RSC Advances

PAPER

View Article Online
View Journal | View Issue

Check for updates

Cite this: *RSC Adv.*, 2020, **10**, 24830

Copper(II)-catalyzed synthesis of multisubstituted indoles through sequential Chan–Lam and cross-dehydrogenative coupling reactions†

Xin Chen,[ab] Yunyun Bian,[a] Baichuan Mo,[ab] Peng Sun,[ab] Chunxia Chen*[ab] and Jinsong Peng *[a]

Received 24th May 2020
Accepted 22nd June 2020

DOI: 10.1039/d0ra04592f

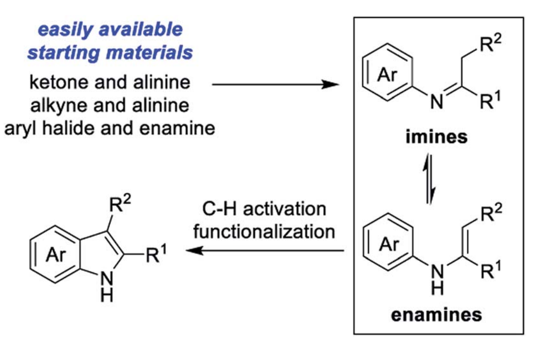
rsc.li/rsc-advances

Starting from arylboronic acids and ester (*Z*)-3-aminoacrylates, one-pot syntheses of diverse indole-3-carboxylic esters have been described through copper(II)-catalyzed sequential Chan–Lam *N*-arylation and cross-dehydrogenative coupling (CDC) reactions. The initial Chan–Lam arylation can proceed in DMF at 100 °C for 24 h to give ester (*Z*)-3-(arylamino)acrylate intermediates in the presence of $Cu(OAc)_2$/tri-*tert*-butylphosphine tetrafluoroborate, a catalytic amount of myristic acid as the additive, $KMnO_4$ and $KHCO_3$. Sequentially, these *in situ* arylated intermediates can undergo an intramolecular oxidative cross-dehydrogenative coupling process in mixed solvents (DMF/DMSO = 2 : 1) at 130 °C to give C3-functionalized multi-substituted indole derivatives.

1. Introduction

The indole unit is not only one of the most abundant structural motifs in natural products,[1] but is also ubiquitous among agrochemicals,[2] marketed medicines (such as dolasetron, tropisetron, indomethacin, proglumetacin, and ondansetron),[3] and progressive functional materials.[4] In particular, substituted indoles have been utilized as "privileged scaffolds" for drug discovery of anti-inflammatory, antihypertensive, anti-tumor, anti-HIV, and antimigraine agents.[5] Considering the importance of indole scaffolds for pharmaceutical research, the development of practical syntheses of indole derivatives is of immense interest to synthetic chemists.

Over the past century, a variety of approaches for indole preparation have been well established.[6] While numerous classical procedures based on condensation and cyclization have been developed,[6b] there is still a great demand to explore new strategies and methodologies for the modular synthesis of functionalized indoles from easily available starting materials. Over the past decades, transition metal-mediated inter- and intramolecular C–C and C–N bond forming reactions have emerged as one of the most powerful and popular tools for indole syntheses.[7] Following this tendency, an attractive C–H activation/cyclization strategy relying on the use of *N*-arylated enamine or imine intermediates have emerged in recent years (Scheme 1). In 2008, Glorius group[8a] reported the first Pd-catalyzed oxidative cyclization of *N*-aryl enaminones/esters for indole syntheses with $Cu(OAc)_2$ as the oxidant. Shortly afterward, Cacchi[9] demonstrated a copper-catalyzed aerobic version for the synthesis of indoles from *N*-aryl enaminones in DMF. Subsequent to these original works, different catalytic system (Pd,[10] Cu,[11] Fe,[12] PIDA,[13] I_2,[14] visible light,[15] photoredox/metal,[16] and electricity[17]) have been widely investigated to enlarge the substrate scope. Using simple and easily available substrates, domino one-pot processes combining the *in situ* formation of *N*-arylated enamines or imines with subsequent cyclization have also been developed for the synthesis of indoles. For instance, Jiao group[18] pioneered studies to construct an indole backbone through an efficient Pd-catalyzed aerobic oxidative C–H functionalization approach from simple anilines and activated

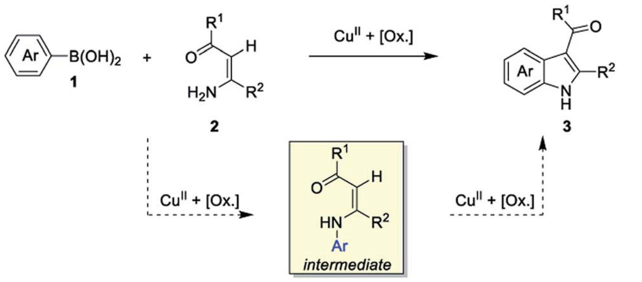


Scheme 1 Metal-catalyzed indole syntheses based on the *N*-arylated enamines and imines.

[a]College of Chemistry, Chemical Engineering and Resource Utilization, Northeast Forestry University, No. 26 Hexing Road, Harbin, 150040, P. R. China

[b]Material Science and Engineering College, Northeast Forestry University, No. 26 Hexing Road, Harbin, 150040, P. R. China. E-mail: ccx1759@163.com; jspeng1998@nefu.edu.cn

† Electronic supplementary information (ESI) available: Copies of ^1H, ^{13}C NMR, HRMS and IR spectra for new compounds. See DOI: 10.1039/d0ra04592f

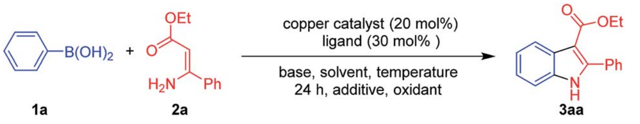


Scheme 2 Prospected sequence for the synthesis of indoles.

alkynes. Recently, Zhang and Cao[19] reported a one-pot synthesis of 2-(perfluoroalkyl)indoles through sequential Michael-type addition and Pd(II)-catalyzed cross-dehydrogenative coupling reaction of anilines and methyl perfluoroalk-2-ynoates with oxygen as the sole oxidant. Yoshikai group[20] developed a Pd-catalyzed method for the synthesis of indoles from *N*-aryl imines directly derived from simple and obtainable anilines and ketones. In addition, using simple anilines[21] or aniline derivatives with directing groups,[22–27] various transitional metal-catalyzed (such as Rh,[22] Ru,[23] Pd,[24] Au,[25] Ni,[26] and Co[27]) protocols have been well established through group-directed oxidative C–H annulation of alkynes.

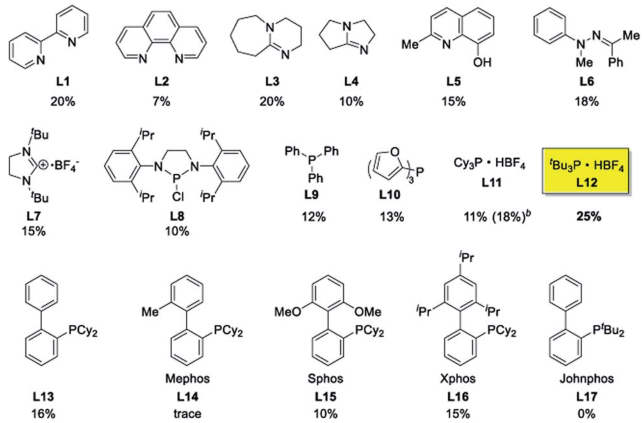
We have been devoting our efforts to develop metal-catalyzed sequential one-pot processes containing a direct C–H functionalization step for the construction of heterocyclic frameworks.[28] Over the past decades, oxidative cross-dehydrogenative coupling (CDC) reactions have emerged as one of the most powerful routes for C–C bond formations in organic synthesis.[29]

Table 1 Condition optimization for the copper-catalyzed synthesis of indole **3aa**[a]



