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Metal-free synthesis of quinoline-2,4-dicarboxylate derivatives using aryl amines and acetylenedicarboxylates through a pseudo three-component reaction†

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An efficient, useful and one-pot protocol for the synthesis of quinoline-2,4-dicarboxylate scaffolds is accomplished from aryl amines and dimethyl/diethyl acetylenedicarboxylates using 20 mol% molecular iodine as a catalyst in acetonitrile at 80 °C. In addition, the mechanistic explanation for the formation of the desired products is disclosed. The pivotal role of molecular iodine in the formation of the major products, diester quinoline derivatives, and the minor product, triesters, in two cases is described in the mechanism. The notable advantages of this method are non-involvement of a metal catalyst, avoiding of metal contamination in the final product as well as waste generation, use of a low cost and eco-friendly catalyst, ease of handling, high regioselectivity, shorter reaction time, the formation of one C–N and two C–C bonds and a broad substrate scope with good yields.

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Introduction

Quinolines are privileged heterocyclic frameworks present in numerous naturally occurring alkaloids and some of them are used as potent drugs.[1a–c] They also exhibit a broad spectrum of biological activities,[1d] such as antimalarial,[1e] antituberculosis,[1f,g] anticancer,[1h,i] anti-HIV,[1j] antiasthmatic[1k] and antihypertensive activities.[1l] Very recently, quinoline derivatives have been used for the treatment of SARS-CoV-2.[1m–o] Additionally, naturally occurring alkaloids, namely, quinine and cinchonidine, have been exploited extensively as chiral ligands for asymmetric synthesis.[2] Moreover, many synthetic quinoline derivatives are marketed as antimalarial drugs and some of the derivatives have been explored in materials science.[3a,b] Due to their immense importance in medicinal chemistry, materials science and organic synthesis, synthetic organic chemists have put tremendous efforts to develop new methodologies for the synthesis of new substituted quinoline derivatives. Some classical procedures are well recognized for the synthesis of quinolines and their derivatives, such as Skraup,[4a] Conard–Limpach,[4b] Pfitzinger,[4c,d] Doebner–von Miller,[4e] Friedlaender[4f] and many others.[5] The quinoline-2-carboxylate backbone is an integral part of naturally occurring alkaloids, namely, ascidiathiazone A and B.[6a] Therefore, the synthetic community has devoted considerable efforts to achieve the synthesis of quinoline mono-carboxylate derivatives. Wang *et al.* first demonstrated the synthesis of 4-aryl-quinoline-2-carboxylate derivatives from functionalized glycine derivatives and olefins/alkynes under catalytic radical cation salt induced conditions.[6b] Later on, Zhang and co-workers reported the synthesis of 4-substituted quinoline-2-carboxylate derivatives from similar kinds of substrates involving a photocatalyst in the presence of blue LED light.[6c,d] Similarly, Balaraman and co-workers reported the synthesis of quinoline-3-carboxylate derivatives from aniline and alkyne in the presence of a rhodium catalyst.[7a]

The Bayer Pharma Group used quinoline-2,4-carboxylate as the key precursor for the synthesis of glucose transport inhibitors, namely N^4-(2-(4-cyanobenzyl)-4-methylthiazol-5-yl)quinoline-2,4-dicarboxylate and its derivatives.[7b] It reflects the importance of this key precursor in medicinal chemistry. Despite the importance of quinoline-2,4-carboxylate and its derivatives, only a few methods are known so far for the synthesis of quinoline-2,4-dicarboxylate, as shown in Scheme 1. Peet and co-workers[8a] first reported an antiallergic quinolinone derivative obtained in two steps using *o*-nitroaniline and acetylenedicarboxylate (Scheme 1a). However, they did not obtain quinoline-2,4-dicarboxylate. Similarly, Pitchumani and co-workers showed the use of enamines (derived from aryl amines and dimethyl acetylenedicarboxylate) in a multi-component reaction for the synthesis of highly functionalized pyr-

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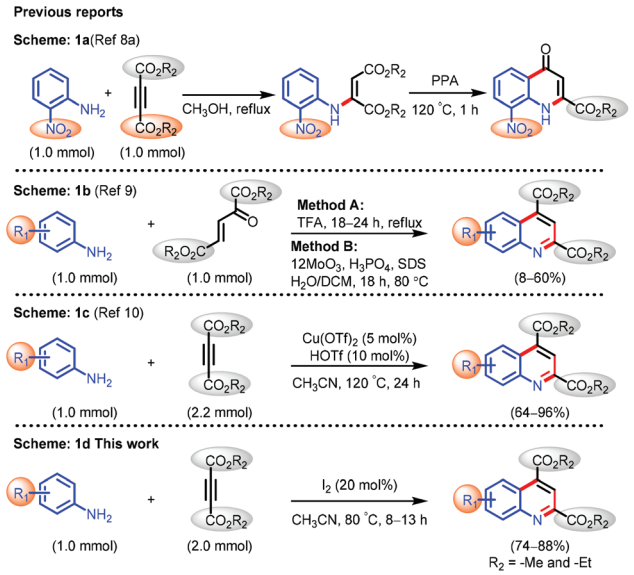


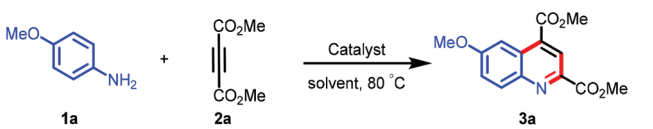
Scheme 1 Previous reports and present work.

rolidines.[8b] It is to be noted that none of them reported the synthesis of quinoline-2,4-dicarboxylate derivatives. Pietrancosta and co-workers[9] reported a method for the synthesis of quinoline-2,4-dicarboxylate derivatives *via* an improved Doebner Miller reaction using aryl amines and an unsaturated keto-ester (synthesized from ketoglutaric acid in three steps) (Scheme 1b). Recently, Yi and co-workers[10] disclosed a one-pot synthesis of 2,4-disubstituted quinolines through the copper(II) triflate catalyzed reaction of aryl amines and acetylenedicarboxylates (Scheme 1c). Despite the great utility of these earlier reported methods, they have some demerits, such as the use of the expensive metal catalyst $Cu(OTf)_2$, the requirement of the hazardous triflic acid, high reaction temperature, longer reaction time and restricted substrate scope. In order to overcome all these complications, the development of a straightforward protocol is still highly desirable in terms of green and sustainable chemistry. Molecular iodine has emerged as a Lewis acid catalyst that has been utilized in various organic transformations.[11] Recently, our research group has shown the efficacy of molecular iodine for the synthesis of various nitrogen heterocycles,[12a–e] which encouraged us to develop a new methodology for the synthesis of quinoline-2,4-dicarboxylate derivatives using molecular iodine as a catalyst due its low cost, easy availability, nontoxicity, versatility and environmental friendliness.[12f] Iodine has structural features and reactivity patterns that are similar to those of transition metals[12f–h] and it can be used in place of transition metals to make the process greener and eco-friendly. Recently, it has been utilized for several organic transformations, such as C–N, C–O, and C–C bond formations in organic compounds, which have been reviewed.[12f,i] Keeping in mind the growing concerns about environment protection and waste generation, we considered that molecular iodine can be used to develop a sustainable method for the synthesis of dimethyl/diethyl quinoline-2,4-dicarboxylate derivatives (Scheme 1d). Dialkyl acetylenedicarboxylates are readily available starting materials, which have been extensively used for the synthesis of various heterocycles.[13] These can act as Michael acceptors[14] as well as dienophiles[15] due to the presence of two ester groups. Our group has accomplished the synthesis of various heterocycles using acetylenedicarboxylates.[12a,16] Due to that motivation, we are still encouraged to explore them in our laboratory and use them for the synthesis of dimethyl/diethyl quinoline-2,4-dicarboxylate derivatives. In continuation of our efforts towards the synthesis of various quinolines,[17] herein, we disclose the metal-free synthesis of dimethyl/diethyl quinoline-2,4-dicarboxylate derivatives using aryl amines and acetylenedicarboxylates in the presence of 20 mol% I_2 in acetonitrile at 80 °C (Scheme 1d). To date, there is no literature precedent of the molecular iodine catalyzed domino reaction of arylamines and dimethyl/diethyl acetylenedicarboxylates.

