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Triple zirconocene/brønsted acid/CuO cooperative and relay catalysis system for tandem Mannich addition/C–C formative cyclization/oxidation†

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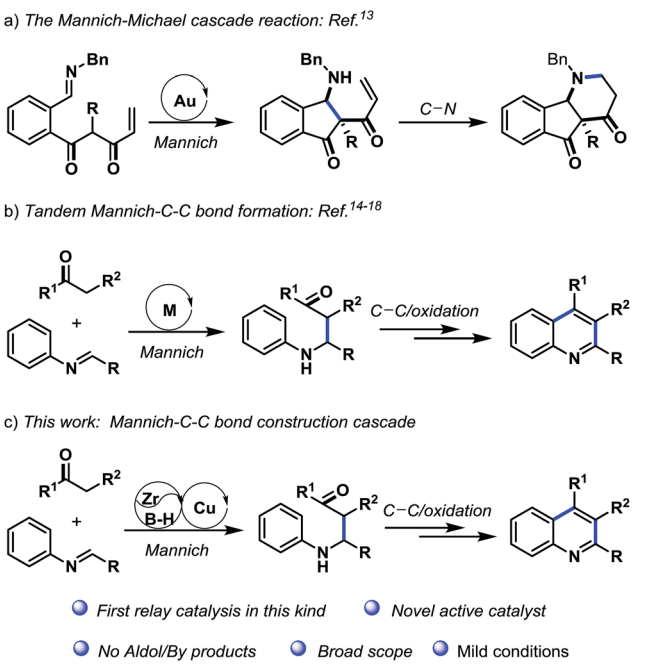
A new triple cooperative and relay catalysis system featuring the Mannich addition followed by C–C construction and oxydehydrogenation is described. The zirconocene dichloride and trimellitic acid synergic catalysis triggered the Mannich addition and C–C bond construction reactions, while CuO allowed relay catalysis for oxydehydrogenation. This novel strategy demonstrated superior activity for the synthesis of substituted quinolines from commercially available anilines, aldehydes and ketones. The corresponding substituted quinolines were synthesized with 32 examples in 90–96% yields under mild reaction conditions. A novel zirconocene–Brønsted acid complex, generated *in situ* and acting as an active catalyst, was validated from the mechanistic studies.

Introduction

Relay catalysis reactions are the one-pot multi-catalysis cascade reactions in which each catalytic system promotes one type of transformation in a consecutive fashion. The strategy of relay catalysis obviates the requirement of isolation and purification of products resulting from the each independent transformation. More importantly, the advent of one-pot orthogonal relay catalysis reactions made intricate organic syntheses feasible, which were inaccessible and inefficient by the classical step-wise catalysis. However, establishing such processes need to overcome a number of challenging issues, such as the chemo selectivity and the compatibility between the catalytic systems. The combined metal/metal and metal/organo catalyst dual catalysis are potential kinds of relay catalysis that has stimulated intensive interest in recent years. A number of significant reactions have been developed using metal/metal relay catalysis including Au/Ni,[1] Au/Ag,[2] Au/Yb,[3] Au/Sc,[4] Ru/Pd/Cu[5] and Pd/Ag/Bi[6] catalyst systems. Regarding to the metal/organo relay catalysis, the metal-Brønsted acid based systems have contributed largely.[7–12] The metal catalysts such as Au, Rh, Pd, Ag and Ru are used in combination with a variety of Brønsted acids. In this context, the development of divergent relay catalysis approaches employing new catalysts is highly desirable.

The cascade reactions for the Mannich reaction followed by the C–C or C–N bond formation are of highly appealing (Scheme 1). This is because such kind of reactions could construct these fundamental bonds of organic molecules in a single step. In literature, two divergent synthetic procedures with such cascade reaction were available. In 2010, Shin[13] discovered an one pot redox-pinacol-Mannich–Michael cascade reaction leading to the synthesis of 1-aminoindanes and 5,6-



Scheme 1 The reactions involving the Mannich reaction followed by C–C/C–N bond formation.

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fused azacycles (Scheme 1, eq. a). In this reaction, the gold catalyst rendered the Mannich reaction followed by C–N formation in an intramolecular manner. Very recently, HCl,[14] iodine,[15] $CuCl_2$,[16] $FeCl_3$ (ref. 17) and AgOTf[18] catalyzed three components tandem reactions of anilines, aldehydes and ketones for the construction of multi-functionalized quinoline had been reported (Scheme 1, eq. b). This approach undergone intermolecular Mannich reaction followed by intramolecular C–C bond formation and oxydehydrogenation.

In this paper, combination with the advantages of cascade reaction integrating the Mannich addition and C–C/C–N bond construction, the development of new catalytic systems is highly desirable in organic synthesis. Herein, we report an unprecedented cooperative and relay catalysis by zirconocene dichloride, trimellitic acid and CuO triple catalytic system for the Mannich addition/C–C bond formation/oxydehydrogenation sequence (Scheme 1, eq. c). This triple cooperative and relay catalytic system demonstrated superior activity for synthesis of polysubstituted quinoline from arylamines, aldehydes and ketones under mild condition.

Results and discussion

We choose aniline, benzaldehyde and methyl pyruvate as substrates to optimize the conditions of cascade Mannich addition, C–C bond construction and oxydehydrogenation reaction (Table 1). At first, simple copper salts such as $CuCl_2$, $CuBr_2$, $Cu(acac)_2$, $Cu(OAc)_2$, $CuSO_4 \cdot 5H_2O$, CuO, $Cu(OTf)_2$ and $Cu(ClO_4)_2$ were used as catalysts in the presence of both Cp_2TiCl_2 and PhCOOH (Table 1, entries 1–8). Among these metal salts, CuO was found to be the most effective catalyst and the desired product **4aa** was obtained in 31% yield (Table 1, entry 6). Other commercially available metallocene complexes such as Cp^*TiCl_3 and Cp_2ZrCl_2 were also used as Lewis acid catalysts for the three-component sequence reactions, which demonstrated that Cp_2ZrCl_2 was the best catalyst for this transformation (Table 1, entries 9 and 10). In light of our previous findings that salicylato–titanocene complexes and phenols–titanocene complexes function as organometallic Lewis acids,[19] a selection of oxygen donor ligands such as phenol and benzenesulfonic acid were evaluated in the reaction of aniline, benzaldehyde and methyl pyruvate (Table 1, entries 11 and 12). None of them provide satisfactory results, which suggested that monofunctional acids were unsuitable for this three-component cascade reaction. With the assistance of *o*-aminobenzoic acid, salicylic acid and phthalic acid, the Zr catalyst was slightly activated and the tandem reaction afforded desired product with 41%, 42% and 47% yields, respectively (Table 1, entries 13–15). When glutaric acid and proline were introduced into this triple catalytic system, the desired products were obtained in 29% and 28% yields (Table 1, entries 16 and 17). The above results indicated that the aromatic diacids show up higher activity than the aliphatic diacids and amino acids. We hypothesized that higher activity of this catalytic system could be achieved by employing multifunctional acids such as 2-aminobenzene-1,4-disulfonic acid, trimellitic acid and 5-sulfosalicylic acid (Table 1, entries 18–20). To our pleased, trimellitic acid is the most potent catalyst among the three multifunctional aromatic acids, which promotes the reaction to afford the desired product in 54% yield, higher than 5-sulfosalicylic acid and 2-aminobenzene-1,4-disulfonic acid. When the reaction time extended to 2 h, the yield increases to 88%, but the yield increased slightly with further extension of the reaction time (Table 1, entry 21). After an extensive screening of the reaction parameters (see the ESI†), the best yield of **4aa** was obtained when reaction was performed in *i*-propanol/water (3 : 1) at 60 °C.

