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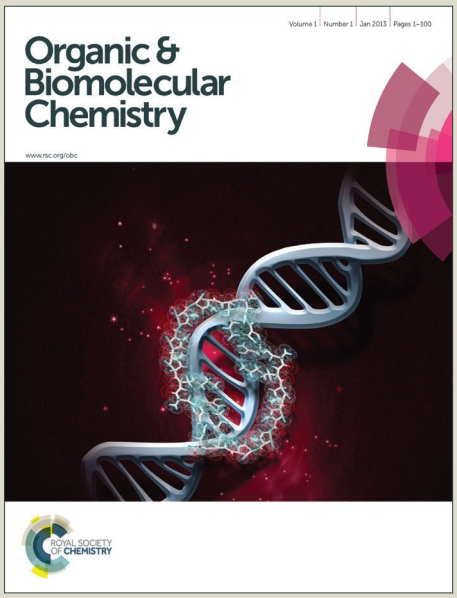

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Rhodium-Catalyzed *ortho* C-H Bond Activation of Arylamines for the Synthesis of Quinoline Carboxylates

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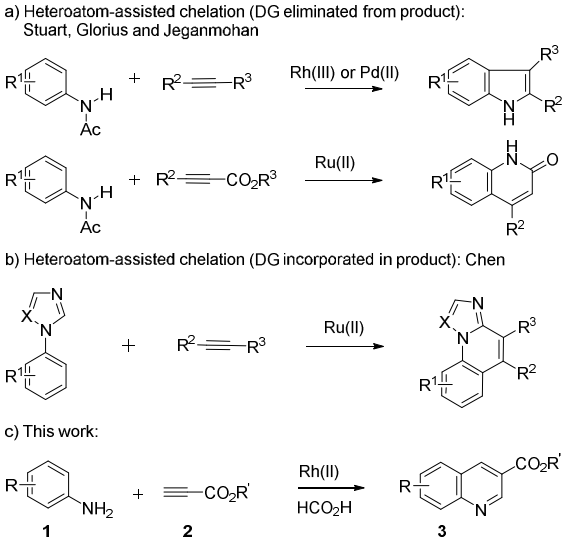
The rhodium catalyzed annulation of anilines with alkynic esters providing for the high yield synthesis of quinoline carboxylates with excellent regioselectivity is described. This unprecedented reaction employs either formic acid as C1 source and reductant or Copper(II) as oxidant and is proposed to proceed *via* rhodacycle of *in situ* generated amide and enamine ester followed by *ortho* C-H activation of arylamines with rhodium catalyst.

Introduction

Quinoline carboxylates are ubiquitous heterocyclic units found extensively in many natural products and pharmaceuticals and possess anti-malarial, anti-HIV, anti-microbial and anti-TB activities.[1,2] The prevalence of quinoline units in bioactive molecules has prompted the development of many useful methods for their synthesis and functionalization.[3] In particular, the literature related to synthesis of quinoline 3-carboxylates found to be scarce to the best of our knowledge.[4] Despite significant advances, most of the methods suffer from limited availability of substrates,[4a,4c] complicated multi-step procedures,[4b,4e] and low regioselectivity, leading to low yields of products[4d] in most cases. More recently, transition metal-catalyzed functionalization of a variety of less active C-H bonds has received substantial importance in the construction of heterocyclic scaffolds.[5] In particular, Rh(III), Ru(II), Pd(II) and Cu(II) metal complexes have provided exciting opportunities for the efficient synthesis of condensed heterocycles *via* chelation-assisted directing group C-H bond functionalization (*e.g.* indoles, pyrroles, pyridines, isoquinolones, isocoumarins, and indolines).[6-11] However, for directing group-assisted intermolecular cyclization with alkynes, the elimination of heteroatom-assisted chelation is often required in the early reaction stage[12, 13] (Scheme 1).



Scheme 1 Transition metal-catalysed synthesis of heterocycles *via* heteroatom-assisted chelation

Quite recent reports[14] have described utilization of a directing group that is incorporated in the product. In this context, we reasoned that N-formyl derivative **4a** generated *in situ* could serve as a directing group for C-H functionalization to construct the quinoline carboxylate units. Recently, we have reported rhodium catalyzed directing group assisted annulations of phenol acetates with acrylates *via ortho* C-H bond activation giving coumarin derivatives in high yields.[15] In this communication, we disclose the first efficient and direct approach to quinoline carboxylates **3 & 6** from simple and readily available anilines **1** and alkynic esters **2** by using C-H activation *via* Rh catalysis with either formic acid as C1 source or $Cu(OAc)_2$ as oxidant (Scheme 2 & 6).

Results and discussion

We commenced our optimization study by examining reaction of 3,5-dimethoxyaniline **1a** (1 mmol) with ethyl propiolate **2a** (1.2 equiv) in excess of formic acid (1 mL) at various temperatures under N_2 atmosphere (Table 1). When $[Rh_2(OAc)_4]$ (5 mol %) was

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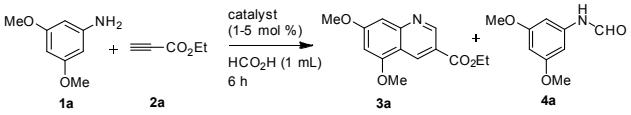
employed at 100 °C, a mixture of cyclized quinoline-3-carboxylate (3a, 48%) along with N-formyl derivative (**4a**, 45%) was obtained (entry 1). In order to improve the yield of **3a**, both Rh catalyst concentration and temperature were reduced. At 70 °C, the cyclization efficiency was significantly improved to give 3a in 61% yield. Interestingly, on further lowering the temperature to 50 °C, a dramatic improvement in the yield of **3a** (84%) was realized (entry 3), probably due to the higher stability of rhodacycle **II** at lower temperature. Finally, the best result could be obtained when the reaction was conducted at 50 °C with the lowered catalyst concentration (2.5 mol %; entry 5). However, further lowering of either the temperature (35 °C) of the reaction or the catalyst loadings (1 mol %) had a deleterious effect on the product distribution (entry 4 & 7). Surprisingly, other catalysts were found to be less effective in improving the product distribution (entry 8, 9, 11 & 13); so also with the use of other solvents such as toluene or chlorinated solvents for the reaction. We noticed that lowering the amount of HCO_2H resulted in reduced yield of the product **3a**. The catalyst control experiment, however, gave exclusively the N-formyl derivative **4a** (91%), also in the absence of Rh catalyst, neither coupling reaction proceeded nor deuterium exchange occurred.