Entry	Cu/ligand	Base	Solvent	Oxidant	Yield[b] [%]
1	CuI/L1	$KHCO_3$	DMF	Air	10/6[c]/7[d]
2	CuBr/L1	$KHCO_3$	DMF	Air	Trace
3	CuCl/L1	$KHCO_3$	DMF	Air	Trace
4	Cu_2O/L1	$KHCO_3$	DMF	Air	Trace
5	$Cu(OTf)_2$/L1	$KHCO_3$	DMF	Air	5
6	$CuCl_2$/L1	$KHCO_3$	DMF	Air	8
7	$CuBr_2$/L1	$KHCO_3$	DMF	Air	7
8	$CuSO_4\cdot 5H_2O$/L1	$KHCO_3$	DMF	Air	10
9	$Cu(OAc)_2$/L1	$KHCO_3$	DMF	Air	20
10	$Cu(acac)_2$/L1	$KHCO_3$	DMF	Air	14
11	CuO/L1	$KHCO_3$	DMF	Air	0
12[e]	$Cu(OAc)_2$/L2-L17	$KHCO_3$	DMF	Air	0–25
13	$Cu(OAc)_2$	$KHCO_3$	DMF	Air	0
14[f]	$Cu(OAc)_2$/L12	$KHCO_3$	DMF	—	0
15	$Cu(OAc)_2$/L12	K_2CO_3	DMF	Air	15
16	$Cu(OAc)_2$/L12	NaOH	DMF	Air	0
17	$Cu(OAc)_2$/L12	Li_2CO_3	DMF	Air	0
18	$Cu(OAc)_2$/L12	K_3PO_4	DMF	Air	20
19	$Cu(OAc)_2$/L12	$NaHCO_3$	DMF	Air	17
20	$Cu(OAc)_2$/L12	NaOAc	DMF	Air	18
21	$Cu(OAc)_2$/L12	$KHCO_3$	DMSO	Air	10
22	$Cu(OAc)_2$/L12	$KHCO_3$	THF	Air	15
23	$Cu(OAc)_2$/L12	$KHCO_3$	1,4-Dioxane	Air	Trace
24	$Cu(OAc)_2$/L12	$KHCO_3$	DMA	Air	19
25	$Cu(OAc)_2$/L12	$KHCO_3$	*tert*-Pentyl alcohol	Air	20
26	$Cu(OAc)_2$/L12	$KHCO_3$	DMF/DMSO	Air	33 (37)[g]
27[g]	$Cu(OAc)_2$/L12	$KHCO_3$	DMF/DMSO	$KMnO_4$	48
28[g]	$Cu(OAc)_2$/L12	$KHCO_3$	DMF/DMSO	$K_2S_2O_8$	21
29[g]	$Cu(OAc)_2$/L12	$KHCO_3$	DMF/DMSO	TBHP	20
30[g]	$Cu(OAc)_2$/L12	$KHCO_3$	DMF/DMSO	MnO_2	30
31[g]	**$Cu(OAc)_2$/L12**	**$KHCO_3$**	**DMF/DMSO**	**$KMnO_4$**	**55**[h]
32[g]	$Cu(OAc)_2$/L12	$KHCO_3$	DMF/DMSO	$KMnO_4$	47[i]
33[g]	$Cu(OAc)_2$/L12	$KHCO_3$	DMF/DMSO	$KMnO_4$	48[j]
34[g]	$Cu(OAc)_2$/L12	$KHCO_3$	DMF/DMSO	$KMnO_4$	45[k]

[a] Reaction conditions unless otherwise stated: **1a** (0.5 mmol), **2a** (0.2 mmol), base (0.6 mmol), catalyst (20 mol%), ligand (30 mol%), solvent (1.0 mL), air or oxidant, 70 °C, 24 h, air. [b] Isolated yield. [c] 1.5 equiv. of **1a**. [d] 2.0 equiv. of **1a**. [e] The effect of various ligands was investigated, see Scheme 1. [f] N_2. [g] DMF (1.0 mL), 100 °C, 24 h; then DMSO (0.5 mL), 130 °C, 24 h. [h] 20 mol% of myristic acid was added. [i] 20 mol% of palmitic acid was added. [j] 20 mol% of stearic acid was added. [k] 20 mol% of trimethylacetic acid was added.



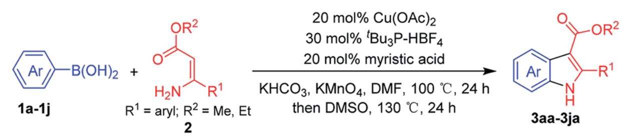
Scheme 3 Effect of ligands on the copper-catalyzed annulations reaction. [a] Reaction conditions: 20 mol% $Cu(OAc)_2$, $KHCO_3$, DMF, air, 70 °C, 24 h; isolated yields. [b] PCy_3 was directly used.

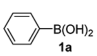
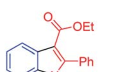
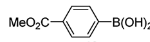
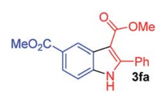
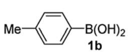
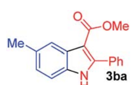
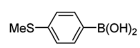
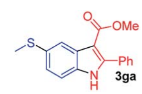
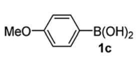
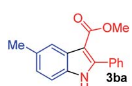
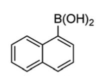
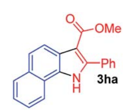
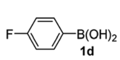
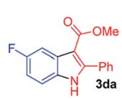
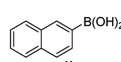
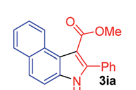
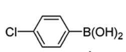
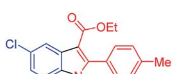
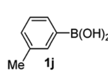
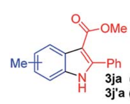
For indole syntheses, we recently developed a Cu(I)-catalyzed 2-fold arylation process through a tandem Ullmann-type C–N and cross-dehydrogenative coupling sequence from enamines and aryl iodides.[30] More recently, a one-pot synthesis of 2-aryl indole-3-carboxylate derivatives has also been established by our group through stoichiometric copper salt-mediated sequential hydroamination and cross-dehydrogenative coupling reaction from simple anilines and ester arylpropiolates.[31] Subsequent to our previous works, we became interested in developing a new entry to multi-substituted indoles from arylboronic acids and enamines through sequential copper(II)-catalyzed Chan–Lam oxidative *N*-arylation and cross-dehydrogenative coupling reaction (Scheme 2). Several potential issues need to be addressed: (1) the Chan–Lam arylation has been extended to numerous nucleophilic partners for carbon–heteroatom bonds formation,[32] but not to enamines. (2) The Chan–Lam *N*-arylation involving arylboronic acids is known to occur in the presence of Cu(II) catalyst, while the Cu(I) catalyst has usually been employed in the C–H functionalization step.[9,30] Merging fundamentally different copper catalysis into one-pot reaction is still challenging.

2. Results and discussion

Ethyl (*Z*)-3-amino-3-phenylacrylate (**2a**) was selected as the substrate to react with phenylboronic acid (**1a**) in the presence of different combinations of copper catalysts, ligands, bases, solvents and oxidants (Table 1). The blank experiment (without copper catalyst and ligand) was examined in DMF at 70 °C for 24 h using $KHCO_3$ as the base, and no desired product **3aa** was obtained. A survey of copper catalysts showed that $Cu(OAc)_2$ provided better results (20% yield) than CuI, CuBr, CuCl, Cu_2O, $Cu(OTf)_2$, $CuCl_2$, $CuBr_2$, $CuSO_4 \cdot 5H_2O$, $Cu(acac)_2$ and CuO (0–

Table 2 The substrate scope of arylboronic acids[a]

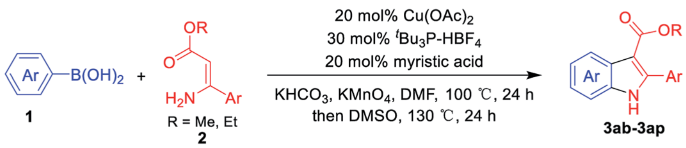


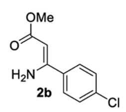
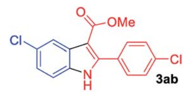
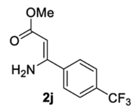
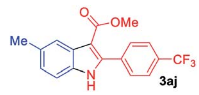
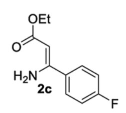
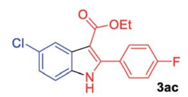
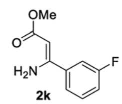
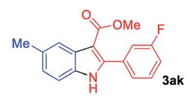
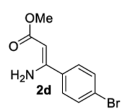
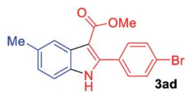
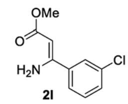
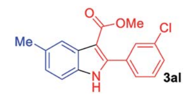
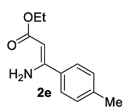
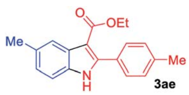
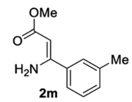
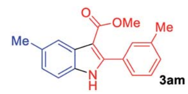
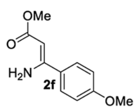
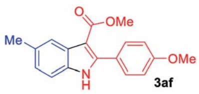
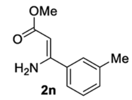
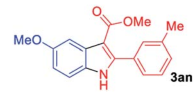
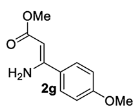
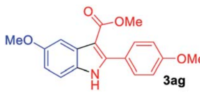
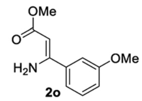
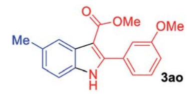
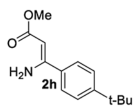
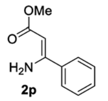
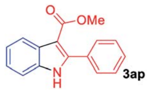
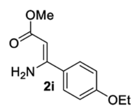
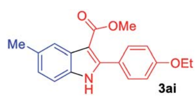
Entry	S-1	P-3	Yield[b]	Entry	S-1	P-3	Yield[b]
1	 1a	 3aa	55	6	 1f	 3fa	44
2	 1b	 3ba	54	7	 1g	 3ga	50
3	 1c	 3ba	51	8	 1h	 3ha	49
4	 1d	 3da	47	9	 1i	 3ia	50
5	 1e	 3ea	46	10[c]	 1j	 3ja (6-Me) 3j'a (4-Me)	52 (2 : 1)

[a] Reaction conditions: **2** (0.2 mmol), arylboronic acids **1** (0.5 mmol), $Cu(OAc)_2$ (20 mol%), $^tBu_3P \cdot HBF_4$ (30 mol%), myristic acid (0.04 mmol), $KHCO_3$ (0.6 mmol), $KMnO_4$ (0.1 mmol), DMF (1 mL), 100 °C, 24 h; then DMSO (0.5 mL), 130 °C, 24 h, air. [b] Yield of the isolated product. [c] The ratio of the regioisomers was determined by NMR analysis.