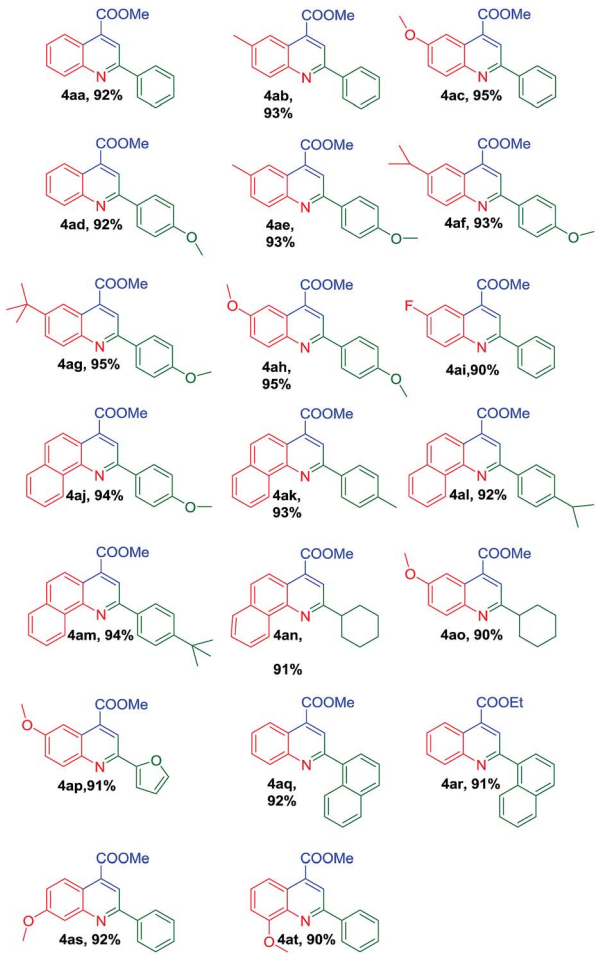
With the optimal reaction conditions in hand, we set out to expand the generality and scope of Cp_2ZrCl_2, trimellitic acid and CuO catalyzed three-component cascade reaction. 1 mmol aldehyde, 1.1 mmol of anilines and 1.5 mmol of ketones with 5 mol% of Cp_2ZrCl_2, 5 mol% of trimellitic acid, 5 mol% of CuO at 60 °C for 2 h were operated as the typical selection. It is found that the reaction proceeded smoothly with aldehydes and aromatic amines bearing either electron-withdrawing or donating groups (Table 2). The substituents with different electron properties has little impact on this transformation, such as anilines containing methyl (**4ab**), methoxyl (**4ac**) or fluorous (**4ai**) group, benzaldehydes with methyl (**4ak**), *i*-propyl (**4al**), *t*-butyl (**4am**) or methoxyl (**4ad**) group and pyruvate with

Table 1 Catalyst and Brønsted acid screening for three-component sequence reaction[a]

Entry	Catalyst	Brønsted acid	Yield[b] (%)
1	$Cp_2TiCl_2/CuCl_2$	PhCOOH	30
2	$Cp_2TiCl_2/CuBr_2$	PhCOOH	28
3	$Cp_2TiCl_2/Cu(acac)_2$	PhCOOH	25
4	$Cp_2TiCl_2/Cu(OAc)_2$	PhCOOH	22
5	$Cp_2TiCl_2/CuSO_4 \cdot 5H_2O$	PhCOOH	24
6	Cp_2TiCl_2/CuO	PhCOOH	31
7	$Cp_2TiCl_2/Cu(OTf)_2$	PhCOOH	26
8	$Cp_2TiCl_2/Cu(ClO_4)_2$	PhCOOH	27
9	Cp^*TiCl_3/CuO	PhCOOH	29
10	**Cp_2ZrCl_2/CuO**	**PhCOOH**	**34**
11	Cp_2ZrCl_2/CuO	PhOH	20
12	Cp_2ZrCl_2/CuO	$PhSO_3H$	26
13	Cp_2ZrCl_2/CuO	Ph $(COOH)NH_2$	41
14	Cp_2ZrCl_2/CuO	Ph (COOH)OH	42
15	Cp_2ZrCl_2/CuO	Ph $(COOH)_2$	47
16	Cp_2ZrCl_2/CuO	$(CH_2)_3(COOH)_2$	29
17	Cp_2ZrCl_2/CuO	HNC_4H_7COOH	28
18	Cp_2ZrCl_2/CuO	$H_2NPh\ (SO_3H)_2$	45
19	Cp_2ZrCl_2/CuO	5-$SO_3HPhCOOH$ (OH)	48
20	**Cp_2ZrCl_2/CuO**	**Ph $(COOH)_3$**	**54**
21	Cp_2ZrCl_2/CuO	Ph $(COOH)_3$	88[c]

[a] All reactions were conducted using the aniline (1.0 mmol), benzaldehyde (1.0 mmol), methyl pyruvate (1.0 mmol), catalyst (0.05 mmol, 5 mol%), Brønsted acid (0.05 mmol, 5 mol%), 50 °C, 1 h. [b] Isolated yields. [c] 50 °C, 2 h.

Table 2 Zirconocene dichloride/trimellitic acid/copper oxide catalyzed three components tandem reaction of aldehydes, arylamines and pyruvates[a,b]



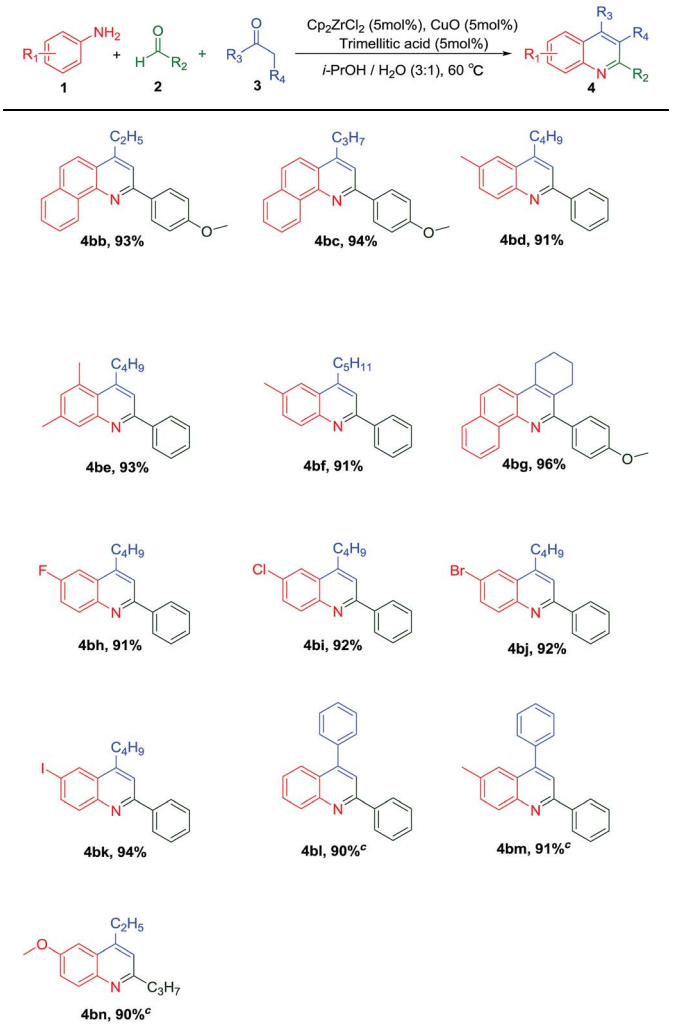
[a] All reactions were conducted using aldehyde (1.0 mmol); arylamine (1.1 mmol); pyruvate (1.5 mmol); Cp_2ZrCl_2 (0.05 mmol, 5 mol%); CuO (0.05 mmol, 5 mol%); trimellitic acid (0.05 mmol, 5 mol%); *i*-PrOH : H_2O (3 : 1, 0.5 mL); all reactions were carried out at 60 °C for 2 h. [b] Isolated yield.

methyl or ethyl group. Aniline with methyl (**4ab**) and methoxyl (**4ac**) substituents led to the excellent results (90–91%), when benzaldehyde and methyl pyruvate were used. The *p*-substituents of anilines were changed from methyl (**4ae**), *i*-propyl (**4af**), *t*-butyl (**4ag**) to methoxyl (**4ah**) reacted with 4-methoxybenzaldehyde and methyl pyruvate, the yields of the condensation reaction were 93–95%. Under the similar condition, treating 4-fluroaniline and benzaldehyde with methyl pyruvate afforded the substituted quinoline (**4ai**) in 90% yield. Benzaldehydes with methoxyl (**4aj**), methyl (**4ak**), *i*-propyl (**4al**) or *t*-butyl (**4am**) substituents obtained 92–94% yields when they reacted with 1-naphthylamine and methyl pyruvate, which provided a convenient route for the construction of tricyclic–quinolines. Aliphatic aldehydes such as cyclohexanecarbaldehyde was also readily introduced into this reaction, reacted with 1-naphthylamine or 4-methoxy aniline and methyl pyruvate afforded the desired products (**4an**, **4ao**) in 91% and 90% yields, respectively. Heterocyclic furfuraldehyde afforded the desired product in 91% yield (**4ap**). 1-Naphthaldehyde reacted with aniline and methyl pyruvate or ethyl pyruvate under standard conditions afforded the multiply substituted quinolines in 92% and 91% yield (**4aq** and **4ar**). As expected, *m*-substituted aniline and aldehyde (**4as**) produced desired quinoline in 92% yield. Gratifyingly, the sterically hindered *ortho*-substituted anilines (**4at**) still furnished the desired product in more than 90% yield.

