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Recyclable nano copper oxide catalyzed synthesis of quinoline-2,3-dicarboxylates under ligand free conditions†

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An efficient protocol was developed for the recyclable nano CuO powder catalyzed synthesis of quinoline derivatives from acetylenedicarboxylates and 2-aminocarbonyl compounds using acetonitrile as solvent at 40 °C in air. A variety of quinoline derivatives were synthesized in good yields with good chemoselectivity in the presence of a catalytic amount of CuO nano powder under ligand/additive free conditions. The catalyst is air-stable, inexpensive and recyclable up to four cycles.

Introduction

Heterocyclic aromatic aza compounds especially quinoline derivatives are widely used in several compounds[1] (*e.g.*: quinine, chloroquine, primaquine, mefloquine *etc.* compounds are biologically anti-malarial active (Fig. 1))[1d] and these pharmacologically active derivatives display a broad range of biological activity.[2] Quinolines are an important group of heterocyclic compounds, which have been found to possess useful biological activity, such as anti-malarial, anti-bacterial, anti-inflammatory, anti-asthmatic and anti-hypertensive properties[3] and tyrokinase PDGF-RTK inhibiting agents, as well as being general synthetic building blocks.[4] In addition to medicinal applications, quinolines have been employed in the study of bioorganic and bioorganometallic processes.[5] These quinoline derivatives are valuable synthons for the preparation of nano and mesostructures with electronic and photonic functional applications.[6–11] Skraup, Combes, Friedlander, Doebner–Von Miller quinoline syntheses,[12] are some well known methods for quinoline synthesis. Many new methodologies are being reported frequently using various starting materials.

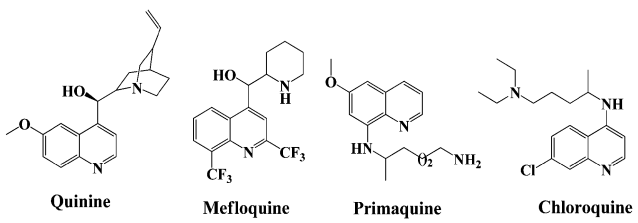

Fig. 1 Biologically active compounds with anti-malarial activity.

Recently Gabriele[13] synthesized substituted quinolines from 2-amino arylketones by initial reaction with a Grignard reagent and further cyclization in the presence of Cu/Pd catalysts. Francis[14] reported quinoline synthesis from 2-amino benzylalcohol and a variety of ketones catalyzed by ruthenium catalysts. Che[15] and co-workers introduced gold catalyzed quinoline synthesis under microwave-assisted conditions. Lewis acids,[16] Brønsted acids,[17] molecular iodine,[18] proline,[19] ionic liquids[20] and transition metals[21] were some of the catalysts used for various types of quinoline syntheses, but many of the aforementioned reactions require strong acids or bases, organic solvents, hazardous and expensive catalysts at elevated temperatures and the reaction conditions are also tedious and yields are low even after prolonged reaction times.

Verpoort *et al.* reported a ruthenium catalyzed approach to the Friedlander quinoline synthesis in 1,4-dioxane as the solvent at 80 °C by using different basic conditions with good yields.[30] Adapa and co-workers developed an efficient and rapid Friedlander synthesis of functionalized quinolines catalyzed by using neodymium(III) nitrate hexahydrate as a catalyst in ethanol at room temperature which afforded good yields.[31] However, these aforementioned reactions are also homogeneous.