14% yields) with 2,2′-bipyridine (**L1**) as the ligand and air as the oxidant (entries 1–11). To increase the yield of **3aa**, we then investigated the effect of various ligands (nitrogen-containing ligands **L2–L6**,[33] *N*-heterocarbene ligand **L7**, monophosphorous ligands **L8–L12**, and Buchwald-type bulky biaryl phosphine ligands **L13–L17**, Scheme 3) on the reaction using $Cu(OAc)_2$ as the catalyst (entry 7, Table 1). It turned out that $^tBu_3P\cdot HBF_4$ (**L12**) performed best, and the yield was improved to 25% with $KHCO_3$ as the base under air atmosphere (Scheme 3). It is worth noting that ligand and oxidant are essential to this transformation and **3aa** was not produced in the absence of ligand (entry 13) or oxidant (entry 14). The effect of other bases such as K_2CO_3, NaOH, Li_2CO_3, K_3PO_4, $NaHCO_3$, and NaOAc on the reaction was next examined (entries 15–20), $KHCO_3$ provided a better result with 25% isolated yield. A survey of reaction media showed that the use of DMF provided better results than those obtained in DMSO, THF, 1,4-dioxane, DMA, and *tert*-pentyl alcohol (entries 21–25). The binary mixed solvent composed of DMF and DMSO (DMF/DMSO, 2 : 1) gave the final product **3aa** in 33% yield at 70 °C (entry 26). With increased reaction temperature and time, the yield of **3aa** can been improved from 33% to 37% (entry 26). Among the range of oxidants ($KMnO_4$, $K_2S_2O_8$, TBHP, MnO_2, and O_2, entries 26–30) that were surveyed, $KMnO_4$ appeared to be optimal and gave **3aa** with an enhanced yield (48%, entry 27). Attempts have been made under higher air or O_2 pressure (3 atm), however, the yields cannot obviously be improved. In 2001, Buchwald and co-workers demonstrated that aliphatic acid can increase the

Table 3 Variation of the enamine unit[a]



Entry	S-1	P-3	Yield[b]	Entry	S-1	P-3	Yield[b]
1	 2b	 3ab	47	9	 2j	 3aj	49
2	 2c	 3ac	42	10	 2k	 3ak	47
3	 2d	 3ad	46	11	 2l	 3al	46
4	 2e	 3ae	49	12	 2m	 3am	49
5	 2f	 3af	53	13	 2n	 3an	49
6	 2g	 3ag	51	14	 2o	 3ao	48
7	 2h	 3ah	52	15	 2p	 3ap	51
8	 2i	 3ai	46				

[a] Reaction conditions: **2** (0.2 mmol), arylboronic acids **1** (0.5 mmol), $Cu(OAc)_2$ (20 mol%), $^tBu_3P\cdot HBF_4$ (30 mol%), myristic acid (0.04 mmol), $KHCO_3$ (0.6 mmol), $KMnO_4$ (0.1 mmol), DMF (1 mL), 100 °C, 24 h; then DMSO (0.5 mL), 130 °C, 24 h, air. [b] Yield of the isolated product.

copper-catalyzed coupling reaction rate of arylboronic acids and amines through the coordination of aliphatic acid to the copper center to improve solubility of the copper catalyst in organic solvents.[34] Given the importance of aliphatic acids in achieving a homogeneous catalyst system, various carboxylic acids such as myristic acid, palmitic acid, stearic acid, and trimethylacetic acid were explored as the additive. It was found that the addition of 1 equiv of myristic acid relative to $Cu(OAc)_2$ improved the yield of **3aa** to 55% (entry 31), while other carboxylic acids had little effect on the reaction (entries 32–34). In general, in the presence of combinations of $Cu(OAc)_2$, $^t Bu_3P \cdot HBF_4$, $KHCO_3$, myristic acid and $KMnO_4$, the synthesis of indoles **3** was conducted in a one-pot fashion using DMF/DMSO as mixed solvents.

Having established the feasibility of indole synthesis *via* copper(II)-catalyzed sequential oxidative Chan–Lam arylation/CDC process, we then explored the generality of arylboronic acids using methyl or ethyl (*Z*)-3-amino-3-phenylacrylate as the coupling partner (Table 2). As shown in Table 2, diverse substituents (such as Me, OMe, F, Cl, ester, and methylthio) on the aromatic moiety of boronic acids were applicable, and the corresponding indole products **3aa–3ja** can be obtained in 44–55% yields. Arylboronic acids containing electron-donating groups at the *para* (**1b**, **1c**, and **1g**), or *meta* (**1j**) position were generally more reactive than those bearing electron-withdrawing substituents (**1d–1f**) and provided higher yields (entries 2–7, and 10, Table 2). However, the incorporation of substituents in the *ortho* position of arylboronic acid seriously hampered copper-catalyzed oxidative annulation process, and the corresponding indoles cannot be obtained. In addition, *α*- or *β*-naphthyl boronic acids **1h** and **1i** can also be smoothly transformed into the corresponding products **3ha** and **3ia** in 49% and 50% yields, respectively (entries 8 and 9). For β-naphthyl boronic acid **1i**, there are two possible C–H activation sites (*α*- and *β*-position), the CDC process occurred only at the *α*-site to give a single regioisomer **3ia** (entry 9). The specificity of site selectivity (α/β) implies that the aromatic C–H alkenylation is probably an outcome of electrophilic aromatic substitutions. However, regioselectivity issues surfaced for *meta*-substituted arylboronic acid (**1j**), and a mixture of two regioisomers (**3ja** and **3j′a**) was obtained in a nearly 2 : 1 ratio, indicating intramolecular CDC reaction occurred at the most sterically accessible site (entry 10).

The scope and limitation of ester (*Z*)-3-aminoacrylate substrates were finally investigated in this one-pot sequential oxidative process. As shown in Table 3, several functional groups (such as Me, OMe, OEt, ^{t}Bu, F, Cl, Br and CF_3) are tolerated under the standard conditions. For ester (*Z*)-3-amino-3-arylpropiolates, the electronic nature of the aromatic motifs did not seem to affect the efficiency: both electron-donating (Me, MeO, EtO, and ^{t}Bu) and electron-withdrawing substituents (F, Cl, Br, and CF_3) can be incorporated at the *para* (**2b–2j**, entries 1–9) and *meta* (**2k–2o**, entries 10–14) position, providing indole derivatives **3ab–3ao** in 42–53% yields. However, ester (*Z*)-3-amino-3-arylpropiolates (**2p–2r**, Fig. 1) with substituents in the *ortho* position of aromatic ring cannot proceed to give the corresponding products, probably because of the strong steric

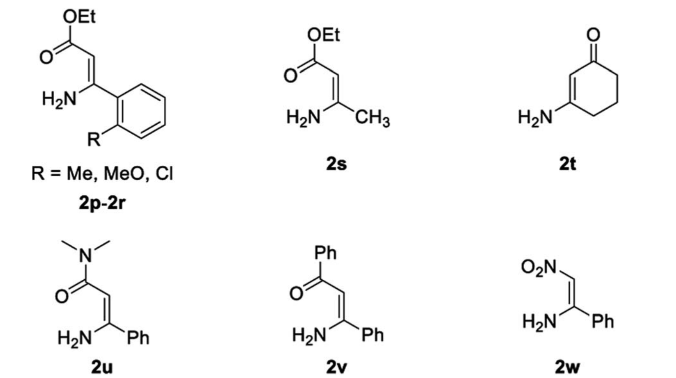
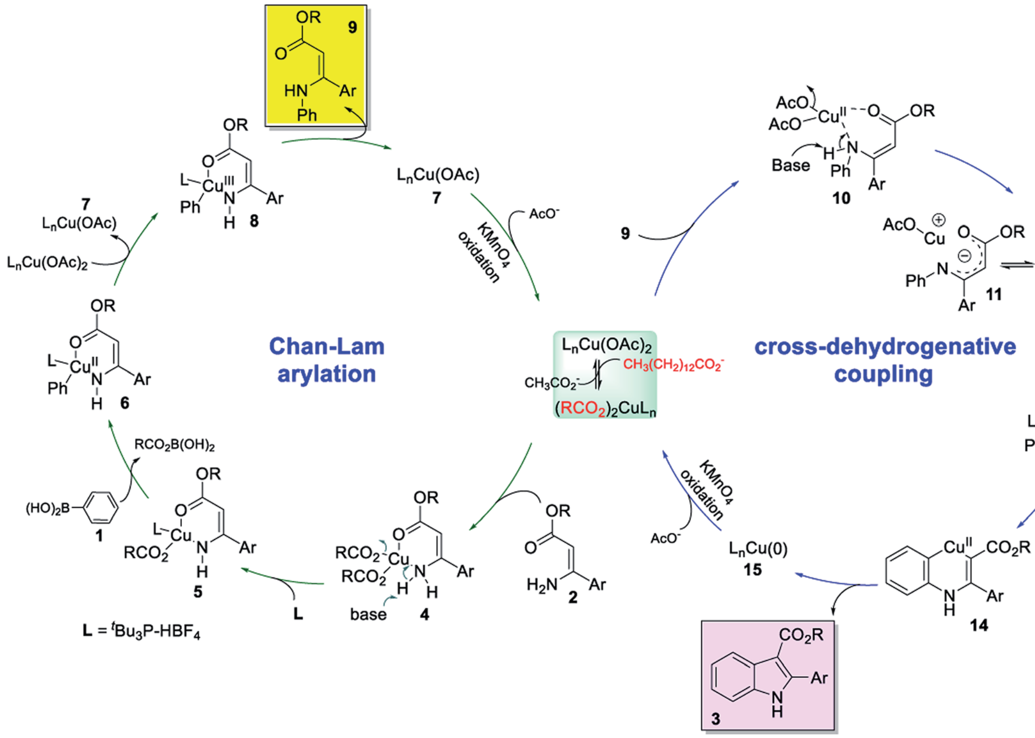


Fig. 1 Unsuccessful enamine substrates.

repulsion of the *ortho* substituent. In addition, when the scope of substrates was extended to aliphatic and carbocyclic enamines [for example, ethyl (*Z*)-3-aminobut-2-enoate **2s** and 3-aminocyclohex-2-en-1-one **2u**, Fig. 1], the reaction did not happen to give the corresponding products. Enamine substrates with an amide (**2t**), aromatic ketone (**2v**) or nitro group (**2w**) were also examined under the standard conditions; however, no product can be obtained. These unsuccessful results indicated that the electron density of olefin moiety was highly essential for CDC process.