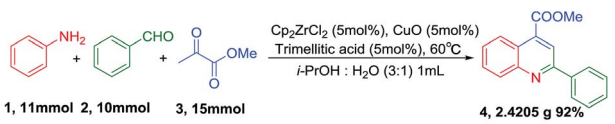
The zirconocene dichloride/trimellitic acid/CuO cooperative and relay catalytic system was successfully applied in the three-component coupling sequence reaction of aliphatic ketones and aromatic ketones under the optimized conditions (Table 3). The reaction results had not significantly effected by aliphatic ketones. The catalytic sequence reaction of 2-butanone with benzaldehyde and 1-naphthylamine afforded the products (**4bb**) in 93% yields, whereas other chain ketones including 2-pentone, 2-hexanone and 2-heptanone afforded 2,4-substituted quinolines in 91–93% yield (**4bd**), (**4be**), (**4bf**). Cyclic ketones such as cyclohexanone (**4bg**) was also readily introduced into this reaction, the desired product being formed with yield of 96%. Various halogens, such as fluorine, chlorine, bromine, iodine and electron-donating groups such as methyl were all tolerated in this reaction, afforded the products with 91–94% yields (**4bh**, **4bi**, **4bj**, **4bk** and **4be**). This triple cooperative and relay catalytic system were also applied in the three-component cascade reaction of aromatic ketone, such as anilines, benzaldehyde reacted with acetophenone afforded 2,4-diphenylquinoline in 90% and 91% yield(**4bl** and **4bm**), albeit with longer reaction time (12 h). To our pleased, chain aldehyde can also be used as substrate for this reaction afforded 6-methoxy-4-ethyl-2-propylquinoline in 90% yield with 12 h(**4bn**). More importantly, this cooperative and relay catalytic system for synthesis of substituted quinoline could be easily scaled up and the desired disubstituted quinoline was obtained in 92% yield (Scheme 2).

To get more information about the reaction mechanism, several control experiments (Table 4) and parallel experiment (Scheme 3) were set up under the standard conditions. The three components cascade reaction of aniline, benzaldehyde and methyl pyruvate without catalyst or with 5 mol% CuO did not get the desired product at 60 °C for 2 h (Table 4, entries 1 and 2). In the presence of 5 mol% trimellitic acid, three-component sequence reaction afforded the desired quinoline in 14% yield (Table 4, entry 3). With addition of 5 mol% Cp_2ZrCl_2 in the reaction only obtained 17% yield of quinoline (Table 4, entry 4), which eliminated the possibility that *i*-propanol or water coordination with zirconocene dichloride released HCl promotes this reaction. With the assistance of 5 mol% Cp_2ZrCl_2 and 5 mol% trimellitic acid, the desired product was isolated in 44% yield (Table 4, entries 5). Adding 5 mol% CuO into this catalytic system, the yield of 4-methoxycarbonyl-2-phenylquinoline was up to 92% (Table 4, entry 6). It is clear

Table 3 Zirconocene dichloride/trimellitic acid/copper oxide catalyzed three components tandem reaction of aldehydes, arylamines and ketones[a,b]



[a] Reaction conditions: a mixture of aldehyde (1.0 mmol); arylamine (1.1 mmol); ketone (1.5 mmol); Cp_2ZrCl_2 (0.05 mmol, 5 mol%); CuO (0.05 mmol, 5 mol%); trimellitic acid (0.05 mmol, 5 mol%); *i*-PrOH : H_2O (3 : 1,0.5 mL), 60 °C for 8 h. [b] Isolated yield. [c] 12 h.



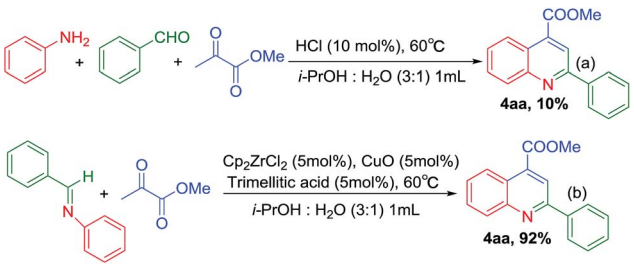
Scheme 2 Scaled up for the gram scale.

that the high efficiency of the coupling sequence reaction should not be attributed to zirconocene dichloride, trimellitic acid or CuO individually. We proposed that the cooperation of zirconocene dichloride, trimellitic acid and the relay of CuO, resulted in the efficient cooperative and relay catalysis. The control experiments using 10 mol% HCl afforded the substituted quinolines in 10% yield, indicating HCl was not

Table 4 Control experiment[a]

Entry	CuO (mol%)	Trimellitic acid (mol%)	Cp_2ZrCl_2 (mol%)	Yield[b] (%)
1	—	—	—	ND
2	5	—	—	ND
3	—	5	—	14
4	—	—	5	17
5	—	5	5	44
6	5	5	5	92

[a] Reaction conditions: a mixture of aldehyde (1.0 mmol); aniline (1.1 mmol); methyl pyruvate (1.5 mmol); *i*-PrOH : H_2O (3 : 1, 0.5 mL); all reactions were carried out at 60 °C for 2 h, ND = no detected. [b] Isolated yield.



Scheme 3 The paralleled experiment.

catalytic species (Scheme 3a). This control experiments and parallel experiment indicated that zirconocene dichloride and trimellitic acid demonstrated good compatibility with CuO in three components cascade reaction, which presented a new cooperative and relay catalysis system for synthesis of multiply substituted quinolines from anilines, aldehydes and ketones. *N*-Arylimines and methyl pyruvate under the standard condition also afforded the desired product in 92% yield (Scheme 3b), which indicated that the imine was firstly formed in this reaction, followed by Mannich addition and cyclization.

The interaction of zirconocene dichloride and trimellitic acid in three-component coupling sequence reaction for synthesis of substituted quinolines were investigated by ^{1}H NMR and HRMS analyses. ^{1}H NMR experiments, which were conducted using Cp_2ZrCl_2 in D_2O (Fig. 1), showed that no coordination occurred and only one Cp singlet of Cp_2ZrCl_2 at $\delta = 6.49$ ppm (●) was detected. When adding 1 equiv. trimellitic acid, a new zirconocene complex species II formed, which resonated at $\delta = 6.57$ ppm (★). Intensity of the Cp singlet at $\delta = 6.57$ didn't increase as the time went on. Adding 2 equiv. aniline into this transformation, zirconocene dichloride (I) was consumed gradually in D_2O and transformed to a new zirconocene species $Cp_2Zr(OOC)_2PhCOOH$ (II).[20] The above conclusion was also certified by HRMS analysis, corresponding to the $[II + H]^+$ signal at m/z 428.9921 (Fig. S3–S6†). These observations clearly demonstrated that during the reaction, zirconocene dichloride readily converted into zirconocene complexes II, and presumably it was the organometallic binary acid catalyst.

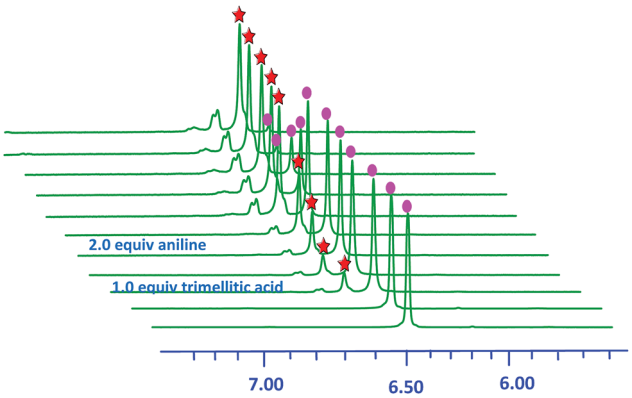
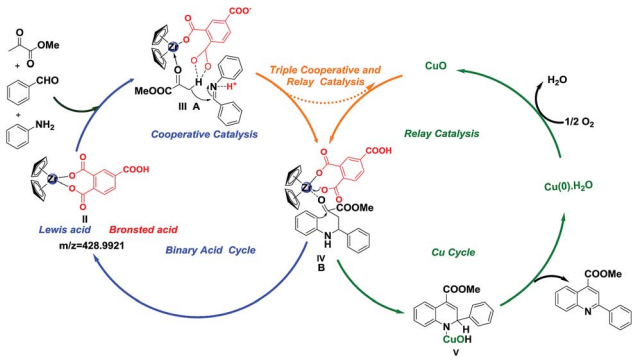


Fig. 1 Partial 400 MHz ^{1}H NMR spectra (D_2O) of a mixture of Cp_2ZrCl_2 (1.0 equiv.) and trimellitic acid (1.0 equiv.) with $PhNH_2$ (2.0 equiv). 6.49 ppm I●[Cp_2ZrCl_2]; 6.57 ppm II★$Cp_2Zr(OOC)_2PhCOOH$.