Table 1 Rh-catalyzed reaction of 3,5-dimethoxyaniline **1a** with ethyl propiolate **2a** and HCO_2H: optimization studies[a]

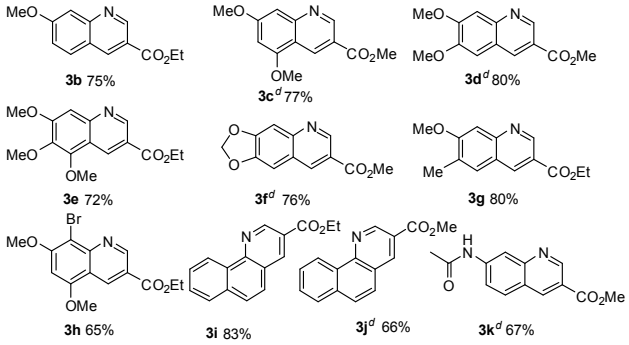


No.	catalyst	Catalyst (mol %)	t (^{o}C)	products (%)[b] 3a	4a
1	$Rh_2(OAc)_4$	5	100	48	45
2	$Rh_2(OAc)_4$	5	70	61	34
3	$Rh_2(OAc)_4$	5	50	84	11
4	$Rh_2(OAc)_4$	5	35	50	40
5	$Rh_2(OAc)_4$	2.5	50	85	10[c]
6	$Rh_2(OAc)_4$	2.5	35	40	45
7	$Rh_2(OAc)_4$	1	50	41	42
8	$[RhCOCl_2]_2$	2.5	50	30	48
9	Rh/Al_2O_3	2.5	50	10	85
10	$[RhCp^*Cl_2]_2$	2.5	50	-	90
11	$RuCl_3$	2.5	50	22	68
12	$Co(NO_3)_2$	2.5	50	-	90
13	$Pd(OAc)_2$	2.5	50	31	44
14	No catalyst	-	50	-	91

[a] Arylamines (1 mmol), ethyl propiolate (1.2 mmol), HCO_2H (1 mL), 6 h. [b] Isolated yield after chromatographic purification. [c] No change in yield of **4a** was observed even after 24 h.

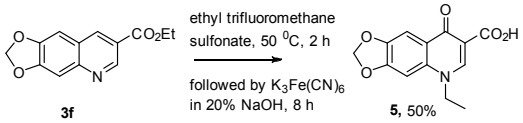
With the optimized reaction conditions established, we next examined the reaction scope of a variety of anilines with alkynic esters. The results are summarized in Table 2. Activated aniline bearing bromo, methoxy, methylenedioxy, amide and methyl groups on the aromatic nucleus including naphthyl group were well-tolerated under the reaction conditions. In all substrate evaluation study, we observed that the *ortho* C-H bond activation was strongly promoted by the electron-donating groups present at the *meta* to NH_2 group of the substrates. For all the cases studied, the annulated products **3a-k** were indeed obtained in high yields (65-83%) with excellent regioselectivity. However, in the case of substrates with weakly electron-donating groups (aniline, 3,4-dimethyl or dichloroaniline), only 5-10% of the required quinoline-3-carboxylate **3** was formed (GCMS analysis) with the major product being N-formyl derivative **4** (~90%). Also, in the case of internal alkynes, there was no annulated product formed.

Table 2 Rh-catalyzed synthesis of quinoline-3-carboxylates: substrate scope[a-c]



[a] Arylamines (1 mmol), ethyl propiolate (1.2 mmol), $Rh_2(OAc)_4$ (2.5 mol %), HCO_2H (1 mL), 50 °C, 6 h. [b] Isolated yield after column purification. [c] 5-10% yield of N-formyl derivative **4b-k** was isolated in all the cases studied; [d] Methyl propiolate was used.

The catalytic method was successfully extended to the synthesis of oxolinic acid **5**, a quinolone antibiotic and antibacterial used in the treatment of urinary tract infections and psoriasis. Thus, quinoline carboxylate **3f**, obtained from 3,4-methylenedioxyaniline by the present protocol, was subjected to N-alkylation with ethyl trifluoromethane sulfonate followed by oxidation with $K_3Fe(CN)_6$[16] in a single step to give oxolinic acid[17] **5** in 50% yield (Scheme 2).



Scheme 2 Short synthesis of oxolinic acid (5)

To gain some insight into the mechanistic details of the reaction, the following experiments were conducted (Scheme 3): (i) when N-formyl derivative **4a** was reacted with ethyl propiolate in the presence of Rh(II)/HCO_2H combination, **3a** was obtained in 70% yield, thereby suggesting that **4a** could be an intermediate in the catalytic cycle; (ii) also, when **4a** was treated with D_2O in the absence of ethyl propiolate under Rh(II)/HCO_2H reaction conditions, deuterated N-formyl derivative **d_3-4a** was isolated in 72% yield, in which deuterium incorporation of 43% at C-4 carbon and 57% each at C-2 and C-6 carbons was observed (^{1}H NMR proven). This observed deuteration at the *ortho* and *para* positions in absence of alkyne indicates that a reversible, electrophilic C-H metallation has

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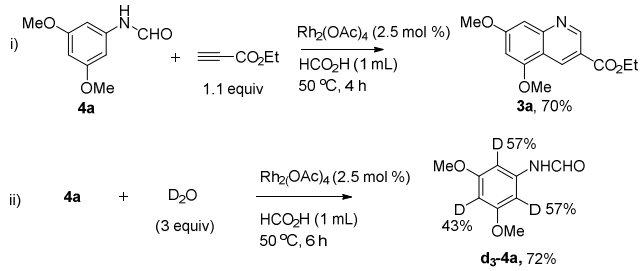
occurred under the reaction condition. The fact that no *para* C-H alkynation of N-formyl derivative was observed in presence of alkyne, probably suggests that Rh atom is inserted in the *ortho* position and stabilized by coordination with carbonyl of amide group possibly leading to rhodacycle as intermediate;[18] (iii) the UV-visible absorptions of $[Rh_2(OAc)_4]$ catalyst showed two maxima at λ_{max} 590 nm and 445 nm which have been shifted to λ_{max} 420 nm on addition of HCO_2H. This blue shift may be assigned to the Rh(I) species[19] (see SI).



