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Short communication

Hafnium (IV) bis(perfluorooctanesulfonyl)imide complex catalyzed synthesis of polyhydroquinoline derivatives via unsymmetrical Hantzsch reaction in fluorous medium

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ABSTRACT

A facile and efficient synthesis of polyhydroquinoline derivatives was reported via four-component condensation reaction of aldehydes, dimedone, active methylene compounds, and ammonium acetate in the presence of $Hf(NPf_2)_4$ in $C_{10}F_{18}$ at 60 °C. The method offers several advantages including high yields, short reaction time, simple work-up procedure and catalyst reusability.

1. Introduction

4-Substituted 1,4-dihydropyridines (DHPs) comprise a large family of medicinally important compounds. They can cure the disordered heart ratio as a chain-cutting agent of factor IV channel, possess the calcium channel agonist–antagonist modulation activities [1] and also behave as neuroprotectants, cerebral antiischaemic agents and chemosensitizers [2]. A recent computational analysis of the comprehensive medicinal chemistry database found that the DHP framework to be the most prolific chemotypes. Quinolines having 1,4-dihydropyridine nucleus are very important compounds because of their pharmacological properties. Members of this family are being used as antimalarial, antiinflammatory, anti-asthamatic, antibacterial, and tyrosine kinase inhibiting agents [3]. For these reasons, polyhydroquinoline compounds not only attract the attention of chemists to synthesize but also represent an interesting research challenge.

The classical methods involve the three-component condensation of an aldehyde with ethyl acetoacetate, and ammonia in acetic acid or in refluxing alcohol [4–6]. However, these methods suffer from drawbacks such as long reaction time, use of large quantities of organic solvents, lower product yields or harsh refluxing conditions. Researchers recently have developed several alternate and more efficient methods for the synthesis of polyhydroquinoline derivatives, which include the use of microwaves [7], autoclave [8], ionic liquids [9], iodine [10], metal triflates [11], ceric ammonium nitrate (CAN) [12], L-proline [13], PTSA-SDS [14] and BINOL-phosphoric acid derivatives [15]. But some of those methods still have their own limitation in terms of yields, longer reaction time, difficult work-up. In some cases, catalysts used are harmful to environment and cannot be reused. Therefore, a novel method for the preparation of polyhydroquinoline derivatives is still desired.

Our previous works in FBS have found that metal (e.g. Hf, Yb, Sc) complexes with bis(perfluorooctanesulfonyl)imide ponytails are active and recyclable catalysts which could be immobilized in the fluorous phase for synthesis of substituted quinolines [16] and 14-substituted-14*H*-dibenzo[*a*,*j*] xanthenes [17] and allylation of 1,3-dicarbonyl compounds [18]. As part of a continuing effort in our laboratory toward the development of lanthanide complexes catalysts for fluorous phase organic synthesis [19], we present our results about a hafnium (IV) bis(perfluorooctanesulfonyl)imide complex catalyzed four-component Hantzsch reaction in fluorous medium.

2. Results and discussion

First a mixture of benzaldehyde, 5,5-dimethylcyclohexane-1,3-dione, ethyl acetoacetate, and ammonium acetate in perfluorodecalin ($C_{10}F_{18}$, *cis*- and *trans*-mixture) was chosen as the model

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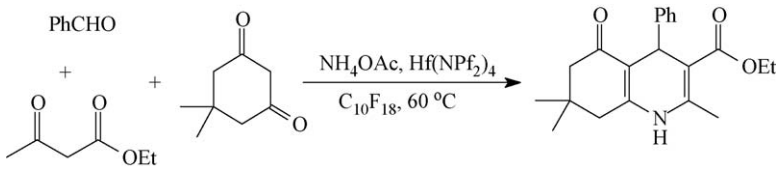


Scheme 1. Optimizing the reaction conditions.