Taken ^{1}HNMR, HRMS, control experiments and paralleled experiments together, a plausible catalytic cycle of zirconocene dichloride/trimellitic acid/CuO triple cooperative and relay catalytic system in three-component sequence reaction was illustrated in Scheme 4. Zirconocene dichloride I pre-catalyst activated by trimellitic acid and transformed to binary acid catalyst II in the presence of aniline. The incoming ketone coordinated to Zr center of II. In transition state A, enolation was accelerated as the carbonyl coordinated to oxytropic Zr and methyl formed hydrogen bond with the carboxyl oxygen of trimellitic acid. The carbon–carbon bond formation is illustrated in transition state A. The coordinated enolate then undergoes addition to the aldimine, which is activated by H^+ from the other carboxyl group of trimellitic acid. This transition state show cases the cooperative nature of this binary acid catalytic system. In transition state B, the electron-rich benzene ring attacked the keto-carbonyl group to formed the intermediate dihydroquinoline. After the dihydroquinoline was released, the zirconocene catalyst II was regenerated from the transition state B by coordination of the carboxyl group again. The coordination of the dihydroquinoline and CuO may induce a combination of electron transfer and intramolecular rearrangement to give the desired product[21] and Cu(0)·H_2O, which should be more stable than Cu(0) due to its coordination with H_2O. Active Cu(0)·H_2O is facilely oxidized by oxygen in the air to restore CuO, which enters next catalytic cycle.



Scheme 4 Proposed mechanism of zirconocene dichloride/trimellitic acid/CuO cooperative and relay catalysis for synthesis of substituted quinolines.

Conclusions

In summary, we have developed a triple cooperative and relay catalysis system that the combination of organometallic Lewis acids and Brønsted acids with metal were developed for three-component cascade Mannich addition/C–C formative cyclization/oxidation reaction. The green syntheses of substituted quinolines were achieved from readily available anilines, aldehydes and aromatic or aliphatic ketones in good to excellent yields. ^{1}H NMR and HRMS analysis unveiled that $Cp_2Zr(OOC)_2PhCOOH$ was catalytic specis, which significantly accelerated the condensation of aldehydes, anilines and ketones into dihydroquinolines with *i*-propanol and water as solvent. Meanwhile, CuO catalyzed oxydehydrogenation of dihydroquinolines to generate quinolines.

Experimental

General methods and materials

All manipulations were performed in an atmosphere of air. All reagents were purchased from the commercial approaches and used without further purification unless specified otherwise. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker EQUINX55 (400 MHz for ^{1}H; 101 MHz for ^{13}C) spectrometer in $CDCl_3$. For ^{1}H NMR, tetramethylsilane (TMS) served as internal standard (δ = 0) and ^{1}H NMR chemical shifts are reported in ppm downfield of tetramethylsilane and referenced to residual solvent peak ($CDCl_3$ at 7.26 ppm) unless otherwise noted. The data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet), and coupling constant in Hz. For ^{13}C NMR, $CDCl_3$ was used as internal standard (δ = 77.0) and spectra were obtained with complete proton decoupling. HRMS (ESI) analysis was performed and (HRMS) data were reported with sodium mass/charge (*m*/*z*) ratios as values in atomic mass units. Column chromatography was performed on silica gel (230–400 mesh) and analytical thin layer chromatography was carried out using 250 μm commercial silica gel plates. Visualization of the developed chromatogram was performed by UV absorbance and stained with an iodine vapor.

Typical procedures for synthesis of substituted quinolones

A 10 mL test tube equipped with a magnetic stirrer and a septum, was charged with aldehyde (1.0 mmol), amine (1.1 mmol), and the ketone (1.5 mmol) in one portion. Cp_2ZrCl_2 (0.05 mmol, 5 mol%), CuO (0.05 mmol, 5 mol%) and trimellitic acid (0.05 mmol, 5 mol%) were stirred in *i*-PrOH : H_2O (3 : 1) 0.5 mL. The reaction mixture was heated to 60 °C and stirred until the reaction was completed as indicated by TLC, then the reaction mixture was quenched with distilled water (5.0 mL). The aqueous phase was extracted with dichloride methane (3–5 mL), dried over Na_2SO_4 and concentrated *in vacuo* to give the

crude product. The crude product was purified by flash column chromatography on neutral silica gel (ethyl acetate:petroleum ether). Full experimental details and characterization data for all quinolines product are included in the ESI.†

4-Methoxycarbonyl-2-phenylquinoline (4aa). Yield, 92%; primrose yellow solid; mp 217–218 °C; Rf 0.51 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1728, 1593, 1346, 1250, 1203, 1149, 771, 694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, J = 8.5 Hz, 1H), 8.41 (s, 1H), 8.22 (s, 3H), 7.77 (s, 1H), 7.63 (s, 1H), 7.55 (s, 2H), 7.50 (d, J = 7.1 Hz, 1H), 4.07 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.85, 156.71, 149.29, 138.81, 135.61, 130.35, 129.91, 129.74, 128.94, 127.81, 127.48, 125.43, 124.00, 120.34, 52.72. HRMS (ESI): m/z called for $C_{17}H_{13}NO_2$ $[M + H]^+$, 264.1019; found, 264.1026.

6-Methyl-4-methoxycarbonyl-2-phenylquinoline (4ab). Yield, 93%; primrose yellow solid; mp 212–213 °C; Rf 0.45 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1730, 1608, 1352, 1254, 1209, 1153, 775, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.35 (s, 1H), 8.19 (d, J = 7.3 Hz, 2H), 8.12 (d, J = 8.6 Hz, 1H), 7.61–7.57 (m, 1H), 7.54 (s, 2H), 7.47 (s, 1H), 4.06 (s, 3H), 2.58 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.97, 155.72, 147.94, 138.90, 138.01, 134.81, 132.18, 129.99, 129.53, 128.90, 127.36, 124.24, 124.02, 120.23, 52.65, 22.13. HRMS (ESI): m/z called for $C_{18}H_{15}NO_2$ $[M + H]^+$, 278.1176; found, 278.1177.

6-Methoxy-4-methoxycarbonyl-2-phenylquinoline (4ac). Yield, 95%; primrose yellow solid; mp 215–219 °C; Rf 0.47(petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1726, 1591, 1344, 1253, 1206, 1152, 774, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.21 (d, J = 2.7 Hz, 1H), 8.16 (d, J = 7.5 Hz, 2H), 8.10 (d, J = 9.2 Hz, 1H), 7.52 (s, 2H), 7.42 (d, J = 2.6 Hz, 2H), 4.04 (s, 3H), 3.97 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.91, 159.05, 154.03, 145.70, 138.92, 133.17, 131.72, 129.29, 128.88, 127.14, 125.55, 122.79, 120.69, 103.22, 55.57, 52.56. HRMS (ESI): m/z called for $C_{17}H_{13}NO_2$ $[M + H]^+$, 294.1130; found, 294.1125.

4-Methoxycarbonyl-2-[4-methoxyl]phenylquinoline (4ad). Yield, 92%; primrose yellow solid; mp 220–221 °C; Rf 0.49 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1731, 1596, 1349, 1253, 1206, 1152, 778, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 8.3 Hz, 1H), 8.36 (s, 1H), 8.18 (d, J = 8.9 Hz, 3H), 7.75 (d, J = 1.2 Hz, 1H), 7.59 (s, 1H), 7.06 (d, J = 8.8 Hz, 2H), 4.07 (s, 3H), 3.89 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.96, 161.15, 156.27, 149.28, 135.50, 131.38, 130.10, 129.83, 128.85, 127.39, 125.40, 123.67, 119.93, 114.33, 55.42, 52.70. HRMS (ESI): m/z called for $C_{18}H_{15}NO_3$ $[M + H]^+$, 294.1125; found, 294.1130.

6-Methyl-4-methoxycarbonyl-2-[4-methoxyl]phenylquinoline (4ae). Yield, 93%; yellow solid; mp 224–225 °C; Rf 0.52 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1729, 1596, 1348, 1254, 1207, 1151, 773, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.32 (s, 1H), 8.16 (d, J = 8.8 Hz, 2H), 8.08 (d, J = 8.6 Hz, 1H), 7.59 (dd, J = 8.6, 1.6 Hz, 1H), 7.26 (s, 2H), 7.05 (d, J = 8.8 Hz, 2H), 4.07 (s, 3H), 3.90 (s, 3H), 2.58 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.81, 167.07, 160.97, 155.31, 147.91, 137.53, 134.73, 132.07, 131.98, 131.48, 129.76, 128.69, 124.22, 123.67, 119.81, 114.31, 114.28, 55.39, 52.62, 22.08. HRMS (ESI): m/z called for $C_{19}H_{17}NO_3$ $[M + H]^+$, 308.1281; found, 308.1289.