To gain insight into the mechanism of the reaction, some designed control experiments were conducted. When the reaction of **1a** and **2a** was conducted in DMF for 24 h, the Chan–Lam *N*-arylated intermediate **9** and **3aa** can be isolated in 68% and 10% yields, respectively. Then, the intermediate **9** was carried out under the optimized reaction conditions, 65% of the desired product **3aa** was obtained. Based on the above results and previous literature reports from our group[30,31] and others,[35] a reaction mechanism for the copper(II)-catalyzed oxidative annulation of enamines with arylboronic acids was proposed. The Scheme 4 showed a simplified sequence of events beginning with the $Cu(OAc)_2$. First, a soluble active cupric tetradecanoate species was formed through the anion exchange reaction of $Cu(OAc)_2$ and myristic acid in the presence of base.[34] The coordination of (*Z*)-enamine **2** to the Cu(II) center to form **4**, which then reacted with a base to form a Cu–N bond and afforded an intermediate complex **5**. Engagement of arylboronic acid **1** led to transmetalation *via* 4-membered transition state[35a] and delivered aryl-Cu(II) species **6**. The intermediate **6** was then oxidized by Cu(II) to form an Cu(III) species **8**, and the subsequent reductive elimination gave *N*-arylated intermediate **9** and a Cu(I)OAc species **7**. Completion of the catalytic cycle was achieved *via* oxidation to Cu(II) in the presence of $KMnO_4$ (Chan–Lam C–N coupling process). The coordination of *N*-arylated intermediate **9** to Cu(II) gave a six-membered chelate ring complex **10**. A new C–Cu(II) complex **12** was then formed through sequential a base-promoted deprotonation of N–H, dissociation of acetate anion and complexation of the resulting cationic Cu(II) species at *α*-carbon of **11**. A deprotonation/re-protonation process of alkyl-Cu(II) complex **12** afforded an alkenyl copper **13** under basic conditions. *Ortho*-cupration of



Scheme 4 Proposed catalytic pathway for the formation of indole **3**.

phenyl ring of **13** provided a six-membered copper-cycle intermediate **14**,[9] which was then transformed into the product **3** and Cu(0) species **15** through reductive elimination process. Finally, Cu(0) was oxidized to the active Cu(II) catalyst by $KMnO_4$ for the next Chan–Lam arylation reaction.

3. Conclusions

In summary, we have developed a new one-pot approach to diverse multi-substituted indoles through copper-catalyzed oxidative annulations of enamines with readily accessible arylboronic acids. The accomplished reaction comprises an intermolecular Chan–Lam arylation followed by an intramolecular cross-dehydrogenative coupling reaction promoted by the same copper catalyst. The success of the reaction heavily relies on the careful selection of proper additive and oxidant. The combination of myristic acid and $KMnO_4$ was found to be essential for the formation of C3-functionalized multi-substituted indoles. Considering a broad substrate scope and considerable valance of the products for medicinal science, this novel synthetic method could be of utility for the discovery of drugs.

4. Experimental section

4.1. General information

Chemicals were all purchased from commercial supplies and used without further purification unless otherwise stated. Solvents were dried and purified according to the standard procedures before use. Reactions were monitored by analytical thin-layer chromatography (TLC). All reactions were conducted in dried glassware. Purification of reaction products was done by flash chromatography with 230–400 mesh silica gel. Ester (*Z*)-3-aryl-3-aminoacrylate substrates were prepared according to the literature methods.[36] Melting points were determined on a melting point apparatus in open capillaries and are uncorrected. Infrared spectra of samples were recorded from 4000 to 500 cm^{-1} in ATR (attenuated total reflectance) mode using an FT-IR instrument. ^1H NMR spectra were recorded on a 400 or 500 MHz spectrometer, and ^{13}C NMR spectra were recorded at 100, 125 or 150 MHz. Unless otherwise stated, deuterochloroform ($CDCl_3$) was used as a solvent. Chemical shifts (δ) are given in parts per million downfield relative to tetramethylsilane (TMS). Chemical shifts for carbon resonances are reported in parts per million and are referenced to the carbon resonance of the solvent $CHCl_3$ (δ = 77.16 ppm). The splitting patterns are reported as s (singlet), d (doublet), dd (double doublet), td (triplet of doublet), t (triplet), q (quartet), br (broad), and m (multiplet). Coupling constants are given in hertz. High-resolution mass spectra were recorded on a BIO TOF Q mass spectrometer equipped with an electrospray ion source (ESI), operated in the positive mode.

4.2. General procedure for synthesis of indole-3-carboxylate derivatives

A 10 mL Schlenk tube or standard vial equipped with a magnetic stirring bar was charged with ester (*Z*)-3-aryl-3-aminoacrylates (0.2 mmol, 1.0 equiv.), aryl boronic acid (0.5 mmol, 2.5 equiv.), $KMnO_4$ (0.1 mmol, 15.8 mg), and $KHCO_3$ (60 mg, 0.6 mmol, 3.0 equiv.), and then $Cu(OAc)_2$ (0.04 mmol, 8.0 mg), $^tBu_3P\cdot HBF_4$ (0.06 mmol, 17.4 mg) and myristic acid (0.04 mmol, 9.1 mg) were added. Finally, DMF (1.0 mL) was added to the mixture *via* syringe at room temperature under air. The vial was sealed and put into a preheated oil bath at 100 °C for 24 h. The mixture was cooled to room temperature, dimethyl sulfoxide (0.5 mL) was then added *via* syringe, and the reaction mixture was heated to 130 °C for another 24 h. Finally, the mixture was cooled to room temperature, quenched with water (3 mL), and diluted with ethyl acetate (5 mL). The layers were separated, and the aqueous layer was extracted with 3 × 5 mL of ethyl acetate. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under vacuum. The crude product was then purified by a chromatography silica gel (H), eluting with ethyl acetate/petroleum ether (10–15%).

Ethyl 2-phenyl-1*H*-indole-3-carboxylate (3aa).[37] Yield, 55% (29.2 mg); white solid, mp 155–158 °C; IR (KBr, cm^{-1}): 3254, 1662, 1450, 1430, 1270, 1212, 1129, 1047, 744, 690; ^1H NMR (400 MHz, $CDCl_3$) δ 8.76 (br, 1H), 8.22–8.20 (d, J = 7.2 Hz, 1H), 7.61–7.59 (m, 2H), 7.37–7.35 (m, 3H), 7.33–7.31 (m, 1H), 7.27–7.21 (m, 2H), 4.26 (q, J = 7.1 Hz, 2H), 1.28 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.5, 143.6, 134.2, 131.0, 128.6, 128.1, 127.0, 126.5, 122.1, 121.0, 120.9, 110.1, 103.4, 58.7, 13.3.

Methyl 5-chloro-2-(4-chlorophenyl)-1*H*-indole-3-carboxylate (3ab). Yield, 47% (30.0 mg); light yellow solid, mp 163–165 °C; IR (KBr, cm^{-1}): 3249, 1677, 1666, 1485, 1444, 1296, 1210, 1135, 1091, 786, 800, 823; ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.17–8.16 (d, J = 1.6 Hz, 1H), 7.58–7.56 (d, J = 8.5 Hz, 2H), 7.42–7.40 (d, J = 8.5 Hz, 2H), 7.30–7.28 (m, 1H), 7.25–7.22 (m, 1H), 3.85 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.3, 143.3, 134.7, 132.5, 129.8, 128.7, 127.5, 127.4, 127.1, 122.9, 120.8, 111.1, 103.5, 50.2. HRMS-ESI (*m*/*z*) calcd for $C_{16}H_{12}Cl_2NO_2^+$ (M + H)$^+$ 320.02396, found 320.02390.