reaction (Scheme 1) to detect whether the use of catalyst hafnium (IV) bis(perfluorooctanesulfonyl)imide complex is efficient and to investigate the optimal conditions. The results are summarized in Table 1. As shown in Table 1, hafnium (IV), tin (IV), and lanthanide (III) bis(perfluorooctanesulfonyl)imide complexes screened were effective in catalyzing the reaction with the product yield in the order of hafnium (IV) > tin (IV) > lanthanide (III) (Table 1, entries 2, 4, 5, 8 and 11–14). It was also found that metal (e.g. Sc, Yb) complexes with the $-N(SO_2C_8F_{17})_2$ ($-NPf_2$) ligand gave better yields than those with the $-OSO_2C_8F_{17}$ ($-OPf$) ligand or $-OSO_2CF_3$ (OTf) ligand in fluorous solvent (Table 1, entries 5–10). It is reasonable to speculate that the stronger electron-withdrawing ligand of $M[N(SO_2C_8F_{17})_2]_n$ ($n = 3, 4$) complex renders it super Lewis acidity in fluorous solvent and hence shows better catalytic activity. Bis(perfluorooctanesulfonyl)imide ($NHPf_2$) itself can promote the reaction, but it was found to be less effective than the corresponding metal complexes. We also carried out the reaction without any catalyst, poor yield (<5%) (Table 1, entry 16) of the desired product was isolated, and the major product isolated was dimedone/aldehyde adduct. The use of just 1 mol% of $Hf(NPf_2)_4$ in fluorous solvent is sufficient. After the reaction was completed, the fluorous phase containing catalyst could be reused for several times. As indicated in Table 1, almost the similar catalyst activity remained after five successive runs. The yields obtained were between 93 and 95%.

To handle the procedure more easily, we then studied the reaction in different co-solvent systems using a common organic solvent. As indicated in Table 2, the polar solvents such as ethanol and acetonitrile were found much better than the non-polar solvents like cyclohexane. The results could be interpreted with the much better solubility of the catalyst and the reactants in the polar solvents, which would have an influence on the effective miscibility of fluorous phase and organic phase. Toluene proved to be efficient (Table 2, entry 3) probably because toluene showed better miscibility with fluorous solvents. Comparing the use of perfluorodecalin as the sole solvent, the use of co-solvent system resulted in lower product yield under the similar conditions. Based on these results, we employed only perfluorodecalin as the sole solvent in the further experiments. The temperature was optimized by conducting the reaction at 60 °C and room temperature. As a result, the reaction was completed with higher yield and in shorter reaction time at 60 °C (Table 2, entries 6 and 7).

A variety of substrates were submitted to the optimum reaction conditions and the desired products were obtained in good to excellent yields (Scheme 2). As can be seen from the results in Table 3, aromatic aldehydes containing both electron-withdrawing and electron-donating groups as well as heterocyclic systems reacted smoothly with 1,3-cyclohexanediones and β-ketoesters (methyl and ethyl acetoacetate) to produce high yields of products. Aromatic aldehydes with electron-withdrawing groups showed increased reaction rate (Table 3, entries 5–7). However, with aliphatic aldehydes, lower yields of the products were witnessed (Table 3, entries 10 and 11).

Table 1
The reaction of benzaldehyde, ethyl acetoacetate, dimedone and ammonium acetate: effect of catalysts[a].

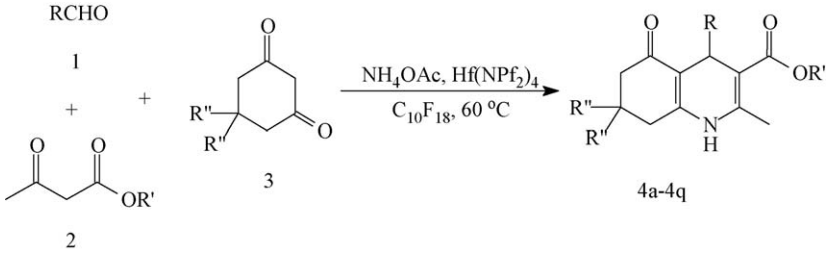
Entry	Catalyst	Amount of catalyst (mol%)	Yield (%)[b]
1	$Hf(NPf_2)_4$	0.5	73
2	$Hf(NPf_2)_4$	1	95, 95, 93, 93, 94[c]
3	$Hf(NPf_2)_4$	1.5	96
4	$Sn(NPf_2)_4$	1	91
5	$Yb(NPf_2)_3$	2	82
6	$Yb(OPf)_3$	2	73
7	$Yb(OTf)_3$	5	65
8	$Sc(NPf_2)_3$	2	85
9	$Sc(OPf)_3$	2	77
10	$Sc(OTf)_3$	5	68
11	$La(NPf_2)_3$	2	60
12	$Nd(NPf_2)_3$	2	65
13	$Y(NPf_2)_3$	2	71
14	$Sm(NPf_2)_3$	2	73
15	$NHPf_2$	2	42
16	–	–	<5

[a] All reactions were carried out in $C_{10}F_{18}$ at 60 °C.
[b] Isolated yields.
[c] Catalyst was reused five times.