6-*i*-Propyl-4-methoxycarbonyl-2-[4-methoxyl]phenylquinoline (4af). Yield, 93%; yellow solid; mp 210–211 °C; Rf 0.51 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1732, 1595, 1349, 1251, 1205, 1152, 774, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 1.4 Hz, 1H), 8.33 (s, 1H), 8.15 (s, 3H), 7.66 (d, J = 1.8 Hz, 1H), 7.05 (d, J = 8.8 Hz, 2H), 4.07 (s, 3H), 3.89 (s, 3H), 3.14 (d, J = 13.6, 6.8 Hz, 1H), 1.37 (d, J = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.11, 160.97, 155.45, 148.29, 148.21, 134.92, 131.60, 130.00, 129.50, 128.72, 123.75, 121.70, 119.84, 114.29, 55.41, 52.60, 34.56, 23.88. HRMS (ESI): m/z called for $C_{21}H_{21}NO_3$ $[M + H]^+$, 336.1594; found, 336.1589.

6-*t*-Butyl-4-methoxycarbonyl-2-[4-methoxyl]phenylquinoline (4ag). Yield, 95%; yellow solid; mp 207–208 °C; Rf 0.50 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1733, 1596, 1349, 1252, 1205, 1143, 774, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 2.0 Hz, 1H), 8.34 (s, 1H), 8.15 (dd, J = 15.5, 8.8 Hz, 3H), 7.85 (dd, J = 8.9, 2.1 Hz, 1H), 7.05 (d, J = 8.8 Hz, 2H), 4.08 (s, 3H), 3.89 (s, 3H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.12, 160.97, 155.62, 150.36, 147.90, 135.08, 131.62, 129.59, 128.73, 123.44, 120.40, 119.88, 114.29, 55.41, 52.61, 35.29, 31.22. HRMS (ESI): m/z called for $C_{21}H_{21}NO_3$ $[M + H]^+$, 350.1751; found, 350.1756.

6-Methoxy-4-methoxycarbonyl-2-[4-methoxyl]phenylquinoline (4ah). Yield, 95%; yellow solid; mp 210–211 °C; Rf 0.48 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1725, 1591, 1343, 1247, 1201, 1146, 767, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.20 (d, J = 2.3 Hz, 1H), 8.14 (d, J = 8.6 Hz, 2H), 8.08 (d, J = 9.2 Hz, 1H), 7.41 (d, J = 9.2 Hz, 1H), 7.05 (d, J = 8.6 Hz, 2H), 4.06 (s, 3H), 3.98 (s, 3H), 3.89 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.06, 160.79, 158.78, 153.78, 145.70, 133.23, 131.59, 131.52, 128.47, 125.15, 122.65, 120.32, 114.28, 103.32, 55.57, 55.40, 52.55. HRMS (ESI): m/z called for $C_{19}H_{17}NO_4$ $[M + H]^+$, 324.1230; found, 324.1234.

6-Fluoro-4-methoxycarbonyl-2-[4-methoxyl]phenylquinoline (4ai). Yield, 90%; yellow solid; mp 230–231 °C; Rf 0.46 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1723, 1585, 1342, 1245, 1200, 1144, 767, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.87 (d, J = 8.5 Hz, 1H), 8.57 (s, 1H), 8.43 (s, 3H), 7.92 (s, 1H), 7.89 (s, 1H), 7.74 (s, 2H), 7.70 (d, J = 7.1 Hz, 1H), 4.11 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.91, 164.83, 158.21, 148.78, 144.31, 140.25, 138.90, 138.60, 137.94, 138.83, 138.45, 134.39, 133.05, 129.33, 51.65. HRMS (ESI): m/z called for $C_{17}H_{12}FNO_2$ $[M + H]^+$, 282.1019; found, 282.1012.

4-Methoxycarbonyl-2-[4-methoxylphenyl]benzoquinoline (4aj). Yield, 94%; yellow solid; mp 213–214 °C; Rf 0.49 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1733, 1597, 1351, 1255, 1209, 1154, 778, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.48 (d, J = 7.8 Hz, 1H), 8.59 (d, J = 9.2 Hz, 1H), 8.42 (s, 1H), 8.33 (d, J = 8.6 Hz, 2H), 7.90 (d, J = 7.5 Hz, 1H), 7.85 (d, J = 9.2 Hz, 1H), 7.73 (s, 2H), 7.09 (d, J = 8.6 Hz, 2H), 4.09 (s, 3H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.19, 161.03, 154.45, 147.28, 135.39, 133.48, 131.59, 131.52, 128.69, 128.52, 127.59, 126.97, 125.14, 122.37, 122.07, 119.02, 114.25, 55.40, 52.70. HRMS (ESI): m/z called for $C_{22}H_{17}NO_3$ $[M + H]^+$, 344.1281; found, 344.1286.

4-Methoxycarbonyl-2-[4-methylphenyl]benzoquinoline (4ak). Yield, 93%; yellow solid; mp 225–226 °C; Rf 0.53 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1736, 1598, 1352, 1254, 1208, 1155, 778, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.50 (d, J

= 7.8 Hz, 1H), 8.60 (d, J = 9.2 Hz, 1H), 8.45 (s, 1H), 8.27 (d, J = 7.8 Hz, 2H), 7.86 (d, J = 9.2 Hz, 2H), 7.74 (s, 2H), 7.38 (d, J = 7.7 Hz, 2H), 4.09 (s, 3H), 2.47 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.22, 154.89, 147.37, 139.75, 136.16, 135.51, 133.48, 131.66, 129.65, 128.80, 128.54, 127.61, 127.25, 127.06, 125.19, 122.36, 119.38, 52.73, 21.40. HRMS (ESI): m/z called for $C_{22}H_{17}NO_3$ $[M + H]^+$, 328.1332; found, 328.1342.

4-Methoxycarbonyl-2-[4-*i*-propylphenyl]benzoquinoline (4al). Yield, 92%; yellow solid; mp 229–230 °C; Rf 0.52 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1721, 1583, 1340, 1244, 1197, 1141, 762, 683 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.50 (d, J = 8.0 Hz, 1H), 8.61 (d, J = 9.2 Hz, 1H), 8.46 (s, 1H), 8.30 (d, J = 8.2 Hz, 2H), 7.91–7.83 (m, 2H), 7.77–7.68 (m, 2H), 7.45 (d, J = 8.2 Hz, 2H), 4.08 (s, 3H), 3.04 (dt, J = 13.8, 6.9 Hz, 1H), 1.36 (d, J = 7.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.20, 154.99, 150.66, 147.39, 136.64, 135.47, 133.48, 131.68, 128.80, 128.53, 127.60, 127.43, 127.04, 125.22, 122.39, 122.37, 119.50, 52.71, 34.07, 23.97. HRMS (ESI): m/z called for $C_{24}H_{21}NO_3$ $[M + H]^+$, 356.1645; found, 356.1650.

4-Methoxycarbonyl-2-[4-*t*-butylphenyl]benzoquinoline (4am). Yield, 94%; primrose yellow solid; mp 215–216 °C; Rf 0.48 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1721, 1585, 1342, 1245, 1294, 1140, 765, 685 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.51 (d, J = 7.9 Hz, 1H), 8.61 (d, J = 9.2 Hz, 1H), 8.47 (s, 1H), 8.30 (d, J = 8.4 Hz, 2H), 7.88 (s, 2H), 7.78–7.71 (m, 2H), 7.62 (d, J = 8.4 Hz, 2H), 4.09 (s, 3H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.22, 154.97, 152.90, 147.42, 136.24, 135.51, 133.49, 131.69, 128.82, 128.54, 127.60, 127.16, 125.90, 125.22, 122.40, 122.37, 119.54, 52.73, 34.82, 31.33. HRMS (ESI): m/z called for $C_{25}H_{23}NO_3$ $[M + H]^+$, 370.1802; found, 370.1805.

4-Methoxycarbonyl-2-cyclohexylbenzoquinoline (4an). Yield, 91%; primrose yellow solid; mp 213–214 °C; Rf 0.47 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1729, 1595, 1345, 1253, 1204, 1151, 774, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.42 (d, J = 7.7 Hz, 1H), 8.57 (d, J = 9.2 Hz, 1H), 7.89 (s, 2H), 7.85 (d, J = 9.3 Hz, 1H), 7.71 (d, J = 1.7 Hz, 2H), 4.06 (s, 3H), 3.04 (s, 1H), 2.14 (d, J = 11.9 Hz, 2H), 1.96 (d, J = 12.9 Hz, 2H), 1.80 (d, J = 11.7 Hz, 2H), 1.53 (d, J = 12.8 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.41, 164.84, 135.05, 133.30, 131.54, 128.28, 127.48, 126.90, 125.07, 122.40, 120.96, 52.60, 46.99, 32.91, 26.58, 26.18. HRMS (ESI): m/z called for $C_{21}H_{21}NO_3$ $[M + H]^+$, 320.1645; found, 320.1648.