There are few reports[22] in the literature especially for the preparation of 4-substituted quinoline-2,3-dicarboxylates. Taylor synthesized quinoline-2,3-dicarboxylates from 2-aminobenzophenone and dimethylacetylenedicarboxylate in benzene under reflux conditions. As 2-aminoacetophenone did not react with dimethylacetylenedicarboxylate in one pot, they used basic conditions (sodium methoxide in anhydrous conditions) to enable the enamine adduct to cyclize in 26 h.[23] Other methods involved harsh reaction conditions, longer reaction times, toxic organic solvents and very low yields. The chemical industry is a major contributor to environmental pollution, largely due to wide use of hazardous solvents. Benzene is one of the undesired

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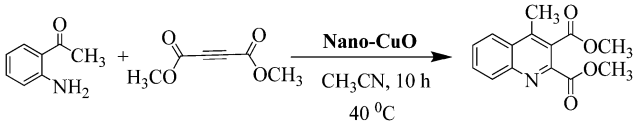
and environmentally hazardous solvents which belongs to red category solvents due to its carcinogenicity and toxicity to humans; hence there is a need to replace hazardous organic solvents with environmentally benign solvents. A number of procedures have been reported for the synthesis of quinolines involving a variety of metal catalysts and Lewis acids.

However, many of these methods suffer from harsh reaction conditions, long reaction times, low yields, difficulties in work-up, and the use of stoichiometric and/or relatively expensive reagents. In view of these drawbacks, the reaction could be further explored and refined to overcome some of these shortcomings by using an environmentally benign solvent with a recyclable catalyst under mild reaction conditions. Moreover, the above reactions are homogeneous, wherein catalyst recovery is the major drawback, as well as the problems of product contamination and the lack of catalyst recyclability.[24] Heterogeneous catalysts are attractive both from economic and industrial points of view as compared to homogeneous catalysts.[25] Furthermore, nanoscale catalysts are more advantageous as more active surface area is available to bind the substrates selectively and enhance the reaction efficacy.[26]

The application of metal nanoparticles for organic reactions has attracted immense attention in recent years.[27] Since the turn of the millennium, interest in metal nanoparticles catalysis has considerably increased because this class of catalysts appears as one of the most promising solutions toward efficient reactions under mild and environmentally benign conditions in the context of Green Chemistry.



Scheme 1 Nano-CuO catalyzed synthesis of dimethyl 4-methylquinoline-2,3-dicarboxylate.

Results and discussion

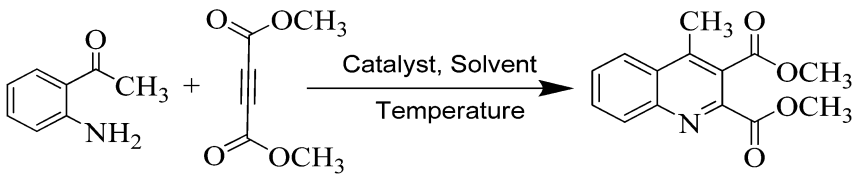
As part of our current studies[28] on the development of new routes in heterocyclic synthesis, we report an efficient synthetic route to quinoline-2,3-dicarboxylates. Hence, the development of ligand-free, air-resistant, inexpensive, recyclable catalytic systems for the formation of quinoline derivatives is highly desirable. To develop a simple, efficient, and reusable catalytic system for the synthesis of quinoline-2,3-dicarboxylates under ligand-free conditions, the role of nano-CuO as a recyclable catalyst was investigated in the synthesis of quinoline and its derivatives.

Initially the reaction between 2-aminoacetophenone and dimethylacetylenedicarboxylate was carried out in acetonitrile solvent catalyzed by nano-CuO resulting in the formation of dimethyl 4-methylquinoline-2,3-dicarboxylate in one pot at 40 °C in 93% yield (Scheme 1). No product formation was observed in the absence of metal catalyst even after a prolonged reaction time, while the reaction afforded a lower yield of product with water as the solvent at 40 °C for 10 h (entries 1 & 2, Table 1).

First, the reaction was optimized with several copper sources like $Cu(acac)_2$, CuI, CuBr, Cu_2O, all these were homogeneous and heterogeneous CuO nanoparticles were proved to be best for this reaction (entries 3–7, Table 1). Lower yield of the product was observed at room temperature (entry 8, Table 1). The optimal conditions for the desired product were found to be **1a** (1 mmol), **2a** (1 mmol), 3.0 mol% nano-CuO, acetonitrile (2.0 mL), 40 °C for 10 h.