Scheme 3 Mechanistic studies

(iv) Cyclic voltammetry study of $[Rh_2OAc_4]$ with HCO_2H has shown that there is a onset reversible reduction potential occurring at -0.710 V attributable to Rh(II) to Rh(I) reduction process[20] (Fig. 1).

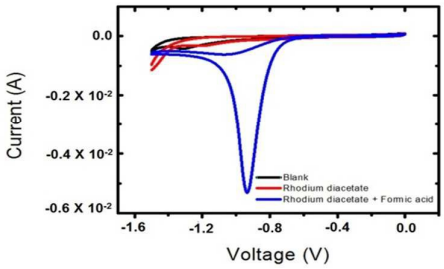
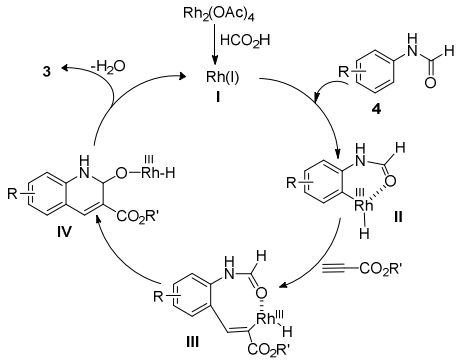


Fig. 1 Cyclic voltammogram of $[Rh_2(OAc)_4]$ in the presence of HCO_2H and 0.1 M lithium perchlorate as supporting electrolyte at 25 °C. Scan Rate: 50 mV/sec.

Based on the results presented above and literature precedence,[21] we have proposed a catalytic cycle for this reaction (Scheme 4). The first step in the catalytic cycle involves the formation of catalytically active Rh(I) species (**I**), obtained from $[Rh_2(OAc)_4]$ on reduction with formic acid. Rh(I) species (**I**) can then undergo a reversible oxidative addition at *ortho* aromatic C-H bond of N-formyl derivative **4** regioselectively to provide a six-membered rhodacycle **II**.

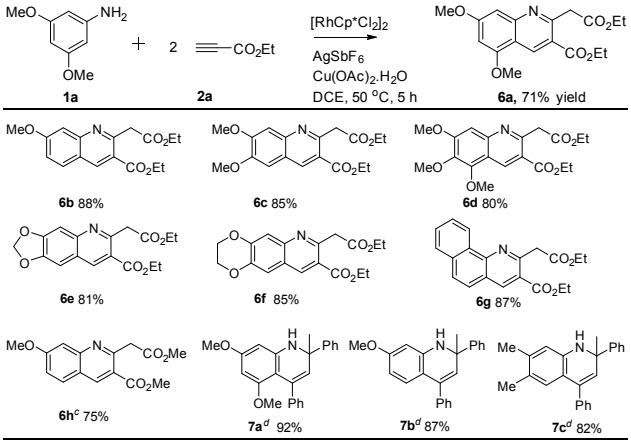


Scheme 4 Rh-catalytic cycle *via ortho* C-H bond activation.

This metallacycle can insert an equivalent of alkyne into the Rh-C bond of species **II** to generate an intermediate **III**, which then undergoes intramolecular cyclization to give intermediate **IV**. Subsequent reductive elimination of **IV** followed by H_2O removal affords the quinoline derivatives **3** with the release of the active Rh(I) catalyst for the next catalytic cycle. The catalytic cycle thus consists of rhodium alternating between the Rh(I) and Rh(III) oxidation states.

During the optimization study we observed that the $[RhCp^*Cl_2]_2/HCO_2H$ system was found to be inactive to afford quinoline-3-carboxylate **3** (Table 1, entry 10). Surprisingly, by changing to a new catalytic system [Rh(III)/Cu(II)], we observed that 3,5-dimethoxyaniline **1a** underwent oxidative coupling with ethyl propiolate **2a** to afford the corresponding 2,3-disubstituted quinoline dicarboxylate **6a** in 71% yield. After several experimentations (see SI), it was thus found that a combination of aniline **1a** (1 mmol), ethyl propiolate (2.1 equiv), $[RhCp^*Cl_2]_2$ (2.5 mol %), $AgSbF_6$ (10 mol %) and $Cu(OAc)_2$ (20 mol %) in DCE at 50 °C for 5 h was the best optimized condition in achieving excellent product yields **6a-h** (70-88%). Table 3 summarises the results of its substrate scope of study.[22]

Table 3 Rh(III)-catalyzed reaction of electron-rich anilines and ethyl propiolates or phenyl acetylene: substrate scope[a, b]



[a] Substrate 1a (1 mmol), ethyl propiolate (2.1 mmol), $[RhCp^*Cl_2]_2$ (2.5 mol %), $AgSbF_6$ (20 mol %), $Cu(OAc)_2{\cdot}H_2O$ (20 mol %), DCE (2 mL), 50 °C, 5 h. [b] Isolated yields. [c] Methyl propiolate was used. [d] Phenyl acetylene was used.

In case of internal alkynyl esters, only the Michael addition products were produced. Additionally, when the coupling partner was changed to simple phenylacetylene (2.1 equiv), under same reaction conditions, 1,2-dihydroquinoline derivatives **7a-c** were obtained in high yields (82-95%). In this case, the regioselectivity observed was remarkable and very well established in the literature.[23] This catalytic pathway can be expalained by the initial formation of imine from aniline and phenylacetylene, its insertion into another metal–alkynyl species followed by intramolecular cyclization, leading to product **7**. This oxidative coupling was found to proceed *via ortho* C-H bond activation of arylamines (For mechanistic and optimization studies; see SI).