6-Methoxy-4-methoxycarbonyl-2-cyclohexylquinoline (4ao). Yield, 90%; primrose yellow solid; mp 203–204 °C; Rf 0.50 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1733, 1598, 1349, 1253, 1206, 1152, 775, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 2.7 Hz, 1H), 7.99 (d, J = 9.2 Hz, 1H), 7.85 (s, 1H), 7.37 (dd, J = 9.2, 2.8 Hz, 1H), 4.03 (s, 3H), 3.96 (s, 3H), 2.01 (s, 1H), 1.77–1.59 (m, 4H), 1.33–1.24 (m, 4H), 1.01–0.89 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.13, 163.49, 158.51, 145.18, 133.01, 130.96, 130.88, 125.14, 122.22, 121.43, 103.32, 55.53, 52.43, 47.08, 32.81, 26.51, 26.04. HRMS (ESI): m/z called for $C_{18}H_{21}NO_3$ $[M + Na]^+$, 322.1414; found, 322.1421.

6-Methoxy-4-methoxycarbonyl-2-furylquinoline (4ap). Yield, 91%; claybank; mp 210–211 °C; Rf 0.51 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1720, 1583, 1340, 1243, 1194, 1142, 764, 683 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.20 (d, J = 2.6 Hz, 1H), 8.06 (d, J = 9.3 Hz, 1H), 7.62 (s, 1H), 7.40 (dd, J = 9.2, 2.6 Hz, 1H), 7.19 (d, J = 3.3 Hz, 1H), 6.98 (s, 1H), 4.05 (s, 3H), 3.97 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.16, 168.26, 166.72, 159.03, 153.30, 146.21, 145.46, 143.92, 133.20, 131.35, 125.50, 122.95, 119.44, 112.27, 109.55, 103.47, 55.59, 52.60. HRMS (ESI): m/z called for $C_{16}H_{13}NO_4$ $[M + H]^+$, 284.0917; found, 284.0922.

4-Methoxycarbonyl-2-naphthylquinoline (4aq). Yield, 92%; primrose yellow solid; mp 233–234 °C; Rf 0.47 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1717, 1585, 1340, 1242, 1195, 1141, 763, 685 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (d, J = 8.5 Hz, 1H), 8.32 (d, J = 8.4 Hz, 1H), 8.27 (s, 1H), 8.16 (d, J = 8.1 Hz, 1H), 8.02–7.96 (m, 2H), 7.85 (t, J = 7.6 Hz, 1H), 7.79–7.71 (m, 2H), 7.64 (t, J = 7.7 Hz, 1H), 7.54 (dt, J = 13.4, 6.6 Hz, 2H), 4.07 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.73, 158.97, 149.15, 137.87, 135.19, 134.05, 131.14, 130.33, 130.07, 129.55, 128.52, 127.99, 126.87, 126.13, 125.53, 124.50, 123.87, 52.76. HRMS (ESI): m/z called for $C_{21}H_{15}NO_3$ $[M + H]^+$, 314.1176; found, 314.1180.

4-Ethoxycarbonyl-2-naphthylquinoline (4ar). Yield, 91%; yellow solid; mp 235–236 °C; Rf 0.46 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1726, 1589, 1343, 1247, 1201, 1145, 763, 688 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (d, J = 8.6 Hz, 1H), 8.29 (d, J = 8.3 Hz, 1H), 8.23 (s, 1H), 8.13 (d, J = 8.2 Hz, 1H), 8.01–7.94 (m, 2H), 7.83 (s, 1H), 7.75 (d, J = 0.9 Hz, 2H), 7.65–7.60 (m, 1H), 7.53 (d, J = 1.8 Hz, 2H), 4.54 (s, 2H), 1.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.34, 158.98, 149.12, 137.94, 135.69, 134.04, 131.17, 130.32, 130.02, 129.51, 128.50, 127.94, 126.85, 126.13, 125.39, 124.30, 123.90, 61.93, 14.31. HRMS (ESI): m/z called for $C_{21}H_{21}NO_3$ $[M + H]^+$, 328.1332; found, 328.1335.

7-Methoxy-4-methoxycarbonyl-2-phenylquinoline (4as). Yield, 92%; primrose yellow solid; mp 215–216 °C; Rf 0.52 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1726, 1589, 1345, 1248, 1186, 1146, 769, 682 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, J = 9.3 Hz, 1H), 8.27 (s, 1H), 8.21–8.17 (m, 2H), 7.55 (s, 3H), 7.52–7.47 (m, 1H), 7.30 (d, J = 2.7 Hz, 1H), 4.07 (s, 3H), 4.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.95, 160.85, 157.16, 151.27, 139.01, 135.33, 129.61, 128.90, 127.44, 126.52, 120.95, 119.26, 118.10, 108.10, 55.55, 52.67. HRMS (ESI): m/z called for $C_{18}H_{15}NO_3$ $[M + H]^+$, 294.1125; found, 294.1133.

8-Methoxy-4-methoxycarbonyl-2-phenylquinoline (4at). Yield, 90%; primrose yellow solid; mp 217–218 °C; Rf 0.49 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 1724, 1588, 1342, 1247, 1187, 1141, 765, 684 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.25 (d, J = 8.5 Hz, 1H), 8.20 (d, J = 8.3 Hz, 2H), 7.51 (s, 1H), 7.10 (d, J = 7.6 Hz, 1H), 7.04 (d, J = 8.3 Hz, 2H), 4.11 (s, 3H), 4.06 (s, 3H), 3.89 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.08, 161.07, 155.59, 155.10, 141.29, 135.71, 131.58, 128.94, 127.54, 124.77, 120.21, 117.13, 114.27, 108.38, 56.25, 55.39, 52.69. HRMS (ESI): m/z called for $C_{19}H_{17}NO_4$ $[M + H]^+$, 323.1154; found, 323.1158.

4-Ethoxyl-2-[4-methylphenyl]benzoquinoline (4bb). Yield, 93%; primrose yellow solid; mp 221–225 °C; Rf 0.43 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 3078, 2962, 2931, 1611, 1510, 1459 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.52 (d, J = 8.0 Hz, 1H), 8.32 (d, J = 8.8 Hz, 2H), 7.91 (d, J = 4.9 Hz, 2H), 7.81 (d, J = 7.4 Hz, 4H), 7.09 (d, J = 8.8 Hz, 2H), 3.91 (s, 3H), 3.18 (s,

2H), 1.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.67, 154.90, 150.16, 146.21, 133.54, 132.75, 132.34, 128.72, 127.84, 127.53, 126.65, 125.17, 123.52, 120.95, 117.52, 114.16, 55.41, 25.84, 14.64. HRMS (ESI): *m/z* called for $C_{21}H_{21}NO_3$ $[M + H]^+$, 336.1594; found, 336.1589. HRMS (ESI): *m/z* called for $C_{22}H_{19}NO$ $[M + H]^+$, 314.1539; found, 314.1542.

4-Propyl-2-[4-methylphenyl]benzoquinoline (4bc). Yield, 94%; white solid; mp 229–221 °C; Rf 0.45 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 3076, 2957, 2929, 1597, 1498, 1456 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.55 (d, J = 8.1 Hz, 1H), 8.33 (d, J = 8.8 Hz, 2H), 7.90 (s, 2H), 7.79 (s, 4H), 7.10 (d, J = 8.8 Hz, 2H), 3.91 (s, 3H), 3.11 (s, 2H), 1.87 (d, J = 7.6 Hz, 2H), 1.09 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.68, 154.66, 148.71, 133.55, 132.72, 132.35, 128.73, 127.86, 127.55, 126.66, 125.18, 123.74, 121.16, 118.48, 114.16, 55.41, 34.90, 23.71, 14.20. HRMS (ESI): *m/z* called for $C_{23}H_{21}NO$ $[M + H]^+$, 328.1696; found, 328.1702.

6-Methyl-4-butyl-2-phenylquinoline (4bd). Yield, 91%; white solid; mp 222–223 °C; Rf 0.47 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 3071, 2954, 2923, 1596, 1491, 1451 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 2H), 7.46 (s, 2H), 7.14 (d, J = 34.7 Hz, 4H), 5.92 (s, 1H), 2.38 (s, 5H), 1.55 (s, 2H), 1.33 (s, 2H), 0.87 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.57, 167.29, 140.31, 135.88, 135.77, 130.67, 129.71, 128.19, 126.99, 125.33, 92.55, 31.95, 30.40, 22.36, 20.94, 13.67. HRMS (ESI): *m/z* called for $C_{20}H_{21}N$ $[M + H]^+$, 276.1713; found, 276.1716.