To check the generality of the reaction, various 2-aminocarbonyl compounds were used as substrates and all the reactions proceeded to get the desired quinolines in good yields. All these reactions were also conducted with diethylacetylenedicarboxylate and di-*tert*-butylacetylenedicarboxylate in the present experimental conditions.

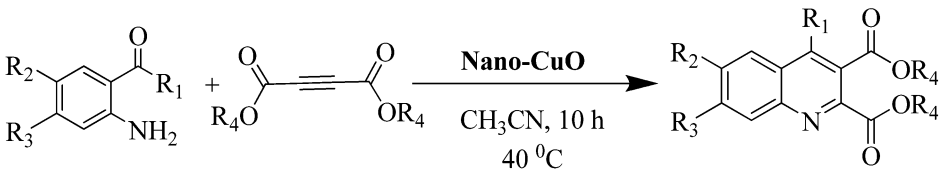
Table 1 Optimization studies for the synthesis of quinoline and its derivatives[a]

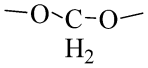
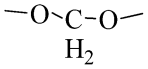


Entry	Catalyst (mol%)	Solvent	Temperature	Yield (%)
1	—	CH_3CN	40 °C	—
2	Nano-CuO	Water	40 °C	40
3	$Cu(acac)_2$	CH_3CN	40 °C	30
4	CuI	CH_3CN	40 °C	35
5	CuBr	CH_3CN	40 °C	30
6	**Nano-CuO**	**CH_3CN**	**40 °C**	**93**
7	Cu_2O	CH_3CN	40 °C	45
8	Nano-CuO	CH_3CN	rt	30

[a] Reaction conditions: 2-aminoacetophenone (1.0 mmol), dimethylacetylenedicarboxylate (1.0 mmol), catalyst (3 mol%).

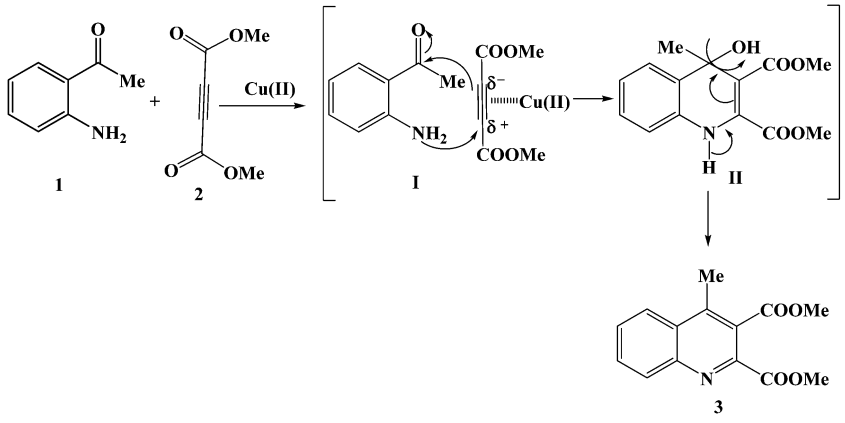
Table 2 Synthesis of quinolinedicarboxylates using the nano-CuO catalyst[a]



Entry	R_1	R_2	R_3	R_4	Product	Yield[b] (%)
1	CH_3	H	H	CH_3	**3a**	93
2	Ph	H	H	CH_3	**3b**	88
3	Ph	Cl	H	CH_3	**3c**	84
4	H	Cl	H	CH_3	**3d**	94
5	Ph	H	Br	CH_3	**3e**	83
6	CH_3	OCH_3	OCH_3	CH_3	**3f**	87
7	CH_3			CH_3	**3g**	86
8	CH_3	H	H	CH_2CH_3	**3h**	89
9	Ph	H	H	CH_2CH_3	**3i**	82
10	Ph	Cl	H	CH_2CH_3	**3j**	81
11	H	Cl	H	CH_2CH_3	**3k**	90
12	Ph	H	Br	CH_2CH_3	**3l**	80
13	CH_3	OCH_3	OCH_3	CH_2CH_3	**3m**	81
14	CH_3			CH_2CH_3	**3n**	80
15	CH_3	H	H	^{t}Bu	**3o**	—
16	Ph	H	H	^{t}Bu	**3p**	—