Ethyl 5-chloro-2-(4-fluorophenyl)-1*H*-indole-3-carboxylate (3ac). Yield, 42% (26.7 mg); light yellow solid, mp 149–151 °C; IR (KBr, cm^{-1}): 3416, 1673, 1497, 1447, 1212, 1130, 840, 804, 786; ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.19–8.18 (d, J = 1.2 Hz, 1H), 7.64–7.60 (dd, J = 8.5, 5.4 Hz, 2H), 7.30–7.27 (m, 1H), 7.24–7.21 (m, 1H), 7.13 (t, J = 8.6 Hz, 2H), 4.32 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.9, 163.4 (164.2, 162.6, d, $^1J_{C-F}$ = 249 Hz), 144.5, 133.4, 131.5 (131.6, 131.5, d, $^3J_{C-F}$ = 8 Hz), 128.6, 128.0, 127.6 (127.6, 127.5, d, $^4J_{C-F}$ = 3 Hz), 123.8, 121.8, 115.3 (115.4, 115.3, d, $^2J_{C-F}$ = 21 Hz), 112.1, 104.6, 60.0, 14.4. HRMS-ESI (*m*/*z*) calcd for $C_{17}H_{14}ClFNO_2^+$ (M + H)$^+$ 318.06916, found 318.06912.

Methyl 2-(4-bromophenyl)-5-methyl-1*H*-indole-3-carboxylate (3ad). Yield, 46% (31.7 mg); orange solid, mp 160–162 °C; IR (KBr, cm^{-1}): 3307, 1672, 1444, 1124, 830, 790; ^1H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 7.98 (s, 1H), 7.57–7.49 (q, J = 7.6 Hz, 4H), 7.27 (d, J = 8.1 Hz, 1H), 7.11 (d, J = 8.1 Hz, 1H), 3.84 (s, 3H), 2.50 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.8, 143.1, 133.5, 131.9, 131.4, 131.1, 131.0, 127.7, 125.2, 123.6, 121.8, 110.7, 104.4, 51.0, 21.7. HRMS-ESI (*m*/*z*) calcd for $C_{17}H_{15}BrNO_2^+$ (M + H)$^+$ 344.02807, found 344.02802.

Ethyl 5-methyl-2-(*p*-tolyl)-1*H*-indole-3-carboxylate (3ae). Yield, 49% (27.4 mg); white solid, mp 157–159 °C; IR (KBr, cm^{-1}): 3280, 1656, 1440, 1267, 1217, 1158, 1143, 1048, 800, 790; ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.04 (s, 1H), 7.57 (d, J = 8.0 Hz, 2H), 7.29–7.27 (m, 3H), 7.11 (d, J = 8.2 Hz, 1H), 4.34 (q, J = 7.1 Hz, 2H), 2.53 (s, 3H), 2.43 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.5, 144.7, 139.2, 133.4, 131.5, 129.5, 129.2, 128.8, 128.0, 124.6, 121.8, 110.6, 104.1, 59.6, 21.8, 21.4, 14.4. HRMS-ESI (*m*/*z*) calcd for $C_{19}H_{20}NO_2^+$ (M + H)$^+$ 294.14886, found 294.14856.

Methyl 2-(4-methoxyphenyl)-5-methyl-1*H*-indole-3-carboxylate (3af). Yield, 53% (31.3 mg); white solid, mp 156–158 °C; IR (KBr, cm^{-1}): 3247, 1668, 1643, 1501, 1454, 1282, 1134, 832, 801, 792; ^1H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.97 (s, 1H), 7.56 (d, J = 8.6 Hz, 2H), 7.23–7.21 (m, 1H), 7.06 (d, J = 8.8 Hz, 1H), 6.92 (d, J = 8.6 Hz, 2H), 3.83 (s, 3H), 3.81 (s, 3H), 2.49 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.1, 159.2, 143.8, 132.3, 130.4, 129.79, 126.8, 123.5, 123.2, 120.6, 112.6, 109.6, 102.4, 54.3, 49.8, 20.7. HRMS-ESI (*m*/*z*) calcd for $C_{18}H_{18}NO_3^+$ (M + H)$^+$ 296.12812, found 296.12836.

Methyl 5-methoxy-2-(4-methoxyphenyl)-1*H*-indole-3-carboxylate (3ag). Yield, 51% (31.8 mg); yellow solid, mp 158–159 °C; IR (KBr, cm^{-1}): 3226, 1664, 1499, 1488, 1454, 1252, 1209, 1172, 1137, 842, 825, 811, 788; ^1H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.70 (d, J = 2 Hz, 1H), 7.58 (d, J = 8.6 Hz, 2H), 7.24 (s, 1H), 6.97 (d, J = 8.6 Hz, 2H), 6.90 (dd, J = 8.6, 2.2 Hz, 1H), 3.91 (s, 3H), 3.85 (s, 3H), 3.83 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.0, 159.3, 154.7, 144.0, 129.8, 129.0, 127.5, 123.3, 112.6, 112.1, 110.6, 102.7, 54.8, 54.3, 49.8. HRMS-ESI (*m*/*z*) calcd for $C_{18}H_{18}NO_4^+$ (M + H)$^+$ 312.12303, found 312.12314.

Methyl 2-[4-(*tert*-butyl) phenyl]-5-methyl-1*H*-indole-3-carboxylate (3ah). Yield, 52% (33.4 mg); white solid, mp 189–190 °C; IR (KBr, cm^{-1}): 3267, 1674, 1443, 1201, 1284, 1158, 1119, 861, 789, 780; ^1H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.00 (s, 1H), 7.61 (d, J = 8.5 Hz, 2H), 7.48 (d, J = 8.5 Hz, 2H), 7.28 (s, 1H), 7.09 (d, J = 8.3 Hz, 2H), 3.86 (s, 3H), 2.51 (s, 3H), 1.36 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.0, 151.3, 143.8, 132.3, 130.5, 128.1, 128.0, 126.8, 124.2, 123.6, 120.7, 109.6, 102.7, 49.9, 33.8, 30.2, 20.7. HRMS-ESI (*m*/*z*) calcd for $C_{21}H_{24}NO_2^+$ (M + H)$^+$ 322.18016, found 322.18030.

Methyl 2-(4-ethoxyphenyl)-5-methyl-1*H*-indole-3-carboxylate (3ai). Yield, 46% (28.4 mg); white solid, mp 195–197 °C; IR (KBr, cm^{-1}): 3257, 1652, 1612, 1457, 1450, 1260, 1250, 1181, 1142, 1048, 848, 799, 790; ^1H NMR (500 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.98 (s, 1H), 7.58 (d, J = 8.8 Hz, 2H), 7.24 (s, 1H), 7.07 (d, J = 9.0 Hz, 2H), 6.94 (d, J = 8.8 Hz, 2H), 4.06 (q, J = 7.0 Hz, 2H), 3.85 (s, 3H), 2.50 (s, 3H), 1.44 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.0, 158.7, 143.7, 132.3, 130.5, 129.8, 126.9, 123.5, 123.1, 120.7, 113.1, 109.5, 102.4, 62.5, 49.8, 20.7, 13.8. HRMS-ESI (*m*/*z*) calcd for $C_{19}H_{20}NO_3^+$ (M + H)$^+$ 310.14377, found 310.14368.

Methyl 5-methyl-2-(4-(trifluoromethyl) phenyl)-1*H*-indole-3-carboxylate (3aj). Yield, 49% (32.6 mg); white solid, mp 165–167 °C; IR (KBr, cm^{-1}): 3288, 1665, 1446, 1325, 1221, 1166, 1134, 1068, 849, 802, 693, 622; ^1H NMR (500 MHz, $CDCl_3$) δ 8.66–8.56 (br, 1H), 8.00 (s, 1H), 7.77–7.69 (m, 4H), 7.31–7.29 (m, 1H), 7.13 (d, J = 8.2 Hz, 1H), 3.85 (s, 3H), 2.51 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.7, 141.5, 134.6, 132.6, 131.0, 129.9 (130.2, 123.0, 129.7, 129.5, q, $^2J_{C-F}$ = 33 Hz), 128.8, 126.4, 125.2 (128.7, 126.5, 124.0, 121.8, q, $^1J_{C-F}$ = 276 Hz), 124.4, 124.0 (124.07, 124.04, 124.01, 123.98, q, $^3J_{C-F}$ = 4 Hz), 120.8, 109.8, 103.8, 50.0, 20.7. HRMS-ESI (*m*/*z*) calcd for $C_{18}H_{15}F_3NO_2^+$ (M + H)$^+$ 334.10494, found 334.10495.

Methyl 2-(3-fluorophenyl)-5-methyl-1*H*-indole-3-carboxylate (3ak). Yield, 47% (26.6 mg); orange solid, mp 121–122 °C; IR (KBr, cm^{-1}): 3267, 1674, 1443, 1201, 1158, 1119, 861, 789, 680; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.98 (s, 1H), 7.38–7.33, (m, 3H), 7.24 (s, 1H), 7.09 (d, *J* = 7.7 Hz, 2H), 3.83 (s, 3H), 2.49 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.8, 162.3 (163.1, 161.5, d, $^1J_{C-F}$ = 246 Hz), 142.8, 134.1 (134.1, 134.0, d, $^3J_{C-F}$ = 8 Hz), 133.5, 131.8, 129.7 (129.7, 129.6, d, $^3J_{C-F}$ = 8 Hz), 127.6, 125.2 (125.23, 125.21, d, $^4J_{C-F}$ = 3 Hz), 125.1, 121.8, 116.7 (116.8, 116.6, d, $^2J_{C-F}$ = 23 Hz), 116.1 (116.1, 116.0, d, $^2J_{C-F}$ = 21 Hz), 110.8, 104.4, 51.0, 21.7. HRMS-ESI (*m*/*z*) calcd for $C_{17}H_{15}FNO_2^+$ (M + H)$^+$ 284.10813, found 284.10825.