Table 2
The reaction of benzaldehyde, ethyl acetoacetate, dimedone and ammonium acetate: effect of solvents and temperature[a].

Entry	Co-solvent	Temp. (°C)	Time (h)	Yield (%)[b]
1	C_2H_5OH	60	4	90
2	CH_3CN	60	4	87
3	Toluene	60	4	83
4	CH_2Cl_2	Reflux	4	52
5	Cyclohexane	60	4	45
6	–	60	3	95
7	–	RT	4	71

[a] All reactions were carried out using 1 mol% $Hf(NPf_2)_4$ in $C_{10}F_{18}$.
[b] Isolated yields.



Scheme 2. $Hf(NPf_2)_4$ catalyzed synthesis of polyhydroquinoline derivatives via Hantzsch reaction.

Table 3
$Hf(NPf_2)_4$ catalyzed Hantzsch synthesis of polyhydroquinoline derivatives[a].

Entry	R	R′	R″	Time (h)	Product	Yield (%)[b]
1	C_6H_5	Et	CH_3	3	**4a**	95
2	4-MeC_6H_4	Et	CH_3	4	**4b**	90
3	4-$MeOC_6H_4$	Et	CH_3	4	**4c**	89
4	4-HOC_6H_4	Et	CH_3	4	**4d**	87
5	4-ClC_6H_4	Et	CH_3	2	**4e**	96
6	4-BrC_6H_4	Et	CH_3	2	**4f**	91
7	3-$NO_2C_6H_4$	Et	CH_3	2	**4g**	95
8	2-Furyl	Et	CH_3	4	**4h**	93
9	3-pyridyl	Et	CH_3	6	**4i**	92
10	C_2H_5	Et	CH_3	7	**4j**	85
11	n-C_3H_7	Et	CH_3	8	**4k**	83
12	C_6H_5	Et	H	4	**4l**	90
13	4-ClC_6H_4	Et	H	3	**4m**	93
14	4-MeC_6H_4	Et	H	5	**4o**	82
15	C_6H_5	CH_3	CH_3	3	**4p**	87
16	4-MeC_6H_4	CH_3	CH_3	4	**4q**	83

[a] All reactions were carried out using 1 mol% $Hf(NPf_2)_4$ at 60 °C in $C_{10}F_{18}$.
[b] Isolated yields.

3. Conclusions

In conclusion, we have achieved a facile and efficient method for the synthesis of a variety of polyhydroquinoline derivatives via an improved Hantzsch reaction using $Hf(NPf_2)_4$ as a reusable catalyst. The method offers several advantages including simple work-up, short reaction time, high yields of products and the use of non-toxic solvent, which makes it a useful process for the synthesis of polyhydroquinoline derivatives.

4. Experimental

4.1. General

Chemicals used were obtained from commercial suppliers and used without further purifications. ^1H NMR and ^{19}F NMR spectra were recorded with a Bruker Advance RX300 spectrometer. Melting points were obtained with Shimadzu DSC-50 thermal analyzer. Mass spectra were recorded on a Saturn 2000GC/MS instrument. Inductively coupled plasma (ICP) spectra were measured on an Ultima2C apparatus. Elemental analysis was performed on a Yanagimoto MT3CHN recorder.

