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1,2-Alkylarylation of Styrenes with α-Carbonyl Alkyl Bromides and Indoles Using Visible-Light Catalysis

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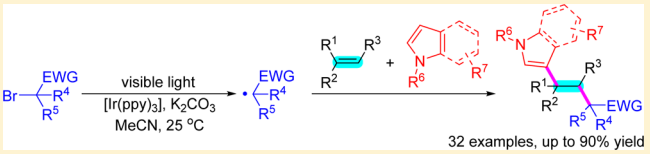
Supporting Information

ABSTRACT: A new intermolecular 1,2-alkylarylation of styrenes with α-carbonyl alkyl bromides and indoles using *fac*-[Ir(ppy)$_3$] as the photoredox catalyst has been developed. The method allows the simultaneous formation of two new carbon−carbon bonds through three component reaction, and represents a new single-electron transfer (SET) strategy for the 1,2-alkylarylation of the styrenes with broad substrate scope and excellent functional group tolerance.

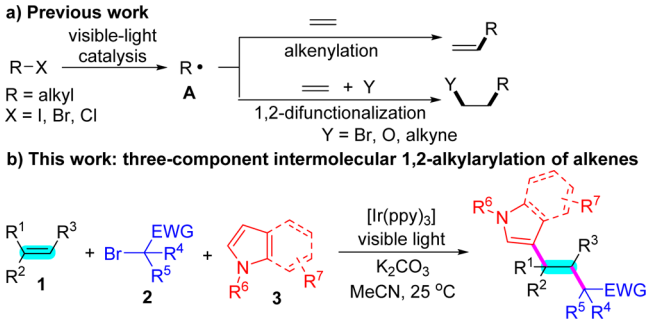


INTRODUCTION

Alkenes Functionalization. Alkenes, which are a class of important organic molecules in the academe and the industry, are present as core motifs in numerous natural products, pharmaceuticals, and polymers, as well as serve as versatile building blocks in synthesis.[1] Accordingly, transformations of alkenes are among the most powerful tools for increasing molecular complexity and continue to draw much attention.[1,2] Typical transformations include the difunctionalization of alkenes, which can efficiently form two new chemical bonds in a single step.[3] Despite these significant advances, the majority of the alkene difunctionalization methods suffer from the harsh reaction conditions (e.g., high reaction temperatures and/or a large loading of transition metal catalysts), and the three-component dicarbofunctionalization of alkenes involving a C−H functionalization manner remains challenging.

Visible-Light-Induced Reactions. The visible-light photoredox catalysis has becoming one of the most powerful strategies for the construction of complex molecules from simple starting materials in synthesis due to its inherently mild, environmentally benign, and low cost features.[4] Among the available methods, the reactions of alkenes with alkyl halides,[5−8] particularly α-carbonyl alkyl bromides,[5b,6a] are particularly attractive, in which alkyl halides were converted into alkyl carbon-centered radicals through visible light-initiated single-electron transfer followed by addition to alkenes. Generally, these transformations proceed via two types of strategies (Scheme 1a): one is the Heck-type alkenylation reaction[5] and the other involves 1,2-difunctionalization reaction.[6−8] However, such successful approaches are less abundant, and the intermolecular three-component dicarbofunctionalization of alkenes with alkyl halides using visible-light catalysis remains an unexploited area. In 2012, Zhang, Yu, and co-workers had first reported the visible-light photoredox catalyzed Heck-type alkenylation of various enamides and enecarbamates with α-carbonyl alkyl bromides involving direct C−H functionalization.[5a] Subsequently, Lei and co-workers

Scheme 1. Transformation of Alkenes with Alkyl Halides with Alkenes Using Photoredox Catalysis



expanded the visible-light catalysis to the alkenylation of simple arylalkenes with various α-carbonyl alkyl bromides and benzyl bromides for producing α-vinyl carbonyls and allylbenzene derivatives.[5b] On the other hand, the 1,2-difunctionalization transformations focus on the 1,2-bromoalkylation,[6] 1,2-alkoxycyanomethylation,[7] and 1,2-dicarbofunctionalization,[8] and the majority of which are restricted to the two-component reactions. In 2014, Lei and co-workers[6a] had developed the first visible-light-initiated three-component 1,2-alkoxycyanomethylation of alkenes with 2-bromoalkylnitriles and alcohols. In light of these results[6a] and our previously reported results,[9] we envisioned that if the carbon nucleophiles had the similar reactivity to alcohols under visible-light catalysis conditions, they would react with alkenes to achieve three-component dicarbofunctionalization. Herein, we report a novel visible-light-induced 1,2-alkylarylation of styrenes with α-carbonyl alkyl bromides and *N*-heterocyclic compounds (e.g., indoles and pyrroles) at room temperature

