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$Cu(OAc)_2$-Promoted Oxidative Cross-Dehydrogenative Coupling Reaction of *α*-Acylmethyl Malonates with Indole Derivatives to Access 3-Functionalized Indoles and Polycyclic Indoles

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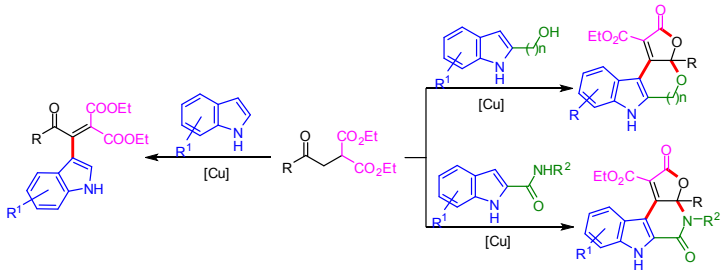


ABSTRACT

A $Cu(OAc)_2$-promoted oxidative cross-dehydrogenative coupling reaction of *α*-acylmethyl malonates with indole derivatives was developed. In the case of indoles, the regioselective coupling products were formed through sequential dehydrogenation-addition-dehydrogenation process. When a second nucleophilic center was located in the 2-positioin of indoles, further successive nucleophilic cyclization occurred to give polycyclic indole derivatives. The $Cu(OAc)_2$ was proved to act as not only an oxidant but also a catalyst.

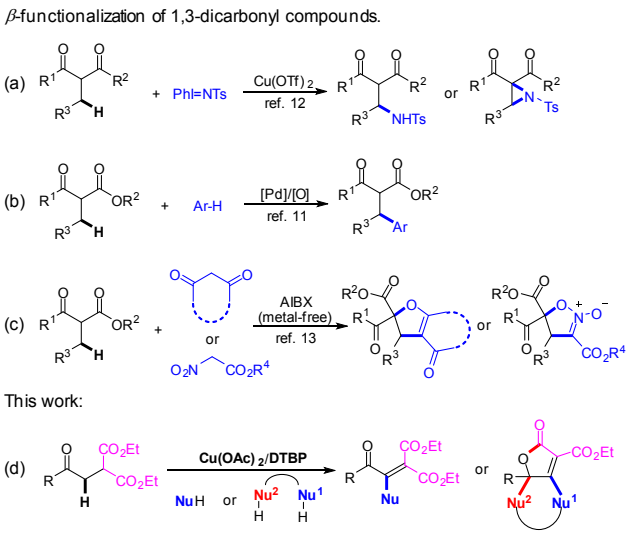
INTRODUCTION

Transition-metal-catalyzed coupling reactions have become a powerful tool in organic synthesis. As a direct way to form C–C bonds, the oxidative cross-dehydrogenative coupling (CDC) of two different C-H bonds constitutes an attractive strategy in the last decades because it avoids preinstalling leaving or activating group on the substrates.[1] In particular, the development

of selective inactive C(sp^3)-H functionalization to form C(sp^3)-X (X = C, N, or O) bond is highly desirable but full of challenge. Carbonyl compounds play a critical role in organic synthesis. Most of the transformation of carbonyl primarily occurs at the electrophilic carbonyl carbon and the nucleophilic α-carbon atom. Recently, direct functionalization of the inactive β-C(sp^3)-H of carbonyls has attracted considerable attentions. A selective C-H activation strategy was usually adopted to achieve such transformation, which requires a transition-metal catalyst such as [Pd][2] or [Ni],[3] and the assistance of an internal or transient directing group.[4] A strategy to combine a dehydrogenation of carbonyl to yield α,β-unsaturated carbonyls with subsequent olefin transformations represents another new avenue to realize the β-functionalization. Nevertheless, most of the developed methods require the participation of [Pd] catalyst and an aryl halide substrate.[5] A direct dehydrogenative coupling of two different C-H bonds to realize the β-functionalization of carbonyls is rare. The key of this strategy is rapid generation of the electrophilic deficient species under mild conditions and easy occurrence of the subsequent addition. Ueno and Kuwano reported the Ni-catalyzed C-N bonds formation at the β-position of ketones.[6] Su reported a Cu(II)-catalyzed direct β-functionalization of saturated ketones.[7] However, the substrates were limited to those without substituents on the β-carbon in these two transformations. Wang and Hayashi developed the use of secondary amine catalyst to generate enamine intermediate, which was oxidized to iminium species followed by Michael addition to realize the β-functionalization.[8] Nevertheless, this method was only suitable for aldehydes. A similar route involves the use of *N*-heterocyclic carbene (NHC) catalyst.[9] In terms of the α-substituted-1,3-dicarbonyl compounds, dehydrogenation affords α,β-unsaturated carbonyls with stronger electrophilicity due to the existence of two electron-withdrawing groups, which is beneficial to the second step of addition. Matsuo and Ishibashi reported a one-pot two-step

functionalization of *β*-position of 1,3-dicarbonyls with *N*-tertbutylbenzenesulfinimidoyl chloride as the oxidant.[10] But the reaction conditions were too harsh involving the oxygen/water free, strong base, and ultra-low temperature, as well as not easy availability of the oxidant. Pihko explored the Pd-catalyzed oxidative coupling of cyclic *β*-keto esters with electron-rich arenes at the *β′*-position (Scheme 1b).[11] Chan developed a $Cu(OTf)_2$-catalyzed *β*-amination and aziridination of 2-alkyl substituted 1,3-dicarbonyl compounds with PhI=NTs (Scheme 1a).[12] Zhang reported a hypervalent-iodine-mediated *α*,*β′*-annulation of *β*-ketoesters with 1,3-diketones or nitroacetates (Scheme 1c).[13] In these limited examples of *β*-functionalization of 1,3-dicarbonyl compounds, expensive [Pd] catalyst or hypervalent iodine reagents were always required. Recently, we reported a $Cu(OAc)_2$-triggered cascade reaction of malonate tethered oxime acetates with indole derivatives to prepare polysubtituted 3-pyrrolin-2-ones *via* a key vicinal dielectrophilic 2*H*-pyrrol-2-one intermediates.[14] We speculated an electron-withdrawing acyl group on the *β*-carbon atom of malonates might be beneficial to yield the electron-deficient alkene intermediate with a low-cost [Cu] reagent to achieve the dehydrogenation process. Subsequent reaction with nucleophiles followed by oxidation would generate coupling products. While a dinucleophiles was employed, further intramolecular attack on carbonyl might occur to form polycyclic compounds (Scheme 1d). To realize such transformation, the choice of suitable nucleophiles having stronger nucleophilicity than malonates was essential because it has been reported that the dehydrogenation of 2-methyl or 2-ethoxycarbonyl malonate underwent *in situ* Michael addition with itself to form a cascade product.[15]

Scheme 1 Functionalization of *β*-C(sp^3)-H of 1,3-dicarbonyl compounds.

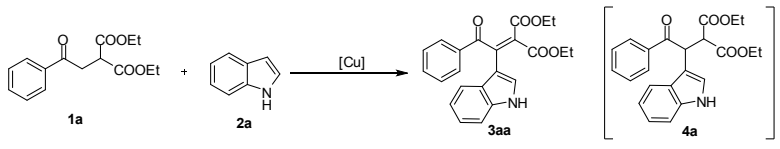


RESULTS AND DISCUSSION

Indole derivatives are widely existed in the biologically active natural products isolated from biological systems and indole alkaloids are one of the largest classes of natural alkaloids. As one of the most important skeleton in drug discovery, indole is also called one of the "privileged scaffolds", which can acts as ligand for a diverse array of receptors.[16] These have stimulated medicinal chemists to apply indole chemistry to drug synthesis and inspired synthetic chemists to develop novel chemical transformations and synthetic strategies.[17] At the outset, we investigated the direct coupling of indole **2a** with diethyl α-benzoylmethyl malonate **1a** (Table 1). Due to the structural similarity of α-benzoylmethyl malonate with malonate tethered oxime acetate,[14] a primary test was conducted by performing the reaction of **1a** and 1.0 equiv of indole **2a** in acetonitrile under the same conditions with $Cu(OAc)_2$ as the oxidant. Disappointingly, no coupling product was formed (entry 1). Adding bases such as K_2CO_3 and Cs_2CO_3 could not initiate the reaction yet (entries 2 and 3). When the reaction were carried out in DMSO with K_2CO_3 as the base, a coupling product **3aa** was formed in 48% yield after 14 h (entry 4). During the reaction, the formation of intermediate **4a** and its smooth conversion to **3aa** was observed. Meanwhile, many indole **2a** remained unreacted due to the self-reaction of **1a**. Increasing the molar ratio of **1a** : **2a** to

1.5 : 1 and tempereture to 100 °C led to the full conversion of **2a** within 5 h, affording **3aa** in 62% yield (entry 5). Using Na_2CO_3 as the base further improved the yield to 74% (entry 6). The requirement of only 2.5 equiv of $Cu(OAc)_2$ demonstrated that the Cu^{II} was finally reduced to Cu^0. In order to reduce the use of $Cu(OAc)_2$ to catalytic amount, a series of external oxidants were evaluated. The results showed di-*tert*-butyl peroxide (DTBP) and pyridine *N*-oxide were effective, and DTBP gave a slightly higher yield of 55% (entries 7-11). A copper catlyst survey showed that $Cu(OAc)_2$ was the most effective (entries 12-14). However, the reaction with catalytic amount of $Cu(OAc)_2$ combined with DTBP proceeded much slower than that of using 2.5 equiv of $Cu(OAc)_2$ directly and much longer reaction time was needed (entry 7). A possible reason was that partial Cu^{II} was reduced to Cu^0, which could not be oxidized to Cu^I/Cu^{II} to enter the next oxidation cycle, thus decreasing the oxidation efficiency greatly. Increasing the amount of $Cu(OAc)_2$ to 1 equiv significantly improved the yield to 77% (entries 15-17). An effort to decrease the amount of $Cu(OAc)_2$ by using a ligand was alao attempted. However, the addition of ligand such as 2,2'-Bpy, Phen, TMEDA, $Me_2NCH_2CO_2H$, or DMAP had no significant improvement on the yield (entries 18-22). It was worth noting that using DMSO as the solvent was crutial because no reaction was observed in other solvents such as toluene, DMF, and 1,4-dioxane (entries 23-25).