Results and discussion

To find out the optimum reaction conditions, *p*-anisidine **1a** and dimethyl acetylenedicarboxylate **2a** were chosen as the model substrates and the results are presented in Table 1. We initiated our studies with the reaction using *p*-anisidine (**1a**,

Table 1 Optimization of reaction conditions[a,b,c,d]



Entry	Catalyst	Mol %	Solvent	Time	Yield **3a**[b] (%)
1[c]	—	—	—	24 h	NR
2	—	—	—	24 h	NR
3[c]	—	—	CH_3CN	24 h	NR
4	—	—	CH_3CN	24 h	NR
5[c]	I_2	5	CH_3CN	24 h	NR
6	I_2	5	CH_3CN	18 h	28
7	I_2	10	CH_3CN	18 h	50
8	I_2	15	CH_3CN	12 h	68
9	**I_2**	**20**	**CH_3CN**	**8 h**	**85**
10	I_2	25	CH_3CN	8 h	83
11	$PhI(OAc)_2$	20	CH_3CN	8 h	NR
12	IBr	20	CH_3CN	8 h	25
13	ICl	20	CH_3CN	8 h	20
14	I_2	20	Dioxane	8 h	NR
15[d]	I_2	20	CH_2Cl_2	8 h	NR
16	I_2	20	$(CH_2Cl)_2$	8 h	NR
17[d]	I_2	20	THF	8 h	NR
18	I_2	20	DMF	8 h	NR
19	I_2	20	DMSO	8 h	NR
20[d]	I_2	20	MeOH	8 h	62
21	I_2	20	H_2O	8 h	48

[a] Reaction conditions: all the reactions were performed using *p*-anisidine (**1a**, 1.0 mmol) and dimethyl acetylenedicarboxylate (**2a**, 2.0 mmol) in solvent (3.0 mL) at 80 °C. [b] Isolated yield. [c] Reaction performed at room temperature. [d] Reaction performed under reflux conditions. NR (no desired product).

1.0 mmol) and dimethyl acetylenedicarboxylate (**2a**, 2.0 mmol) without any solvent and catalyst (Table 1, entries 1 and 2). The reaction did not occur at room temperature as well as upon heating at 80 °C. The reaction did not proceed even when it was examined in acetonitrile in the absence of a catalyst at room temperature as well as at 80 °C (Table 1, entries 3 and 4). The reaction did not proceed in the presence of 5 mol% I_2 at room temperature (Table 1, entry 5); however, upon heating at 80 °C for 18 h, the product **3a** was isolated in 28% yield (Table 1, entry 6). Encouraged by this successful result, we attempted to increase the yield of the desired product **3a** by examining the different reaction parameters, such as catalyst loading, using different catalysts and screening various solvents. When the catalyst loading was increased from 5 mol% to 10 mol%, **3a** was obtained in 50% yield (Table 1, entry 7). Upon increasing the catalyst loading from 10 mol% to 15 mol%, the reaction time was reduced to 12 h and the yield of **3a** was also further improved (Table 1, entry 8). When the catalyst loading was further increased to 20 mol%, the reaction was completed in 8 h and the yield of **3a** was increased significantly to 85% (Table 1, entry 9). However, a further increase in the catalyst loading to 25 mol% did not improve the yield of **3a** (Table 1, entry 10). Next, we carried out the model reaction in the presence of different iodine containing non-metallic catalysts, such as $PhI(OAc)_2$, IBr and ICl (Table 1, entries 11–13).

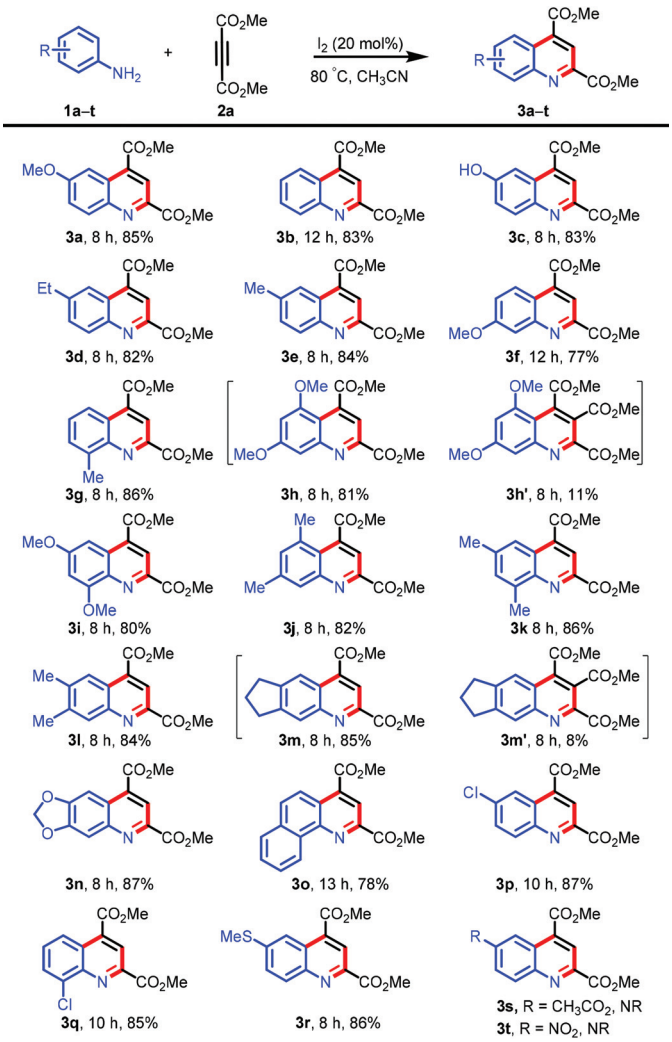
It was observed that none of them was more efficient than I_2. Next, to check the efficiency of the solvent, different solvents, such as 1,4-dioxane, dichloromethane, tetrahydrofuran, dimethyl sulfoxide, methanol and water, were tested (Table 1, entries 14–21) using 20 mol% I_2 as the catalyst. It was noted that in all solvents, either the reaction did not occur or the yield of **3a** was low. Therefore, the best yield of **3a** was obtained in acetonitrile. From all the above observations, the optimum reaction conditions were 20 mol% I_2 in acetonitrile at 80 °C (Table 1, entry 9) in terms of both reaction time and yield.

With the optimized reaction conditions in hand, the scope and generality of the developed method were explored with different aryl amines **1a–t** and dimethyl acetylenedicarboxylate **2a** (Table 2). The reaction of *p*-anisidine **1a** with dimethyl acetylenedicarboxylate **2a** provided the desired product **3a** in 85% yield. The reaction of simple aniline **1b** with **2a** proceeded well and gave the expected product **3b** in 83% yield. Similarly, aryl amine containing a hydroxyl group at the *para* position afforded the corresponding product **3c** in 83% yield.