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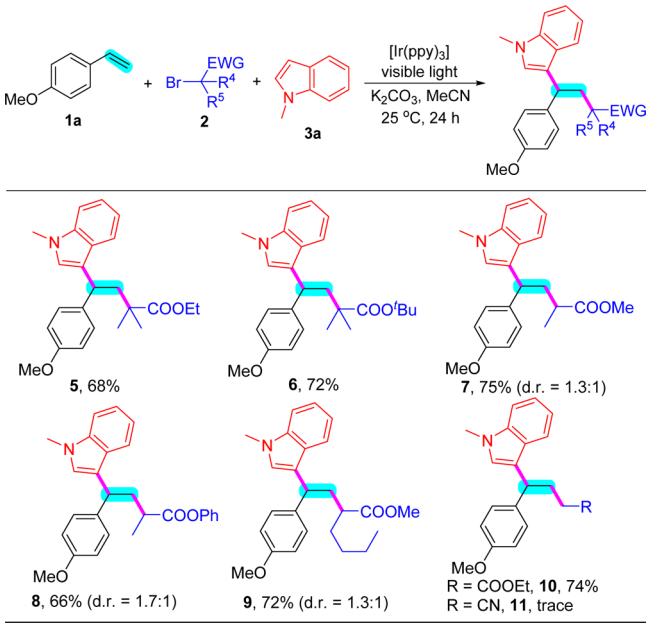
(Scheme 1b);[10] the reaction enables the formation of two new C−C bonds in a single reaction and represents a new mild route to assembling 3-functionalized indoles.

RESULTS AND DISCUSSION

We commenced our study by examining the three-component reaction of 1-methoxy-4-vinylbenzene (**1a**) with diethyl 2-bromo-2-methylmalonate (**2a**) and 1-methyl-1*H*-indole (**3a**) using visible-light catalysis (Table 1). A number of photocatalysts, namely $[Ir(ppy)_3]$, $[Ru(bpy)_3Cl_2]$, and Eosin Y, were initially investigated, and $[Ir(ppy)_3]$ was found to be the most efficient catalyst in terms of yield (entries 1−3). In the presence of $[Ir(ppy)_3]$, K_2CO_3 under irradiation, styrene **1a** underwent the 1,2-alkylarylation reaction with bromide **2a**, 1-methyl-1*H*-indole **3a**, light in MeCN under argon at 25 °C to afford the desired product **4** in a 90% yield (entry 1). However, the reaction could not happen in the absence of photocatalysts (entry 4). A screen of the amount of $[Ir(ppy)_3]$ revealed 1 mol% of $[Ir(ppy)_3]$ as the best choice for further optimization (entries 1, 5, and 6). Notably, without base the reaction delivered trace amount of product **4** (entry 7). This results showed C−Br bond cleavage and deprotonation in this reaction mostly with the aid of bases. Subsequently, three other bases, such as Cs_2CO_3, K_2HPO_4, and Et_3N, were tested; each of which was less effective than K_2CO_3 (entry1 versus entries 8−10). Among the amount of K_2CO_3 and effect of reaction temperature examined, the reaction using 2 equiv of K_2CO_3 at 25 °C turned out to be preferred (entry 1 versus entries 11−14). We found that a series of other solvents, including CH_2Cl_2, toluene, and DMF, displayed lower reactivity for the three-component reaction (entries 15−17). Gratifyingly, a scale of stryene **1a** up to 1 g was successfully performed with good yield (entry 18).

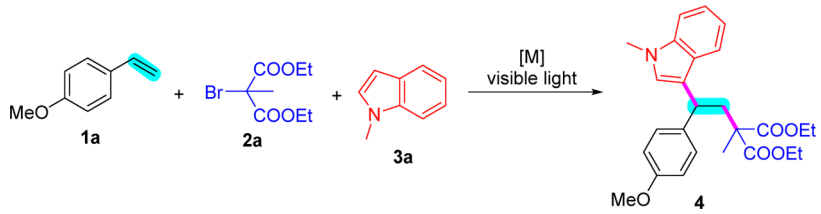
Table 2. Variation of the α-Carbonyl Alkyl Bromides (2)[a]



[a]Reaction conditions: **1a** (0.2 mmol), **2** (0.4 mmol), **3a** (0.4 mmol), $[Ir(ppy)_3]$ (1 mol %), K_2CO_3 (2 equiv), and MeCN (2 mL) under irradiation and argon atmosphere at 25 °C for 24 h. The d.r. value is given in the parentheses as determined by ^1H NMR analysis of the crude product.