Table 1 Screening of the Reaction Conditions[a]



entry	[Cu]	additive	ratio[b]	solvent	T (ºC)	time (h)	yield of **3aa**
1	$Cu(OAc)_2$	-	1:1:2.5	CH_3CN	80	12	0
2	$Cu(OAc)_2$	K_2CO_3	1:1:2.5:2.5	CH_3CN	80	12	0
3	$Cu(OAc)_2$	Cs_2CO_3	1:1:2.5:2.5	CH_3CN	80	12	0
4	$Cu(OAc)_2$	K_2CO_3	1:1:2.5:2.5	DMSO	80	14	48
5	$Cu(OAc)_2$	K_2CO_3	1.5:1:2.5:2.5	DMSO	100	5	62

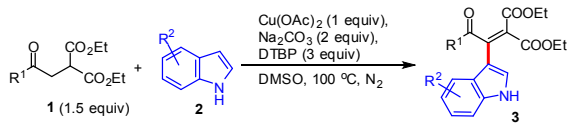
6	$Cu(OAc)_2$	Na_2CO_3	1.5:1:2.5:2.5	DMSO	100	5	74
7	$Cu(OAc)_2$	Na_2CO_3, DTBP	1.5:1:0.2:1:3	DMSO	100	13	55
8	$Cu(OAc)_2$	Na_2CO_3, $K_2S_2O_8$	1.5:1:0.2:1:3	DMSO	100	13	trace
9	$Cu(OAc)_2$	Na_2CO_3, 	1.5:1:0.2:1:3	DMSO	100	13	49
10	$Cu(OAc)_2$	Na_2CO_3, 	1.5:1:0.2:1:3	DMSO	100	11	15
11	$Cu(OAc)_2$	Na_2CO_3, MCPBA	1.5:1:0.2:1:3	DMSO	100	12	38
12	$CuCl_2$	Na_2CO_3, DTBP	1.5:1:0.2:2:3	DMSO	100	16	20
13	$Cu(OTf)_2$	Na_2CO_3, DTBP	1.5:1:0.2:2:3	DMSO	100	16	17
14	CuI	Na_2CO_3, DTBP	1.5:1:0.2:2:3	DMSO	100	11	52
15	$Cu(OAc)_2$	Na_2CO_3, DTBP	1.5:1:0.4:0.8:3	DMSO	100	12	59
16	$Cu(OAc)_2$	Na_2CO_3, DTBP	1.5:1:0.6:1.2:3	DMSO	100	10	66
17	$Cu(OAc)_2$	Na_2CO_3, DTBP	1.5:1:1:2:3	DMSO	100	6	77
18	$Cu(OAc)_2$	2,2'-Bpy, Na_2CO_3, DTBP	1.5:1:0.2:0.2:1:3	DMSO	100	13	47
19	$Cu(OAc)_2$	Phen, Na_2CO_3, DTBP	1.5:1:0.2:0.2:1:3	DMSO	100	6	57
20	$Cu(OAc)_2$	TMEDA, Na_2CO_3, DTBP	1.5:1:0.2:0.2:1:3	DMSO	100	16	42
21	$Cu(OAc)_2$	$Me_2NCH_2CO_2H$, Na_2CO_3, DTBP	1.5:1:0.2:0.2:1:3	DMSO	100	14	50
22	$Cu(OAc)_2$	DMAP, Na_2CO_3, DTBP	1.5:1:0.2:0.4:1:3	DMSO	100	10	51
23	$Cu(OAc)_2$	Na_2CO_3, DTBP	1.5:1:1:2:3	$PhCH_3$	100	8	0
24	$Cu(OAc)_2$	Na_2CO_3, DTBP	1.5:1:1:2:3	DMF	100	8	trace
25	$Cu(OAc)_2$	Na_2CO_3, DTBP	1.5:1:1:2:3	1,4-dioxane	100	8	0

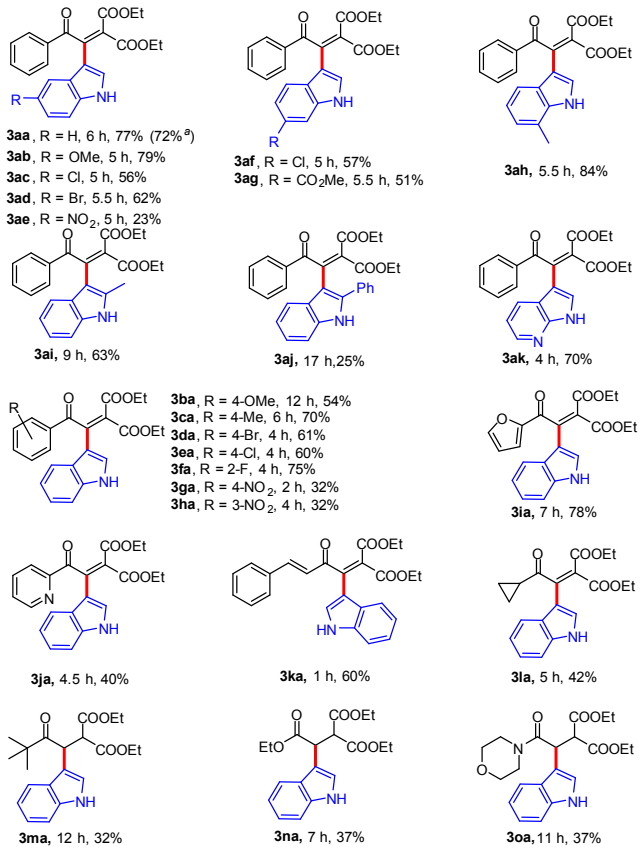
[a] **1a** (0.4 mmol), other reactants and reagents, and 8 mL of solvent. [b] **1a**/**2a**/additive.

Under the optimized conditions (Table 1, entry 17), the scope of this cross-dehydrogenative coupling reaction was examined. As illustrated in Table 2, a variety of indoles with different substitution patterns afforded the corresponding products in moderate to good yields. Both electron-donating and electron-withdrawing substituents like methoxy, alkyl, bromo, chloro, and fluorine groups were well compatible (**3aa**-**3ad** and **3af**-**3ah**). However, when a strong electron-withdrawing group such as -NO_2 linked to the phenyl ring of indole, the coupling product **3ae** was obtained in a low yield (23%). 2-Methyl indole also provided **3ai** in 63% yield, while 2-phenyl indole only give 25% yield of **3aj** probably due to the big steric hindrance. Meanwhile, an analogue of indole, 7-azaindole also provided **3ak** in 70% yield. Next, the scope of α-acylmethyl malonates connecting different substituents (R^1) on the carbonyl carbon was also assessed. Regardless of either electron-rich or electron-deficient aryl groups of R^1, the reaction

was performed well to give **3ba-3fa** moderate to good yields. When a nitro group was located at the phenyl ring, a relatively low yield of **3ga** or **3ha** was obtained. Heteroaryls such as furyl and pyridyl were also tolerated in the reaction (**3ia** and **3ja**). In addition, when R^1 was an alkenyl group and alkyl group, the desired products **3ka** and **3la** were also obtained in 60% and 42% yield, respectively. While an tert-butyl of R^1 only provided the coupling product **3ma** without further oxidation. Changing the acyl to ester or amide group, similar result was obtained with relatively low yield (**3na** and **3oa**).

Table 2. Substrate scopes of indoles and *α*-acylmethyl malonates.

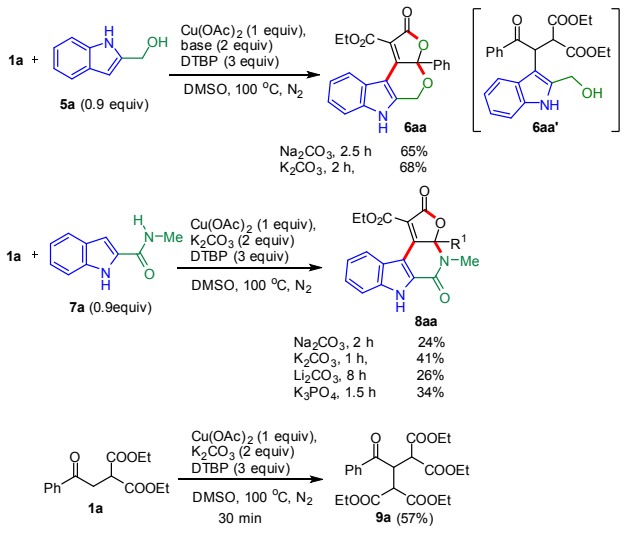




[a] The yield of a 2 mmol scale reaction.

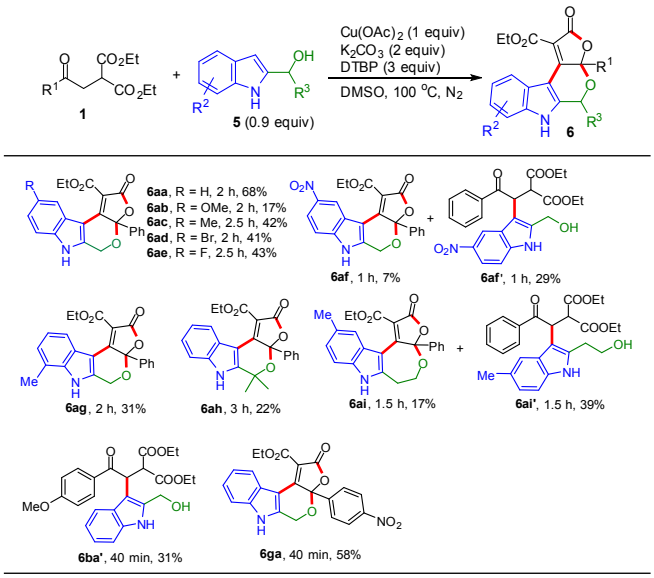
Encouraged by these results obtained from indoles, we envisaged that a second nucleophilic site linking to the 2-position of indole might attack on the carbonyl, leading to the formation of polycyclic indoles. Accordingly, indole-2-methanol **5a** and indole-2-formamide **7a** were subjected to the reaction with **1a**, respectively (Scheme 2). Pleasingly, the reaction of **1a** with **5a** under the optimized conditions afforded the anticipated product **6aa** in 65% yield. Using K_2CO_3 as the base gave slightly high yield (68%). Meanwhile, the intermediate **6aa'** was also determined and transformed to **6aa** smoothly. It was noteworthy that this reaction showed perfect regioselectivity with indole-3-carbon coupling with sp^3-carbon and oxygen atom attacking on the carbonyl carbon. The reaction of **1a** with **7a** with Na_2CO_3 as the base only furnished 24% yield of **8aa**. Replacing Na_2CO_3 by K_2CO_3 improved the yield to 41%. Using Li_2CO_3 as the base gave a comparable yield with that of Na_2CO_3, however, the reaction proceeded very slowly (8 h *vs* 1 h). The K_3PO_4 was also inferior to the K_2CO_3. An organic base like Et_3N and pyridine could not initiate the reaction. An attempt to further improve the yield was failed because large amount of **9a** was formed from the self-reaction of **1a**. A main reason for the low yield lied in the electronegativity of 2-amide group reduced the nucleophilicity of indole-3-carbon, which made the addition reaction difficult.

Scheme 2 The reaction of 1a with 5a/7a and the self-reaction of 1a.



To evaluate the generality of this process, various indole-2-alcohols and indole-2-carboxamides were subjected to the reaction with **1** (Tables 3 and 4). For the indole-2-alcohols **5**, the substituent R^2 on the phenyl ring had siginficant influence on the reaction. Both strong electron-donating and electron-withdrawing group were unfavorable to the reaction. While other groups such as bromo, fluoro have no influence on the reaction, delivering the corresponding products in modest yields. When R^2 is methoxy, **6ab** was obtained in a very low yield of 17%. While a nitro group led to the corresponding product **6af** in only 7% yield accompanied by the formation of **6af'** in 29% yield. A tertiary alcohol tethered indole gave the corresponding products **6ah** in 22% yield. Indole-2-ethanol **5i** was also tolerated in the reaction to give **6ai** in 17% yield accompanied by **6ai'** in 39% yield. Notably, when R^1 was 4-methoxyphenyl, only the coupling intermediate **6ba'** was formed in 31% yield due to the strong electon-donating character of methoxy group, which recduced the electrophilicity of carbonyl. While R^1 was a 4-nitrophenyl, the product **6ga** was formed in 58% yield.