5,7-Dimethyl-4-butyl-2-phenylquinoline (4be). Yield, 93%; white solid; mp 219–220 °C; Rf 0.46 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 3078, 2961, 2929, 1563, 1498, 1457 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 2H), 7.47 (d, J = 6.1 Hz, 2H), 6.91 (s, 1H), 6.85 (s, 2H), 5.95 (s, 1H), 2.47 (s, 2H), 2.36 (s, 6H), 1.60 (s, 2H), 1.38 (s, 2H), 0.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.50, 167.03, 140.37, 138.81, 138.31, 130.69, 128.21, 127.64, 127.03, 122.89, 92.70, 31.97, 30.47, 22.38, 21.24, 13.69. HRMS (ESI): *m/z* called for $C_{21}H_{23}N$ $[M + H]^+$, 290.1817; found, 290.1819.

6-Methyl-4-pentyl-2-phenylquinoline (4bf). Yield, 91%; white solid; mp 215–216 °C; Rf 0.47 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 3075, 2959, 2928, 1599, 1495, 1453 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 6.5 Hz, 2H), 7.47 (s, 2H), 7.20 (d, J = 7.8 Hz, 2H), 7.09 (d, J = 7.8 Hz, 2H), 5.92 (s, 1H), 2.39 (s, 5H), 1.56 (s, 2H), 1.28 (s, 4H), 0.86 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.57, 167.32, 140.32, 135.89, 135.78, 130.67, 129.72, 128.19, 126.99, 125.33, 92.54, 32.21, 31.39, 27.93, 22.19, 20.94, 13.81. HRMS (ESI): *m/z* called for $C_{21}H_{23}N$ $[M + H]^+$, 290.1817; found, 290.1819.

6-(4-Methoxyphenyl)-7,8,9,10-tetrahydrobenzophenanthridine (4bg). Yield, 96%; white solid; mp 182–183 °C; Rf 0.48 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 3078, 2962, 2931, 1591, 1484, 1447 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.37 (d, J = 7.4 Hz, 1H), 7.89 (s, 2H), 7.82 (s, 1H), 7.71–7.63 (m, 4H), 7.05 (d, J = 8.6 Hz, 2H), 3.91 (s, 3H), 3.27 (s, 2H), 2.91 (s, 2H), 2.02 (s, 2H), 1.80 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.54, 142.11, 132.99, 130.85, 129.04, 127.43, 127.41, 126.91, 126.60, 124.94, 120.53, 113.46, 55.38, 29.13, 26.20, 22.89, 22.55. HRMS (ESI): *m/z* called for $C_{24}H_{21}NO$ $[M + H]^+$, 340.1696; found, 340.1708.

6-Fluoro-4-butyl-2-phenylquinoline (4bh). Yield, 91%; white solid; mp 245–246 °C; Rf 0.43 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 3070, 2951, 2922, 1592, 1491, 1453 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, J = 7.5, 1.7 Hz, 2H), 7.46 (s, 2H), 7.16 (d, J = 4.8 Hz, 2H), 7.08 (s, 2H), 5.95 (s, 1H), 2.37 (s, 2H), 1.52 (s, 2H), 1.32 (s, 2H), 0.86 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.92, 167.07, 162.06, 159.61, 140.10, 134.50, 134.47, 130.86, 128.25, 127.38, 127.30, 127.04, 116.10, 92.83, 31.90, 30.34, 22.34, 13.63. HRMS (ESI): *m/z* called for $C_{19}H_{18}FN$ $[M + H]^+$, 280.1455; found, 280.1457.

6-Chloro-4-butyl-2-phenylquinoline (4bi). Yield, 92%; white solid; mp 237–238 °C; Rf 0.45 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 3071, 2953, 2924, 1593, 1491, 1452 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 1.3 Hz, 2H), 7.47 (s, 2H), 7.36 (s, 2H), 7.13 (s, 2H), 5.97 (s, 1H), 2.41 (s, 2H), 1.53 (s, 2H), 1.34 (s, 2H), 0.87 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.04, 166.39, 139.99, 137.17, 131.43, 130.98, 129.30, 128.28, 127.07, 126.42, 93.37, 31.96, 30.33, 22.35, 13.68. HRMS (ESI): *m/z* called for $C_{19}H_{18}ClN$ $[M + H]^+$, 296.1107; found, 296.1109.

6-Bromo-4-butyl-2-phenylquinoline (4bj). Yield, 92%; white solid; mp 240–241 °C; Rf 0.47 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 3073, 2954, 2925, 1597, 1495, 1451 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, J = 7.9, 1.6 Hz, 2H), 7.50 (s, 4H), 7.09 (s, 2H), 5.96 (s, 1H), 2.42 (d, J = 8.0 Hz, 2H), 1.53 (d, J = 7.5 Hz, 2H), 1.34 (d, J = 7.5 Hz, 2H), 0.88 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.12, 166.30, 139.96, 137.68, 132.28, 130.98, 128.28, 127.05, 126.74, 119.23, 93.45, 31.97, 30.34, 22.35, 13.67. HRMS (ESI): *m/z* called for $C_{19}H_{18}BrN$ $[M + H]^+$, 340.0696; found, 340.0693.

6-Iodo-4-butyl-2-phenylquinoline (4bk). Yield, 94%; white solid; mp 245–246 °C; Rf 0.51 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 3075, 2959, 2928, 1599, 1495, 1453 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98–7.90 (m, 2H), 7.71 (d, J = 8.5 Hz, 2H), 7.47 (s, 2H), 6.97 (s, 2H), 5.96 (s, 1H), 2.44 (s, 2H), 1.55 (s, 2H), 1.35 (d, J = 7.5 Hz, 2H), 0.89 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.13, 166.17, 139.95, 138.39, 138.24, 130.99, 128.27, 127.05, 126.90, 93.55, 90.04, 31.98, 30.34, 22.35, 13.67. HRMS (ESI): *m/z* called for $C_{19}H_{18}IN$ $[M + H]^+$, 388.0533; found, 388.0537.

2,4-Diphenylquinoline (4bl). Yield, 90%; white solid; mp 243–245 °C; Rf 0.53 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 3055, 3028, 2920, 1589, 1546, 1488, 1444 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 8.4 Hz, 1H), 8.23 (d, J = 7.3 Hz, 2H), 7.93 (d, J = 8.3 Hz, 1H), 7.85 (s, 1H), 7.75 (s, 1H), 7.58 (d, J = 1.7 Hz, 7H), 7.51–7.46 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.87, 149.15, 148.83, 139.66, 138.41, 130.14, 129.55, 129.49, 129.32, 128.81, 128.58, 128.38, 127.58, 126.31, 125.77, 125.62, 119.33. HRMS (ESI): *m/z* called for $C_{21}H_{15}N$ $[M + H]^+$, 282.1277; found, 282.1279.

6-Methyl-2,4-diphenylquinoline (4bm). Yield, 91%; white solid; mp 244–247 °C; Rf 0.52 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 3054, 2915, 1588, 1544, 1488, 1449 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.99 (s, 2H), 7.71 (s, 1H), 7.41 (s, 6H), 6.94 (s, 2H), 6.72 (d, J = 7.5 Hz, 2H), 6.09 (s, 1H), 2.26 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.40, 161.72, 139.95, 136.78, 135.90, 134.10, 133.85, 133.05, 131.17, 130.78,

129.56, 129.29, 128.48, 128.32, 127.20, 123.19, 96.54, 20.76. HRMS (ESI): *m*/*z* called for $C_{22}H_{17}N$ $[M + H]^+$, 296.1443; found, 295.1445.

6-Methoxy-4-ethyl-2-propylquinoline(4bn). Yield, 90%; yellow oil; mp 241–243 °C; Rf 0.55 (petroleum ether/ethyl acetate = 10 : 1); IR (KBr): 3052, 2913, 1586, 1542, 1487, 1448 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, $J = 9.1$ Hz, 1H), 7.66 (s, 1H), 7.18 (d, $J = 2.6$ Hz, 1H), 6.91 (d, $J = 2.4$ Hz, 1H), 3.80 (s, 3H), 2.83 (s, 2H), 2.71 (s, 2H), 1.74 (s, 2H), 1.23 (s, 3H), 0.97 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.32, 156.13, 141.50, 134.59, 131.87, 128.91, 127.14, 119.73, 103.68, 54.41, 36.54, 24.17, 21.87, 13.45, 13.31.

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Notes and references

1 (*a*) G. Jiang and B. List, *Angew. Chem., Int. Ed.*, 2011, **50**, 9471–9474; (*b*) R. De Vreese and M. D'hooghe, *Beilstein J. Org. Chem.*, 2012, **8**, 398–402.