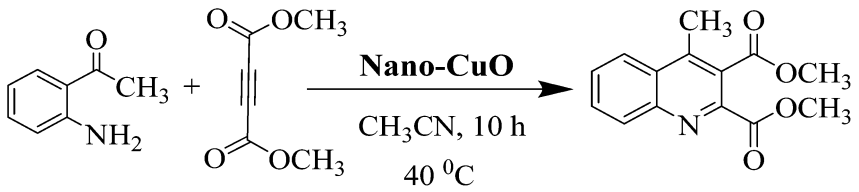
[a] Representative reaction conditions: 2-aminoacetophenone (1 mmol), dimethylacetylenedicarboxylate (1 mmol), nano-CuO (3 mol%, 3 mg), acetonitrile (2.0 mL), 40 °C, 10 h. [b] Isolated yield.

In general, all the reactions were very clean and neat, the quinoline derivatives were obtained in high yields. The compounds were isolated by just passing through a silica gel column. In these reactions, the substitution played a significant role in governing the reactivity of the substrate. Satisfactory yields were obtained in all the cases, in general the reaction of 2-aminobenzophenone offered lower yields compared to 2-aminoacetophenone compounds. Among these 2-aminoacetophenone derivatives, unsubstituted 2-aminoacetophenone (entries 1 & 8, Table 2) afforded good yield and electron-donating methoxy substituted 2-aminoacetophenone compounds (entries 6, 7 & 13, 14, Table 2) resulted in a little lower yields. Similarly reaction with substituted 2-aminobenzophenone compounds gave lower yields compared to unsubstituted 2-aminobenzophenone compounds. Finally, it is also observed that reactions of 2-aminocarbonyl compounds with dimethylacetylenedicarboxylate resulted in higher yields when compared to those with diethylacetylenedicarboxylate. No



Scheme 2 Proposed mechanism for nano-CuO catalyzed synthesis of quinoline derivatives.

Table 3 Recovery of the catalyst[a]



Cycle	Product isolated yield (%)	Catalyst recovery (%)
Native	93	96
1	88	91[b]
2	85	88[b]
3	80	80[b]

[a] Reaction conditions: 2-aminoacetophenone (1.0 mmol), dimethylacetylenedicarboxylate (1.0 mmol), nano-CuO (3 mol%, 3 mg), CH_3CN (2.0 mL), 40 °C, 10 h. [b] With recovered catalyst.

reaction was observed at elevated temperature with di-*tert*-butyldicarboxylate even after prolonged reaction time and all the results are summarized in Table 2.

The actual mechanism of this reaction is not clear at present. However, according to published results,[32] the mechanism can be explained as shown in Scheme 2. Thus the two starting materials of **1** and **2** reacted in the presence of nano-CuO in a concerted manner to form complex **I**, which involves the initial attack of the amine group on the polarized unsaturated diester, followed by attack on the carbonyl group. Finally, the aromatic product **3** is obtained by elimination of a water molecule.

To check the recyclability of the catalyst, after each cycle, the reaction mixture was allowed to cool and the catalyst was recovered by ultracentrifugation, washed with ethyl acetate and acetone, dried under vacuum, and reused for further catalytic reactions. The catalyst maintained its high level of activity even after four cycles as shown in Table 3.

Transmission electron microscope (TEM) studies of both fresh and used catalysts were carried out to understand the shape and size of the particles. Fig. 2a and b show the TEM images of the fresh and the used catalyst after the fourth cycle, respectively. Interestingly, it is observed that the shapes and sizes (the CuO nanoparticle size is <50 nm) of the particles remain unchanged (before and after the reaction) and supports the assumption that the morphology of the catalyst remains the same even after recycling, which further confirmed the heterogeneous nature of the catalyst (Fig. 2).