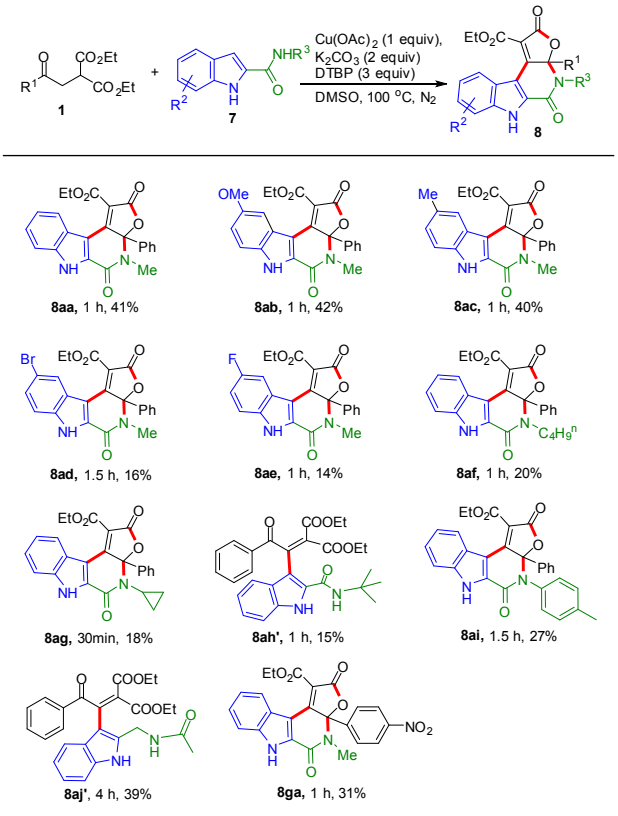
Table 3 Reaction of indole-2-alcohols with *α*-acylmethyl malonates.



In the case of reaction of indole-2-carboxamides **1** with **7** (Table 4), the substituents on both of the substrates had a great influence on the reaction. An electon-withdrawing group on the indole

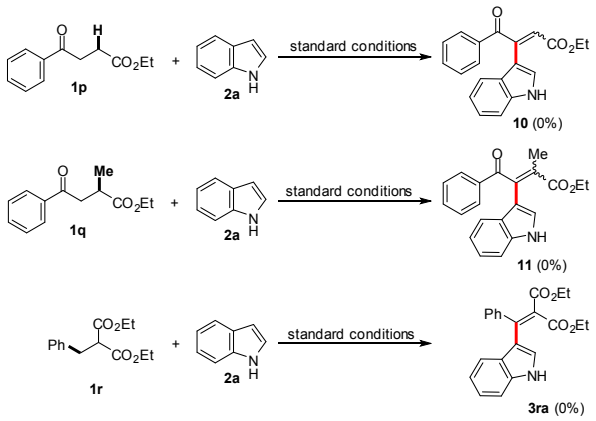
ring was extremely unfavorable to the reaction (**8ad** and **8ae**), and a nitro group led to no formation of the anticipated product, impling that a proper nuclephilicity of indole-3-carbon to trigger the second step of addition was crucial to the success of reaction. Changing the substituent on nitrogen atom from methyl to butyl, cyclopropyl, or 4-methylphenyl, the reaction still worked but the yield was unsatisfatory. A tert-butyl group only gave the uncycled product in 15% yield. In addition, the position of the amide carbony group had great influence on the reaction, when *N*-acetyl indole-2-mehthylamine **7j** was used instead of indole-2-formide **7a**, only coupling product **8aj'** was obtained in 39% yield without further cyclization.

Table 4 Reaction of indole-2-carboxamides with *α*-acylmethyl malonates.



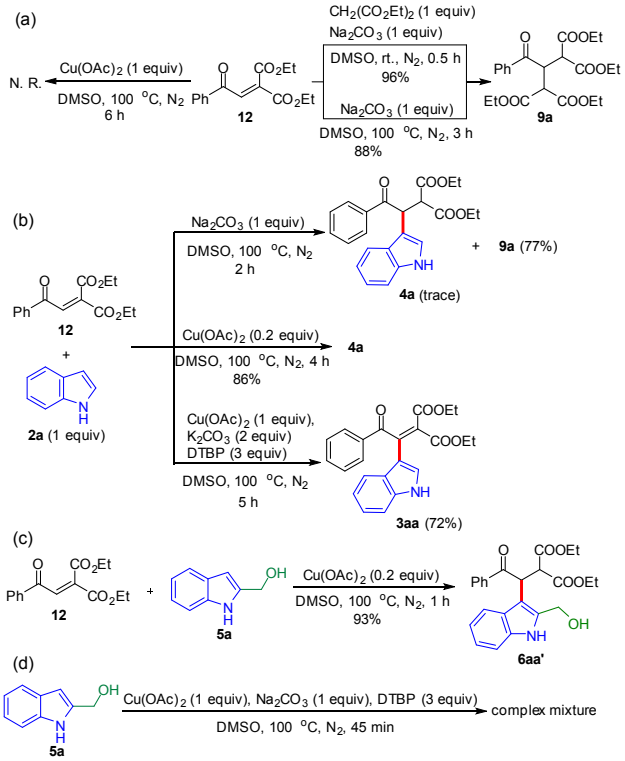
To confirm the role of acyl and malonate group in the cross-dehydrogenative coupling reaction, substrates **1p-r** were prepared and subjected to the reaction with **2a** (Scheme 3). Replacing one of the two ester groups by hydrogen or mehtyl resulted in no reaction occurring (**1p** and **1q**). When the benzoyl group was replaced by a phenyl group, no coupling product **3ra** was formed yet.

Scheme 3 Try of Other Substrates



To have a deep insight into the reaction, compound **12** was prepared through the Wittig reaction of benzoylmethylenetriphenylphosphorane with diethyl 2-oxomalonate. Stirring the mixture of **12** and 1 equiv of $Cu(OAc)_2$ in DMSO at 100 °C for 6 h, most of **12** was recovered. However, when the mixture of **12** and 1 equiv of Na_2CO_3 was stirred at 100 °C, full conversion of **12** was observed after 3 h and **9a** was isolated in 88% yield. When 1 equiv of diethyl malonate was added, the Michael addition to **12** proceeded quickly at room temperature in the presence of Na_2CO_3, giving **9a** in 96% yield (Scheme 4a). This reavealed that the dehydrogenative reaction to generate C=C double bonds was a rate-determine step and therefore we did not observe the formation of **12** during the reaction of **1** with **2**/**5**/**7**. The reaction of **2a** with **12** in the pesence of 1 equiv of Na_2CO_3 at 100 °C only furnished trace of addition product **4a**, and most of **12** was converted to **9a**. While in the presence of 0.2 equiv of $Cu(OAc)_2$, the addition product **4a** was obtained in 86% yield within 4 h (Scheme 4b). Similary, the reaction of **5a** with **12** in the presence of 0.2 equiv of $Cu(OAc)_2$ generated 93% yield of **6aa'** within 1 h (Scheme 4c). These results indicated that the $Cu(OAc)_2$ acted as not only an oxidant but also a catalyst and the base was crucial to the step of dehydrogenation. When the indole **2a** was reacted with equal amount of **12** under standard conditions, **3aa** was obained in 72% yield (Scheme 4b).

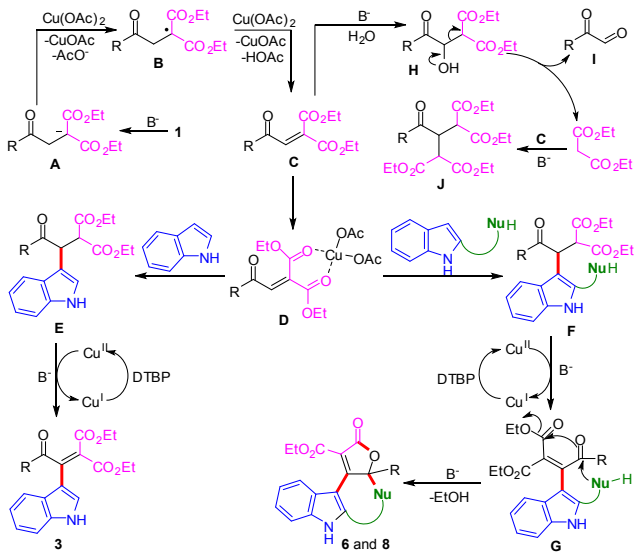
Scheme 4 Control experiments and preliminary mechanistic studies.



On the basis of above results, a plausible reaction mechanism was proposed to clarify the oxidative dehydrogenative coupling reaction (Scheme 5). Deprotonation of **1** followed by single-electron oxidation with $Cu(OAc)_2$ afforded radical **B**, which was further oxidized by $Cu(OAc)_2$ accompanied by release of CuOAc and HOAc to deliver the key intermediate **C**. Coordination of $Cu(OAc)_2$ with the two ester groups increased the electrophilicity of the β-C(sp^2). Reaction of **D** with **2** or **5**/**7** afforded the coupling product **E** or **F**, respectively. Further oxidation of **E** by $Cu(OAc)_2$ under basic conditions furnished **3** with the concurrent release of CuOAc. Similar oxidation of **F** afforded **G**. Under basic conditions, a cascade intramolecular nucleophilic reaction occurred to furnish **6**/**8**. The oxidation process could be promoted by Cu^{II}, which was recycled by oxidation of Cu^{I} with DTBP. Under basic conditions, intermediate **C** might react with the trace amount of water in solvent to yield the addition product **H**, which underwent retro-Aldol reaction to give diethyl malonate and **I**. The Michael addition of diethyl malonate with **C** afforded

the main byproduct **J**. The competition reaction of **C** with H_2O or the coupling partner determined the reaction efficiency. When an electron-withdrawing amide group was linked to the 2-position of indoles, the nucleophilicity of indoles decreased significantly and thus resulted in the increased difficulty of addition with **C**. Additionally, we also observed that stirring the single **5a** under standard conditions gave a complex mixture within 45 min (Scheme 4d). In combined with the steric hindrance of 2-substituent, these were the partial reasons for the low reaction efficiency between **1** and indole-2-alcohols or indole-2-carboxamides.

Scheme 5 Plausible mechanism.



CONCLUSIONS

In summary, we have presented a $Cu(OAc)_2$-promoted oxidative dehydrogenative coupling reaction of α-acylmethyl malonates with indole derivatives. A new $C(sp^2)$–$C(sp^2)$ bonds was directely constructed by connecting the 3-$C(sp^2)$ of indoles and the β-$C(sp^3)$ of malonates under mild conditions. In the case of indoles, a sequential dehydrogenation-addition-dehydrogenation process was involved in the reaction. In terms of indole-2-methanols and indole-2-carboxamides, a futher cascade intramolecular nucleophilic cyclization occurred to give polycyclic indole derivatives. The $Cu(OAc)_2$ acts as not only an oxidant in the step of dehydrogenation but also a

catalyst in the step of addition. The base was essential to the step of oxidative dehydrogenation but at the same time cause the decomposition of intermediate, which is the main reason for the low yield in the reaction of α-acylmethyl malonates with indole-2-methanols and indole-2-carboxamides. An effort to improve the reaction efficiency are ongoing.

EXPERIMENTAL SECTION

General Information

All the reaction was performed on a preheated oil bath (the reaction temperature refers to the temperature of the oil bath). ^{1}H and ^{13}C NMR (proton broadband decoupling) spectra were recorded on 300 and 400 MHz (75 and 100 MHz for ^{13}C NMR) spectrometer at ambient temperature, using TMS as an internal standard. Flash column chromatography was performed over silica gel (200-300 mesh). HRMS was obtained on LTQ Orbitrap XL mass spectrometer.

Straring materials **1a-e**,**1g**,**1i**,**1l-q**, **5a-f**, **5h**, **5i**, **7f-i**,[14] **7j**,[18] and **12**[19] were prepared according to reported method.

General Procedure Preparation of Diethyl Malonate Substituted ketone 1f, 1h, and 1j. The diethyl malonate (12 mmol) was dissolved in dry THF (15 mL). After cooling to 0 ^{o}C, NaH (520 mg, 60 % in oil, 13 mmol) was added in one portion and the mixture was stirred for 30 min at 0 ^{o}C. The corresponding α-bromokenone (10 mmol) was dissolved in THF (15 mL) and added slowly to the reaction mixture. The reaction was warmed to room temperature and quenched by the addition of an equal volume of aq. NH_4Cl. The mixture was extracted with ethyl acetate (3 × 40 mL), and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to provide α-acylmethyl manolates **1**.