With the optimal reaction conditions in hand, we turned our attention to exploit the scope of this visible light-induced three-component reaction with respect to styrenes **1**, α-carbonyl alkyl bromides **2**, and indoles **3** (Table 2). As shown in Table 2, a variety of α-carbonyl alkyl bromides **2** were first investigated in

Table 1. Screening of the Reaction Conditions[a]



entry	[M] [mol %]	base [equiv]	solvent	T [°C]	yield [%][b]
1	$[Ir(ppy)_3]$ (1)	K_2CO_3 (2)	MeCN	25	90
2	$[Ru(bpy)_3Cl_2]$ (1)	K_2CO_3 (2)	MeCN	25	5
3	Eosin Y (1)	K_2CO_3 (2)	MeCN	25	3
4	—	K_2CO_3 (2)	MeCN	25	0
5	$[Ir(ppy)_3]$ (2)	K_2CO_3 (2)	MeCN	25	91
6	$[Ir(ppy)_3]$ (0.5)	K_2CO_3 (2)	MeCN	25	81
7	$[Ir(ppy)_3]$ (1)	—	MeCN	25	trace
8	$[Ir(ppy)_3]$ (1)	Cs_2CO_3 (2)	MeCN	25	36
9	$[Ir(ppy)_3]$ (1)	K_2HPO_4 (2)	MeCN	25	64
10	$[Ir(ppy)_3]$ (1)	Et_3N (2)	MeCN	25	trace
11	$[Ir(ppy)_3]$ (1)	K_2CO_3 (3)	MeCN	25	84
12	$[Ir(ppy)_3]$ (1)	K_2CO_3 (1)	MeCN	25	81
13	$[Ir(ppy)_3]$ (1)	K_2CO_3 (2)	MeCN	10	60
14	$[Ir(ppy)_3]$ (1)	K_2CO_3 (2)	MeCN	40	77
15	$[Ir(ppy)_3]$ (1)	K_2CO_3 (2)	CH_2Cl_2	25	8
16	$[Ir(ppy)_3]$ (1)	K_2CO_3 (2)	toluene	25	5
17	$[Ir(ppy)_3]$ (1)	K_2CO_3 (2)	DMF	25	3
18[c]	$[Ir(ppy)_3]$ (1)	K_2CO_3 (2)	MeCN	25	83

[a]Reaction conditions: **1a** (0.2 mmol); **2a** (0.4 mmol); **3a** (0.4 mmol); [M], base, and solvent (2 mL) under irradiation and argon atmosphere for 24 h. [b]Yield of the isolated product. [c]**1a** (1 g, 7.46 mmol) and MeCN (6 mL) for 48 h.