Aryl amines containing electron-donating groups, such as 4-Et and 4-Me, worked well and gave the expected quinoline derivatives **3d** and **3e** in 82% and 84% yields, respectively. Likewise, the reaction of aryl amines containing the 3-OMe and 2-Me groups with **2a** provided quinoline scaffolds **3f** and **3g** in 77% and 86% yields, respectively. The reaction of aryl amines containing the 3,5-OMe, 2,4-OMe, 3,5-Me, 2,4-Me and 3,4-Me groups with **2a** proceeded smoothly and gave the corresponding quinoline derivatives **3h–l** in 80–86% yields. It is noteworthy that the triester quinoline **3h′** was obtained in 11% yield along with quinoline **3h**. Notably, bicyclic aryl amines, such as 5-aminoindan **1m**, 3,4-(methylenedioxy) aniline **1n**, and 1-naphthylamine **1o**, upon reaction with **2a** provided the fused quinoline derivatives **1m–o** in 78–87% yields. Interestingly, in the reaction with 5-aminoindan **1m**, we isolated the triester quinoline **3m′** in 8% yield along with the desired product **3m**. Gratifyingly, aryl amines containing electron-withdrawing groups such as 4-Cl and 2-Cl also gave the corresponding quinolines **3p** and **3q** in 87% and 85% yields, respectively. In addition, 4-(methylthio)aniline **1r** also provided the desired quinoline **3r** in 86% yield. Unfortunately, aryl amines containing strong electron-withdrawing groups such as $-CO_2Me$ and $-NO_2$ at the *para* position did not give the desired products under standard conditions due to less electron density at the *ortho* position with respect to the $-NH_2$ group.

Inspired by the above-discussed successful results, the scope and generality of the present protocol were extended

Table 2 Reaction of different aryl amines **1a–t** with dimethyl acetylenedicarboxylate **2a** [a,b]



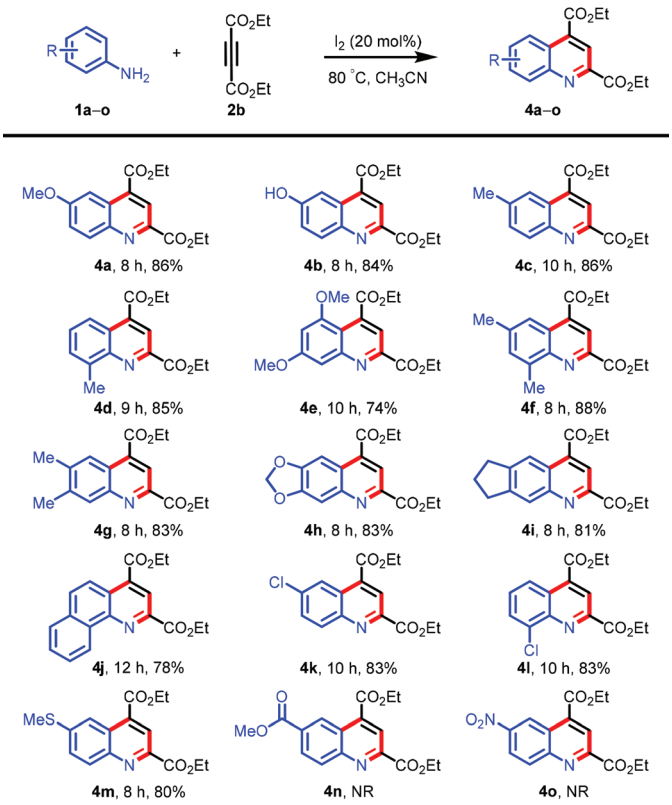
[a] Reaction conditions: all the reactions were performed using aryl amines (**1a–t**, 1.0 mmol) and dimethyl acetylenedicarboxylate (**2a**, 2.0 mmol) in solvent (3.0 mL) at 80 °C. [b] Isolated yield. NR (no desired product).

further using different aryl amines **1a–o** with diethyl acetylenedicarboxylate **2b** (Table 3). The reaction of *p*-anisidine **1a** with diethyl acetylenedicarboxylate **2b** under the standard conditions proceeded smoothly and gave the desired quinoline **4a** in 86% yield. Similarly, the hydroxyl group at the *para* position of aryl amine **1b** was well tolerated and afforded the corresponding quinoline **4b** in 84% yield. The aryl amines containing the 4-Me and 2-Me groups also worked well and provided the desired quinoline derivatives **4c** and **4d** in 86% and 85% yields, respectively. The di-substituted aryl amines containing the 3,5-OMe, 2,4-Me and 3,4-Me groups upon reaction with **2b** gave the expected quinoline scaffolds **4e–g** in 74–88% yields. Notably, the reaction of bicyclic amines, such as 3,4-(methylenedioxy)aniline **1h**, 5-aminoindan **1i**, and 1-naphthylamine **1j**, with **2b** gave the expected quinoline derivatives **4h–j** in 78–83% yields. Interestingly, aryl amines having electron-withdrawing groups, such as 4-Cl and 2-Cl, provided the desired quinolines **4k** and **4l** in 83% and 83% yields, respectively. Additionally, 4-(methylthio)aniline **1m** provided the corresponding quinoline **4m** in 80% yield. Unfortunately, aryl amines containing strong electron-withdrawing groups, such as $-CO_2Me$ and $-NO_2$, at the *para* position did not give the desired products under the standard conditions due to less electron density at the *ortho*-position with respect to the $-NH_2$ group.

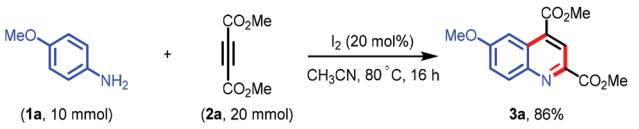
We performed a scale up reaction using *p*-anisidine (**1a**, 10 mmol) and dimethyl acetylenedicarboxylate (**2a**, 20 mmol) to give the desired product **3a** in 86% yield (Scheme 2). All the compounds were characterized using spectroscopic techniques, such as IR, ^{1}H NMR, ^{13}C NMR and HRMS. In addition, the structure of compound **3k** was confirmed using the single X-ray crystallographic data (see the ESI†).

To gain insights into the reaction mechanism, we carried out a series of control experiments (Scheme 2). At first, we performed a reaction of *p*-anisidine **1a** with dimethyl acetylenedicarboxylate **2a** (Scheme 3a) in the absence of molecular iodine. After heating the reaction mixture for a period of 8 h, we isolated hydroamination intermediate **A** (aza-Michael product) and it was characterized using IR, ^{1}H NMR, ^{13}C NMR and HRMS. A similar observation has also been reported by Peet and co-workers.[8a] Next, we carried out the reaction between intermediate **A** and dimethyl acetylenedicarboxylate **2a** under the standard conditions (Scheme 3b). The reaction was completed in another 8 h and quinoline **3a** was obtained in 83% yield. This suggests the formation of intermediate **A** and its

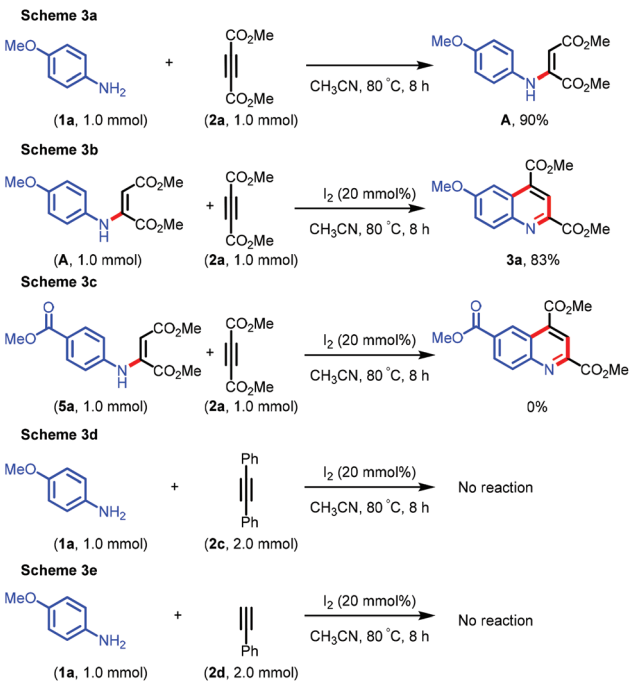
Table 3 Reaction of different aryl amines **1a–o** with diethyl acetylenedicarboxylate **2b** [a,b]



[a] Reaction conditions: all the reactions were performed using aryl amines (**1a–o**, 1.0 mmol) and diethyl acetylenedicarboxylate (**2b**, 2.0 mmol) in solvent (3.0 mL) at 80 °C. [b] Isolated yield. NR (no desired product).