1f (eluent: ethyl acetate / petroleum ether = 1/25-1/15, colorless oil, 2.03 g, 69%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (td, J = 7.6, 1.7 Hz, 1H), 7.61-7.46 (m, 1H), 7.24 (td, J = 7.6, 0.7 Hz, 1 H), 7.16 (dd, J = 11.3, 8.3 Hz, 1H), 4.34-4.16 (m, 4H), 4.05 (t, J = 7.1 Hz, 1H), 3.36 (dd, J = 7.0, 3.2 Hz, 2H), 1.29 (t, J = 7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.8, 194.7, 169.0, 164.0, 160.6, 135.3, 135.2, 130.8, 130.7, 124.7, 124.6, 124.6, 124.5, 117.0, 116.7, 61.8, 47.4, 47.3, 42.5, 42.4, 14.1; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{15}H_{18}FO_5$ 297.1138, found 297.1127.

1h (eluent: ethyl acetate / petroleum ether = 1/20-1/10, colorless solid, 1.87 g, 58%, mp 53-55 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (t, J = 1.8 Hz, 1H), 8.46 (ddd, J = 8.2, 2.2, 1.0 Hz, 1 H), 8.32 (dt, J = 7.8, 1.3 Hz, 1 H), 7.72 (t, J = 8.0 Hz, 1 H), 4.34-4.17 (m, 4H), 4.09 (t, J = 7.1 Hz, 1H), 3.67 (d, J = 7.0 Hz, 2H), 1.31 (t, J = 7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.7, 168.8, 148.5, 137.4, 133.8, 130.1, 127.9, 123.2, 62.1, 47.2, 38.0, 14.1; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{15}H_{18}NO_7$ 324.1083, found 324.1075.

1j (eluent: ethyl acetate / petroleum ether = 1/20-1/12, brown oil, 969.0 mg, 35%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70 (ddd, J = 4.8, 1.6, 0.8 Hz, 1H), 8.03 (dd, J = 7.9, 1.0 Hz, 1 H), 7.85 (td, J = 7.7, 1.7 Hz, 1 H), 7.50 (ddd, J = 7.5, 4.8, 1.1 Hz, 1H), 4.31-4.18 (m, 4H), 4.03 (t, J = 7.2 Hz, 1H), 3.88 (d, J = 6.9 Hz, 2H), 1.29 (t, J = 7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.3, 169.1, 152.6, 149.1, 136.9, 127.5, 121.8, 61.7, 47.2, 37.3, 14.0; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{14}H_{18}NO_5$ 280.1185, found 280.1180.

Preparation of 1k. The process is the same as above only with the (*E*)-1-iodo-4-phenylbut-3-en-2-one (2 mmol) as halide.

1k (eluent: ethyl acetate / petroleum ether = 1/20-1/10, light yellow oil, 346.9 mg, 57%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, J = 16.3 Hz, 1 H), 7.58-7.50 (m, 2 H), 7.45-7.34 (m, 3 H), 6.76 (d, J = 16.3 Hz, 1 H), 4.234 (q, J = 7.2 Hz, 2H), 4.229 (q, J = 7.1 Hz, 2H), 3.99 (t, J = 7.2 Hz, 1H),

3.34 (d, J = 7.2 Hz, 2 H), 1.29 (t, J = 7.1 Hz, 3H); 13C NMR (75 MHz, CDCl3) δ 196.4, 169.1, 143.7, 134.3, 130.8, 129.1, 128.5, 125.5, 62.2, 61.8, 47.1, 39.4, 14.1, 14.0; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{17}H_{21}O_5$ 305.1389, found 305.1378.

Preparation of 5g. To a stirred solution of ethyl 7-methyl-indole-2-carboxylate (1.0 mmol) in 5 mL of THF was added $LiALH_4$ (5 mmol) at room temperature. After completion of the reaction as monitored by TLC, a small amount aqueous NaOH solution was slowly added. The mixture was stirred for 20 minutes and then filtered. The filtrate was added 20 mL of water and then extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (ethyl acetate : petroleum ether = 1 : 2) to provide **5g** (reddish brown solid, 151.0 mg, 94%, mp 63-65 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (br, 1H), 7.40 (d, J = 7.5 Hz, 1H), 7.01 (t, J = 7.4 Hz, 1H), 6.96 (d, J = 6.9 Hz, 1H), 6.34 (d, J = 2.0 Hz, 1H), 4.69 (s, 2 H), 2.51-2.34 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.2, 136.2, 127.6, 122.8, 120.4, 120.2, 118.4, 101.2, 58.7, 16.7; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{10}H_{12}NO$ 162.0919, found 162.0910.

Indole-2-carboxamides 7a-e were prepared according to literature procedure.[20] A mixture of indole-2-carboxylate (1.0 mmol) and 15 mL of aqueous solution of methylamine (25 wt %) was stirred at room temperature until the completion of the reaction as monitored by TLC (about 24-48 h). After filtration, the solid was washed with water and then dried to provide **7a-e**.

7c (white solid, 179.9 mg, 96%, mp 250-253 °C): ^{1}H NMR (300 MHz, d_6-DMSO) δ 11.44 (br, 1H), 8.48-8.33 (m, 1H), 7.37 (d, J = 0.5 Hz, 1H), 7.30 (d, J = 8.3 Hz, 1H), 6.99 (dd, J = 8.4, 1.5 Hz, 1H), 6.96 (d, J = 1.5 Hz, 1H), 2.81 (d, J = 4.6 Hz, 3H), 2.36 (s, 3 H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 161.9, 134.9, 131.9, 128.4, 127.6, 125.2, 120.9, 112.2, 101.8, 26.0, 21.3; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{11}H_{13}N_2O$ 189.1028, found 189.1014.

7d (white solid, 229.2 mg, 91%, mp 296-297 °C): ^{1}H NMR (300 MHz, d_6-DMSO) δ 11.82 (br, 1H), 8.67-8.49 (m, 1H), 7.85 (d, J = 1.6 Hz, 1H), 7.40 (d, J = 8.7 Hz, 1H), 7.30 (dd, J = 8.7, 1.9 Hz, 1H), 7.07 (s, 1H), 2.83 (d, J = 4.6 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 161.2, 135.0, 133.2, 129.0, 125.8, 123.7, 114.4, 112.2, 101.6, 25.9; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{10}H_{10}BrN_2O$ 252.9977, found 252.9959.

General Procedure for the Preparation of 3. A mixture of α-acylmethyl manolates **1** (0.45 mmol), indoles **2** (0.3 mmol), DTBP (0.9 mmol), Na_2CO_3(0.6 mmol), and $Cu(OAc)_2$ (0.3 mmol) in DMSO (3.0 mL) was stirred at 100 °C under N_2 atmosphere. After completion of the reaction as determined by TLC, the mixture was cooled to room temperature and ammonia solution (10%, 30 mL) was added. The mixture was extracted with ethyl acetate (3 × 30 mL). The combined organic phase were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to give the products **3**.

3aa (eluent: ethyl acetate / petroleum ether = 1/5, yellow solid, 90.0 mg, 77%, mp 178-180 °C): ^{1}H NMR (300 MHz, d_6-DMSO) δ 11.94 (br, 1H), 7.86 (d, J = 7.1 Hz, 2H), 7.62-7.54 (m, 2H), 7.47 (t, J = 7.4 Hz, 2H), 7.43 (d, J = 8.4 Hz, 1H), 7.36 (d, J = 8.1 Hz, 1H), 7.14 (td, J = 7.5, 0.8 Hz, 1H), 7.04 (td, J = 7.5, 0.8 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 4.02 (q, J = 7.1 Hz, 2H), 1.09 (t, J = 7.1 Hz, 3H), 1.00 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 193.8, 165.8, 163.2, 149.6, 136.8, 135.4, 133.6, 128.9, 128.6, 124.5, 122.6, 120.9, 120.5, 119.2, 112.7, 108.1, 61.5, 61.3, 13.6, 13.5; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{23}H_{21}NNaO_5$ 414.1317, found 414.1315.

3ab (eluent: ethyl acetate / petroleum ether = 1/5, yellow solid, 99.6 mg, 79%, mp 186-188 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67 (br, 1H), 7.98 (d, J = 7.0 Hz, 2H), 7.48 (tt, J = 7.3, 1.3 Hz, 1H), 7.38 (t, J = 7.4 Hz, 2H), 7.31 (d, J = 3.0 Hz, 1H), 7.17 (d, J = 8.8 Hz, 1H), 7.07 (d, J = 2.3 Hz, 1H), 6.82 (dd, J = 8.8, 2.4 Hz, 1H), 4.15 (q, J = 7.1 Hz, 2H), 4.10 (q, J = 7.1 Hz, 2H), 3.77 (s,

3H), 1.09 (t, *J* = 7.1 Hz, 3H), 1.05 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.5, 166.9, 163.9, 155.3, 150.6, 135.9, 133.5, 131.6, 129.1, 128.8, 128.1, 125.5, 121.7, 113.7, 112.8, 109.9, 101.8, 62.0, 61.8, 55.7, 13.8, 13.7; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{24}H_{24}NO_6$ 422.1604, found 422.1595.

3ac (eluent: ethyl acetate / petroleum ether = 1/5, yellow solid, 71.0 mg, 56%, mp 168-172 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.00 (br, 1H), 7.92 (d, *J* = 7.0 Hz, 2H), 7.61 (s, 1H), 7.48 (tt, J = 7.3, 1.3 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.11-7.13 (m, 2H), 7.09 (d, *J* = 2.9 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.1, 166.7, 163.8, 150.3, 135.5, 135.2, 133.6, 129.1, 128.8, 127.2, 125.4, 123.6, 122.6, 119.1, 113.3, 109.2, 62.6, 61.9, 13.9, 13.7; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{23}H_{21}ClNO_5$ 426.1108, found 426.1104.

3ad (eluent: ethyl acetate / petroleum ether = 1/6, yellow solid, 86.8 mg, 62%, mp 186-188 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.05 (br, 1H), 7.91 (d, *J* = 7.0 Hz, 2H), 7.77 (d, *J* = 1.8 Hz, 1H), 7.48 (tt, *J* = 7.4, 1.3 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.24 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.06 (d, *J* = 8.7 Hz, 1H), 7.03 (d, *J* = 2.9 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.0, 166.7, 163.8, 150.3, 135.5, 135.5, 133.6, 129.1, 129.0, 128.8, 126.2, 126.0, 122.7, 122.2, 114.8, 113.8, 109.1, 62.7, 61.9, 14.0, 13.8; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{23}H_{21}BrNO_5$ 470.0603, found 470.0591.

3ae (eluent: ethyl acetate / dichloromethane = 1/90, yellow solid, 29.8 mg, 23%, mp 216-218 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.51 (br, 1H), 8.63 (d, *J* = 2.0 Hz, 1H), 8.06 (dd, *J* = 9.0, 2.1 Hz, 1H), 7.93 (d, *J* = 7.1 Hz, 2H), 7.51 (tt, J = 7.4, 1.2 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.24 (d, *J* = 9.0 Hz, 1H), 7.16 (d, *J* = 2.8 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.8, 166.5, 163.5, 149.0,

142.9, 139.8, 135.2, 133.9, 130.7, 129.2, 129.0, 123.8, 118.8, 116.7, 112.5, 111.5, 63.0, 62.2, 13.9, 13.8; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{23}H_{21}N_2O_7$ 437.1349, found 437.1339.