Methyl 2-(3-chlorophenyl)-5-methyl-1*H*-indole-3-carboxylate (3al). Yield, 46% (27.5 mg); light yellow solid, mp 152–153 °C; IR (KBr, cm^{-1}): 3266, 1673, 1478, 1443, 1139, 782; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (br, 1H), 7.98 (s, 1H), 7.60 (s, 1H), 7.51 (d, *J* = 7.2 Hz, 1H), 7.37–7.31 (m, 2H), 7.24 (d, *J* = 5.4 Hz, 1H), 7.09 (d, *J* = 7.1 Hz, 1H), 3.83 (s, 3H), 2.49 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.7, 141.6, 133.0, 132.7, 132.5, 130.8, 128.4, 128.3, 128.1, 126.9, 126.6, 124.1, 120.8, 109.7, 103.5, 50.0, 20.7. HRMS-ESI (*m*/*z*) calcd for $C_{17}H_{15}ClNO_2^+$ (M + H)$^+$ 300.07858, found 300.07837.

Methyl 5-methyl-2-(*m*-tolyl)-1*H*-indole-3-carboxylate (3am). Yield, 49% (27.4 mg); light yellow solid, mp 136–138 °C; IR (KBr, cm^{-1}): 3289, 1668, 1447, 1161, 1124, 1049, 786, 731, 698; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (br, 1H), 7.92 (s, 1H), 7.36–7.34 (m, 2H), 7.24–7.21 (m, 1H), 7.17–7.13 (m, 2H), 7.01–6.99 (d, *J* = 7.9 Hz, 1H), 3.74 (s, 3H), 2.42 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.8, 143.7, 136.8, 132.4, 131.0, 130.5, 128.9, 128.8, 127.0, 126.8, 125.8, 123.7, 120.7, 109.5, 102.9, 49.8, 20.7, 20.4. HRMS-ESI (*m*/*z*) calcd for $C_{18}H_{18}NO_2^+$ (M + H)$^+$ 280.13321, found 280.13309.

Methyl 5-methoxy-2-(*m*-tolyl)-1*H*-indole-3-carboxylate (3an). Yield, 49% (29.0 mg); light yellow solid, mp 138–140 °C; IR (KBr, cm^{-1}): 3395, 1667, 1451, 1213, 1195, 1164, 1124, 1050, 1029, 796; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 7.68 (s, 1H), 7.39–7.36 (m, 2H), 7.26–7.24 (m, 1H), 7.20–7.16 (m, 2H), 6.87 (d, *J* = 9.0 Hz, 1H), 3.87 (s, 3H), 3.77 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.1, 154.6, 144.2, 136.7, 130.9, 129.2, 128.8, 128.7, 127.4, 126.9, 125.7, 112.2, 110.9, 102.8, 102.5, 54.7, 49.8, 20.3. HRMS-ESI (*m*/*z*) calcd for $C_{18}H_{18}NO_3^+$ (M + H)$^+$ 296.12812, found 296.12802.

Methyl 2-(3-methoxyphenyl)-5-methyl-1*H*-indole-3-carboxylate (3ao). Yield, 48% (28.3 mg); yellow solid, mp 130–132 °C; IR (KBr, cm^{-1}): 3354, 1686, 1466, 1440, 1286, 1123, 878, 804, 787; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (br, 1H), 8.01 (s, 1H), 7.28–7.26 (m, 1H), 7.22–7.17 (m, 3H), 7.08 (d, *J* = 8.2 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 1H), 3.82 (s, 3H), 3.78 (s, 3H), 2.51 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.0, 158.0, 143.3, 132.4, 132.2, 130.4, 128.5, 128.0, 126.7, 123.7, 120.8, 120.5, 114.1, 113.6, 109.8, 102.7, 54.2, 49.8. HRMS-ESI (*m*/*z*) calcd for $C_{18}H_{18}NO_3^+$ (M + H)$^+$ 296.12812, found 296.12848.

Methyl 2-phenyl-1*H*-indole-3-carboxylate (3ap).[8b,30] Yield, 51% (25.6 mg); yellow solid, mp 137–139 °C; IR (KBr, cm^{-1}): 3300, 1667, 1486, 1447, 1421, 1282, 1214, 1132, 792, 765, 740, 697; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.23–8.21 (m, 1H), 7.69–7.67 (m, 2H), 7.48–7.47 (m, 3H), 7.42–7.40 (m, 1H), 7.30–7.28 (m, 2H), 3.85 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.7, 143.5, 134.0, 130.9, 128.5, 128.3, 127.2, 126.5, 122.3, 121.2, 121.1, 109.9, 103.6, 49.9.

Methyl 5-methyl-2-phenyl-1*H*-indole-3-carboxylate (3ba).[13,38] Yield, 54% (28.6 mg); white solid, mp 154–156 °C; IR (KBr, cm^{-1}): 3287, 2949, 1673, 1452, 1129, 800, 759, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (br, 1H), 7.99 (s, 1H), 7.62–7.60 (m, 2H), 7.40 (br, 3H), 7.23 (d, *J* = 8.1 Hz, 1H), 7.07 (d, *J* = 8.1 Hz, 1H), 3.81 (s, 3H), 2.49 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.9, 143.6, 132.4, 131.1, 130.5, 128.5, 128.5, 128.0, 127.1, 126.7, 123.7, 120.7, 109.7, 49.8, 20.7.

Methyl 5-methoxy-2-phenyl-1*H*-indole-3-carboxylate (3ca).[38] Yield, 49% (27.5 mg); white solid, mp 157–159 °C; IR (KBr, cm^{-1}): 3294, 2950, 1678, 1485, 1462, 1268, 1206, 1167, 1129, 1047, 1035, 804, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (br, 1H), 7.71 (d, *J* = 3 Hz, 1H), 7.61–7.59 (m, 2H), 7.41–7.39 (m, 3H), 7.23 (d, *J* = 8.8 Hz, 1H), 6.90 (dd, *J* = 8.8, 2.5 Hz, 1H), 3.90 (s, 3H), 3.79 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.0, 154.7, 143.9, 131.0, 129.2, 128.4, 128.0, 127.4, 127.1, 112.4, 110.9, 103.0, 102.6, 54.8, 49.8.

Methyl 5-fluoro-2-phenyl-1*H*-indole-3-carboxylate (3da). Yield, 47% (25.3 mg); white solid, mp 156–158 °C; IR (KBr, cm^{-1}): 3282, 1667, 1487, 1464, 1454, 1270, 1213, 1138, 1047, 859, 701, 629; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (br, 1H), 7.86 (dd, *J* = 10.0, 2.4 Hz, 1H), 7.64–7.63 (m, 2H), 7.46–7.44 (m, 3H), 7.31–7.27 (m, 1H), 7.02 (td, *J* = 9, 2.4 Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.5, 159.3 (160.0, 158.5, d, $^1J_{C-F}$ = 236 Hz), 146.1, 131.6 (131.59, 131.55, d, $^3J_{C-F}$ = 6 Hz), 129.5, 129.4, 128.4, 128.3, 111.8, 111.7, 111.6, 107.5 (107.6, 107.5, d, $^2J_{C-F}$ = 26 Hz), 104.7 (104.72, 104.69, d, $^4J_{C-F}$ = 4 Hz), 51.0. HRMS-ESI (*m*/*z*) calcd for $C_{16}H_{13}FNO_2^+$ (M + H)$^+$ 270.09248, found 270.09256.

Ethyl 5-chloro-2-(*p*-tolyl)-1*H*-indole-3-carboxylate (3ea). Yield, 46% (28.8 mg); white solid, mp 190–192 °C; IR (KBr, cm^{-1}): 3429, 3270, 1671, 1431, 1210, 1128, 824, 786; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (br, 1H), 8.17 (d, *J* = 1.6 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.35–7.05 (m, 5H), 4.30 (q, *J* = 7.1 Hz, 2H), 2.37 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.1, 146.0, 139.6, 133.4, 129.4, 128.9, 128.8, 128.5, 127.7, 123.4, 121.7, 112.0, 104.1, 59.9, 21.4, 14.4. HRMS-ESI (*m*/*z*) calcd for $C_{18}H_{17}ClNO_2^+$ (M + H)$^+$ 314.09423, found 314.09406.

Dimethyl 2-phenyl-1*H*-indole-3,5-dicarboxylate (3fa). Yield, 44% (27.2 mg); white solid, mp 202–204 °C; IR (KBr, cm^{-1}): 3328, 1693, 1674, 1452, 1437, 1288, 1105, 762, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.68 (s, 1H), 8.00 (dd, *J* = 8.6, 1.3 Hz, 1H), 7.69–7.67 (m, 2H), 7.48–7.41 (m, 4H), 3.96 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.9, 164.2, 144.8, 136.6, 130.3, 128.6, 128.5, 127.3, 126.1, 124.0, 123.7, 123.1, 109.8, 104.5, 51.0, 50.2. HRMS-ESI (*m*/*z*) calcd for $C_{18}H_{16}NO_4^+$ (M + H)$^+$ 310.10738, found 310.10748.