4.1.1. Preparation of bis(perfluorooctanesulfonyl)imide

$(C_8F_{17}SO_2)_2NH$ was prepared according to the literature [20,21]. Ammonia gas (300 mmol) was added into perfluorooctanesulfonyl fluoride (50 g, 99.6 mmol) at −20 °C. After the stirring was held at −20 °C for about 1 h, it was then continued at room temperature for another 1 h. The solid product was acidified with 2 M HCl followed by addition of Et_2O. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure, dried under vacuum at 80 °C for 16 h to give $C_8F_{17}SO_2NH_2$ (87% yield). Then the mixture of perfluorooctanesulfonyl fluoride (45.4 g, 91 mmol), perfluorooctanesulfonamide (43.4 g, 87 mmol) and Et_3N (76 mL) was heated at reflux for 23 h. The lower brown fluorous layer was washed with 4 M HCl and dried under vacuum at 70 °C for 6 h to afford $(C_8F_{17}SO_2)_2N\ HNEt_3$. Free $(C_8F_{17}SO_2)_2NH$ was obtained in 50% yield by passing through acidic ion exchange resin column. Anal. Calcd. for $(C_8F_{17}SO_2)_2NH$: C, 19.58; N: 1.43; H: 0.10. Found: C, 19.61; N: 1.45; H, 0.16. ^{19}F NMR (300 MHz, a,a,a-trifluorotoluene): δ −126.2, −121.8, −114.0, −81.2.

4.1.2. Preparation of $Hf(NPf)_4$

$Hf(NPf)_4$ was prepared according to the literatures [20]. A mixture of $HN(SO_2C_8F_{17})_2$ (0.981 g, 1 mmol) and hafnium (IV) chloride (0.080 g, 0.25 mmol) and anhydrous methanol (10 mL) was added to a flask, and the whole was stirred continuously at 50 °C for 16 h. After being cooled to room temperature, the mixture was evaporated and dried at 80 °C/0.01 mmHg for 16 h to give white powder of hafnium (IV) bis(perfluorooctanesulfonyl)imide complex in 96% yield (0.984 g). ICP: Calcd. for $C_{64}N_4O_{16}F_{136}S_8Hf$: Hf, 4.35%. Found: Hf, 4.31%. Anal. Calcd. for $Hf[N(SO_2C_8F_{17})_2]_4$: C, 18.75. Found: C, 18.67.

4.2. Typical procedure for the synthesis of polyhydroquinoline derivatives

A mixture of benzaldehyde (106 mg, 1 mmol), dimedone (140 mg, 1 mmol), ethyl acetoacetate (130 mg, 1 mmol), ammonium acetate (77 mg, 1 mmol), $Hf(NPf)_4$ (1 mol%) was heated at 60 °C in perfluorodecalin (1.5 mL) for 3 h. The reaction mixture was cooled to room temperature and ethanol (10 mL) was added, and the mixture was stirred for another 5 min. The fluorous layer on the bottom was separated for the next cycle. The upper ethanol layer was evaporated under reduced pressure, washed with water, recrystallized from ethanol to afford 2,7,7-trimethyl-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester.

2,7,7-Trimethyl-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (compound **4a**): mp 202–204 °C [204–205 °C, Ref. [10b]]. ^1H NMR ($CDCl_3$, 300 MHz) δ: 0.93 (s, 3H), 1.07 (s, 3H), 1.19 (t, J = 7.1 Hz, 3H), 2.13–2.32 (m, 4H), 2.37 (s, 3H), 4.05 (q, J = 7.2 Hz, 2H), 5.05 (s, 1H), 6.21 (s, 1H), 7.06–7.31 (m, 5H). MS (EI) m/z 339 (M^+).

2,7,7-Trimethyl-5-oxo-4-(4-methxylphenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (compound **4b**): mp 260–262 °C [261–262 °C, Ref. [10b]]. ^1H NMR ($CDCl_3$, 300 MHz) δ: 0.94 (s, 3H), 1.08 (s, 3H), 1.21 (t, J = 7.1 Hz, 3H), 2.10–2.24 (m, 4H), 2.26 (s, 3H), 2.37 (s, 3H), 4.06 (q, J = 7.1 Hz, 2H), 5.03 (s, 1H), 5.96 (s, 1H), 7.02 (d, J = 8 Hz, 2H), 7.19 (d, J = 8 Hz, 2H). MS (EI) m/z 353 (M^+).