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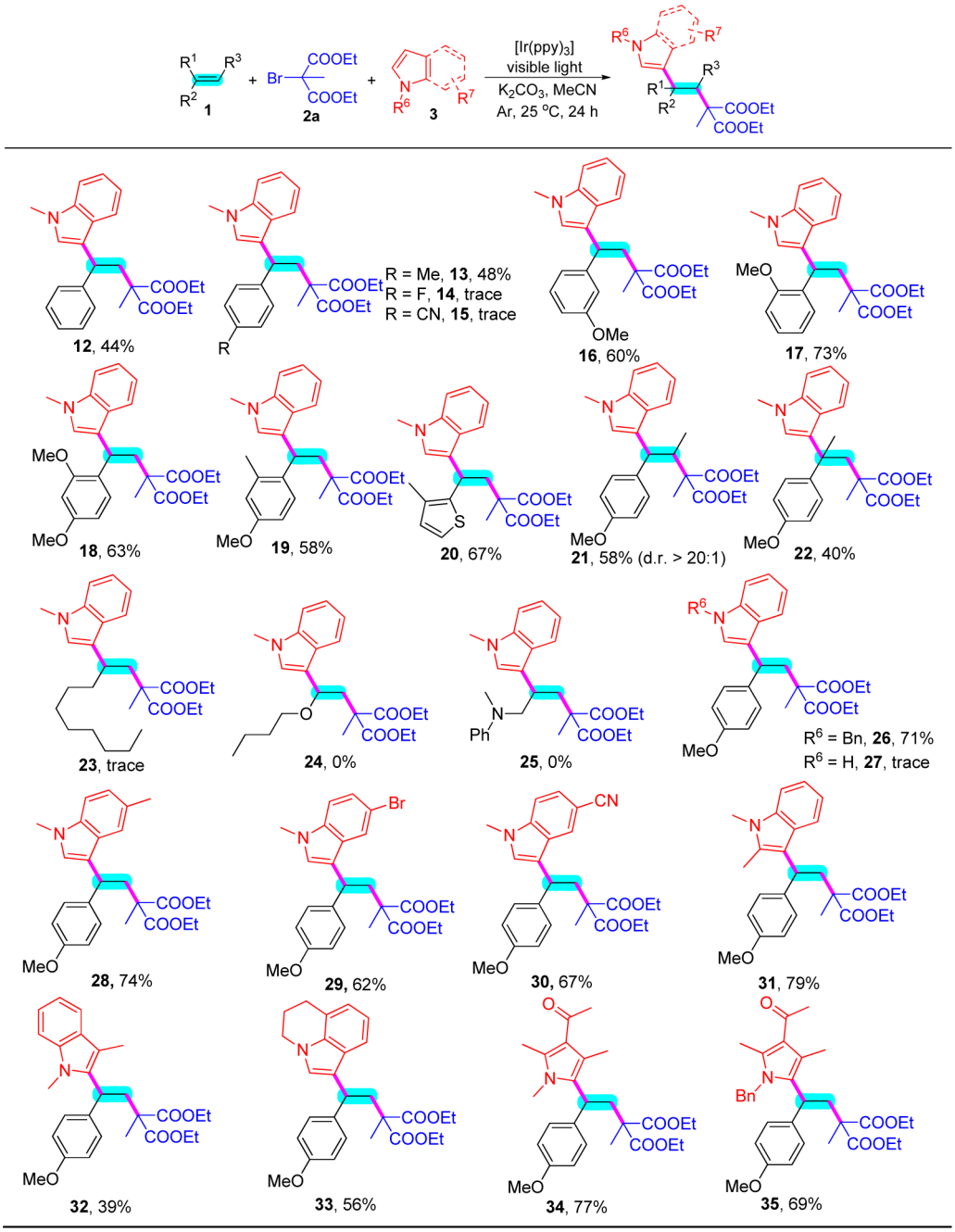
Table 3. Variation of the Alkenes (1) and *N*-Heterocyclic Compounds (3)[a]



[a]Reaction conditions: **1** (0.2 mmol), **2a** (0.4 mmol), **3** (0.4 mmol), [Ir(ppy)$_3$] (1 mol %), K_2CO_3 (2 equiv), and MeCN (2 mL) under irradiation and argon atmosphere at 25 °C for 24 h. The d.r. value given in the parentheses was determined by ^{1}H NMR analysis of the crude product.

the presence of styrene **1a**, indole **3a**, [Ir(ppy)$_3$], and K_2CO_3 under irradiation. To our delight, the optimal conditions were compatible with a wide range of α-carbonyl alkyl bromides **2b**−**2g**, including primary, secondary, and tertiary α-bromoalkyl esters (products **5**−**10**). For example, treatment of tertiary α-bromoalkyl esters **2b** or **2c** with styrene **1a** and indole **3a** [Ir(ppy)$_3$], K_2CO_3 under irradiation smoothly afforded products **5** and **6** in 68 and 72% yields, respectively. Using secondary α-bromoalkyl esters **2d**−**f**, the reaction delivered the corresponding products **7**−**9** with good yields. The experiment result showed that primary α-bromoalkyl ester **2g** was also viable for three-component reaction, providing product **10** in 74% yield. However, only a trace amount of 1,2-alkylarylation product **11** was detected by GC-MS analysis when bromoacetonitrile was used as substrates.

Encouraged by the results described above, we next set out to examine the generality of alkenes **1** and *N*-heterocyclic derivatives **3** under the optimal conditions (Table 3). Initially, an array of alkenes were investigated (products **12**−**25**). The results showed that the optimal conditions were compatible with various substituted styrenes with eletron-donating groups **1b**−**c** and **1f**−**l** (products **12**−**13** and **16**−**22**), but were inert to styrenes with eletron-withdrawing groups **1c,d** and aliphatic alkenes **1k** (products **14,15**, and **23**−**25**). In the presence of bromide **2a** and indole **3a**, [Ir(ppy)$_3$], K_2CO_3 under irradiation, styrene **1b** was a suitable substrate for assembling product **12** in moderate yield.