Methyl 5-(methylthio)-2-phenyl-1*H*-indole-3-carboxylate (3ga). Yield, 50% (29.7 mg); white solid, mp 131–133 °C; IR (KBr, cm^{-1}): 3286, 1665, 1439, 1215, 1131, 1077, 766, 697; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.18 (s, 1H), 7.64–7.63 (m, 2H), 7.45–7.44 (m, 3H), 7.31–7.25 (m, 2H), 3.83 (s, 3H), 2.57 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.6, 144.0, 132.6, 130.7, 130.1, 128.4, 128.3, 127.3, 127.2, 123.4, 120.5, 110.5, 102.9, 50.0, 17.0. HRMS-ESI (*m/z*) calcd for $C_{17}H_{16}NO_2S^+$ $(M + H)^+$ 298.08963, found 298.08957.

Methyl 2-phenyl-1*H*-benzo[*g*]indole-3-carboxylate (3ha). Yield, 49% (29.5 mg); white solid, mp 185–187 °C; IR (KBr, cm^{-1}): 3219, 1668, 1472, 1436, 1199, 1128, 811, 746, 684; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.16 (s, 1H), 8.31 (d, J = 8.8 Hz, 1H), 8.02 (d, J = 8.1 Hz, 1H), 7.97 (d, J = 8.1 Hz, 1H), 7.73–7.70 (m, 3H), 7.56 (t, J = 7.6 Hz, 1H), 7.51–7.45 (m, 4H), 3.88 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.8, 141.3, 131.1, 129.7, 129.0, 128.6, 128.0, 127.9, 127.2, 124.9, 123.6, 123.0, 121.8, 120.3, 120.0, 118.3, 105.2, 50.0. HRMS-ESI (*m/z*) calcd for $C_{20}H_{16}NO_2^+$ $(M + H)^+$ 302.11756, found 302.11707.

Methyl 2-phenyl-3*H*-benzo[*e*]indole-1-carboxylate (3ia). Yield, 50% (30.0 mg); white solid, mp 192–193 °C; IR (KBr, cm^{-1}): 3310, 1666, 1460, 1442, 1195, 1145, 806, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (d, J = 8.5 Hz, 1H), 8.71 (s, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.67 (d, J = 8.7 Hz, 1H), 7.60–7.54 (m, 3H), 7.49–7.42 (m, 5H), 3.82 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.9, 138.7, 131.5, 131.4, 129.4, 127.8, 127.6, 127.5, 127.4, 127.0, 125.1, 124.3, 123.8, 123.0, 120.0, 111.1, 107.3, 50.6. HRMS-ESI (*m/z*) calcd for $C_{20}H_{16}NO_2^+$ $(M + H)^+$ 302.11756, found 302.11691.

Mixture of methyl 6-methyl-2-phenyl-1*H*-indole-3-carboxylate (3ja) and methyl 4-methyl-2-phenyl-1*H*-indole-3-carboxylate (3j′a).[30,39] Yield, 52% (27.6 mg); yellow solid, the ratio (**3ja** : **3j′a** = 2 : 1) is determined by NMR; IR (KBr, cm^{-1}): 3297, 2949, 1682, 1452, 1214, 1127, 1048, 813, 768, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (br, $1.5H_{overlap}$), 8.07 (d, J = 8.2 Hz, $1H_{3ja}$), 7.65–7.63 (m, $2H_{3ja}$), 7.55–7.51 (m, $1H_{3j'a}$), 7.45–7.40 (m, $4.50H_{overlap}$), 7.22 (d, J = 8.0 Hz, $0.55H_{3j'a}$), 7.17–7.10 (m, $2.54H_{overlap}$), 7.01 (d, J = 7.1 Hz, $0.53H_{3j'a}$), 3.83 (s, $3H_{3ja}$), 3.76 (s, $1.56H_{3j'a}$), 2.65 (s, $1.50H_{3j'a}$), 2.47 (s, $3H_{3ja}$).

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We are grateful for financial support from Special Project for Double First-Class-Cultivation of Innovative Talents (201815), the Fundamental Research Funds for the Central Universities (2572017DB07), and Natural Science Foundation of Heilongjiang Province (B2017002, LC2018003).

Notes and references

1 A. J. Kochanowska-Karamyan and M. T. Hamann, *Chem. Rev.*, 2010, **110**, 4489.
2 C.-L. Do-Thanh, J. J. Vargas, J. W. Thomas, G. R. Armel and M. D. Best, *J. Agric. Food Chem.*, 2016, **64**, 3533.
3 (*a*) E. Vitaku, D. T. Smith and J. T. Njardarson, *J. Med. Chem.*, 2014, **57**, 10257; (*b*) N. Chadha and O. Silakari, *Eur. J. Med. Chem.*, 2017, **134**, 159.
4 (*a*) Y. Liu, K. Ai and L. Lu, *Chem. Rev.*, 2014, **114**, 5057; (*b*) M. Vlasselaer and W. Dehaen, *Molecules*, 2016, **21**, 785.
5 (*a*) F. R. de Sa Alves, E. J. Barreiro and C. A. M. Fraga, *Mini-Rev. Med. Chem.*, 2009, **9**, 782; (*b*) T. V. Sravanthi and S. L. Manju, *Eur. J. Pharm. Sci.*, 2016, **91**, 1; (*c*) N. K. Kaushik, N. Kaushik, P. Attri, N. Kumar, C. H. Kim, A. K. Verma and E. H. Choi, *Molecules*, 2013, **18**, 6620; (*d*) T. P. Singh and O. M. Singh, *Mini-Rev. Med. Chem.*, 2018, **18**, 9.
6 (*a*) G. R. Humphrey and J. T. Kuethe, *Chem. Rev.*, 2006, **106**, 2875; (*b*) F. T. Douglass and K. T. Pavan, *Tetrahedron*, 2011, **67**, 7195; (*c*) R. Vicente, *Org. Biomol. Chem.*, 2011, **9**, 6469; (*d*) M. Inman and C. J. Moody, *Chem. Sci.*, 2013, **4**, 29; (*e*) G. Bartoli, R. Dalpozzo and M. Nardi, *Chem. Soc. Rev.*, 2014, **43**, 4728; (*f*) M. M. Heravi, S. Rohani, V. Zadsirjan and N. Zahedi, *RSC Adv.*, 2017, **7**, 52852.
7 (*a*) G. Battistuzzi, S. Cacchi and G. Fabrizi, *Eur. J. Org. Chem.*, 2002, 2671; (*b*) K. Kruger, A. Tillack and M. Beller, *Adv. Synth. Catal.*, 2008, **350**, 2153; (*c*) S. Cacchi and G. Fabrizi, *Chem. Rev.*, 2011, **111**, PR215; (*d*) M. Platon, R. Amardeil, L. Djakovitch and J. C. Hierso, *Chem. Soc. Rev.*, 2012, **41**, 3929; (*e*) T. L. Guo, F. Huang, L. Yu and Z. Yu, *Tetrahedron Lett.*, 2015, **56**, 296; (*f*) S. W. Youn and T. Y. Ko, *Asian J. Org. Chem.*, 2018, **7**, 1467.
8 (*a*) S. Würtz, S. Rakshit, J. J. Neumann, T. Dröge and F. Glorius, *Angew. Chem., Int. Ed.*, 2008, **47**, 7230; (*b*) J. J. Neumann, S. Rakshit, T. Dröge, S. Würtz and F. Glorius, *Chem. - Eur. J.*, 2011, **17**, 7298.
9 R. Bernini, G. Fabrizi, A. Sferrazza and S. Cacchi, *Angew. Chem., Int. Ed.*, 2009, **48**, 8078.
10 (*a*) X.-L. Lian, Z.-H. Ren, Y.-Y. Wang and Z.-H. Guan, *Org. Lett.*, 2014, **16**, 3360; (*b*) A. Mishra and I. Deb, *Adv. Synth. Catal.*, 2016, **358**, 2267.
11 (*a*) F. Huang, P. Wu, L. Wang, J. Chen, C. Sun and Z. Yu, *J. Org. Chem.*, 2014, **79**, 10553; (*b*) P. Drouhin and R. J. K. Taylor, *Eur. J. Org. Chem.*, 2015, 2333; (*c*) J. Liu, W. Wei, T. Zhao, X. Liu, J. Wu, W. Yu and J. Chang, *J. Org. Chem.*, 2016, **81**, 9326; (*d*) F.-Z. Hu, S.-H. Zhao, H. Chen, S.-W. Yu, X.-Y. Xu, W.-C. Yuan and X.-M. Zhang, *ChemistrySelect*, 2017, **2**, 1409.
12 Z.-H. Guan, Z.-Y. Yan, Z.-H. Ren, X.-Y. Liu and Y.-M. Liang, *Chem. Commun.*, 2010, 2823.
13 W. Yu, Y. Du and K. Zhao, *Org. Lett.*, 2009, **11**, 2417.
14 (*a*) Z. He, W. Liu and Z. Li, *Chem.–Asian J.*, 2011, **6**, 1340; (*b*) Z. Jia, T. Nagano, X. Li and A. S. C. Chan, *Eur. J. Org. Chem.*, 2013, 858.
15 (*a*) C.-J. Wu, Q.-Y. Meng, T. Lei, J.-J. Zhong, W.-Q. Liu, L.-M. Zhao, Z.-J. Li, B. Chen, C.-H. Tung and L.-Z. Wu, *ACS Catal.*, 2016, **6**, 4635; (*b*) W.-Q. Liu, T. Lei, Z.-Q. Song, X.-L. Yang, C.-J. Wu, X. Jiang, B. Chen, C.-H. Tung and L.-Z. Wu, *Org. Lett.*, 2017, **19**, 3251.
16 J. Zoller, D. C. Fabry, M. A. Ronge and M. Rueping, *Angew. Chem., Int. Ed.*, 2014, **53**, 13264.
17 S. Tang, X. Gao and A. Lei, *Chem. Commun.*, 2017, **53**, 3354.
18 (*a*) Z. Shi, C. Zhang, S. Li, D. Pan, S. Ding, Y. Cui and N. Jiao, *Angew. Chem., Int. Ed.*, 2009, **48**, 4572; (*b*) L. Ren, Z. Shi and N. Jiao, *Tetrahedron*, 2013, **69**, 4408.