2,7,7-Trimethyl-5-oxo-4-(4-methoxyphenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (compound **4c**): mp 255–257 °C [258–259 °C, Ref. [10b]]. ^1H NMR ($CDCl_3$, 300 MHz) δ: 0.94 (s, 3H), 1.07 (s, 3H), 1.21 (t, J = 7.2 Hz, 3H), 2.13–2.27 (m, 3H), 2.31–2.37 (m, 4H), 3.74 (s, 3H), 4.06 (q, J = 7.2 Hz, 2H), 5.00 (s, 1H), 6.01 (s, 1H), 6.72–6.75 (m, 2H), 7.20–7.26 (m, 2H). MS (EI) m/z 369 (M^+).

2,7,7-Trimethyl-5-oxo-4-(4-hydroxyphenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (compound **4d**): mp 232–234 °C [232–234 °C, Ref. [10a]]. ^1H NMR ($CDCl_3$, 300 MHz) δ: 0.93 (s, 3H), 1.07 (s, 3H), 1.19 (t, J = 7.2 Hz, 3H), 2.09–2.19 (m, 3H), 2.20–2.34 (m, 4H), 4.06 (q, J = 7.6 Hz, 2H), 4.98 (s, 1H), 5.61 (s, 1H), 6.10 (s, 1H), 6.65 (d, J = 8.9 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H). MS (EI) m/z 356 (M^+).

2,7,7-Trimethyl-5-oxo-4-(4-chlorophenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (compound **4e**): mp 244–246 °C [245–247 °C, Ref. [14]]. ^1H NMR ($CDCl_3$, 300 MHz) δ: 0.93 (s, 3H), 1.07 (s, 3H), 1.19 (t, J = 7.2 Hz, 3H), 2.12–2.35 (m, 4H), 2.37 (m, 3H), 4.06 (q, J = 7.2 Hz, 2H), 5.02 (s, 1H), 6.13 (s, 1H), 7.15 (d, J = 8 Hz, 2H), 7.31 (d, J = 8 Hz, 2H). MS (EI) m/z 374 (M^+).

2,7,7-Trimethyl-5-oxo-4-(4-bromophenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (compound **4f**): mp 253–255 °C [254–255 °C, Ref. [10b]]. ^1H NMR ($CDCl_3$, 300 MHz) δ: 0.93 (s, 3H), 1.07 (s, 3H), 1.19 (t, J = 7.2 Hz, 3H), 2.19–2.27 (m, 3H), 2.34–2.41 (m, 4H), 4.05 (q, J = 7.2 Hz, 2H), 5.03 (s, 1H), 5.78 (s, 1H), 7.19 (d, J = 8 Hz, 2H), 7.34 (d, J = 8 Hz, 2H). MS (EI) m/z 417 (M^+).

2,7,7-Trimethyl-5-oxo-4-(3-nitrophenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (compound **4g**): mp 173–175 °C [174–176 °C, Ref. [14]]. ^1H NMR ($CDCl_3$, 300 MHz) δ: 0.93 (s, 3H), 1.07 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H), 2.12–2.41 (m, 7H), 3.69 (q, J = 7.1 Hz, 2H), 5.15 (s, 1H), 6.86 (s, 1H), 7.35 (t, J = 7.9 Hz,

1H), 7.72 (d, J = 7.9 Hz, 1H), 7.96 (m, 1H), 7.98 (m, 1H). MS (EI) m/z 385 (M^+).

2,7,7-Trimethyl-5-oxo-4-(2-furyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (compound **4h**): mp 245–247 °C [246–248 °C, Ref. [10a]]. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.02 (s, 3H), 1.10 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H), 2.21–2.28 (m, 3H), 2.32–2.38 (m, 4H), 4.12–4.18 (m, 2H), 5.21 (s, 1H), 5.81 (s, 1H), 6.05 (s, 1H), 6.24 (s, 1H), 7.19 (s, 1H). MS (EI) m/z 316 (M^+).

2,7,7-Trimethyl-5-oxo-4-(3-pyridyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (compound **4i**): mp 64–66 °C [66–67 °C, Ref. [10a]]. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.93 (s, 3H), 1.08 (s, 3H), 1.21 (t, J = 7.1 Hz, 3H), 2.16–2.38 (m, 4H), 2.39 (s, 3H), 4.06 (q, J = 7.1 Hz, 2H), 5.07 (s, 1H), 6.02 (s, 1H), 7.23–7.28 (m, 2H), 8.26–8.35 (m, 2H). MS (EI) m/z 316 (M^+).