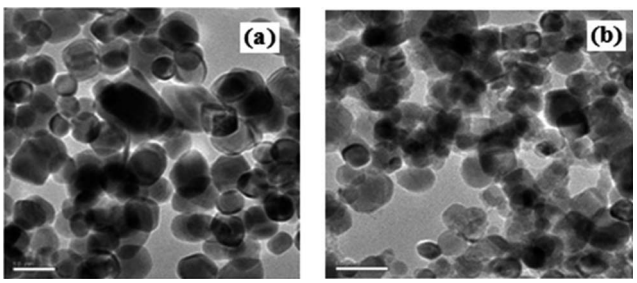


Fig. 2 TEM images of (a) fresh nano-CuO particles and (b) nano-CuO particles after the fourth cycle.

Conclusion

In conclusion, an inexpensive, air-stable recyclable catalytic system was developed for the synthesis of quinoline and its derivatives under ligand-free conditions. To the best of our knowledge, this is the first novel nano-CuO catalyzed synthesis of quinoline-2,3-dicarboxylates, which is of potential industrial significance because of its simplicity in operation, high yields, environmental and economic advantages, using a commercially available, economically viable, air-stable and recyclable heterogeneous catalyst.

Experimental section

General methods

Nano-CuO (99.9%), all the starting materials (carbonyl and acetylene compounds) were commercially available and purchased from Sigma Aldrich and used without purification. Column chromatography was carried out with 60–120 sized mesh silica gel using ethyl acetate and hexane as eluents. Analytical TLC was performed with Merck silica gel 60 F_{254} plates, and the products were visualized by UV detection. ^1H NMR and ^{13}C NMR (Avance 300, Innova 400 MHz and Bruker Gemini 200 MHz) spectra were recorded in $CDCl_3$ using TMS as an internal standard. Chemical shifts (δ) were reported in ppm, and spin–spin coupling constants (J) are in Hz. Melting points were determined on a Fischer-Johns melting point apparatus. TEM analysis was recorded on Philips CM200 model instrument operating voltages at 20–200 kV and resolution was 2.4 Å. EI-MS were recorded on a Finnegan MAT 1020 mass spectrometer operating at 70 eV.

Typical procedure for the synthesis of dimethyl 4-methylquinoline-2,3-dicarboxylate. To a stirred solution of 2-aminoacetophenone (**1a**) (1.0 mmol), dimethylacetylenedicarboxylate (**2a**) (1.0 mmol) in acetonitrile (2.0 mL) was added CuO nano-

powder (3 mol%, 3 mg) and the reaction mixture was heated at 40 °C under air. After the completion of the reaction over 10 h, as monitored by TLC, the reaction mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried with anhydrous Na_2SO_4. The solvent was evaporated under vacuum to give the crude product, which was purified by column chromatography with hexane and ethyl acetate as eluent to get the expected product **3a** (93%) as a yellow solid in good yield. The purity of the product was confirmed by ^{1}H NMR, ^{13}C NMR and mass spectroscopy and compared with the literature values.

Representative procedure for recycling. After extraction of the organic compounds with ethyl acetate, the recovered heterogeneous catalyst was placed in a 25 mL round-bottomed flask. 2-Aminoacetophenone (**1a**) (1.0 mmol) and dimethylacetylenedicarboxylate (**2a**) (1.0 mmol) were added under air, followed by addition of acetonitrile (2.0 mL) and the reaction mixture was stirred at 40 °C for 10 h. After completion of the reaction (as monitored by TLC), the heterogeneous mixture was then cooled to room temperature and treated with ethyl acetate (2 mL). The aqueous layer was separated and extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried with anhydrous Na_2SO_4 and concentrated under reduced pressure to yield the product, which was purified by column chromatography using silica gel (ethyl acetate–hexane) to obtain the pure product **3a** (89%) as a yellow solid. The product was characterized by ^{1}H and ^{13}C NMR, and MS analysis and compared with the literature values. The same procedure was extended for further cycles.