Scheme 2 Gram scale synthesis.

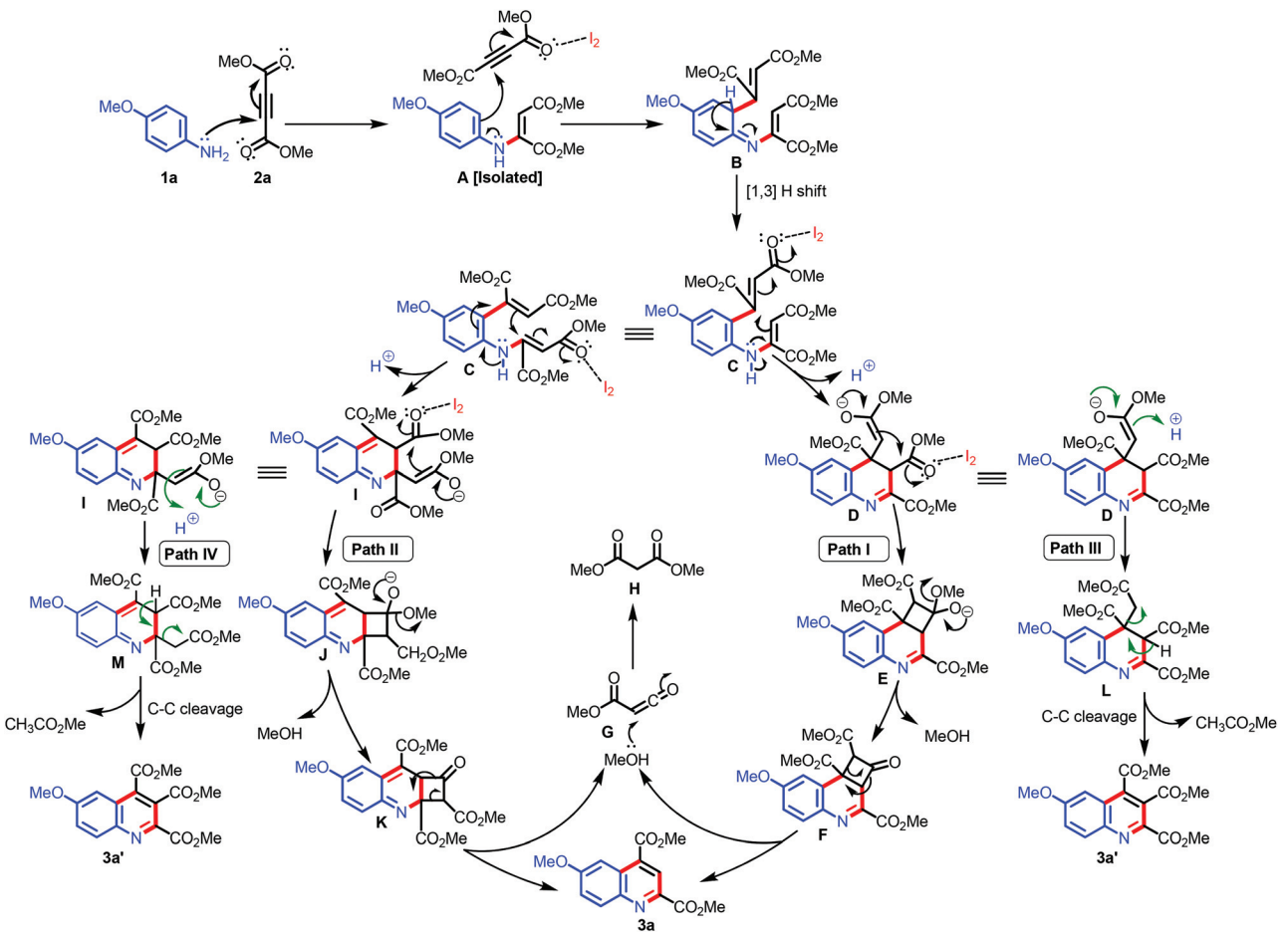


Scheme 3 Control experiments.

involvement in the reaction mechanism. The reaction using intermediate **5a** with dimethyl acetylenedicarboxylate **2a** under identical conditions did not provide the expected product (Scheme 3c). The reason for reaction failure might be the less electron density at the *ortho*-position of the ring with respect to the –NH group due to the presence of the strong electron-withdrawing ester group. Next, we carried out the reactions using *p*-anisidine **1a** with diphenylacetylene **2c** and phenylacetylene **2d** under identical conditions, and the reactions did not proceed at all in both the cases (Scheme 3d and e). In both the cases, the formation of the four membered ring fused tetrahydroquinoline intermediate was not possible. Therefore, we did not obtain the corresponding products using diphenylacetylene and acetylene. These two experiments suggest that the presence of the two ester groups in acetylene is necessary for the formation of the product, which also supports our proposed reaction mechanism.

From the observation of control experiments and literature precedents, the plausible mechanism for the formation of quinoline-2,4-dicarboxylate derivatives and triester quinoline derivatives is shown in Scheme 4. We presumed that the reaction can occur *via* two pathways, path **I** or path **II**, to form the desired diester products. According to path I, at first, aryl amine **1a** reacts with acetylenedicarboxylate **2a** to give aza-Michael product **A**.[12i] The intermediate product (**A**) reacts with the second molecule of **2a** assisted by molecular iodine *via* the Michael reaction, leading to the annulated intermediate **B**. Then intermediate **B** undergoes a [1,3] H shift to provide intermediate **C**, which on intramolecular cyclization *via* the Michael reaction promoted by molecular iodine affords reactive anion species **D**. Next, intermediate **D** undergoes intramolecular cyclization which is also assisted by molecular iodine to generate a four membered ring fused with tetrahydroquinoline **F** through intermediate **E**. Due to ring strain, intermediate **F** undergoes cleavage to give the desired quinoline **3a** and reactive ketene intermediate **G**, which is attacked by the generated methanol in the reaction medium to give malonic ester **H**. Alternatively, the formation of diesters can also be explained through path **II**. We detected malonic ester **H** in the crude ^{1}H NMR spectrum of compound **3a** (see the ESI†). In addition, malonic ester **H** was also detected by HRMS (see the ESI†).

The formation of the minor product, triester quinoline derivatives, occurs *via* two possible pathways, path **III** or path **IV**. According to path **III**, intermediate **L** can also be formed from intermediate **D** after protonation, which undergoes C–C



Scheme 4 The plausible mechanism for the formation of quinoline derivative **3a** and triester quinolines **3h′** and **3m′**.

bond cleavage with the elimination of CH_3CO_2Me to give the expected triester quinoline derivatives. In path **IV**, intermediate **M** can also be generated after protonation from intermediate **I**, which undergoes an almost similar type of reaction like C–C bond cleavage to provide triester quinoline derivatives. Similar C–C bond cleavage has also been reported by others.[10,18a,b] The formation of products **3h** and **3h′** and **3m** and **3m′** occurs *via* all four possible pathways among which path I and path II are more predominant; otherwise, in all other cases, path **I** and path **II** are solely favoured for the formation of diesters.