19 D. Shen, J. Han, J. Chen, H. Deng, M. Shao, H. Zhang and W. Cao, *Org. Lett.*, 2015, **17**, 3283.

20 Y. Wei, I. Deb and N. Yoshikai, *J. Am. Chem. Soc.*, 2012, **134**, 9098.

21 (*a*) S. Kramer, K. Dooleweerdt, A. T. Lindhardt, M. Rottländer and T. Skrydstrup, *Org. Lett.*, 2009, **11**, 4208; (*b*) G. Zhang, H. Yu, G. Qin and H.-M. Huang, *Chem. Commun.*, 2014, **50**, 4331; (*c*) D. Shen, J. Han, J. Chen, H. Deng, M. Shao, H. Zhang and W. Cao, *Org. Lett.*, 2015, **17**, 3283.

22 (*a*) D. R. Stuart, M. Bertrand-Laperle, K. M. N. Burgess and K. Fagnou, *J. Am. Chem. Soc.*, 2008, **130**, 16474; (*b*) J. Chen, G. Song, C.-L. Pan and X. Li, *Org. Lett.*, 2010, **12**, 5426; (*c*) D. R. Stuart, P. Alsabeh, M. Kuhn and K. Fagnou, *J. Am. Chem. Soc.*, 2010, **132**, 18326; (*d*) C. Wang, H. Sun, Y. Fang and Y. Huang, *Angew. Chem., Int. Ed.*, 2013, **52**, 5795; (*e*) C. Wang and Y. Huang, *Org. Lett.*, 2013, **15**, 5294; (*f*) D. Zhao, Z. Shi and F. Glorius, *Angew. Chem., Int. Ed.*, 2013, **52**, 12426; (*g*) B. Liu, C. Song, C. Sun, S. Zhou and J. Zhu, *J. Am. Chem. Soc.*, 2013, **135**, 16625; (*h*) T. Matsuda and Y. Tomaru, *Tetrahedron Lett.*, 2014, **55**, 3302; (*i*) L. Zheng and R. Hua, *Chem. - Eur. J.*, 2014, **20**, 2352; (*j*) K. Muralirajan and C. H. Cheng, *Adv. Synth. Catal.*, 2014, **356**, 1571; (*k*) Y. Hoshino, Y. Shibata and K. Tanaka, *Adv. Synth. Catal.*, 2014, **356**, 1577; (*l*) P.-Y. Tao and Y.-X. Jia, *Chem. Commun.*, 2014, **50**, 7367; (*m*) S. Kathiravan and I. A. Nicholls, *Chem. Commun.*, 2014, **50**, 14964; (*n*) B. Zhou, Y. Yang, H. Tang, J. Du, H. Feng and Y. Li, *Org. Lett.*, 2014, **16**, 3900; (*o*) Z.-L. Fan, S.-S. Song, W. Li and A. Zhang, *Org. Lett.*, 2015, **17**, 310; (*p*) L. Kong, F. Xie, S. Yu, Z. Qi and X. Li, *Chin. J. Catal.*, 2015, **36**, 925; (*q*) Z. Zhou, G.-X. Liu, Y. Chen and X.-Y. Lu, *Adv. Synth. Catal.*, 2015, **357**, 2944; (*r*) Y. Kim and S. Hong, *Chem. Commun.*, 2015, **51**, 11202; (*s*) H. Yan, H. Wang, X. Li, X. Xin, C. Wang and B. Wan, *Angew. Chem., Int. Ed.*, 2015, **54**, 10613; (*t*) H. J. Kim, D. C. Fabry, S. Madera and M. Rueping, *Org. Chem. Front.*, 2019, **6**, 2319.

23 (*a*) L. Ackermann and A. V. Lygin, *Org. Lett.*, 2012, **14**, 764; (*b*) Z. Zhang, H. Jiang and Y. Huang, *Org. Lett.*, 2014, **16**, 5976; (*c*) S. Allu and K. C. Kumara Swamy, *Adv. Synth. Catal.*, 2015, **357**, 2665.

24 (*a*) F. Zhou, X.-L. Han and X.-Y. Lu, *Tetrahedron Lett.*, 2011, **52**, 4681; (*b*) J.-L. Chen, Q. Y. Pang, Y. B. Sun and X. Li, *J. Org. Chem.*, 2011, **76**, 3523.

25 S. Kramer, K. Dooleweerdt, A. T. Lindhardt, M. Rottländer and T. Skrydstrup, *Org. Lett.*, 2009, **11**, 4208.

26 W. Song and L. Ackermann, *Chem. Commun.*, 2013, **49**, 6638.

27 (*a*) Z.-Z. Zhang, B. Liu, J.-W. Xu, S.-Y. Yan and B.-F. Shi, *Org. Lett.*, 2016, **18**, 1776; (*b*) H. Wang, M. Moselage, M. J. González and L. Ackermann, *ACS Catal.*, 2016, **6**, 2705; (*c*) Q. Lu, S. Vásquez-Céspedes, T. Gensch and F. Glorius, *ACS Catal.*, 2016, **6**, 2352; (*d*) A. Lerchen, S. Vasquez-Cespedes and F. Glorius, *Angew. Chem., Int. Ed.*, 2016, **55**, 3208; (*e*) Y. J. Liang and N. Jiao, *Angew. Chem., Int. Ed.*, 2016, **55**, 4035.

28 (*a*) C. Chen, G. Shang, J. Zhou, Y. Yu, B. Li and J. Peng, *Org. Lett.*, 2014, **16**, 1872; (*b*) G. Zhao, C. Chen, Y. Yue, Y. Yu and J. Peng, *J. Org. Chem.*, 2015, **80**, 2827; (*c*) Y. Yue, J. Peng, D. Wang, Y. Bian, P. Sun and C. Chen, *J. Org. Chem.*, 2017, **82**, 5481; (*d*) X. Li, Y. Bian, X. Chen, H. Zhang, W. Wang, S. Ren, X. Yang, C. Lu, C. Chen and J. Peng, *Org. Biomol. Chem.*, 2019, **17**, 321; (*e*) X. Li, X. Chen, H. Wang, C. Chen, P. Sun, B. Mo and J. Peng, *Org. Biomol. Chem.*, 2019, **17**, 4014.

29 (*a*) C. Li, *Acc. Chem. Res.*, 2009, **42**, 335; (*b*) C. S. Yeung and V. M. Dong, *Chem. Rev.*, 2011, **111**, 1215; (*c*) C. Liu, J.-W. Yuan, M. Gao, S. Tang, W. Li, R.-Y. Shi and A.-W. Lei, *Chem. Rev.*, 2015, **115**, 12138.

30 Y. Li, J. Peng, X. Chen, B. Mo, X. Li, P. Sun and C. Chen, *J. Org. Chem.*, 2018, **83**, 5288.

31 P. Sun, J. Yang, Z. Song, Y. Cai, Y. Liu, C. Chen, X. Chen and J. Peng, *Synthesis*, 2020, **52**, 75.

32 Selected reviews, see: (*a*) J. X. Qiao and P. Y. S. Lam, *Synthesis*, 2011, 829; (*b*) K. S. Rao and T.-S. Wu, *Tetrahedron*, 2012, **68**, 7735; (*c*) X. Ma, F. Liu and D. Mo, *Chinese J. Org. Chem.*, 2017, **37**, 1069; (*d*) X. Duan, N. Liu, J. Wang and J. Ma, *Chinese J. Org. Chem.*, 2019, **39**, 661.

33 J. E. Steves and S. S. Stahl, *J. Am. Chem. Soc.*, 2013, **135**, 15742.

34 J. C. Antilla and S. L. Buchwald, *Org. Lett.*, 2001, **3**, 2077.

35 (*a*) J. C. Vantourout, H. N. Miras, A. Isidro-Llobet, S. Sproules and A. J. B. Watson, *J. Am. Chem. Soc.*, 2017, **139**, 4769; (*b*) A. E. King, T. C. Brunold and S. S. Stahl, *J. Am. Chem. Soc.*, 2009, **131**, 5044; (*c*) J. P. Collman and M. Zhong, *Org. Lett.*, 2000, **2**, 1233.

36 G. Hou, W. Li, M. Ma, X. Zhang and X. Zhang, *J. Am. Chem. Soc.*, 2010, **132**, 12844.

37 X. Guo, J. Han, Y. Liu, M. Qin, X. Zhang and B. Chen, *J. Org. Chem.*, 2017, **82**, 11505.

38 X. Zhang, D. Zhang-Negrerie, J. Deng, Y. Du and K. Zhao, *J. Org. Chem.*, 2013, **78**, 12750.

39 V. A. Bodunov, E. E. Galenko, A. V. Galenko, M. S. Novikov and A. F. Khlebnikov, *Synthesis*, 2018, **50**, 2784.