ($CDCl_3$): δ=2.63 (s, 6H, Me), 3.58 (s, 6H, OMe), 7.32–7.50 (m, 6H), 7.57–7.73 (m, 4H); ^{13}C NMR ($CDCl_3$): δ=22.9, 52.1, 126.6, 126.7, 126.9, 127.6, 128.1, 128.8, 135.2, 140.0, 141.0, 145.7, 155.5, 168.4; Anal. Calcd for $C_{23}H_{21}NO_4$: C 73.58, H 5.64, N 3.73; found: C 73.5, H 5.5, N 3.7.

4.3.7. 2,6-Dimethyl-3,5-diisopropoxycarbonyl-4-phenyl-pyridine (**56**)

Pale yellow crystals; yield: 0.33 g (93%); R_f (CH_2Cl_2/EtOAc, 9:1)=0.37; mp 84.0–89.0 °C; IR (KBr): ν=2979, 1727, 1714, 1555, 1536, 1455, 1374, 1290, 1234, 1095, 1036 cm^{-1}; ^1H NMR ($CDCl_3$): δ=0.86 (d, 12H, $CHMe_2$, J=6.2), 2.51 (s, 6H, Me), 4.80–4.84 (m, 2H, $CHMe_2$), 7.18–7.19 (m, 2H); 7.27–7.28 (m, 3H); ^{13}C NMR ($CDCl_3$): δ=20.7, 22.3, 68.5, 126.7, 127.4, 127.5, 127.8, 127.9, 135.9, 145.1, 154.5, 166.8; Anal. Calcd for $C_{21}H_{25}NO_4$: C 70.96, H 7.09, N 3.94; found: C 70.8, H 6.9, N 3.8.

4.3.8. 2,6-Dimethyl-3,5-di-(tert-butoxycarbonyl)-4-phenyl-pyridine (**57**)

Colourless crystals; yield: 0.32 g (83%); R_f (CH_2Cl_2/EtOAc, 9:1)=0.41; mp 88.0–92.0 °C; IR (KBr): ν=3437, 3064, 3004, 2996, 2983, 2931, 1731, 1719, 1563, 1496, 1476, 1457, 1410, 1393, 1366, 1305, 1251, 1157, 1107, 1076, 1045, 1026 cm^{-1}; ^1H NMR ($CDCl_3$): δ=1.18 (s, 18H, CMe_3), 2.58 (s, 6H, Me), 7.26–7.29 (m, 2H), 7.36–7.37 (m, 3H); ^{13}C NMR ($CDCl_3$): δ=22.7, 27.5, 82.2, 127.8, 128.0, 128.2, 128.8, 136.4, 145.0, 154.3, 166.9; Anal. Calcd for $C_{23}H_{29}NO_4$: C 72.04, H 7.62, N 3.65; found: C 71.8, H 7.5, N 3.6.

4.3.9. 2,6-Di-n-propyl-3,5-dimethoxycarbonyl-4-phenyl-pyridine (**58**)

Pale yellow oil; yield: 0.38 g (99%); R_f(CH_2Cl_2/EtOAc, 9:1)=0.35; IR (film): ν=2964, 2934, 2873, 1728, 1557, 1496, 1465, 1446, 1385, 1367, 1302, 1255, 1216, 1173, 1155, 1109, 1053, 1028 cm^{-1}; ^1H NMR ($CDCl_3$): δ=0.89 (t, 6H, CH_2CH_3, J=7.1), 0.98 (t, 6H, $CH_2CH_2CH_3$), 1.74–1.82 (m, 4H, $CH_2CH_2CH_3$), 2.78–2.83 (m, 4H, $CH_2CH_2CH_3$), 3.98 (q, 4H, CH_2CH_3, J=14.3), 7.24–7.28 (m, 2H), 7.34–7.36 (m, 3H); ^{13}C NMR ($CDCl_3$): δ=13.5, 14.0, 23.1, 38.3, 61.2, 126.7, 128.0, 128.2, 128.3, 136.7, 146.0, 159.1, 168.0; Anal. Calcd for $C_{23}H_{29}NO_4$: C 72.04, H 7.62, N 3.65; found: C 71.8, H 7.5, N 3.6.

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