Conclusion

We have devised a simple and efficient method for the synthesis of dimethyl/diethyl quinoline-2,4-dicarboxylate derivatives by employing a domino reaction using readily available aryl amines and acetylenedicarboxylates in the presence of 20 mol% I_2 under mild conditions. From the reaction mechanism, the role of molecular iodine in the reaction for the formation of intermediate **B** from product **A** is quite clear, *i.e.*, the Michael reaction as well as the other steps which are proposed in the mechanism. This transformation occurs under metal-free conditions, avoiding the use of metal catalysts with no formation of metal waste. The important features of this protocol are its ease of handling, use of low cost and environmentally benign catalysts, high regioselectivity, use of commercially available starting materials, no requirement for an inert atmosphere or dry solvent, shorter reaction time, the consecutive formation of one C–N and two C–C bonds and a broad substrate scope with good to excellent yields. We are still exploring the synthetic application of quinoline-2,4-dicarboxylate and studies to obtain quinoline-2,3,4-tricarboxylate derivatives by tuning the reaction conditions are underway in our laboratory.

Experimental

General information and methods

Melting points were determined on a melting point apparatus (Buchi-540). ^{1}H and ^{13}C NMR spectra were recorded on 400, 500 and 600 MHz and 100, 125 and 150 MHz NMR spectrometers (Bruker), respectively. TMS was used as an internal reference; chemical shifts (δ scale) are reported in parts per million (ppm). ^{1}H NMR spectra are reported in the order: multiplicity, coupling constant (J value) in hertz (Hz) and no. of protons; signals are characterized as s (singlet), d (doublet), t (triplet), m (multiplet) and bs (broad). IR spectra were recorded on an IR spectrophotometer (PerkinElmer). HRMS spectra were recorded using a TOF mass analyzer.

General procedure for the synthesis of quinoline-2,4-dicarboxylate derivatives

Into a 10 mL round-bottomed flask, a mixture of aryl amine (**1**, 1.0 mmol) and acetylenedicarboxylate (**2**, 2.0 mmol) in 3 mL of acetonitrile was added. After five minutes of stirring, molecular iodine (20 mol%, 50 mg) was added into it. The resultant mixture was stirred at room temperature for 10 min and subsequently it was kept for heating at 80 °C in a pre-heated oil-bath. After completion of the reaction, it was cooled to room temperature and acetonitrile was evaporated on a rotary evaporator. After this, a saturated solution of sodium thiosulphate was added dropwise to the reaction mixture to decolorize the iodine. Then it was extracted with ethyl acetate (3 × 5 mL). The combined organic layer was washed with water (2 × 5 mL) followed by brine solution (5 mL) and dried over anhydrous sodium sulphate. The solvent was evaporated on a rotary evaporator. Finally, the crude mixture was purified using silica gel (60–120 mesh) column chromatography.

Dimethyl 6-methoxyquinoline-2,4-dicarboxylate (3a).[9] (234 mg, 85%, light yellow solid); mp 152–153 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.30 (d, J = 2.8 Hz, 1H), 8.23 (d, J = 9.3 Hz, 1H), 7.48 (dd, J = 9.3, 2.8 Hz, 1H), 4.09 (s, 3H), 4.05 (s, 3H), 4.00 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.5, 165.7, 161.3, 145.3, 144.7, 133.4, 132.9, 128.7, 124.2, 123.4, 103.2, 55.9, 53.5, 52.9; V_{max}/cm^{-1} 2926, 1745, 1640, 1478, 1336; HRMS (ESI) calcd for $C_{14}H_{14}NO_5$ 276.0872 (M + H$^+$); found 276.0872.

Dimethyl 6-methoxyquinoline-2,4-dicarboxylate (3b).[9] (204 mg, 83%, yellow solid); mp 128–129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (d, J = 8.5 Hz, 1H), 8.70 (s, 1H), 8.37 (d, J = 8.5 Hz, 1H), 7.86 (t, J = 7.6 Hz, 1H), 7.78 (t, J = 7.6 Hz, 1H), 4.11 (s, 3H), 4.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 165.6, 148.8, 147.7, 136.3, 131.5, 130.8, 130.6, 126.5, 125.77, 122.5, 53.6, 53.1; V_{max}/cm^{-1} 2956, 1721, 1507, 1434, 1355; HRMS (ESI) calcd for $C_{13}H_{12}NO_4$ 246.0766 (M + H$^+$); found 246.0766.

Dimethyl 6-hydroxyquinoline-2,4-dicarboxylate (3c). (217 mg, 83%, yellow solid); mp 215–216 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.84 (s, 1H), 8.44 (s, 1H), 8.12 (d, J = 9.2 Hz, 1H), 8.07 (d, J = 2.5 Hz, 1H), 7.50 (dd, J = 9.2, 2.6 Hz, 1H), 3.99 (s, 3H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6,) δ 165.7, 164.8, 159.5, 143.6, 143.4, 132.7, 132.7, 127.6, 123.8, 122.1, 106.2, 52.9, 52.6; V_{max}/cm^{-1} 3394, 1722, 1655, 1600, 1354; HRMS (ESI) calcd for $C_{13}H_{12}NO_5$ 262.0715 (M + H$^+$); found 262.0715.

Dimethyl 6-ethylquinoline-2,4-dicarboxylate (3d). (224 mg, 86%, light yellow solid); mp 136–137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.63 (d, J = 0.8 Hz, 1H), 8.27 (d, J = 8.7 Hz, 1H), 7.71 (dd, J = 8.7, 1.9 Hz, 1H), 4.10 (s, 3H), 4.06 (s, 3H), 2.90 (q, J = 7.6 Hz, 2H), 1.36 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 165.7, 147.7, 147.4, 146.7, 135.4, 132.1, 131.3, 126.7, 123.3, 122.6, 53.5, 53.0, 29.7, 15.4; V_{max}/cm^{-1} 2964, 1725, 1649, 1498, 1333; HRMS (ESI) calcd for $C_{15}H_{16}NO_4$ 274.1079 (M + H$^+$); found 274.1093.

Dimethyl 6-methylquinoline-2,4-dicarboxylate (3e).[9] (218 mg, 84%, gray solid); mp 131–132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.58 (s, 1H), 8.22 (d, J = 8.7 Hz, 1H), 7.65 (dd, J = 8.6, 1.1 Hz, 1H), 4.08 (s, 3H), 4.04 (s, 3H), 2.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 165.6, 147.5, 146.6, 141.3, 135.2, 133.1, 131.1, 126.5, 124.4, 122.5, 53.5, 53.0, 22.5; V_{max}/cm^{-1} 2962, 1721, 1633, 1500, 1352; HRMS (ESI) calcd for $C_{14}H_{14}NO_4$ 260.0923 (M + H$^+$); found 260.0923.

Dimethyl 7-methoxyquinoline-2,4-dicarboxylate (3f). (214 mg, 77%, light yellow solid); mp 148–149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, J = 9.4 Hz, 1H), 8.56 (s, 1H), 7.66 (d, J = 2.5 Hz, 1H), 7.41 (dd, J = 9.4, 2.5 Hz, 1H), 4.10 (s, 3H), 4.06 (s, 3H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 165.7, 161.4, 150.9, 147.8, 135.9, 126.7, 124.2, 122.0, 120.4, 108.7, 55.9, 53.6, 53.1; V_{max}/cm^{-1} 2968, 1738, 1615, 1600, 1366; HRMS (ESI) calcd for $C_{14}H_{14}NO_5$ 276.0872 (M + H$^+$); found 276.0895.