A plausible mechanism for the formation of **6** *via* addition reaction followed by *ortho*-C-H bond activation pathway is depicted in Scheme 5. At the beginning, aniline **1** undergoes Michael addition onto ethyl propiolate **2a** to form enamine ester **8**. The additive $AgSbF_6$ probably removes the Cl^- ligand from the catalyst

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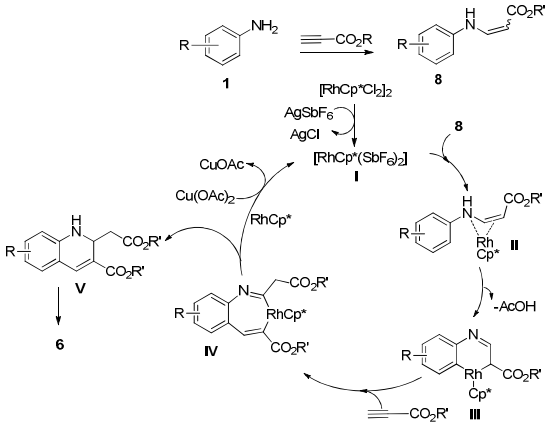
$[RhCp^*Cl_2]_2$ complex, giving a cationic rhodium species **I**. Coordination of lone pair of nitrogen and double bond of imine species **8** to a cationic species **I** provides the intermediate **II** followed by acetate accelerated *ortho*-metalation affords a six-membered rhodacycle **III**. The coordinative insertion of second molecule of ethyl propiolate into the Rh-C bond of rhodacycle **III** gives intermediate **IV**. Species **IV** then on intramolecular cyclization and reductive elimination leads to the cyclized intermediate **V** together with a Rh(I) species, which is reoxidized in the presence of $Cu(OAc)_2$ to the active rhodium species **I** for the next catalytic cycle. Finally, intermediate **V** can be easily converted to product **6** by oxidation with Cu(II). Cu(I) is probably reoxidized back to Cu(II) by air.[12h]



Scheme 5 Plausible mechanism for 2,3-disubstituted quinoline carboxylates **6**

Conclusion

In summary, we have presented, for the first time, a simple annulation strategy that affords quinoline carboxylates (**3a-k** and **6a-h**) in high yields from the corresponding substituted anilines **1a-k** *via* rhodium catalyzed cyclization in a single step. This cyclization strategy involves rhodacycle as the possible intermediate formed by the *ortho* C-H activation of aniline supported by deuterium incorporation studies. We believe that this single-step cyclization strategy will find tremendous applications in the synthesis of bioactive heterocyclic scaffolds as demonstrated here in the high yield synthesis of oxolinic acid (**5**). Further exploration of the reaction scope and other types of cyclizations is currently under investigation.

Experimental Section:

General

Solvents were purified and dried by standard procedures before use; petroleum ether of boiling range 60-80 °C was used. Melting points were uncorrected and recorded on a Buchi B-542 instrument. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AC-200 spectrometer unless mentioned otherwise. Infrared spectra were recorded on Shimadzu FTIR-8400 spectrometer and absorption is expressed in cm^{-1}. ESI-MS were recorded on a Thermo Finnigan LCQ Advantage spectrometer in ESI mode with a spray voltage of 4.8 kV. All chemicals are purchased from Sigma-Aldrich and used without further purification. Purification was done using column chromatography (230-400 mesh).

General experimental procedure for the preparation of quinoline 3-carboxylate derivatives (3a-j):

To a mixture of substituted aniline (**1a-j**) (0.1 g, 1 mmol), $Rh_2(OAc)_4$ (2.5 mol %) and formic acid (1 mL) under a nitrogen atmosphere was added followed by ethyl propiolate **2a** (1.2 mmol). The resulting brown solution was stirred at 50 °C for 6 h. After completion of reaction (monitored by TLC), it was diluted with ethyl acetate (10 mL), and washed with water (10 mL), 5% aqueous sodium bicarbonate (15 mL), and brine (10 mL). The organic layer was dried (Na_2SO_4) and concentrated in *vacuo* to give a brown solid. On purification with flash chromatography using pet ether and ethyl acetate (7:3), quinoline 3-carboxylic acid ester (**3a-j**) was eluted as a solid.

Ethyl 5,7-dimethoxyquinoline-3-carboxylate (3a):

Yield: 85%; 0.144 g; colorless solid, **mp:** 122-123 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 1722, 1618, 1599, 1505, 1432; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 9.31 (s, 1H), 9.05 (s, 1H), 7.05 (s, 1H), 6.51 (s, 1H), 4.46 (q, *J* = 7.3 Hz, 2H), 4.00 (s, 3H), 3.96 (s, 3H), 1.46 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 165.5, 163.5, 156.9, 152.1, 150.9, 133.4, 120.3, 115.6, 99.8, 98.8, 61.1, 55.8, 55.7, 14.5; HRMS (ESI): calc. for $[(C_{14}H_{15}NO_4)H]$ (M+Na) 284.0899, found 284.0893.

Ethyl 7-methoxyquinoline-3-carboxylate (3b):

Yield: 78%; 0.146 g; yellow solid, **mp:** 110-112 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2981, 1717, 1601, 1279, 1243, 1027; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 9.36 (d, *J* = 1.7 Hz, 1H), 8.73 (d, *J* = 1.7, 1H), 7.79 (d, *J* = 9.0 Hz, 1H), 7.26 (d, *J* = 2.2 Hz, 1H), 7.23 (d, *J* = 9.0, 2.5 Hz, 1H), 4.45 (q, *J* = 7.1 Hz, 2H), 3.98 (s, 3H), 1.46 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 165.5, 162.6, 152.0, 150.5, 138.0, 130.1, 122.1, 121.3, 120.9, 107.5, 61.2, 55.6, 14.5; HRMS (ESI): calc. for $[(C_{13}H_{13}NO_3)H]$ (M+H) 232.0974, found 232.0968.

Methyl 5,7-dimethoxyquinoline-3-carboxylate (3c):

Yield: 77%; 0.124 g; colorless solid, **mp:** 134-135 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 1722, 1618, 1599, 1505, 1432; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 9.31 (d, *J* = 1.4 Hz, 1H), 9.06 (d, *J* = 1.4 Hz, 1H), 7.05 (s, 1H), 6.51 (d, *J* = 2.3 Hz, 1H), 4.00 (s, 3H), 3.99 (s, 3H), 3.96 (s, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 166.0, 163.6, 156.9, 152.2, 151.0, 133.5, 120.0, 115.6, 99.8, 98.8, 55.9, 55.7, 52.2; HRMS (ESI): calc. for $[(C_{13}H_{13}NO_4)H]$ (M+H) 248.0845, found 248.0858.

Ethyl 6,7-dimethoxyquinoline-3-carboxylate (3d):

Yield: 80%; 0.129 g; colorless solid, **mp:** 160-161 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 1722, 1618, 1599, 1505, 1432; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 9.20 (d, *J* = 1.8 Hz, 1H), 8.61 (d, *J* = 1.8 Hz, 1H), 7.41 (s, 1H), 7.07 (s, 1H), 4.00 (s, 3H), 3.97 (s, 3H), 3.93 (s, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 166.5, 154.7, 150.7, 148.3, 147.6, 136.8, 122.8, 121.6, 108.1, 106.2, 56.6, 56.4, 52.5; HRMS (ESI): calc. for $[(C_{13}H_{13}NO_4)H]$ (M+H) 248.0923, found 248.0924.