3af (eluent: ethyl acetate / petroleum ether = 1/5, yellow solid, 72.4 mg, 57%, mp 165-168 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.93 (br, 1H), 7.94 (d, J = 7.1 Hz, 2H), 7.53 (d, J = 8.6 Hz, 1H), 7.48 (tt, J = 7.3, 1.3 Hz, 1H), 7.38 (t, J = 7.4 Hz, 2H), 7.30 (d, J = 2.4 Hz, 1H), 7.21 (d, J = 1.6 Hz, 1H), 7.09 (dd, J = 8.7, 1.9 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 4.11 (q, J = 7.1 Hz, 2H), 1.13 (t, J = 7.1 Hz, 3H), 1.10 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.4, 166.6, 163.7, 149.8, 137.1, 135.6, 133.7, 129.2, 129.1, 128.8, 128.2, 123.3, 123.0, 122.1, 120.8, 112.0, 109.9, 62.2, 62.0, 13.9, 13.8; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{23}H_{21}ClNO_5$ 426.1108, found 426.1092.

3ag (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/5/1, yellow solid, 68.6 mg, 51%, mp 151-153 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.29 (br, 1H), 7.95 (d, J = 7.2 Hz, 2H), 7.85 (s, 1H), 7.79 (dd, J = 8.6, 1.3 Hz, 1H), 7.64 (d, J = 8.6 Hz, 1H), 7.48 (t, J = 7.3 Hz, 1H), 7.43-7.33 (m, 3H), 4.21 (q, J = 7.1 Hz, 2H), 4.12 (q, J = 7.1 Hz, 2H), 3.90 (s, 3H), 1.15 (t, J = 7.1 Hz, 3H), 1.10 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.3, 167.6, 166.5, 163.7, 149.9, 136.1, 135.5, 133.7, 130.4, 129.1, 128.9, 128.1, 124.8, 123.4, 122.2, 119.4, 114.4, 110.0, 62.3, 62.0, 52.2, 13.9, 13.8; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{25}H_{24}NO_7$ 450.1553, found 450.1540.

3ah (eluent: ethyl acetate / petroleum ether =1/6, yellow solid, 102.3 mg, 84%, mp 170-172 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.85 (br, 1H), 7.94 (d, J = 7.0 Hz, 2H), 7.51-7.41 (m, 2H), 7.35 (t, J = 7.4 Hz, 2H), 7.19 (d, J = 3.0 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 6.96 (d, J = 7.1 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 4.11 (q, J = 7.1 Hz, 2H), 2.29 (s, 3H), 1.16 (t, J = 7.1 Hz, 3H), 1.09 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.2, 166.8, 163.9, 151.1, 136.3, 135.8, 133.4, 129.1, 128.7, 127.7, 124.3, 123.8, 122.1, 121.6, 121.5, 117.5, 110.2, 62.1, 61.7, 16.4, 13.9, 13.8; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{24}H_{24}NO_5$ 406.1654, found 406.1644.

3ai (eluent: ethyl acetate / petroleum ether =1/5, yellow solid, 76.8 mg, 63%, mp 113-116 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.38 (br, 1H), 7.92 (d, J = 7.0 Hz, 2H), 7.64-7.55 (m, 1H), 7.44 (tt, J = 7.3, 1.3 Hz, 1H), 7.34 (t, J = 7.4 Hz, 2H), 7.20-7.14 (m, 1H), 7.14-7.05 (m, 2H), 4.12 (q, J = 7.1 Hz, 2H), 4.04 (q, J = 7.1 Hz, 2H), 2.17 (s, 3H), 1.08 (t, J = 7.1 Hz, 3H), 0.99 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.2, 166.0, 164.4, 151.3, 136.9, 135.9, 135.6, 133.3, 129.1, 128.6, 126.6, 126.5, 122.2, 120.8, 118.8, 111.2, 106.4, 61.8, 61.8, 13.8, 13.6, 13.0; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{24}H_{24}NO_5$ 406.1654, found 406.1641.

3aj (eluent: ethyl acetate / petroleum ether =1/5, yellow oil, 35.3 mg, 25%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (br, 1H), 7.63 (d, J = 7.1 Hz, 3H), 7.51-7.43 (m, 2H), 7.38-7.31 (m, 4H), 7.30-7.24 (m, 1H), 7.22-7.12 (m, 4H), 4.04 (q, J = 7.1 Hz, 2H), 3.93 (q, J = 7.1 Hz, 2H), 1.00 (t, J = 7.1 Hz, 3H), 0.87 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.9, 165.4, 164.4, 149.9, 138.9, 136.2, 136.0, 132.9, 131.1, 129.9, 129.1, 128.9, 128.6, 128.3, 127.1, 123.1, 121.2, 119.4, 111.6, 107.5, 61.9, 61.6, 13.6, 13.5; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{29}H_{26}NO_5$ 468.1811, found 468.1801.

3ak (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/5/1, white solid, 82.3 mg, 70%, mp 199-200 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.38 (br, 1H), 8.32 (dd, J = 4.7, 1.2 Hz, 1H), 8.05 (dd, J = 8.1, 1.4 Hz, 1H), 7.98 (d, J = 7.0 Hz, 2H), 7.72 (s, 1H), 7.49 (tt, J = 7.3, 1.3 Hz, 1H), 7.39 (t, J = 7.4 Hz, 2H), 7.14 (dd, J = 8.1, 4.8 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 4.12 (q, J = 7.1 Hz, 2H), 1.113 (t, J = 7.1 Hz, 3H) , 1.107 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.1, 166.5, 163.3, 149.2, 148.7, 143.4, 135.5, 133.6, 129.9, 129.1, 128.8, 128.3, 123.1, 118.5, 117.3, 108.2, 62.0, 61.9, 13.9, 13.8; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{22}H_{21}N_2O_5$ 393.1450, found 393.1434.

3ba (eluent: ethyl acetate / petroleum ether = 1/4, yellow solid, 68.4 mg, 54%, mp 174-175 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.89 (br, 1H), 7.92 (d, J = 8.9 Hz, 2H), 7.62 (d, J = 7.5 Hz, 1H), 7.27 (d, J = 6.4 Hz, 2H), 7.16 (td, J = 7.1, 1.3 Hz, 1H), 7.11 (td, J = 7.1, 1.2 Hz, 1H), 6.82 (d, J = 8.9 Hz, 2H), 4.14 (q, J = 7.1 Hz, 2H), 4.11 (q, J = 7.1 Hz, 2H), 3.77 (s, 3H), 1.10 (t, J = 7.1 Hz, 3H), 1.07 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.4, 166.9, 163.9, 163.8, 150.6, 136.7, 131.4, 128.9, 127.8, 124.8, 123.2, 121.9, 121.3, 120.0, 114.1, 112.2, 110.2, 62.0, 61.7, 55.5, 13.79, 13.76; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{24}H_{24}NO_6$ 422.1604, found 422.1591.

3ca (eluent: ethyl acetate / petroleum ether = 1/6, yellow solid, 85.3 mg, 70%, mp 189-190 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.76 (br, 1H), 7.86 (d, J = 8.2 Hz, 2H), 7.63 (d, J = 7.5 Hz, 1H), 7.26-7.31 (m, 2H), 7.21-7.08 (m, 4H), 4.14 (q, J = 7.1 Hz, 2H), 4.11 (q, J = 7.1 Hz, 2H), 2.32 (s, 3H), 1.10 (t, J = 7.1 Hz, 3H), 1.07 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.2, 166.8, 163.9, 150.8, 144.4, 136.7, 133.3, 129.5, 129.2, 127.8, 124.8, 123.2, 122.0, 121.3, 120.0, 112.1, 110.0, 62.0, 61.8, 21.8, 13.79, 13.78; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{24}H_{24}NO_5$ 406.1654, found 406.1635.

3da (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/5/1, yellow solid, 85.6 mg, 61%, mp 196-198 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.82 (br, 1H), 7.81 (d, J = 8.6 Hz, 2H), 7.60 (d, J = 7.7 Hz, 1H), 7.50 (d, J = 8.6 Hz, 2H), 7.34-7.26 (m, 2H), 7.23-7.08 (m, 2H), 4.16 (q, J = 7.1 Hz, 2 H), 4.13 (q, J = 7.1 Hz, 2H), 1.13 (t, J = 7.1 Hz, 3H), 1.09 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.4, 166.6, 163.8, 150.0, 136.8, 134.6, 132.1, 130.5, 128.6, 127.8, 124.7, 123.5, 122.4, 121.6, 119.9, 112.2, 109.6, 62.1, 61.9, 13.9, 13.8; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{23}H_{20}BrNNaO_5$ 492.0423, found 492.0414.

3ea (eluent: ethyl acetate / petroleum ether = 1/9, yellow solid, 76.8 mg, 60%, mp 200-202 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.82 (br, 1H), 7.88 (d, J = 8.6 Hz, 2H), 7.60 (d, J = 7.7 Hz, 1H),

7.33 (d, J = 8.6 Hz, 2H), 7.31-7.27 (m, 2H), 7.23-7.08 (m, 2H), 4.16 (q, J = 7.1 Hz, 2H), 4.13 (q, J = 7.1 Hz, 2H), 1.13 (t, J = 7.1 Hz, 3H), 1.09 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.2, 166.6, 163.8, 150.0, 139.8, 136.8, 134.2, 130.4, 129.1, 127.8, 124.7, 123.5, 122.4, 121.6, 119.9, 112.2, 109.6, 62.1, 61.9, 13.9, 13.8; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{23}H_{21}ClNO_5$ 426.1108, found 426.1102.

3fa (eluent: ethyl acetate / petroleum ether = 1/9, yellow solid, 92.2 mg, 75%, mp 175-176 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73 (br, 1H), 8.05 (td, J = 7.6, 1.8 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.48-7.38 (m, 1H), 7.31-7.25 (m, 2H), 7.23-7.10 (m, 3H), 6,98 (ddd, J = 10.9, 8.3, 0.8 Hz, 1 H), 4.16 (q, J = 7.1 Hz, 2H), 4.12 (q, J = 7.1 Hz, 2H), 1.14 (t, J = 7.1 Hz, 3H), 1.05 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 190.4, 166.1, 164.0, 161.8 ($^1J_{C\text{-}F}$ = 257.8 Hz), 151.7, 137.2, 136.4 ($^3J_{C\text{-}F}$ = 9.3 Hz), 131.0, 129.6, 125.2 ($J_{C\text{-}F}$ = 3.2 Hz), 125.1, 124.0 ($^3J_{C\text{-}F}$ = 9.5 Hz), 122.9, 121.2, 119.8 ($J_{C\text{-}F}$ = 3.0 Hz), 119.4, 117.3 ($^2J_{C\text{-}F}$ = 21.9 Hz), 113.0, 107.3, 61.7, 13.9, 13.9; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{23}H_{21}FNO_5$ 410.1404, found 410.1394.

3ga (eluent: dichloromethane / petroleum ether = 1/2-1/1, yellow solid, 42.0 mg, 32%, mp 179-180 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.78 (br, 1H), 8.21 (d, J = 9.0 Hz, 2H), 8.10 (d, J = 9.0 Hz, 2H), 7.62 (d, J = 7.8 Hz, 1H), 7.39 (d, J = 3.0 Hz, 1H), 7.33 (d, J = 7.6 Hz, 1H), 7.23 (td, J = 7.4, 1.3 Hz, 1H), 7.17 (td, J = 7.3, 1.2 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 4.15 (q, J = 7.1 Hz, 2H), 1.18 (t, J = 7.1 Hz, 3H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.5, 166.3, 163.9, 150.2, 149.6, 140.3, 136.8, 129.8, 128.1, 124.5, 124.0, 123.7, 122.5, 121.8, 119.8, 112.3, 108.9, 62.3, 62.2, 13.9, 13.8; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{23}H_{21}N_2O_7$ 437.1349, found 437.1334.