Dimethyl 8-methylquinoline-2,4-dicarboxylate (3g).[9] (224 mg, 86%, light yellow solid); mp 125–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (t, J = 3.9 Hz, 2H), 7.71–7.61 (m, 2H), 4.08 (s, 3H), 4.06 (s, 3H), 2.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 165.8, 148.0, 146.4, 139.53, 136.4, 130.8, 130.3, 126.5, 123.5, 122.1, 53.3, 53.1, 18.6; V_{max}/cm^{-1} 2920, 1725, 1654, 1492, 1344; HRMS (ESI) calcd for $C_{14}H_{14}NO_4$ 260.0923 (M + H$^+$); found 260.0924.

Dimethyl 5,7-dimethoxyquinoline-2,4-dicarboxylate (3h). (248 mg, 81%, light yellow liquid); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (d, J = 2.2 Hz, 1H), 6.63 (s, 1H), 6.42 (d, J = 2.3 Hz, 1H), 4.04 (s, 3H), 3.95 (s, 3H), 3.92 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 162.7, 162.1, 155.9, 149.9, 140.5, 108.2, 107.7, 100.0, 97.4, 56.5, 55.8, 53.7, 52.7; V_{max}/cm^{-1} 2948, 1739, 1621, 1596, 1348; HRMS (ESI) calcd for $C_{15}H_{16}NO_6$ 306.0978 (M + H$^+$); found 306.0979.

Trimethyl 5,7-dimethoxyquinoline-2,3,4-tricarboxylate (3h′). (41 mg, 11%, yellow liquid); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, J = 2.2 Hz, 1H), 6.63 (d, J = 2.2 Hz, 1H), 4.01 (s, 3H), 3.99 (s, 3H), 3.94 (s, 3H), 3.93 (s, 3H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 166.4, 165.6, 163.8, 156.1, 150.8, 150.1, 139.9, 118.8, 112.1, 101.9, 101.4, 57.0, 56.2, 53.5, 53.3, 52.9; V_{max}/cm^{-1} 3277, 2935, 1728, 1666, 1550; HRMS (ESI) calcd for $C_{17}H_{18}NO_8$ 364.1032 (M + H$^+$); found 364.1059.

Dimethyl 6,8-dimethoxyquinoline-2,4-dicarboxylate (3i). (245 mg, 80%, yellow solid); mp 161–162 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.74 (s, 1H), 7.89 (s, 1H), 6.78 (s, 1H), 4.06 (s, 3H), 4.05 (s, 3H), 4.03 (s, 3H), 3.99 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.5, 165.8, 162.4, 157.3, 143.2, 138.1, 133.3, 129.6, 124.1, 102.4, 95.2, 56.5, 56.0, 53.3, 52.9; V_{max}/cm^{-1} 2954, 1720, 1615, 1436, 1285; HRMS (ESI) calcd for $C_{15}H_{16}NO_6$ 306.0978 (M + H$^+$); found 306.0978.

Dimethyl 5,7-dimethylquinoline-2,4-dicarboxylate (3j). (225 mg, 82%, yellow solid); mp 133–134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.99 (s, 1H), 7.36 (s, 1H), 4.07 (s, 3H), 4.03 (s, 3H), 2.58 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 165.5, 149.4, 146.7, 140.9, 139.9, 134.7, 133.5, 128.9, 122.5, 119.2, 53.5, 53.3, 21.7, 21.0; V_{max}/cm^{-1} 2953, 1732, 1631, 1561, 1338; HRMS (ESI) calcd for $C_{15}H_{16}NO_4$ 274.1079 (M + H$^+$); found 274.1079.

Dimethyl 6,8-dimethylquinoline-2,4-dicarboxylate (3k).[9] (236 mg, 86%, light yellow solid); mp 138–139 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.40 (s, 1H), 7.53 (s, 1H), 4.07 (s, 3H), 4.05 (s, 3H), 2.87 (s, 3H), 2.55 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.7, 165.9, 146.7, 145.3, 140.9, 138.9, 135.4, 133.3, 126.7, 122.3, 122.2, 53.3, 52.9, 22.6, 18.4; V_{max}/cm^{-1} 2956, 1728, 1627, 1568, 1339; HRMS (ESI) calcd for $C_{15}H_{16}NO_4$ 274.1079 (M + H$^+$); found 274.1079.

Dimethyl 6,7-dimethylquinoline-2,4-dicarboxylate (3l). (231 mg, 84%, white solid); mp 139–140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.59 (s, 1H), 8.12 (s, 1H), 4.09 (s, 3H), 4.06 (s, 3H), 2.52 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 165.8, 148.1, 146.6, 141.6, 141.4, 134.9, 132.2, 130.6, 124.8, 121.8, 53.5, 53.0, 21.0, 20.5; V_{max}/cm^{-1} 2923, 1723, 1614, 1585, 1356; HRMS (ESI) calcd for $C_{15}H_{16}NO_4$ 274.1079 (M + H$^+$); found 274.1096.

Dimethyl 7,8-dihydro-6*H*-cyclopenta[*g*]quinoline-2,4-dicarboxylate (3m). (244 mg, 85%, yellow solid); mp 142–143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.59 (s, 1H), 8.15 (s, 1H), 4.09 (s, 3H), 4.06 (s, 3H), 3.14 (t, J = 7.3 Hz, 4H), 2.20 (quint, J = 7.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 165.8, 149.4, 149.2, 148.8, 146.3, 135.5, 125.8, 125.6, 121.6, 119.6, 53.4, 53.0, 33.4, 32.9, 26.2; V_{max}/cm^{-1} 2953, 1725, 1614, 1436, 1351; HRMS (ESI) calcd for $C_{16}H_{16}NO_4$ 286.1079(M + H$^+$); found 286.1079.

Trimethyl 7,8-dihydro-6*H*-cyclopenta[*g*]quinoline-2,3,4-tricarboxylate (3m′). (28 mg, 8%, brown liquid); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.81 (s, 1H), 4.04 (s, 3H), 4.03 (s, 3H), 3.95 (s, 3H), 3.15–3.10 (m, 4H), 2.20 (quint, J = 7.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 166.5, 166.2, 151.4, 149.0, 147.8, 146.7, 139.6, 125.0, 123.2, 122.2, 119.7, 53.6, 53.4, 53.4, 33.2, 33.1, 26.1; V_{max}/cm^{-1} 3222, 2922, 1731, 1650, 1554; calcd for $C_{18}H_{18}NO_6$ 344.1134 (M + H$^+$); found 344.1137.

Dimethyl [1,3]dioxolo[4,5-*g*]quinoline-6,8-dicarboxylate (3n). (252 mg, 87%, gray solid); mp 164–165 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.25 (s, 1H), 7.61 (s, 1H), 6.19 (s, 2H), 4.08 (s, 3H), 4.04 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.5, 165.7, 151.7, 151.7, 147.9, 145.2, 134.2, 125.2, 121.4, 107.1, 102.7, 101.3, 53.4, 53.0; V_{max}/cm^{-1} 2948, 1738, 1640, 1578, 1367; HRMS (ESI) calcd for $C_{14}H_{12}NO_6$ 290.0665 (M + H$^+$); found 290.668.