Ethyl 5,6,7-trimethoxyquinoline-3-carboxylate (3e):

Yield: 72%; 0.114 g; colorless solid, **mp:** 170-172 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 3000, 1718, 1607, 1479, 1278, 1020; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 9.28 (s, 1H), 8.98 (s, 1H), 7.28 (s, 1H), 4.47 (q, *J* = 7.2 Hz, 2H), 4.12

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(s, 3H), 4.04 (s, 3H), 3.97 (s, 3H), 1.47 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 165.8, 158.4, 149.9, 148.2, 148.0, 147.9, 141.4, 133.4, 121.5, 104.3, 61.0, 61.5, 56.5, 30.0, 14.8; HRMS (ESI): calc. for $[(C_{15}H_{17}NO_5)H]$ (M+H) 292.1185, found 292.1179.

Ethyl [1,3]dioxolo[4,5-*g*]quinoline-7-carboxylate (3f):

Yield: 76%; 0.128 g; colorless solid, **mp:** 205-206 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 1709, 1611, 1277, 1203, 1077; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 9.23 (d, *J* = 2.3 Hz, 1H), 8.62 (d, *J* = 1.8 Hz, 1H), 7.42 (s, 1H), 7.14 (s, 1H), 6.16 (s, 2H), 3.99 (s, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 166.1, 152.7, 148.8, 148.6, 148.1, 137.0, 124.0, 121.5, 105.9, 103.6, 102.2, 52.3; HRMS (ESI): calc. for $[(C_{12}H_9NO_4)H]$ (M+H) 232.0610, found 232.0615.

Ethyl 7-methoxy-6-methylquinoline-3-carboxylate (3g):

Yield: 80%; 0.142 g; colorless solid, **mp:** 110-112 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 3081, 1716, 1611, 1299, 1250, 1033; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 9.30 (s, 1H), 8.65 (s, 1H), 7.61 (s, 1H), 7.40 (s, 1H), 4.45 (q, *J* = 6.9 Hz, 2H), 4.01 (s, 3H), 2.39 (s, 3H), 1.46 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 165.6, 161.6, 150.9, 149.4, 137.2, 130.5, 129.0, 121.9, 121.1, 106.2, 61.0, 55.7, 16.8, 14.4; HRMS (ESI): calc. for $[(C_{14}H_{15}NO_3)H]$ (M+H) 246.1130, found 246.1125.

Ethyl 8-bromo-5,7-dimethoxyquinoline-3-carboxylate (3h):

Yield: 65%; 0.095 g; colorless solid, **mp:** 156-158 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2987, 1717, 1605, 1478, 1264, 1002; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 9.50 (d, *J* = 1.8 Hz, 1H), 9.13 (d, *J* = 1.8 Hz, 1H), 6.72 (s, 1H), 4.46 (q, *J* = 7.0 Hz, 2H), 4.10 (s, 3H), 4.08 (s, 3H), 1.45 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 165.4, 159.3, 157.1, 152.2, 148.0, 134.8, 134.0, 120.9, 115.9, 94.2, 61.4, 57.0, 56.1, 14.4; HRMS (ESI): calc. for $[(C_{14}H_{14}BrNO_4)H]$ (M+H) 340.0184, found 340.0182.

Ethyl benzo[*h*]quinoline-3-carboxylate (3i):

Yield: 83%; 0.145 g; colorless solid, **mp:** 105-107 °C; lit[4d] mp 106-107 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2983, 1716, 1598, 1314, 1260, 1212, 750; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 9.56 (d, *J* = 1.8 Hz, 1H), 9.34 (dd, *J* = 7.2, 1.8 Hz, 1H), 8.84 (d, *J* = 1.8 Hz, 1H), 7.94 (d, *J* = 8.6 Hz, 1H), 7.87 (d, *J* = 8.8 Hz, 1H), 7.76-7.80 (m, 3H), 4.48 (q, *J* = 7.1 Hz, 2H), 1.49 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 165.6, 149.0, 148.9, 137.7, 134.5, 131.1, 129.3, 128.7, 127.9, 127.4, 125.5, 125.2, 125.1, 123.9, 61.5, 14.4; HRMS (ESI): calc. for $[(C_{16}H_{13}NO_2)H]$ (M+H) 252.1025, found 252.1019.

Methyl benzo[*h*]quinoline-3-carboxylate (3j):

Yield: 66%; 0.108 g; colorless solid, **mp:** 124-125 °C; lit[4a] mp 125-127 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2980, 1717, 1600, 1374, 1250, 1222, 750; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 9.49 (d, *J* = 1.8 Hz, 1H), 9.29 (dd, *J* = 9.1, 2.3 Hz, 1H), 8.76 (d, *J* = 2.3 Hz, 1H), 7.88 (dd, *J* = 6.9, 1.8 Hz, 1H), 7.81 (d, *J* = 8.7 Hz, 1H), 7.75-7.69 (m, 3H), 4.02 (s, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 165.9, 148.9, 148.9, 137.7, 134.5, 131.1, 129.3, 128.7, 127.8, 127.4, 125.5, 125.4, 125.2, 125.6, 123.6, 52.4; HRMS (ESI): calc. for $[(C_{15}H_{11}NO_2)H]$ (M+H) 238.0868, found 238.0860.

Methyl 7-acetamidoquinoline-3-carboxylate (3k):

Yield: 67%; 0.109 g; pale yellow solid, mp: 120-121 °C; IR ($CHCl_3$, cm^{-1}): υ_{max} 3330, 2940, 1720, 1650; ^{1}H NMR (200 MHz, $CDCl_3$/DMSO-d_6 (1:1)): δ 9.50 (s, 1H), 8.40 (d, *J* = 2.1 Hz, 1H), 7.93 (d, *J* = 1.8 Hz, 1H), 7.63 (s, 1H), 7.11 (d, *J* = 8.9 Hz, 1H), 6.95 (dd, *J* = 2.0, 8.7 Hz, 1H), 3.10 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$/DMSO-d_6): δ 169.0, 165.2, 150.3, 149.6, 142.3, 137.6, 129.4, 122.5, 120.9, 120.8, 115.4, 51.9, 24.0; HRMS (ESI) calcd. for $C_{13}H_{13}N_2O_3[M+H]^+$: 245.0916, found: 245.0921.