Spectroscopic data

Dimethyl 4-methylquinoline-2,3-dicarboxylate.[29] (3a) (entry 1, Table 2) Light yellow solid, m.p. 95–97 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.06 (d, J = 8.3 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 6.59 (t, J = 6.9 Hz, 1H), 6.48 (t, J = 8.1 Hz, 1H), 2.81 (s, 3H), 2.76 (s, 3H), 1.50 (s, 3H). ^{13}C (75 MHz, $CDCl_3$): δ 168.3, 165.5, 146.1, 144.8, 144.2, 131.0, 130.9, 129.2, 128.1, 127.3, 124.1, 53.4, 52.9, 15.6. Mass ESI (m/z) 260 $(M + H)^+$.

Dimethyl 4-phenylquinoline-2,3-dicarboxylate.[29] (3b) (entry 2, Table 2) Yellow solid, m.p. 129–130 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.39 (d, J = 8.4 Hz, 1H), 7.83 (t, J = 6.6 Hz, 1H), 7.68–7.56 (m, 2H), 7.53–7.49 (m, 3H), 7.39–7.35 (m, 2H), 4.08 (s, 3H), 3.64 (s, 3H). ^{13}C (75 MHz, $CDCl_3$): δ 167.4, 165.3, 148.3, 146.7, 144.7, 134.3, 131.1, 130.4, 130.3, 129.2, 128.8, 128.2, 127.6, 127.1, 126.5, 53.4, 52.4. Mass ESI (m/z) 322 $(M + H)^+$.

Dimethyl 6-chloro-4-phenylquinoline-2,3-dicarboxylate.[23] (3c) (entry 3, Table 2) White solid, m.p. 162–164 °C, ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.26 (s, 0.5H), 8.25 (s, 0.5H), 7.77 (d, J = 2.2 Hz, 0.5H), 7.72 (d, J = 2.9 Hz, 0.5H), 7.61–7.53 (m, 4H), 7.40–7.27 (m, 2H), 4.08 (s, 3H), 3.62 (s, 3H). ^{13}C (75 MHz, $CDCl_3$): δ 167.4, 165.2, 147.3, 145.6, 145.1, 135.5, 133.7, 132.2, 129.2, 129.1, 128.6, 128.4, 128.1, 125.3, 53.8, 52.5. Mass ESI (m/z) 356 $(M + H)^+$.

Dimethyl 6-chloroquinoline-2,3-dicarboxylate.[29] (3d) (entry 4, Table 2) Brown solid, m.p. 163–164 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.56 (s, 1H), 8.05 (d, J = 8.8 Hz, 1H), 7.82 (s, 1H), 7.70 (d, J = 9.0 Hz, 1H), 3.96 (s, 3H), 3.90 (s, 3H). ^{13}C (75 MHz, $CDCl_3$): δ 167.1, 165.1, 147.2, 145.3, 144.9, 135.5, 133.7, 132.1, 129.1, 128.4, 125.3, 53.5, 52.5. Mass ESI (m/z) 280 $(M + H)^+$. HRMS calcd $C_{13}H_{11}NO_4Cl$ $(M + H)^+$: 280.0376, found 280.0386.

Dimethyl 7-bromo-4-phenylquinoline-2,3-dicarboxylate.[29] (3e) (entry 5, Table 2) Yellow solid, m.p. 166–167 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.26 (d, J = 8.3 Hz, 1H), 7.80–7.75 (m, 1H), 7.65–7.53 (m, 4H), 7.26 (d, J = 7.5 Hz, 2H), 4.01 (s, 3H), 3.62 (s, 3H). ^{13}C (75 MHz, $CDCl_3$): δ 167.3, 165.3, 147.1, 146.5, 145.1, 133.2, 131.7, 131.2, 130.9, 130.6, 129.5, 127.2, 127.1, 126.1, 123.4, 53.5, 52.6. Mass ESI (m/z) 400 $(M + H)^+$. HRMS calcd $C_{19}H_{15}NO_4Br$ $(M + H)^+$: 400.0184, found 400.0174.