Dimethyl benzo[*h*]quinoline-2,4-dicarboxylate (3o). (233 mg, 78%, gray solid); mp 172–173 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.44 (d, J = 8.1 Hz, 1H), 8.78 (s, 1H), 8.70 (d, J = 9.3 Hz, 1H), 8.03 (d, J = 9.3 Hz, 1H), 7.95 (d, J = 7.4 Hz, 1H), 7.82–7.77 (m, 2H), 4.13 (s, 3H), 4.09 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.6, 165.8, 147.7, 146.0, 135.9, 133.5, 132.2, 131.6, 129.6, 128.2, 128.0, 126.0, 125.6, 123.1, 122.2, 53.4, 53.2; V_{max}/cm^{-1} 2965, 1739, 1642, 1600, 1368; HRMS (ESI) calcd for $C_{17}H_{14}NO_4$ 296.0923(M + H$^+$); found 296.0927.

Dimethyl 6-chloroquinoline-2,4-dicarboxylate (3p).[9] (243 mg, 87%, light yellow solid); mp 152–153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (d, J = 2.3 Hz, 1H), 8.71 (s, 1H), 8.28 (d, J = 9.1 Hz, 1H), 7.78 (dd, J = 9.1, 2.3 Hz, 1H), 4.11 (s, 3H), 4.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 165.2, 147.9, 147.2, 137.2, 135.1, 132.8, 131.9, 127.0, 124.9, 123.4, 53.57, 53.19; V_{max}/cm^{-1} 2959, 1722, 1606, 1494, 1236; HRMS (ESI) calcd for $C_{13}H_{11}ClNO_4$ 280.0381 (M + H$^+$); found 280.0391.

Dimethyl 8-chloroquinoline-2,4-dicarboxylate (3q). (239 mg, 85%, light yellow solid); mp 143–144 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (d, J = 8.7 Hz, 1H), 8.71 (s, 1H), 7.95 (d, J = 7.5 Hz, 1H), 7.65 (t, J = 8.7 Hz, 1H), 4.09 (s, 3H), 4.06 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 165.3, 148.2, 145.2, 136.9, 135.7, 130.9, 130.2, 127.9, 124.8, 123.2, 53.5, 53.2; V_{max}/cm^{-1}

2962, 1728, 1450, 1242; HRMS (ESI) calcd for $C_{13}H_{11}ClNO_4$ 280.0381 (M + H^+); found 280.0390.

Dimethyl 6-(methylthio)quinoline-2,4-dicarboxylate (3r). (253 mg, 86%, light yellow solid); mp 138–139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 8.63 (s, 1H), 8.18 (d, J = 9.0 Hz, 1H), 7.66 (d, J = 8.9 Hz, 1H), 4.08 (s, 3H), 4.05 (s, 3H), 2.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 165.5, 147.1, 146.1, 143.9, 133.4, 131.1, 129.7, 127.2, 123.5, 118.7, 53.5, 52.9, 15.2; V_{max}/cm^{-1} 2958, 1717, 1602, 1450, 1243; HRMS (ESI) calcd for $C_{14}H_{14}SNO_4$ 292.0644 (M + H^+); found 292.0655.

Diethyl 6-methoxyquinoline-2,4-dicarboxylate (4a).[10] (261 mg, 86%, yellow solid); mp 158–159 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (s, 1H), 8.28 (s, 1H), 8.24 (d, J = 9.3 Hz, 1H), 7.47 (d, J = 9.2 Hz, 1H), 4.55 (dq, J = 22.1, 7.0 Hz, 4H), 4.00 (s, 3H), 1.50 (t, J = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 165.3, 161.2, 145.4, 145.2, 133.9, 133.0, 128.6, 124.0, 123.2, 103.2, 62.5, 62.1, 55.9, 14.6, 14.5; V_{max}/cm^{-1} 2981, 1719, 1622, 1600, 1229; HRMS (ESI) calcd for $C_{16}H_{18}NO_5$ 304.1185 (M + H^+); found 304.1188.

Diethyl 6-hydroxyquinoline-2,4-dicarboxylate (4b).[10] (243 mg, 84%, light yellow solid); mp 220–221 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.41 (s, 1H), 8.12 (d, J = 9.2 Hz, 1H), 8.04 (d, J = 2.6 Hz, 1H), 7.49 (dd, J = 9.2, 2.6 Hz, 1H), 4.44 (dq, J = 14.3, 7.1 Hz, 4H), 1.39 (dt, J = 12.1, 7.2 Hz, 6H); ^{13}C NMR (100 MHz, DMSO) δ 165.3, 164.4, 159.4, 143.7, 143.6, 133.2, 132.6, 127.5, 123.8, 121.9, 106.1, 61.8, 61.5, 14.2, 14.0; V_{max}/cm^{-1} 3397, 2946, 1719, 1655, 1310; HRMS (ESI) calcd for $C_{15}H_{16}NO_5$ 290.1028 (M + H^+); found 290.1028.

Diethyl 6-methylquinoline-2,4-dicarboxylate (4c).[10] (247 mg, 86%, yellow solid); mp 135–136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.59 (s, 1H), 8.26 (d, J = 8.6 Hz, 1H), 7.67 (d, J = 8.7 Hz, 1H), 4.58 (q, J = 7.2 Hz, 2H), 4.54 (q, J = 7.2 Hz, 2H), 2.61 (s, 3H), 1.50 (td, J = 7.2, 3.9 Hz, 6H); V_{max}/cm^{-1} 2982, 1722, 1623, 1369, 1234; HRMS (ESI) calcd for $C_{16}H_{18}NO_4$ 288.1236 (M + H^+); found 288.1238.

Diethyl 8-methylquinoline-2,4-dicarboxylate (4d). (244 mg, 85%, light yellow solid); mp 126–127 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (d, J = 12.7 Hz, 2H), 7.68 (d, J = 7.0 Hz, 1H), 7.63 (t, J = 7.7 Hz, 1H), 4.54 (p, J = 7.8 Hz, 4H), 2.92 (s, 3H), 1.50 (q, J = 7.3 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 165.4, 148.0, 146.8, 139.6, 136.9, 130.7, 130.1, 126.5, 123.5, 121.8, 62.36, 62.27, 18.50, 14.53; V_{max}/cm^{-1} 2983, 1717, 1619, 1468, 1342; HRMS (ESI) calcd for $C_{16}H_{18}NO_4$ 288.1236 (M + H^+); found 288.1237.

Diethyl 5,7-dimethoxyquinoline-2,4-dicarboxylate (4e). (248 mg, 74%, light yellow liquid); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (d, J = 2.3 Hz, 1H), 6.61 (s, 1H), 6.41 (d, J = 2.3 Hz, 1H), 4.48 (q, J = 7.1 Hz, 2H), 4.42 (q, J = 7.2 Hz, 2H), 3.91 (s, 3H), 3.87 (s, 3H), 1.41 (dt, J = 9.1, 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 162.5, 162.0, 155.9, 150.1, 140.8, 108.1, 107.9, 99.9, 97.2, 62.1, 61.8, 56.2, 55.8, 14.8, 14.5; V_{max}/cm^{-1} 2938, 1737, 1623, 1596, 1332; HRMS (ESI) calcd for $C_{17}H_{20}NO_6$ 334.1291 (M + H^+); found 334.1294.

Diethyl 6,8-dimethylquinoline-2,4-dicarboxylate (4f). (265 mg, 88%, light yellow solid); mp 144–145 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.38 (s, 1H), 7.52 (s, 1H), 4.53 (quint, J = 7.1 Hz, 4H), 2.87 (s, 3H), 2.55 (s, 3H), 1.49 (td, J = 7.2, 5.6 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 165.5, 146.8, 145.7, 140.7, 139.0, 135.9, 133.1, 126.6, 122.3, 121.9, 62.3, 62.1, 22.5, 18.4, 14.5, 14.5; V_{max}/cm^{-1} 2983, 1717, 1619, 1468, 1342; HRMS (ESI) calcd for $C_{17}H_{20}NO_4$ 302.1392 (M + H^+); found 302.1394.