Procedure for the synthesis of oxolinic acid (5):

A mixture of quinoline (0.1 g) **3f** and ethyl trifluoromethane sulfonate (0.15 g) was warmed at 50 °C for 1 h. After removal of ethyl trifluoromethane sulfonate in *vaccuo*, the residue was added to a suspension of $K_3Fe(CN)_6$ (0.25 g) in 20% NaOH (10 mL) and stirred at room temperature for 2 h. The mixture was extracted with ethyl acetate, and the extract was washed with brine and dried over $MgSO_4$. After removal of ethyl acetate, the residue was purified by silica gel (CH_2Cl_2:MeOH = 50:1) to give quinolone **5** (0.053 g, 50%) as a colorless solid.

mp: 314-316 °C; lit[15] mp 314-316 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 3420, 1620, 1600, 1580, 1550, 1298, 1250, 1033; **^{1}H NMR** (200 MHz, CF_3CO_2D): δ 9.12 (s, 1H), 7.83 (s, 1H), 7.40 (s, 1H), 6.38 (s, 2H), 4.71 (q, *J* = 7.2 Hz, 2H), 1.69 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (50 MHz, CF_3CO_2D): δ 169.8, 158.6, 151.0, 146.3, 139.7, 123.3, 117.7, 112.0, 105.1, 101.7, 96.2, 53.5, 13.9; HRMS (ESI): calc. for $[(C_{13}H_{11}NO_5)H]$ (M+H) 262.0715, found 261.0711.

General experimental procedure for the preparation of quinoline carboxylate derivatives (6a-j), (7a-c):

A two-neck round-bottomed flask with septum was charged with $[RhCp^*Cl_2]_2$ (2.5 mol %), $Cu(OAc)_2{\cdot}H_2O$ (20 mol %) and $AgSbF_6$ (20 mol %) and evacuated, purged with nitrogen gas three times ($AgSbF_6$ was added inside the glove box). To the reaction mixture, was added anilines **1a-j** (1 mmol), ethyl propiolate **2a** (2.1 equiv), and 1,2-dichloroethane (2.0 mL) *via* syringes and again the reaction mixture was evacuated and purged with nitrogen gas three times. The reaction mixture was then allowed to stir at 50 °C for 5 h. It was cooled to room temperature and diluted with CH_2Cl_2, filtered through Celite. The filtrate was washed with water and the organic layer was extracted with CH_2Cl_2 and dried over anhyd. Na_2SO_4. Later, the solution was concentrated under reduced pressure. The crude residue was purified through silica gel column using pet ether and ethyl acetate (7:3) as eluent to give pure 2,3-disubstituted quinoline carboxylates (**6a-j).**

Also, the same procedure was followed for the formation of 1,2-dihydroquinolines (**7a-c**) using phenyl acetylene (2.1 equiv). In case of formation of 1,4-dihydropyridine derivatives (**9i-m**), an excess amount ethyl propiolate **2a** (3 equiv) was used under the same procedure.

Ethyl 2-(2-ethoxy-2-oxoethyl)-5,7-dimethoxyquinoline-3-carboxylate (6a):

Yield: 88%; 0.198 g; colorless solid; **mp:** 128-129 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2949, 1718, 1692, 1628, 1577, 1514, 1439, 1319, 1245, 1221, 1171, 1145, 993; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 9.05 (s, 1H), 6.97 (s,

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1H), 6.48 (s, 1H), 4.39 (q, *J* = 7.0 Hz, 2H), 4.36 (s, 2H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.99 (s, 3H), 3.94 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H), 1.25 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 170.6, 166.1, 163.6, 156.7, 155.7, 151.0, 135.1, 120.3, 114.9, 99.5, 98.6, 61.1, 60.6, 55.8, 55.7, 44.7, 14.4, 14.2; HRMS (ESI): calc. for $[(C_{18}H_{21}NO_6)H]$ (M+H) 348.1447, found 348.1442.

Ethyl 2-(2-ethoxy-2-oxoethyl)-7-methoxyquinoline-3-carboxylate (6b):

Yield: 88%; 0.226 g; colorless solid; **mp:** 132-134 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2954, 1722, 1706, 1638, 1577, 1559, 1507, 1439, 1369, 1336, 1284, 1224, 1179, 1147, 808; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 8.75 (s, 1H), 7.76 (d, *J* = 9.2 Hz, 1H), 7.38 (s, 1H), 7.20 (d, *J* = 8.5 Hz, 1H), 4.42-4.37 (m, 4H), 4.18 (q, *J* = 6.9 Hz, 2H), 3.96 (s, 3H), 1.42 (t, *J* = 7.2 Hz, 3H), 1.26 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 170.7, 165.9, 162.7, 155.1, 150.6, 139.9, 129.6, 121.5, 121.3, 120.6, 106.9, 61.2, 60.7, 55.6, 44.7, 14.3, 14.2; HRMS (ESI): calc. for $[(C_{17}H_{19}NO_5)H]$ (M+H) 318.1341, found 318.1331.

Ethyl 2-(2-ethoxy-2-oxoethyl)-6,7-dimethoxyquinoline-3-carboxylate (6c):

Yield: 85%; 0.192 g; colorless solid; **mp:** 150-152°C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2890, 1718, 1692, 1628, 1577, 1514, 1439, 1319, 1245, 1221, 1171, 1145, 993; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 8.69 (s, 1H), 7.39 (s, 1H), 7.11 (s, 1H), 4.48-4.33 (m, 4H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.05 (s, 3H), 4.02 (s, 3H), 1.47-1.39 (m, 3H), 1.26 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 171.0, 166.1, 154.5, 152.6, 150.3, 146.2, 138.3, 121.9, 121.7, 107.6, 105.5, 61.2, 60.7, 56.2, 56.0, 44.5, 14.3, 14.2; HRMS (ESI): calc. for $[(C_{18}H_{21}NO_6)H]$ (M+H) 348.1446, found 348.1448.