Dimethyl 6,7-dimethoxy-4-methylquinoline-2,3-dicarboxylate.[29] (3f) (entry 6, Table 2) Brown solid, m.p. 135–136 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (s, 1H), 7.26 (s, 1H), 4.02–3.66 (m, 12H), 2.60 (s, 3H). ^{13}C (75 MHz, $CDCl_3$): δ 168.5, 165.4, 153.3, 151.8, 143.6, 142.5, 140.5, 126.3, 123.9, 109.1, 101.2, 56.1, 55.8, 52.9, 52.6, 15.6. HRMS calcd $C_{16}H_{17}NO_6Na$ $(M + Na)^+$: 342.0953, found 342.0952.

Dimethyl 8-methyl-[1,3]dioxolo[4,5-*g*]quinoline-6,7-dicarboxylate.[29] (3g) (entry 7, Table 2) Yellow solid, m.p. 223–224 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50 (s, 1H), 7.28 (s, 1H), 6.20 (s, 2H), 4.03 (s, 3H), 3.91 (s, 3H), 2.63 (s, 3H). ^{13}C (75 MHz, $CDCl_3$): δ 168.5, 165.6, 151.8, 150.9, 144.9, 142.5, 141.7, 125.8, 114.2, 107.4, 102.5, 99.6, 53.2, 52.9, 15.5. Mass ESI (m/z) 304 $(M + H)^+$.

Diethyl 4-methylquinoline-2,3-dicarboxylate.[29] (3h) (entry 8, Table 2) Yellow oil, ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (d, J = 8.3 Hz, 1H), 7.96 (d, J = 8.3 Hz, 1H), 7.69 (t, J = 6.7 Hz, 1H), 7.56 (t, J = 7.1 Hz, 1H), 4.46–4.31 (m, 4H), 2.65 (s, 3H), 1.44–1.30 (m, 6H). ^{13}C (75 MHz, $CDCl_3$): δ 167.1, 165.0, 146.3, 146.1, 143.1, 131.1, 130.3, 128.5, 127.8, 127.1, 123.8, 96.1, 61.9, 61.4, 15.3, 14.2, 14.0. Mass ESI (m/z) 288 $(M + H)^+$.

Diethyl 4-phenylquinoline-2,3-dicarboxylate.[29] (3i) (entry 9, Table 2) Yellow solid, m.p. 95–97 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.30 (d, J = 8.3 Hz, 1H), 7.79 (t, J = 6.7 Hz, 1H), 7.63–7.45 (m, 5H), 7.38–7.33 (m, 2H), 4.56–4.47 (q, J = 6.7 Hz, J = 14.3 Hz, 2H), 4.09–4.02 (q, J = 6.7 Hz, J = 14.3 Hz, 2H), 1.49 (t, J = 6.7 Hz, 3H), 0.99 (t, J = 6.7 Hz, 3H). ^{13}C (75 MHz, $CDCl_3$): δ 167.0, 165.2, 147.8, 147.0, 145.7, 134.6, 130.8, 130.5, 129.3, 128.9, 128.6, 128.1, 127.4, 126.9, 126.5, 62.5, 61.4, 14.1, 13.5. Mass ESI (m/z) 350 $(M + H)^+$.

Diethyl 6-chloro-4-phenylquinoline-2,3-dicarboxylate.[29] (3j) (entry 10, Table 2) White solid, m.p. 154–155 °C, ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.61 (d, J = 3.0 Hz, 1H), 8.12–8.04 (m, 1H), 7.89–7.85 (m, 4H), 7.77–7.70 (m, 2H), 4.55–4.44 (q, J = 7.0 Hz, J = 14.0 Hz, 2H), 4.09–3.98 (q, J = 7.0 Hz, J = 14.0 Hz, 2H), 1.46 (t, J = 7.0 Hz, J = 14.0 Hz, 3H), 0.99 (t, J = 7.0 Hz, J = 14.0 Hz, 3H). ^{13}C (75 MHz, $CDCl_3$): δ 167.5, 165.3, 146.3, 146.2, 143.1, 131.2, 130.3, 128.6, 127.9, 127.2, 123.8, 61.9, 61.4, 14.3, 14.1. Mass ESI (m/z) 384.7 $(M + H)^+$.