Diethyl 6,7-dimethylquinoline-2,4-dicarboxylate (4g). (258 mg, 85%, light yellow solid); mp 147–148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 2.0 Hz, 2H), 8.13 (s, 1H), 4.60–4.55 (m, 2H), 4.52 (t, J = 7.2 Hz, 2H), 2.52 (s, 3H), 2.50 (s, 3H), 1.49 (td, J = 7.1, 3.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 165.4, 148.2, 147.1, 141.2, 141.2, 135.4, 130.7, 125.2, 124.8, 121.6, 62.5, 62.1, 20.9, 20.4, 14.6, 14.5; V_{max}/cm^{-1} 2981, 1721, 1464, 1230; HRMS (ESI) calcd for $C_{17}H_{20}NO_4$ 302.1392 (M + H^+); found 302.1397.

Diethyl [1,3]dioxolo[4,5-*g*]quinoline-6,8-dicarboxylate (4h). (264 mg, 83%, yellow solid); mp 175–176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.22 (s, 1H), 7.61 (s, 1H), 6.19 (s, 2H), 4.54 (q, J = 7.1 Hz, 2H), 4.50 (q, J = 7.1 Hz, 2H), 1.48 (td, J = 7.1, 4.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 159.9, 156.8, 151.5, 147.9, 145.7, 134.7, 125.1, 121.2, 107.3, 102.6, 101.3, 62.5, 62.2, 14.6, 14.5; V_{max}/cm^{-1} 2993, 1721, 1621, 1477, 1233; HRMS (ESI) calcd for $C_{16}H_{16}NO_6$ 318.0978 (M + H^+); found 318.0985.

Diethyl 7,8-dihydro-6*H*-cyclopenta[*g*]quinoline-2,4-dicarboxylate (4i). (256 mg, 81%, light yellow solid); mp 150–152 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.60 (s, 1H), 8.55 (s, 1H), 8.15 (s, 1H), 4.60–4.55 (m, 2H), 4.54–4.49 (m, 2H), 3.14 (t, J = 7.4 Hz, 4H), 2.20 (p, J = 7.4 Hz, 2H), 1.49 (td, J = 7.2, 5.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 165.4, 149.1, 148.9, 148.9, 146.7, 135.9, 125.7, 125.7, 121.4, 119.6, 62.5, 62.2, 33.4, 32.9, 26.2, 14.6, 14.5; V_{max}/cm^{-1} 2979, 1719, 1454, 1369, 1232; HRMS (ESI) calcd for $C_{18}H_{20}NO_4$ 314.1492 (M + H^+); found 314.1495.

Diethyl benzo[*h*]quinoline-2,4-dicarboxylate (4j). (253 mg, 78%, yellow solid); mp 184–185 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.45 (d, J = 7.7 Hz, 1H), 8.74 (s, 1H), 8.67 (d, J = 9.3 Hz, 1H), 8.01 (d, J = 9.3 Hz, 1H), 7.94 (d, J = 8.8 Hz, 1H), 7.84–7.75 (m, 2H), 4.62–4.53 (m, 4H), 1.52 (dd, J = 14.0, 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 165.4, 147.6, 146.4, 136.4, 133.5, 131.9, 131.7, 129.4, 128.1, 127.9, 125.9, 125.7, 122.8, 122.2, 62.4, 62.4, 14.6, 14.5; V_{max}/cm^{-1} 2982, 1720, 1605, 1368, 1237; HRMS (ESI) calcd for $C_{19}H_{18}NO_4$ 324.1236 (M + H^+); found 324.1236.

Diethyl 6-chloroquinoline-2,4-dicarboxylate (4k). (257 mg, 83%, yellow solid); mp 163–164 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (d, J = 2.3 Hz, 1H), 8.69 (s, 1H), 8.30 (d, J = 9.0 Hz, 1H), 7.77 (dd, J = 9.1, 2.3 Hz, 1H), 4.56 (dd, J = 16.0, 7.2 Hz, 4H), 1.50 (q, J = 4.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 164.8, 148.3, 147.3, 137.0, 135.6, 132.9, 131.8, 127.1, 124.9, 123.3, 62.8, 62.6, 14.6, 14.5; V_{max}/cm^{-1} 2987, 1723, 1605, 1448, 1240; HRMS (ESI) calcd for $C_{15}H_{15}ClNO_4$ 308.0690 (M + H^+); found 308.0697.

Diethyl 8-chloroquinoline-2,4-dicarboxylate (4l). (254 mg, 82%, light yellow solid); mp 157–158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (d, J = 2.3 Hz, 1H), 6.61 (s, 1H), 6.41 (d, J = 2.3

Hz, 1H), 4.48 (q, J = 7.1 Hz, 2H), 4.42 (q, J = 7.2 Hz, 2H), 3.91 (s, 3H), 3.87 (s, 3H), 1.41 (dt, J = 9.1, 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 162.5, 162.0, 155.9, 150.1, 140.8, 108.1, 107.9, 99.9, 97.2, 62.1, 61.8, 56.2, 55.8, 14.8, 14.5; V_{max}/cm^{-1} 2983, 1722, 1446, 1370, 1239; HRMS (ESI) calcd for $C_{15}H_{15}ClNO_4$ 308.0690 (M + H$^+$); found 309.0709.

Diethyl 6-(methylthio)quinoline-2,4-dicarboxylate (4m). (258 mg, 80%, light yellow solid); mp 152–153 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.63 (s, 1H), 8.21 (d, J = 9.1 Hz, 1H), 7.67 (d, J = 9.0 Hz, 1H), 4.55 (dq, J = 22.6, 7.1 Hz, 4H), 2.64 (s, 3H), 1.50 (td, J = 7.1, 2.7 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 165.2, 147.2, 146.6, 143.6, 134.0, 131.3, 129.7, 127.2, 123.4, 118.8, 62.6, 62.2, 15.2, 14.6, 14.5; V_{max}/cm^{-1} 2924, 1719, 1602, 1448, 1234; HRMS (ESI) calcd for $C_{16}H_{18}NO_4S$ 320.0957 (M + H$^+$); found 320.0985.

Dimethyl 2-(4-methoxyphenylamino)maleate (A). (240 mg, 90%, yellow liquid); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.55 (s, 1H), 6.85 (d, J = 8.9 Hz, 2H), 6.79 (d, J = 8.9 Hz, 2H), 5.27 (s, 1H), 3.74 (s, 3H), 3.69 (s, 3H), 3.63 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 164.9, 157.0, 149.1, 133.5, 123.1, 114.5, 91.7, 55.5, 52.7, 51.1; V_{max}/cm^{-1} 3287, 2952, 1739, 1669, 1277; HRMS (ESI) calcd for $C_{13}H_{16}NO_5$ 266.1028 (M + H$^+$); found 266.1041.

Dimethyl 2-(4-(methoxycarbonyl)phenylamino)maleate (5a). (232 mg, 79%, yellow liquid); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.71 (s, 1H), 7.93 (d, J = 9.0 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 5.52 (s, 1H), 3.86 (s, 3H), 3.73 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.6, 166.6, 164.6, 146.5, 144.6, 131.0, 125.3, 119.2, 96.9, 53.1, 52.1, 51.5; V_{max}/cm^{-1} 3286, 2949, 1716, 1597, 1268; HRMS (ESI) calcd for $C_{14}H_{16}NO_6$ 294.0978 (M + H$^+$); found 294.0982.

Conflicts of interest

There are no conflicts to declare.

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