Ethyl 2-(2-ethoxy-2-oxoethyl)-5,6,7-trimethoxyquinoline-3-carboxylate (6d):

Yield: 75%; 0.192 g; gummy liquid; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2880, 1716, 1680, 1577, 1514, 1446, 1255, 1220, 1160; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 9.01 (s, 1H), 7.22 (s, 1H), 4.41 (q, *J* = 7.0 Hz, 2H), 4.38 (s, 2H), 4.18 (q, *J* = 7.2 Hz, 2H), 4.12 (s, 3H), 4.02 (s, 3H), 3.98 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H), 1.25 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 170.8, 166.2, 158.1, 154.2, 147.5, 146.5, 140.8, 134.7, 121.2, 117.4, 103.6, 61.7, 61.2, 61.2, 60.7, 56.2, 44.6, 14.2, 14.1; HRMS (ESI): calc. for $[(C_{19}H_{23}NO_7)H]$ (M+H) 378.1553, found 378.1557.

Ethyl 6-(2-ethoxy-2-oxoethyl)-[1,3]dioxolo[4,5-*g*]quinoline-7-carboxylate (6e):

Yield: 81%; 0.195 g; colorless solid; **mp:** 168-170 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2990, 1718, 1692, 1628, 1577, 1514, 1439, 1319, 1245, 1221, 1171, 1145, 993; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 8.63 (s, 1H), 7.34 (s, 1H), 7.11 (s, 1H), 6.15 (s, 2H), 4.38 (q, *J* = 7.2 Hz, 2H), 4.33 (s, 2H), 4.18 (q, *J* = 7.2 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 170.9, 166.0, 152.6, 148.2, 147.4, 138.6, 123.2, 121.6, 105.4, 103.0, 102.0, 61.2, 60.6, 44.3, 14.2, 14.1; HRMS (ESI): calc. for $[(C_{17}H_{17}NO_6)H]$ (M+H) 332.1134, found 332.1129.

Ethyl 7-(2-ethoxy-2-oxoethyl)-2,3-dihydro-[1,4]dioxino[2,3-*g*]quinoline-8-carboxylate (6f):

Yield: 85%; 0.193 g; colorless solid; **mp:** 110-112 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2954, 1740, 1730, 1577, 1559, 1507; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 8.64 (s, 1H); 7.48 (s, 1H), 7.27 (s, 1H), 4.41-4.31 (m, 4H), 4.17 (q, *J* = 7.2 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 171.0, 166.1, 153.0, 148.9, 144.8, 138.9, 122.3, 121.9, 113.9, 112.7, 64.5, 64.2, 61.3, 60.7, 44.5, 29.7, 14.3, 14.2; HRMS (ESI): calc. for $[(C_{18}H_{19}NO_6)H]$ (M+H) 346.1291, found 346.1290.

Ethyl 2-(2-ethoxy-2-oxoethyl)benzo[*h*]quinoline-3-carboxylate (6g):

Yield: 87%; 0.204 g; colorless solid; **mp:** 174-176 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2980, 1740, 1729, 1570, 1589, 1507; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 9.39-9.22 (m, 1H), 8.81 (s, 1H), 7.89 (dd, *J* = 9.1, 2.8 Hz, 1H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.72 (dd, *J* = 8.9, 2.3 Hz, 3H), 4.54 (s, 2H), 4.43 (q, *J* = 7.1 Hz, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 1.46 (t, *J* = 7.2 Hz, 3H), 1.28 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 171.0, 166.1, 153.8, 147.5, 139.4, 134.6, 130.9, 129.1, 128.4, 127.8, 127.3, 125.4, 125.1, 124.5, 123.9, 61.4, 60.7, 44.9, 14.4, 14.3; HRMS (ESI): calc. for $[(C_{20}H_{19}NO_4)H]$ (M+H) 338.1392, found 338.1387.

Methyl 7-methoxy-2-(2-methoxy-2-oxoethyl)quinoline-3-carboxylate (6h):

Yield: 80%; 0.187 g; colorless solid; **mp**:107-109 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2954, 1722, 1706, 1638, 1577, 1559, 1507, 1439, 1369, 1336, 1284, 1224, 1179, 1147, 808; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 8.77 (s, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.38 (d, *J* = 2.0 Hz, 1H), 7.22 (dd, *J* = 8.9, 2.3 Hz, 1H), 4.39 (s, 3H), 3.97 (s, 3H), 3.94 (s, 3H), 3.72 (s, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 171.2, 166.4, 162.9, 155.0, 150.8, 140.1, 129.7, 121.5, 120.8, 107.0, 55.7, 52.3, 52.0, 44.5; HRMS (ESI): calc. for $[(C_{17}H_{19}NO_5)H]$ (M+H) 290.1028, found 290.1025.

5,7-Dimethoxy-2-methyl-2,3-diphenyl-1,2-dihydroquinoline (7a):

Yield: 95%; 0.221 g; colorless solid; **mp**:128-130 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 3399, 2934, 2832, 1606, 1494, 1247, 699; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 7.48 (d, *J* = 7.6 Hz, 2H), 7.30-7.25 (m, 2H), 7.22 (s, 4H), 7.20-7.14 (m, 2H), 5.86 (d, *J* = 2.2 Hz, 1H), 5.76 (d, *J* = 2.0 Hz, 1H), 5.50 (s, 1H), 4.31 (br. s., 1H), 3.74 (s, 3H), 3.28 (s, 3H), 1.67 (s, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 161.2, 158.0, 148.4, 146.4, 142.9, 134.9, 128.2, 127.9, 127.4, 127.1, 126.7, 126.0, 125.4, 103.9, 92.0, 89.9, 56.3, 55.0, 54.9, 29.4; HRMS (ESI): calc. for $[(C_{24}H_{23}NO_2)H]$ (M+H) 358.1807, found 358.1805.

7-Methoxy-2-methyl-2,3-diphenyl-1,2-dihydroquinoline (7b):

Yield: 87%; 0.230 g; colorless solid; **mp**:108-110 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 3381, 2955, 2928, 1613, 1465, 1166, 823; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 7.51 (d, *J* = 7.2 Hz, 2H), 7.40-7.24 (m, 7H), 7.23-7.14 (m, 1H), 6.79 (d, *J* = 8.3 Hz, 1H), 6.13-6.04 (m, 2H), 5.47 (s, 1H), 4.16 (br. s., 1H), 3.70 (s, 3H), 1.73 (s, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 160.5, 148.8, 144.5, 139.6, 135.4, 128.9, 128.4, 128.1, 127.3, 126.8, 126.5, 125.3, 114.0, 102.5, 57.1, 98.7, 55.0, 30.1; HRMS (ESI): calc. for $[(C_{23}H_{21}NO)H]$ (M+H) 328.1701, found 328.1708.