3ha (eluent: ethyl acetate / petroleum ether = 1/4, yellow solid, 41.4 mg, 32%, mp 152-155 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.87-8.73 (m, 2H), 8.30 (ddd, J = 8.2, 2.3, 1.0 Hz, 1H), 8.23 (ddd, J

= 7.7, 1.3, 0.9 Hz, 1H), 7.65 (d, *J* = 7.2 Hz, 1H), 7.55 (t, *J* = 7.9 Hz, 1H), 7.41 (d, *J* = 2.9 Hz, 1H), 7.32 (dd, *J* = 7.2, 1.3 Hz, 1H), 7.26-7.14 (m, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.11 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.0, 166.3, 163.9, 149.5, 148.6, 137.2, 136.8, 134.5, 130.0, 127.9, 127.5, 124.6, 123.7, 123.6, 122.8, 121.8, 119.8, 112.2, 108.9, 62.3, 62.1, 13.9, 13.8; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{23}H_{21}N_2O_7$ 437.1349, found 437.1344.

3ia (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/5/1, yellow solid, 89.7 mg, 78%, mp 165-167 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.92 (br, 1H), 7.63-7.50 (m, 2H), 7.40-7.29 (m, 2H), 7.23-7.05 (m, 3H), 6.44 (dd, *J* = 3.6, 1.7 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 1.16 (t, *J* = 7.1 Hz, 3H), 1.07 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.6, 166.6, 163.8, 151.9, 148.2, 147.3, 136.6, 127.8, 125.1, 123.3, 123.0, 121.4, 120.0, 119.5, 112.5, 112.1, 110.0, 62.0, 61.9, 13.83, 13.76; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{21}H_{20}NO_6$ 382.1291, found 382.1279.

3ja (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/5/1, yellow solid, 47.1 mg, 40%, mp 167-169 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.11 (br, 1H), 8.56 (ddd, *J* = 4.7, 1.6, 0.8 Hz, 1H), 8.12 (d, *J* = 7.8 Hz, 1H), 7.78 (td, *J* = 7.7, 1.7 Hz, 1H), 7.65 (d, *J* = 6.8 Hz, 1H), 7.33 (ddd, *J* = 7.6, 4.7, 1.2 Hz, 1H), 7.27 (d, *J* = 2.9 Hz, 1H), 7.25-7.19 (m, 1H), 7.16-7.02 (m, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 4.10 (q, *J* = 7.1 Hz, 2H), 1.12 (t, *J* = 7.1 Hz, 3H), 1.05 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.4, 166.6, 164.1, 153.0, 151.8, 149.6, 137.1, 136.7, 127.7, 127.0, 125.2, 123.0, 122.3, 121.1, 120.4, 112.0, 109.6, 61.8, 61.7, 13.9, 13.8; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{22}H_{21}N_2O_5$ 393.1450, found 393.1439.

3ka (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/6/1, yellow solid, 75.0 mg, 60%, mp 178-180 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.93 (br, 1H), 7.65 (d, *J* = 7.3 Hz, 1H), 7.56

(d, J = 16.3 Hz, 1H), 7.47-7.39 (m, 2H), 7.38-7.27 (m, 5H), 7.23-7.09 (m, 2H), 6.86 (d, J = 16.3 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 4.14 (q, J = 7.1 Hz, 2H), 1.24 (t, J = 7.1 Hz, 3H), 1.08 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.7, 166.7, 164.0, 150.4, 145.1, 136.7, 134.3, 130.8, 128.9, 128.6, 127.7, 125.9, 125.1, 123.3, 122.2, 121.4, 120.1, 112.1, 109.9, 61.95, 61.86, 14.0, 13.8; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{25}H_{24}NO_5$ 418.1654, found 418.1642.

3la (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/7/1, yellow oil, 45.0 mg, 42%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.82 (br, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 7.8 Hz, 1H), 7.30 (d, J = 2.9 Hz, 1H), 7.22 (td, J = 7.5, 1.1 Hz, 1H), 7.15 (ddd, J = 8.1, 7.0, 1.1 Hz, 1H), 4.27 (q, J = 7.1 Hz, 2H), 4.11 (q, J = 7.1 Hz, 2H), 2.11 (tt, J = 7.9, 4.6 Hz, 1H), 1.31 (t, J = 7.1 Hz, 3H), 1.25-1.21 (m, 2H), 1.06 (t, J = 7.1 Hz, 3H), 0.97-0.92 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.4, 166.7, 164.2, 151.8, 136.6, 127.7, 125.4, 123.2, 121.2, 121.1, 120.1, 112.0, 109.1, 61.9, 61.8, 21.8, 14.1, 13.8, 13.2; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{20}H_{22}NO_5$ 356.1498, found 356.1485.

3ma (eluent: ethyl acetate / petroleum ether = 1/8, brown oil, 35.3 mg, 32%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (br, 1H), 7.66 (d, J = 7.5 Hz, 1H), 7.32 (d, J = 7.2 Hz, 1H), 7.22-7.08 (m, 2H), 6.96 (d, J = 2.2 Hz, 1H), 5.15 (d, J = 11.2 Hz, 1H), 4.34 (d, J = 11.3 Hz, 1H), 4.14-4.25 (m, 2H), 3.82-3.60 (m, 2H), 1.26 (t, J = 7.1 Hz, 3H), 1.10 (s, 9H), 0.76 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.6, 168.7, 168.6, 136.4, 126.4, 124.0, 122.5, 120.1, 119.2, 111.4, 109.1, 61.7, 61.4, 56.3, 44.7, 43.7, 27.8, 14.1, 13.5; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{21}H_{26}NO_5$ 374,1967, found 374.1953.

3na (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/8/2, brown oil, 40.2 mg, 37%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 (br, 1H), 7.73 (d, J = 7.5 Hz, 1H), 7.31 (d, J = 7.4 Hz, 1H), 7.21-7.07 (m, 3H), 4.64 (d, J = 11.7 Hz, 1H), 4.38 (d, J = 11.7 Hz, 1H), 4.30-4.20 (m, 2H),

4.20-4.11 (m, 1H), 4.05 (dq, J = 10.8, 7.1 Hz, 1H), 3.93-3.76 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H), 1.17 (t, J = 7.1 Hz, 3H), 0.84 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5, 168.3, 167.7, 136.2, 126.4, 123.5, 122.4, 119.9, 119.4, 111.4, 109.5, 62.0, 61.5, 61.4, 55.1, 42.5, 14.11, 14.10, 13.6; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{19}H_{24}NO_6$ 362.1604, found 362.1591.

3oa (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/3/1, yellow oil, 45.0 mg, 37%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.66 (br, 1H), 7.67 (d, J = 7.9 Hz, 1H), 7.34 (d, J = 7.9 Hz, 1H), 7.18 (td, J = 7.4, 1.0 Hz, 1H), 7.14-7.06 (m, 2H), 4.85 (d, J = 11.1 Hz, 1H), 4.42 (d, J = 11.1 Hz, 1H), 4.32-4.10 (m, 2H), 3.86-3.69 (m, 2H), 3.67-3.42 (m, 6H), 3.40-3.26 (m, 1H), 3.14-2.96 (m, 1H), 1.27 (t, J = 7.1 Hz, 3H), 0.79 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 168.8, 168.5, 136.1, 126.0, 123.7, 122.5, 120.1, 118.8, 111.5, 109.6, 66.8, 66.3, 61.8, 61.4, 56.4, 46.3, 42.8, 39.9, 14.1, 13.6; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{21}H_{27}N_2O_6$ 403.1869, found 403.1855.

4a (eluent: ethyl acetate / petroleum ether = 1/6, yellow oil, it is an intermediate in the reaction of **1a** with **2a** and can be isolated within a short reaction time): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (br, 1H), 8.00(d, J = 7.1 Hz, 2H), 7.73-7.82 (m, 1H), 7.42 (tt, J = 7.3, 1.3 Hz, 1H), 7.32 (t, J = 7.5 Hz, 2H), 7.24-7.29 (m, 1H), 7.12-7.19 (m, 2H), 7.04 (d, J = 2.6 Hz, 1H), 5.65 (d, J = 11.3 Hz, 1H), 4.54 (d, J = 11.3 Hz, 1H), 4.10-4.27 (m, 2H), 3.70-3.89 (m, 2H), 1.15 (t, J = 7.1 Hz, 3H), 0.73 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.4, 168.6, 136.3, 136.0, 133.1, 128.8, 128.6, 126.2, 124.2, 122.5, 120.2, 119.0, 111.5, 109.2, 61.9, 61.5, 55.9, 44.2, 14.1, 13.6; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{23}H_{24}NO_5$ 394.1654, found 394.1644.

Synthesis of 3aa with 2 mmol of 2a and 3 mmol of 1a. A 50 mL round-bottom flask was charged with diethyl α-benzoylmethyl manolate **1a** (3 mmol), indole **2a** (2 mmol), DTBP (6 mmol), Na_2CO_3 (4 mmol), $Cu(OAc)_2$ (2 mmol), and DMSO (15 mL). The mixture was stirred at

100 °C under N_2 atmosphere for 8 h. After cooling to room temperature, water (150 mL) and ammonium hydroxide (25%, 15 mL) were added and the mixture was extracted with ethyl acetate (3 × 80 mL). The combined organic phase were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (ethyl acetate/petroleum ether = 1/6 to 1/4) to give the product **3aa** (565.1 mg, 72%).

General Procedure for the Preparation of 6. A mixture of *α*-acylmethyl manolates **1** (0.33 mmol), indole-2-alcohols **5** (0.3 mmol), DTBP (0.9 mmol), K_2CO_3 (0.6mmol), and $Cu(OAc)_2$ (0.3 mmol) in DMSO (3.0 mL) was stirred at 100 °C under N_2 atmosphere. After completion of the reaction as determined by TLC, the mixture was cooled to room temperature and ammonia solution (10%, 30 mL) was added. The mixture was extracted with ethyl acetate (3 × 30 mL). The combined organic phase were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to give the products **6**.

6aa (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/5/4, yellow solid, 76.4 mg, 68%, mp 237-240 °C): ^{1}H NMR (300 MHz, d_6-DMSO) δ 12.37 (br, 1H), 7.82-7.71 (m, 1H), 7.55-7.47 (m, 1H), 7.47-7.40 (m, 5H), 7.37-7.25 (m, 2H), 5.43 (d, J = 17.1 Hz, 1H), 4.70 (d, J = 17.0 Hz, 1H), 4.51-4.30 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 165.5, 162.2, 158.6, 142.3, 137.6, 135.4, 130.0, 128.9, 126.4, 123.7, 123.5, 122.2, 121.7, 112.6, 107.8, 105.6, 102.5, 61.5, 61.2, 14.1; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{22}H_{18}NO_5$ 376.1185, found 376.1169.

6aa' (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/4/4, coloreless oil, it is an intermediate in the reaction of **1a** with **5a** and can be isolated within a short reaction time): ^{1}H NMR (300 MHz, d_6-DMSO) δ 11.16 (br, 1H), 8.06 (d, J = 7.5 Hz, 2H), 7.56 (t, J = 7.3 Hz, 1H), 7.55-7.37 (m, 3 H), 7.31 (d, J = 7.6 Hz, 1H), 7.14-6.85 (m, 2H), 5.59 (d, J = 11.4 Hz, 1H), 5.52

(br, 1H), 4.57-5.09 (m, 2H), 4.49 (d, J = 10.2 Hz, 1H), 4.27-4.06 (m, 2H), 3.62-4.01 (m, 2H), 1.19 (t, J = 7.1 Hz, 3H), 0.77 (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 196.7, 167.9, 167.6, 137.6, 135.5, 135.4, 133.2, 128.6, 128.5, 120.9, 119.1, 118.3, 111.5, 101.8, 61.3, 60.9, 55.0, 53.3, 44.1, 13.9, 13.3; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{24}H_{26}NO_6$ 424.1760, found 424.1746.