2 J. Li, L. L. Lin, B. W. Hu, X. J. Lian, G. Wang, X. H. Liu and X. F. Feng, *Angew. Chem., Int. Ed.*, 2016, **55**, 6075–6078.

3 B. D. Robertson, R. E. M. Brooner and R. A. Widenhoefer, *Chem.–Eur. J.*, 2015, **21**, 5714–5717.

4 S. Zhang, Z. L. Xu, J. Jia, C. H. Tung and Z. H. Xu, *Chem. Commun.*, 2014, **50**, 12084–12087.

5 G. B. Dong, P. Teo, Z. K. Wickens and R. H. Grubbs, *Science*, 2011, **333**, 1609–1612.

6 S. Dhiman, U. K. Mishra and S. Ramasastry, *Angew. Chem., Int. Ed.*, 2016, **55**, 7737–7741.

7 (*a*) Z. Y. Han, H. Xiao, X. H. Chen and L. Z. Gong, *J. Am. Chem. Soc.*, 2009, **131**, 9182–9183; (*b*) C. Wang, Z. Y. Han, H. W. Luo and L. Z. Gong, *Org. Lett.*, 2010, **12**, 2266–2269; (*c*) Z. Y. Han, D. F. Chen, Y. Y. Wang, R. Guo, P. S. Wang, C. Wang and L. Z. Gong, *J. Am. Chem. Soc.*, 2012, **134**, 6532–6535; (*d*) J. Mo, D. Eom, E. Lee and P. H. Lee, *Org. Lett.*, 2012, **14**, 3684–3687; (*e*) H. Wu, Y. P. He and L. Z. Gong, *Org. Lett.*, 2013, **15**, 460–463; (*f*) D. Qian and J. L. Zhang, *Chem.–Eur. J.*, 2013, **19**, 6984–6988; (*g*) Y. Horino, Y. Takahashi, Y. Nakashima and H. Abe, *RSC Adv.*, 2014, **4**, 6215–6218; (*h*) X. Wu, M. L. Li and P. S. Wang, *J. Org. Chem.*, 2014, **79**, 419–425; (*i*) S. Dhiman and S. S. V. Ramasastry, *Org. Lett.*, 2015, **17**, 5116–5119; (*j*) Y. N. Gao, F. C. Shi, Q. Xu and M. Shi, *Chem.–Eur. J.*, 2016, **22**, 6803–6807; (*k*) F. Zhao, N. Li, Y. F. Zhu and Z. Y. Han, *Org. Lett.*, 2016, **18**, 1506–1509.

8 (*a*) M. Terada and Y. Toda, *Angew. Chem., Int. Ed.*, 2012, **51**, 2093–2097; (*b*) Z. Y. Cao, Y. L. Zhao and J. Zhou, *Chem. Commun.*, 2016, **52**, 2537–2540; (*c*) Y. L. Zhao, Z. Y. Cao, X. P. Zeng, J. M. Shi, Y. H. Yu and J. Zhou, *Chem. Commun.*, 2016, **52**, 3943–3946.

9 G. X. Jiang and B. List, *Adv. Synth. Catal.*, 2011, **353**, 1667–1670.

10 H. Zhang, L. Zhu, S. Z. Wang and Z. J. Yao, *J. Org. Chem.*, 2014, **79**, 7063–7074.

11 (*a*) K. Sorimachi and M. Terada, *J. Am. Chem. Soc.*, 2008, **130**, 14452–14453; (*b*) Q. A. Chen, D. S. Wang, Y. G. Zhou, Y. Duan, H. J. Fan, Y. Yang and Z. Zhang, *J. Am. Chem. Soc.*, 2011, **133**, 6126–6129.

12 (*a*) H. Wu, Y. P. He and L. Z. Gong, *Adv. Synth. Catal.*, 2012, **354**, 975–980; (*b*) D. F. Chen, P. Y. Wu and L. Z. Gong, *Org. Lett.*, 2013, **15**, 3958–3961; (*c*) D. F. Chen, F. Zhao, Y. Hu and L. Z. Gong, *Angew. Chem., Int. Ed.*, 2014, **53**, 10763–10767; (*d*) L. Deiana, Y. Jiang, C. P. Nieto, S. Afewerki, C. Pradillos, O. Verho, C. Tai, E. V. Johnston and A. Córdova, *Angew. Chem., Int. Ed.*, 2014, **53**, 3447–3451; (*e*) D. F. Chen, Z. Y. Han, X. L. Zhou and L. Z. Gong, *Acc. Chem. Res.*, 2014, **47**, 2365–2377; (*f*) X. P. Yin, X. P. Zeng, Y. L. Liu, F. M. Liao, J. S. Yu, F. Zhou and J. Zhou, *Angew. Chem., Int. Ed.*, 2014, **53**, 13740–13745; (*g*) T. Suzuki, Ismiyarto, Y. Ishizaka, D. Y. Zhou, K. Asano and H. Sasai, *Org. Lett.*, 2015, **17**, 5176–5179; (*h*) X. L. Lian, J. Meng and Z. Y. Han, *Org. Lett.*, 2016, **18**, 4270–4273; (*i*) C. C. Pattillo, I. I. Strambeanu, P. Calleja, N. A. Vermeulen, T. Mizuno and M. C. White, *J. Am. Chem. Soc.*, 2016, **138**, 1265–1272; (*j*) M. Lesieur, Y. D. Bidal, F. Lazreg, F. Nahra and C. S. J. Cazin, *ChemCatChem*, 2015, **7**, 2108–2112.

13 H. Yeom, Y. Lee, J. Jeong, E. So, S. Hwang, J. E. Lee, S. S. Lee and S. Shin, *Angew. Chem., Int. Ed.*, 2010, **49**, 1611–1614.

14 (*a*) N. G. Kozlov and L. I. Basalaeva, *Russ. J. Org. Chem.*, 2009, **45**, 587–590; (*b*) N. G. Kozlov and L. I. Basalaeva, *Russ. J. Org. Chem.*, 2001, **71**, 250–256.

15 X. S. Wang, Q. Li, J. R. Wu, Y. L. Li, C. S. Yao and S. J. Tu, *Synthesis*, 2008, **12**, 1902–1910.

16 F. H. Xiao, W. Chen, Y. F. Liao and G. J. Deng, *Org. Biomol. Chem.*, 2012, **10**, 8593–8596.

17 W. Wei, J. W. Wen, D. S. Yang, X. J. Sun, J. M. You, Y. R. Suo and H. Wang, *Tetrahedron*, 2013, **69**, 10747–10751.

18 X. F. Xu, W. M. Liu, Z. Q. Wang, Y. Q. Feng, Y. L. Yan and X. Zhang, *Tetrahedron Lett.*, 2016, **57**, 226–229.

19 (*a*) Y. Wu, C. Chen, G. Jia, X. Y. Zhu, H. M. Sun, G. F. Zhang, W. Q. Zhang and Z. W. Gao, *Chem.–Eur. J.*, 2014, **20**, 8530–8535; (*b*) X. Y. Zhu, C. Chen, B. X. Yu, G. F. Zhang, W. Q. Zhang and Z. W. Gao, *Chem. Lett.*, 2014, **43**, 1832–1834; (*c*) Y. Wu, X. Wang, Y. L. Luo, J. Wang, Y. J. Jian, H. M. Sun, G. F. Zhang, W. Q. Zhang and Z. W. Gao, *RSC Adv.*, 2016, **6**, 15298–15303; (*d*) X. Wang, Z. H. Wang, G. F. Zhang, W. Q. Zhang, Y. Wu and Z. W. Gao, *Eur. J. Org. Chem.*, 2016, **3**, 502–507; (*e*) Y. L. Luo, Y. Wu, Y. Y. Wang, H. M. Sun, Z. Y. Xie, W. Q. Zhang and Z. W. Gao, *RSC Adv.*, 2016, **6**, 66074–66077.

20 M. Daigle, W. H. Bi, M. A. Legare, J. F. Morin and F. G. Fontaine, *Inorg. Chem.*, 2015, **54**, 5547–5555.
21 (*a*) D. Zhan, T. B. Li, H. D. Wei, W. Weng, K. Ghandi and Q. L. Zeng, *RSC Adv.*, 2013, **3**, 9325–9329; (*b*) R. Jalil, W. Voelter and M. Saeed, *Tetrahedron Lett.*, 2004, **45**, 3475–3476; (*c*) I. E. Marko, P. R. Giles, M. Tsukazaki, S. M. Brown and C. J. Urch, *Science*, 1996, **274**, 2044–2046; (*d*) S. Velusamy and T. Punniyamurthy, *Tetrahedron Lett.*, 2003, **44**, 8955–8957.