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2,6,7-Trimethyl-2,3-diphenyl-1,2-dihydroquinoline (7c):

Yield: 82%; 0.220 g; colorless solid; **mp**: 119-120 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 3381, 3022, 1631, 1493, 1443, 699; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 7.6 (d, *J* = 2.0 Hz, 2H), 7.52 (d, *J* = 1.9 Hz, 2H), 7.51 (s, 1H), 7.39-7.36 (m, 3H), 7.34-7.33 (m, 3H), 7.31-7.29 (m, 1H), 7.26 (s, 1H), 2.17 (s, 6H), 1.57 (s, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 149.0, 141.3, 132.5, 131.5, 129.2, 128.9, 128.8, 128.8, 128.6, 128.4, 128.3, 128.2, 126.3, 121.9, 108.2, 81.5, 74.1, 30.1, 29.8, 29.7; HRMS (ESI): calc. for [($C_{23}H_{21}NO$)H] (M+H) 326.1909, found 326.1905.

Diethyl 4-(2-ethoxy-2-oxoethyl)-1-phenyl-1,4-dihydropyridine-3,5-dicarboxylate (9k):

Yield: 88%; 0.366 g; gummy liquid; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2951, 1713, 1596, 1495, 1436, 1211, 1084, 755, 715, 696; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 7.55 (s, 2H), 7.41 (s, 2H), 7.27-7.25 (m, 1H), 7.24-7.22 (m, 2H), 4.25-4.23 (m, 5H), 4.03 (q, *J* = 7.3 Hz, 2H), 2.57 (d, *J* = 4.9 Hz, 2H), 1.18 (t, *J* = 7.0 Hz, 3H), 1.32 (t, *J* = 7.0 Hz, 6H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 171.5, 166.6, 143.2, 137.6, 129.9, 126.4, 121.1, 120.9, 108.4, 60.3, 60.0, 40.5, 29.7, 14.5, 14.3; HRMS (ESI): calc. for [($C_{21}H_{25}NO_6$)Na] (M+Na) 410.1580, found 410.1574.

Diethyl-1-(3,4-dimethylphenyl)-4-(2-ethoxy-2-oxoethyl)-1,4-dihydropyridine-3,5-dicarboxylate (9l):

Yield: 82%; 0.280 g; gummy liquid; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2900, 1719, 1586, 1429, 1221, 1004, 758; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 7.51 (s, 2H), 7.14 (d, *J* = 8.2 Hz, 1H), 6.99-6.95 (m, 2H), 4.26-4.22 (m, 5H), 4.03 (q, *J* = 7.0 Hz, 2H), 2.56 (d, *J* = 4.9 Hz, 2H), 2.29 (s, 3H), 2.26 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 6H), 1.18 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 171.5, 166.7, 141.1, 138.3, 138.0, 134.9, 130.7, 122.2, 118.3, 107.8, 60.2, 60.0, 40.7, 29.7, 19.9, 19.2, 14.4, 14.2; HRMS (ESI): calc. for [($C_{23}H_{29}NO_6$)H] (M+H) 416.2073, found 416.2070.

Diethyl-1-(4-bromophenyl)-4-(2-ethoxy-2-oxoethyl)-1,4-dihydropyridine-3,5-dicarboxylate (9m):

Yield: 85%; 0.230 g; gummy liquid; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2947, 1728, 1696, 1638, 1438, 1362, 1337, 1259, 1238, 1196, 1177, 881; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 7.53 (d, *J* = 8.6 Hz, 2H), 7.50 (s, 2H), 7.11 (d, *J* = 8.6 Hz, 2H), 4.26-4.21 (m, 5H), 4.02 (q, *J* = 7.1 Hz, 2H), 2.58 (d, *J* = 4.9 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 6H), 1.18 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 171.4, 166.4, 142.2, 137.1, 132.9, 122.3, 119.6, 108.9, 60.4, 60.0, 40.2, 29.6, 14.4, 14.3; HRMS (ESI): calc. for [($C_{21}H_{24}BrNO_6$)H] (M+H) 466.0865, found 466.0860.

Diethyl-1-(2,3-dihydro-1*H*-inden-5-yl)-4-(2-ethoxy-2-oxoethyl)-1,4-dihydropyridine-3,5-dicarboxylate (9n):

Yield: 86%; 0.276 g; gummy liquid; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2960, 1715, 1600, 1490, 1209, 1004, 750, 710; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 7.51 (s, 2H), 7.20 (d, *J* = 8.0 Hz), 7.07 (s, 1H), 6.99 (dd, *J* = 8.0, 2.0 Hz, 2H), 4.28-4.18 (m, 5H), 4.05 (q, *J* = 7.1 Hz, 2H), 2.90 (q, *J* = 7.1 Hz, 4H), 2.55 (d, *J* = 4.8 Hz, 2H), 2.19-2.04 (m, 2H), 1.31 (t, *J* = 7.1 Hz, 6H), 1.20 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 171.5, 166.6, 146.1, 142.6, 141.8, 138.1, 125.2, 119.2, 117.4, 107.6, 60.1, 59.9, 40.5, 32.9, 32.3, 29.6, 25.7, 14.4, 14.2; HRMS (ESI): calc. for [($C_{24}H_{29}NO_6$)H] (M+H) 428.2073, found 428.2070.

Diethyl-4-(2-ethoxy-2-oxoethyl)-1-(9*H*-fluoren-2-yl)-1,4-dihydropyridine-3,5-dicarboxylate (9o):

Yield: 80%; 0.209 g; gummy liquid; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 2945, 1710, 1590, 1510, 1430, 1211, 1084; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 7.76 (t, *J* = 8.3 Hz, 2H), 7.60 (s, 2H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 7.3 Hz, 2H), 7.31 (d, *J* = 7.3 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 1H), 4.28-4.24 (m, 5H), 4.04 (q, *J* = 7.2 Hz, 2H), 3.92 (s, 2H), 2.60 (d, *J* = 4.7 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 6H), 1.19 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 171.5, 166.6, 145.0, 14.3, 143.1, 142.0, 140.6, 140.3, 138.0, 127.1, 125.1, 120.8, 119.9, 117.9, 112.0, 108.2, 60.3, 60.0, 40.6, 37.0, 29.7, 14.5; HRMS (ESI): calc. for [($C_{28}H_{29}NO_6$)H] (M+H) 476.2073, found 476.2072.

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