6ab (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/5/5, yellow solid, 20.4 mg, 17%, mp 284-286 °C): ^{1}H NMR (300 MHz, d_6-DMSO) δ 12.21 (br, 1H), 7.47-7.33 (m, 6H), 7.25 (d, J = 2.1 Hz, 1H), 6.92 (dd, J = 8.8, 2.2 Hz, 1H), 5.35 (d, J = 16.9 Hz, 1H), 4.62 (d, J = 16.9 Hz, 1H), 4.50-4.22 (m, 2H), 3.82 (s, 3H), 1.26 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 165.5, 162.4, 158.8, 154.9, 142.5, 135.6, 132.3, 130.0, 128.9, 126.4, 124.5, 113.2, 112.7, 107.3, 105.7, 105.3, 102.6, 61.5, 61.2, 55.3, 14.1; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{23}H_{20}NO_6$ 406.1291, found 406.1278.

6ac (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/5/5, yellow solid, 49.4 mg, 42%, mp 239-242 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (br, 1H), 7.52 (s, 1H), 7.37 (d, J = 7.0 Hz, 2H), 7.33-7.22 (m, 4H), 7.09 (d, J = 8.3 Hz, 1H), 5.11 (d, J = 16.7 Hz, 1H), 4.62 (d, J = 16.7 Hz, 1H), 4.54-4.43 (m, 1H), 4.43-4.32 (m, 1H), 2.50 (s, 3H), 1.30 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 165.5, 162.2, 158.3, 142.2, 135.9, 135.5, 130.6, 130.0, 128.9, 126.4, 125.0, 123.7, 121.8, 112.3, 107.4, 105.3, 102.6, 61.5, 61.2, 21.3, 14.0; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{23}H_{20}NO_5$ 390.1341, found 390.1332.

6ad (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/5/5, yellow solid, 56.2 mg, 41%, mp 274-278 °C): ^{1}H NMR (300 MHz, d_6-DMSO) δ 12.49 (br, 1H), 7.95 (dd, J = 1.5, 0.7 Hz, 1H), 7.48-7.36 (m, 7H), 5.40 (d, J = 17.1 Hz, 1H), 4.67 (d, J = 17.1 Hz, 1H), 4.49-4.22 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 165.3, 161.9, 158.5, 143.3, 136.4,

135.2, 130.0, 128.9, 126.5, 126.1, 125.3, 124.9, 114.5, 114.2, 108.4, 105.1, 102.4, 61.4, 61.3, 14.0; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{22}H_{17}BrNO_5$ 454.0290, found 454.0282.

6ae (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/5/5, cyan solid, 51.1 mg, 43%, mp 241-245 °C): ^{1}H NMR (300 MHz, d_6-DMSO) δ 12.43 (br, 1H), 7.56 (dd, J = 10.4, 2.5 Hz, 1H), 7.48 (dd, J = 8.9, 4.6 Hz, 1H), 7.45-7.35 (m, 5H), 7.15 (td, J = 9.1, 2.6 Hz, 1H), 5.39 (d, J = 17.1 Hz, 1H), 4.66 (d, J = 17.1 Hz, 1H), 4.46-4.27 (m, 2H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 165.28, 162.03, 158.0 ($^1J_{C\text{-}F}$ = 235.0 Hz), 156.39, 143.85, 135.34, 134.25, 130.05, 128.93, 126.47, 124.4 ($^3J_{C\text{-}F}$ = 11.2 Hz), 113.7 ($^3J_{C\text{-}F}$ = 10.0 Hz), 111.6 ($^2J_{C\text{-}F}$ = 25.8 Hz), 108.2 ($^2J_{C\text{-}F}$ = 26.1 Hz), 107.99, 105.8 ($^4J_{C\text{-}F}$ = 4.1 Hz), 102.44, 61.48, 61.21, 14.05; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{22}H_{17}FNO_5$ 394.1091, found 394.1080.

6af (eluent: methanol / dichloromethane = 1/150, yellow solid, 8.2 mg, 7%, mp 281-283 °C): ^{1}H NMR (300 MHz, d_6-DMSO) δ 12.91 (br, 1H), 8.82 (d, J = 2.0 Hz, 1H), 8.17 (dd, J = 9.0, 2.1 Hz, 1H), 7.67 (d, J = 9.0 Hz, 1H), 7.52-7.36 (m, 5H), 5.46 (d, J = 17.3 Hz, 1H), 4.73 (d, J = 17.3 Hz, 1H), 4.52-4.47 (m, 2H), 1.25 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 165.5, 162.0, 158.5, 145.9, 142.5, 141.3, 135.0, 130.5, 129.3, 126.8, 123.4, 119.5, 119.2, 113.6, 109.8, 107.1, 102.8, 61.8, 14.2; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{22}H_{17}N_2O_7$ 421.1036, found 421.1020.

6af' (eluent: methanol / dichloromethane = 1/150, off-white solid, 40.8 mg, 29%, mp 183-186 °C): ^{1}H NMR (300 MHz, d_6-DMSO) δ 11.94 (br, 1H), 8.49 (br, 1H), 8.04 (d, J = 7.5 Hz, 2H), 7.94 (dd, J = 9.0, 2.2 Hz, 1H), 7.56 (t, J = 7.3 Hz, 1H), 7.37-7.49 (m, 3H), 5.73 (s, 1 H), 5.64 (d, J = 11.3 Hz, 1H), 4.56-5.02 (m, 2H), 4.47 (d, J = 11.2 Hz, 1H), 4.23-4.09 (m, 2H), 3.63-3.97 (m, 2H), 1.16 (t, J = 7.1 Hz, 3H), 0.73 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 167.7, 167.6, 142.2, 140.9, 139.2, 135.3, 133.7, 128.9, 128.6, 116.6, 115.5, 112.1, 104.2, 61.7, 61.2, 55.1, 53.4, 43.6, 13.9, 13.4; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{24}H_{24}N_2NaO_8$ 491.1430, found 491.1423.

6ag (eluent: ethyl acetate / dichloromethane = 1/10, yellow solid, 36.4 mg, 31%, mp 231-236 °C): ^{1}H NMR (300 MHz, d_6-DMSO) δ 12.27 (br, 1H), 7.54 (d, J = 7.7 Hz, 1H), 7.49-7.35 (m, 5H), 7.17 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 7.1 Hz, 1H), 5.39 (d, J = 17.0 Hz, 1H), 4.65 (d, J = 17.0 Hz, 1H), 4.46-4.25 (m, 2H), 2.43 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 165.5, 162.2, 158.5, 142.0, 137.0, 135.5, 130.0, 128.9, 126.4, 124.4, 123.3, 121.91, 121.87, 119.7, 107. 8, 106.0, 102.6, 61.5, 61.2, 16.5, 14.1; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{23}H_{20}NO_5$ 390.1341, found 390.1328.

6ah (eluent: ethyl acetate / petroleum ether = 1/4, yellow solid, 26.3 mg, 22%, mp 229-233 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.85 (br, 1H), 7.87 (d, J = 6.9 Hz, 1H), 7.41 (d, J = 7.4 Hz, 1H), 7.34-7.16 (m, 7H), 4.50-4.25 (m, 2H), 1.65 (s, 3H), 1.29 (t, J = 7.5 Hz, 3H), 1.15 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 162.8, 160.1, 148.8, 139.7, 137.9, 129.6, 128.3, 127.3, 124.3, 123.7, 123.0, 122.4, 112.7, 109.2, 105.4, 103.0, 76.1, 61.7, 32.5, 26.8, 14.4; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{24}H_{22}NO_5$ 404.1498, found 404.1486.

6ai (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/5/5, yellow solid, 20.9 mg, 17%, mp 285-287 °C): ^{1}H NMR (300 MHz, d_6-DMSO) δ 11.95 (br, 1H), 7.42-7.25 (m, 5H), 7.23 (d, J = 8.2 Hz, 1H), 6.94 (dd, J = 8.2, 0.9 Hz, 1H), 6.71 (s, 1H), 4.48-4.20 (m, 2H), 4.20-3.98 (m, 2H), 3.52 (ddd, J = 18.6, 10.5, 4.2 Hz, 1H), 3.27 (d, J = 18.8 Hz, 1H), 2.27 (s, 3H), 0.96 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 166.6, 162.0, 161.8, 142.0, 138.8, 134.8, 129.3, 128.6, 125.7, 125.2, 123.8, 118.6, 116.0, 111.4, 111.2, 103.4, 64.5, 61.2, 30.7, 21.2, 13.6; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{24}H_{22}NO_5$ 404.1498, found 404.1487.

6ai' (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/4/5, brown solid, 52.5 mg, 39%, mp 52-54 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64 (br, 1H), 7.93 (d, J = 7.2 Hz, 2H), 7.48 (s, 1H), 7.40 (t, J = 7.3 Hz, 1H), 7.29 (t, J = 7.6 Hz, 2H), 7.09 (d, J = 8.2 Hz, 1H), 6.91 (d, J = 7.1 Hz,

1H), 5.55 (s, 1H), 4.68 (d, J = 79.1 Hz, 1H), 4.31-4.11 (m, 2H), 3.86 (d, J = 33.3 Hz, 4H), 3.01 (s, 2H), 2.45 (s, 3H), 2.17 (s, 1H), 1.24 (t, J = 7.1 Hz, 3H), 0.81 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.4, 169.0, 168.7, 136.3, 133.9, 132.9, 129.0, 128.6, 128.5, 126.8, 123.2, 119.2, 117.5, 110.4, 103.6, 61.9, 61.7, 61.5, 54.4, 53.4, 45.3, 43.6, 28.9, 21.8, 14.1, 13.5; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{26}H_{30}NO_6$ 452.2073, found 452.2065.

6ba' (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/4/4, brown oil, 41.9 mg, 31%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.80 (br, 1H), 7.94 (d, J = 8.8 Hz, 2H), 7.72 (s, 1H), 7.25-7.18 (m, 1H), 7.17-7.02 (m, 2H), 6.75 (d, J = 8.9 Hz, 2H), 5.62 (d, J = 11.3 Hz, 1H), 4.82 (d, J = 13.1 Hz, 2H), 4.75 (br, 1H), 4.28-4.12 (m, 2H), 3.89-3.72 (m, 2H), 3.72 (s, 3H), 3.22 (s, 1H), 1.23 (t, J = 7.1 Hz, 3H), 0.74 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.8, 169.6, 168.5, 163.5, 135.8, 135.7, 131.0, 128.9, 126.9, 126.8, 122.4, 120.2, 113.8, 111.3, 105.5, 62.0, 61.8, 56.6, 55.4, 54.1, 44.4, 14.1, 13.4; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{25}H_{27}NNaO_7$ 476.1685, found 476.1678.

6ga (eluent: methanol / dichloromethane = 1/300-1/150, brick red solid, 72.5 mg, 58%, mp 237-243 °C): ^{1}H NMR (300 MHz, d_6-DMSO) δ 12.45 (br, 1H), 8.24 (d, J = 8.9 Hz, 2H), 7.80-7.73 (m, 1H), 7.70 (d, J = 8.9 Hz, 2H), 7.54-7.43 (m, 1H), 7.35-7.24 (m, 2H), 5.47 (d, J = 17.2 Hz, 1H), 4.73 (d, J = 17.2 Hz, 1H), 4.49-4.27 (m, 2H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 165.0, 161.9, 157.8, 148.3, 142.4, 142.0, 137.7, 128.0, 124.2, 123.9, 123.5, 122.5, 121.8, 112.6, 107.6, 105.4, 101.5, 61.6, 61.3, 14.1; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{22}H_{17}N_2O_7$ 421.1036, found 421.1026.

General Procedure for the Preparation of 8. A mixture of α-acylmethyl manolates **1** (0.44 mmol), indole-2-carboxamides **7** (0.4 mmol), BuOOBu (1.2 mmol), K_2CO_3 (0.8 mmol), and $Cu(OAc)_2$ (0.4 mmol) in DMSO (4.0 mL) was stirred at 100 ^{o}C under N_2 atmosphere. After

completion of the reaction as determined by TLC, the mixture was cooled to room temperature and ammonia solution (10%, 30 mL) was added. The mixture was extracted with ethyl acetate (3 × 35 mL). The combined organic phase were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to give the products **8**.