2,7,7-Trimethyl-5-oxo-4-ethyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (compound **4j**): mp 144–146 °C [146–147 °C, Ref. [10b]]. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.75 (t, J = 7.2 Hz, 3H), 1.11 (s, 6H), 1.29 (t, J = 7.1 Hz, 3H), 1.38–1.46 (m, 2H), 2.15 (d, J = 7.2 Hz, 1H), 2.27 (d, J = 3.2 Hz, 2H), 2.31 (t, J = 7.2 Hz, 4H), 4.03 (t, J = 5.1 Hz, 1H), 4.16–4.20 (m, 2H), 5.56 (s, 1H). MS (EI) m/z 291 (M^+).

2,7,7-Trimethyl-5-oxo-4-(n-propyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (compound **4k**): mp 148–150 °C [150–152 °C, Ref. [10b]]. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.78 (t, J = 7.2 Hz, 3H), 1.07 (s, 6H), 1.10–1.37 (m, 7H), 2.13–2.32 (m, 7H), 4.02 (q, J = 6.1 Hz, 1H), 4.10–4.23 (m, 2H), 5.58 (s, 1H). MS (EI) m/z 305 (M^+).

2-Methyl-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (compound **4l**): mp 238–240 °C [240–241 °C, Ref. [11]]. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.15 (t, J = 6.8 Hz, 3H), 1.78–2.06 (m, 2H), 2.26–2.44 (m, 7H), 4.05 (q, J = 6.8 Hz, 2H), 5.03 (s, 1H), 6.07 (s, 1H), 7.10 (t, J = 7.6 Hz, 1H), 7.20 (t, J = 7.6 Hz, 2H), 7.30 (d, J = 7.6 Hz, 2H). MS (EI) m/z 311 (M^+).

2-Methyl-5-oxo-4-(4-chlorophenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (compound **4m**): mp 235–237 °C [234–235 °C, Ref. [11]]. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.15 (t, J = 7.2 Hz, 3H), 1.79–2.10 (m, 2H), 2.31–2.50 (m, 7H), 4.05 (q, J = 7.2 Hz, 2H), 5.05 (s, 1H), 6.32 (s, 1H), 7.16 (d, J = 8.8 Hz, 2H), 7.24 (d, J = 8.8 Hz, 2H). MS (EI) m/z 345 (M^+).

2-Methyl-5-oxo-4-(4-methylphenyl)-1,4,5,6, 7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (compound **4o**): mp 240–242 °C [241–242 °C, Ref. [11]]. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.18 (t, J = 7.2 Hz, 3H), 1.80–2.10 (m, 2H), 2.21–2.51 (m, 10H), 4.06 (q, J = 7.2 Hz, 2H), 5.05 (s, 1H), 7.02 (d, J = 7.6 Hz, 2H), 7.18 (d, 2H, J = 7.6 Hz), 7.36 (s, 1H). MS (EI) m/z 325 (M^+).

2,7,7-Trimethyl-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid methyl ester (compound **4p**): mp 258–260 °C [260–261 °C, Ref. [8c]]. ^{1}HNMR ($CDCl_3$, 300 MHz) δ: 1.09 (s, 3H), 1.15 (s, 3H), 2.15–2.37 (m, 4H), 2.41 (s, 3H), 3.62 (s, 3H), 5.07 (s, 1H), 5.80 (s, 1H), 7.10-7.34 (m, 5H). MS (EI) m/z 325 (M^+).

2,7,7-Trimethyl-5-oxo-4-(4-methylphenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid methyl ester (compound **4q**): mp 285–287 °C [>270 °C, Ref. [12]]. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.96 (s, 3H), 1.09 (s, 3H), 2.15–2.38 (m, 10H), 3.62 (s, 3H), 5.04 (s, 1H), 5.96 (s, 1H), 7.00 (d, J = 7.9 Hz, 2H), 7.19 (d, J = 7.9 Hz, 2H). MS (EI) m/z 340 (M^+).

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