Diethyl 6-chloroquinoline-2,3-dicarboxylate.[29] (3k) (entry 11, Table 2) Yellow solid, m.p. 99–100 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.62 (s, 1H), 8.15–8.08 (m, 1H), 7.90 (s, 1H), 7.78–7.70 (m, 1H), 4.59–4.45 (m, 4H), 1.47–1.39 (m, 6H). ^{13}C (75 MHz): δ 166.2, 164.5, 150.9, 146.1, 138.1, 134.1, 132.8, 131.1, 127.3, 126.8, 123.1, 61.9, 61.8, 13.8, 13.9. Mass ESI (m/z) 308 $(M + H)^+$. HRMS calcd $C_{15}H_{15}NO_4Cl$ $(M + H)^+$: 308.0689, found 308.0699.

Diethyl 7-bromo-4-phenylquinoline-2,3-dicarboxylate.[29] (3l) (entry 12, Table 2) Yellow solid, m.p. 109–111 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.28 (d, J = 8.1 Hz, 1H), 7.84–7.74 (m, 1H), 7.64 (d, J = 8.3 Hz, 2H), 7.55 (s, 2H), 7.25 (d, J = 8.1 Hz, 2H), 4.50 (q, J = 6.9 Hz, J = 12.2 Hz, 2H), 4.11 (q, J = 7.1 Hz, J = 12.6 Hz, 2H), 1.47 (t, J = 6.9 Hz, J = 7.1 Hz, 3H), 1.06 (t, J = 7.1 Hz, J = 6.9 Hz, 3H). ^{13}C (75 MHz, $CDCl_3$): δ 165.9, 164.1, 150.8, 146.0, 145.7, 138.0, 134.1, 132.7, 131.8, 130.6, 129.05, 127.2, 126.8, 126.0, 123.1, 62.1, 61.7, 14.1, 13.8. Mass ESI (m/z) 428 $(M + H)^+$. HRMS calcd $C_{21}H_{19}NO_4Br$ $(M + H)^+$: 428.0497, found 428.0498.

Diethyl 6,7-dimethoxy-4-methylquinoline-2,3-dicarboxylate.[29] (3m) (entry 13, Table 2) Brown solid, m.p. 114–116 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (s, 1H), 7.06 (s, 1H), 4.47–4.36 (m, 4H), 3.98 (s, 6H), 2.58 (s, 3H), 1.43 (t, J = 6.7 Hz, J = 7.6 Hz, 3H), 1.36 (t, J = 7.6 Hz, J = 6.7 Hz, 3H). ^{13}C (75 MHz, $CDCl_3$): δ 168.0, 165.2, 153.1, 151.5, 143.6, 143.2, 140.7, 126.1, 123.8, 109.1, 101.2, 61.9, 61.5, 56.0, 55.8, 15.5, 14.3, 14.1. Mass ESI (m/z) 348 $(M + H)^+$. HRMS calcd $C_{18}H_{22}NO_6$ $(M + H)^+$: 348.1447, found 348.1449.

Diethyl 8-methyl-[1,3]dioxolo[4,5-*g*]quinoline-6,7-dicarboxylate.[29] (3n) (entry 14, Table 2) Brown solid, m.p. 98–100 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.53 (s, 1H), 7.25 (s, 1H), 6.17 (s, 2H), 4.53–4.40 (m, 4H), 2.61 (s, 3H), 1.50–1.26 (m, 6H). ^{13}C (75 MHz, $CDCl_3$): δ 167.6, 164.9, 151.2, 149.8, 144.5, 143.0, 141.2, 126.0, 125.2, 113.9, 106.3, 102.1, 99.0, 95.8, 61.8, 61.4, 15.5, 14.0, 13.8. Mass ESI (m/z) 332 $(M + H)^+$.

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