8aa (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/10/2, yellow solid, 65.7 mg, 41%, mp 219-222 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.58 (br, 1H), 7.75 (d, J = 8.2 Hz, 1H), 7.62 (d, J = 8.2 Hz, 1H), 7.42 (ddd, J = 8.2, 7.1, 1.1 Hz, 1H), 7.35-7.26 (m, 6H), 4.55-4.28 (m, 2H), 3.28 (s, 3H), 1.32 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0, 163.2, 161.7, 159.6, 138.4, 135.4, 131.2, 130.0, 129.5, 126.8, 125.4, 124.4, 124.3, 123.3, 113.6, 111.8, 110.5, 96.9, 62.2, 28.9, 14.3; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{23}H_{19}N_2O_5$ 403.1294, found 403.1288.

8ab (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/4/1, yellow solid, 72.0 mg, 42%, mp 262-265 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.64 (br, 1H), 7.50 (d, J = 9.0 Hz, 1H), 7.36-7.27 (m, 5H), 7.19 (d, J = 2.3 Hz, 1H), 7.07 (dd, J = 9.0, 2.4 Hz, 1H), 4.57-4.27 (m, 2H), 3.83 (s, 3H), 3.27 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 166.4, 162.6, 161.4, 158.0, 155.6, 135.9, 133.2, 131.6, 129.9, 129.7, 124.9, 124.3, 117.0, 114.8, 109.6, 108.3, 104.5, 96.0, 61.6, 55.3, 28.4, 14.0; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{24}H_{21}N_2O_6$ 433.1400, found 433.1388.

8ac (eluent: ethyl acetate / petroleum ether = 1/4, yellow solid, 67.3 mg, 40%, mp 269-273 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.63 (br, 1H), 7.51 (d, J = 8.5 Hz, 1H), 7.46 (s, 1H), 7.39-7.18 (m, 6H), 4.56-4.28 (m, 2H), 3.27 (s, 3H), 2.44 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 166.4, 162.1, 161.2, 158.1, 136.6, 135.7, 132.0, 131.5, 129.9, 129.7, 127.8, 124.8, 123.6, 122.7, 113.6, 109.9, 108.0, 96.1, 61.6, 28.5, 21.2, 13.8; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{24}H_{21}N_2O_5$ 417.1450, found 417.1444.

8ad (eluent: ethyl acetate / petroleum ether = 1/4, yellow solid, 31.2 mg, 16%, mp 245-249 °C): ^{1}H NMR (300 MHz, d_6-DMSO) δ 13.67 (br, 1H), 7.90 (t, J = 1.2 Hz, 1H), 7.54-7.51 (m, 2H), 7.46-7.37 (m, 3H), 7.22-7.13 (m, 2H), 4.43-4.15 (m, 2H), 3.08 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 166.2, 162.0, 161.0, 157.9, 137.1, 135.5, 132.7, 131.9, 130.1, 129.8, 128.8, 126.2, 125.0, 116.0, 115.4, 110.8, 108.0, 96.0, 61.8, 28.7, 14.0; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{23}H_{18}BrN_2O_5$ 481.0399, found 481.0385.

8ae (eluent: ethyl acetate / petroleum ether = 1/5, yellow solid, 22.9 mg, 14%, mp 258-264 °C): ^{1}H NMR (300 MHz, d_6-DMSO) δ 13.62 (br, 1H), 7.58 (dd, J = 9.0, 4.6 Hz, 1H), 7.48 (dd, J = 10.2, 2.4 Hz, 1H), 7.46-7.35 (m, 3H), 7.28 (td, J = 9.1, 2.6 Hz, 1H), 7.23-7.11 (m, 2H), 4.42-4.22 (m, 2H), 3.08 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 166.1, 162.5, 161.0, 157.8, 158.3 ($^1J_{C\text{-}F}$ = 237.5 Hz), 135.6, 135.0, 133.1, 130.0, 129.7, 124.9, 124.1 ($^3J_{C\text{-}F}$ = 11.6 Hz), 115.4 ($^3J_{C\text{-}F}$ = 9.9 Hz), 114.9 ($^2J_{C\text{-}F}$ = 27.0 Hz), 110.3, 108.9 ($^2J_{C\text{-}F}$ = 25.7 Hz), 108.6 ($^4J_{C\text{-}F}$ = 5.0 Hz), 95.9, 61.6, 28.5, 13.9; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{23}H_{18}FN_2O_5$ 421.1200, found 421.1191.

8af (eluent: ethyl acetate / dichloromethane = 1/50, yellow solid, 35.6 mg, 20%, mp 197-200 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.77 (br, 1H), 7.75 (d, J = 8.2 Hz, 1H), 7.62 (d, J = 8.3 Hz, 1H), 7.41 (ddd, J = 8.1, 7.1, 0.9 Hz, 1H), 7.35-7.26 (m, 6H), 4.58-4.30 (m, 2H), 4.25-4.07 (m, 1H), 3.35-3.05 (m, 1H), 1.94-1.73 (m, 2H), 1.45 (sextet, J = 7.5 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H), 0.99 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 163.5, 161.8, 159.8, 138.6, 136.3, 131.5, 130.0, 129.4, 126.7, 125.5, 124.42, 124.39, 123.2, 113.6, 111.5, 110.5, 97.5, 62.2, 44.5, 31.4, 20.6, 14.3, 13.9; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{26}H_{25}N_2O_5$ 445.1763, found 445.1754.

8ag (eluent: methanol / dichloromethane = 1/100, yellow solid, 30.1 mg, 18%, mp 250-253 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.60 (br, 1H), 7.72 (d, J = 8.2 Hz, 1H), 7.68 (d, J = 8.3 Hz, 1H),

7.43 (ddd, J = 8.1, 7.1, 0.9 Hz, 1H), 7.38-7.27 (m, 6H), 4.58-4.28 (m, 2H), 2.68 (tt, J = 7.0, 4.2 Hz, 1H), 1.32 (t, J = 7.1 Hz, 3H), 1.28-1.19 (m, 1H), 1.14-1.04 (m, 1H), 1.04-0.91 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 163.2, 161.9, 161.5, 138.6, 136.9, 131.6, 129.9, 129.4, 126.9, 125.3, 124.4, 124.2, 123.2, 113.6, 111.7, 110.6, 98.1, 62.2, 26.5, 14.3, 7.9, 6.9; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{25}H_{21}N_2O_5$ 429.1450, found 429.1444.

8ah' (eluent: ethyl acetate / petroleum ether / dichloromethane = 1/12/3, white solid, 29.3 mg, 15%, mp 197-202 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.26 (br, 1H), 8.14 (d, J = 7.1 Hz, 2H), 8.06 (br, 1H), 7.60 (tt, J = 7.3, 1.3 Hz, 1H), 7.55 (d, J = 8.6 Hz, 1H), 7.49 (t, J = 7.4 Hz, 2H), 7.40 (d, J = 8.2 Hz, 1H), 7.21 (ddd, J = 8.1, 7.1, 1.0 Hz, 1H), 7.07 (ddd, J = 8.1, 7.1, 0.9 Hz, 1H), 4.22-4.05 (m, 2H), 3.98-3.81 (m, 2H), 1.55 (s, 9H), 1.09 (t, J = 7.1 Hz, 3H), 0.73 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.4, 164.0, 162.7, 160.4, 147.5, 135.2, 134.5, 134.4, 132.6, 131.5, 129.6, 129.0, 126.5, 124.4, 121.1, 120.5, 112.5, 107.3, 62.4, 61.9, 52.4, 28.8, 13.7, 13.4; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{28}H_{31}N_2O_6$ 491.2182, found 491.2160.

8ai (eluent: ethyl acetate / petroleum ether = 1/4, yellow solid, 51.0 mg, 27%, mp 252-254 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.58 (br, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.40 (d, J = 6.8 Hz, 2H), 7.37-7.26 (m, 6H), 7.19 (d, J = 8.2 Hz, 2H), 7.02 (d, J = 8.3 Hz, 2H), 4.53-4.31 (m, 2H), 2.38 (s, 3H), 1.32 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 163.5, 161.8, 159.2, 138.9, 138.6, 137.0, 132.4, 131.5, 130.0, 129.8, 129.2, 128.8, 126.8, 125.7, 124.4, 124.3, 123.3, 113.8, 111.7, 110.8, 96.9, 62.2, 21.4, 14.3; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{29}H_{23}N_2O_5$ 479.1607, found 479.1601.

8aj' (eluent: acetone / dichloromethane = 1/30, yellow oil, 72.4 mg, 39%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.72 (br, 1H), 7.99 (d, J = 7.1 Hz, 2H), 7.64 (d, J = 6.8 Hz, 1H), 7.50 (tt, J = 7.3, 1.3 Hz, 1H), 7.40 (t, J = 7.4 Hz, 2H), 7.25 (d, J = 6.5 Hz, 1H), 7.18-7.07 (m, 2H), 6.61 (br, 1H), 4.55 (d, J

= 6.2 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.95 (q, *J* = 7.1 Hz, 2H), 1.99 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 3H), 0.81 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.6, 172.1, 165.6, 163.1, 150.2, 136.4, 135.6, 135.2, 133.8, 129.1, 128.8, 128.5, 125.7, 123.0, 120.8, 119.6, 111.7, 106.1, 62.1, 61.8, 35.8, 23.1, 13.7, 13.5; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{26}H_{27}N_2O_6$ 463.1869, found 463.1860.

8ga (eluent: ethyl acetate / petroleum ether = 1/4, yellow solid, 55.9 mg, 31%, mp 209-212 °C): ^{1}H NMR (300 MHz, d_6-DMSO) δ 13.56 (br, 1H), 8.25 (d, *J* = 8.7 Hz, 2H), 7.64 (d, *J* = 8.3 Hz, 1H), 7.58 (d, *J* = 8.3 Hz, 1H), 7.51 (d, *J* = 8.8 Hz, 2H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.26 (t, *J* = 7.5 Hz, 1H), 4.45-4.18 (m, 2H), 3.10 (s, 3H), 1.19 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 165.9, 161.6, 160.9, 157.8, 148.4, 142.6, 138.5, 131.7, 126.8, 126.3, 124.9, 123.7, 123.4, 122.9, 114.0, 110.6, 108.4, 95.3, 61.7, 28.5, 13.9; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{23}H_{18}N_3O_7$ 448.1145, found 448.1139.

9a (eluent: ethyl acetate / petroleum ether = 1/40-1/20, pale yellow oil, it can be isolated from the reaction of **1a** with **2**/**5**/**7** or the self-reaction of **1a** in the presence of Na_2CO_3): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.2 Hz, 2H), 7.56 (t, *J* = 7.3 Hz,1H), 7.46 (t, *J* = 7.4 Hz, 2H), 4.86 (t, *J* = 8.0 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 4H), 4.08 (d, *J* = 8.0 Hz, 2H), 4.03-3.89 (m, 4H), 1.24 (t, *J* = 7.1 Hz, 6H), 1.11 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.0, 167.9, 167.7, 136.8, 133.4, 129.1, 128.5, 62.04, 62.02, 52.8, 43.7, 14.0, 13.8; HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{22}H_{29}O_9$ 437.1812, found 437.1796.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

spectral data (PDF)

NMR spectra of **1f**, **1h**, **1j**, **1k**, **3aa-3ak**, **3ba-3oa**, **4a**,**5g**, **6aa-6ai**, **6ga**, **6aa'**, **6af'**, **6ai'**, **6ba'**, **6aa'**, **7c**, **7d**, **8aa-8ag**, **8ah'**, **8ai**, **8aj'**, **8ga**, and **9a**.

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