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Using 1-methyl-4-vinylbenzene **1c** also delivered **13** in 48% yield. Only a trace amount of 1,2-alkylaryllation product **14** and **15** was detected by GC-MS analysis when styrenes with electron-withdrawing groups, such as 4-F and 4-CN, were used as substrates. Styrenes **1f** and **1g** with a methoxy group at the *meta* or *ortho* position were viable to furnish the corresponding products **16** and **17** in good yields. The optimal conditions were consistent with disubstituted styrenes **1h** and **1i**, thus affording the desired products **18** and **19**. Gratifyingly, 3-methyl-2-vinylthiophene **1j** was successfully transferred into **20** in 67% yield. We were pleased to find that the reaction was applicable to internal styrene **1k** and 1,1-disubstutited styrene **1l** (products **21** and **22**). Unfortunately, attempts to react with aliphatic alkene **1m** failed (product **23**). 1-(Vinyloxy)butane **1n** and *N*-allyl-*N*-methylaniline **1o** were also not suitable substrates under the optimal conditions (products **24** and **25**).

Subsequently, the feasibility of this difunctionalization protocol with respect to *N*-heterocyclic compounds **3** were investigated in the presence of alkene **1a** with bromide **2a**, [Ir(ppy)$_3$], K_2CO_3 under irradiation (products **26**−**35**). While 1-benzyl-1*H*-indole **3b** was converted to the corresponding product **26** in 71% yield, *N*-H-free indole **3c** had no reactivity for the reaction (product **27**). Indole **3d**−**f**, bearing either electron-rich or electron-poor substituents, on the 5 position smoothly underwent the reaction, respectively giving the desired products **28**−**30** in good yields. Using 2-methyl-substituted indole **3g** the reaction successfully furnished **31** in 79% yield. Pleasingly, 3-methyl-substituted indole **3h** was also suitable for the construction of the desired product **32**, albeit giving a lower yield. It was noted that 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline **3i** successfully participated in the reaction and resulted in the formation of **33** in 56% yield. To our delight, the optimized conditions were applicable to pyrroles, 1-(1,2,4-trimethyl-1*H*-pyrrol-3-yl)ethan-1-one (**3j**) and 1-(1-benzyl-2,4-dimethyl-1*H*-pyrrol-3-yl)ethan-1-one (**3k**), and the desired products **34** and **35** were formed in good yields.

The kinetic isotope effect (KIE) experiments of 3-deuterated 1-methylindole (**3a-D**) were carried out: k_H/k_D = 1.13:1 was observed, and rules out a hydrogen atom abstraction (radical) process in the indole trapping step (see the Supporting Information).[10] To understand three-component reaction, a possible mechanism outlined in Scheme 2 was proposed on the basis of the above results and the reported literatures.[5−7] Initially, the photocatalyst *fac*-[Ir(III) (ppy)$_3$] is excited by visible light to generate *fac*-[Ir(III) (ppy)$_3$]*, which then undergoes single-electron transfer (SET) to afford the alkyl radical intermediate **A**, *fac*-[Ir(IV) (ppy)$_3$]$^+$ complex, and a bromide anion via a single-electron transfer (SET) process. Subsequently, the addition of the alkyl radical **A** to the C−C double bond of 1-methoxy-4-vinylbenzene (**1a**) gives the new alkyl radical intermediate **B**, which is then oxidized by *fac*-[Ir(IV) (ppy)$_3$] to form the cationic intermediate **C**. Finally, nucleophilic attack and deprotonation of the cationic intermediate **C** in the presence of base delivers the desired product **4**.

CONCLUSIONS

In summary, we have illustrated the first visible-light-induced three-component 1,2-alkylarylation of styrenes with α-carbonyl alkyl bromides and *N*-heterocyclic compounds using *fac*-[Ir(ppy)$_3$] as the photoredox catalyst. This reaction smoothly proceeds at room temperature to construct two new C−C bonds in a single reaction, and provides a mild and practical way to access diverse 3-fucntionalized indoles and 2-fucntionalized pyrroles with a broad scope with regard to alkenes, α-carbonyl alkyl bromides, and *N*-heterocyclic compounds.

EXPERIMENTAL SECTION

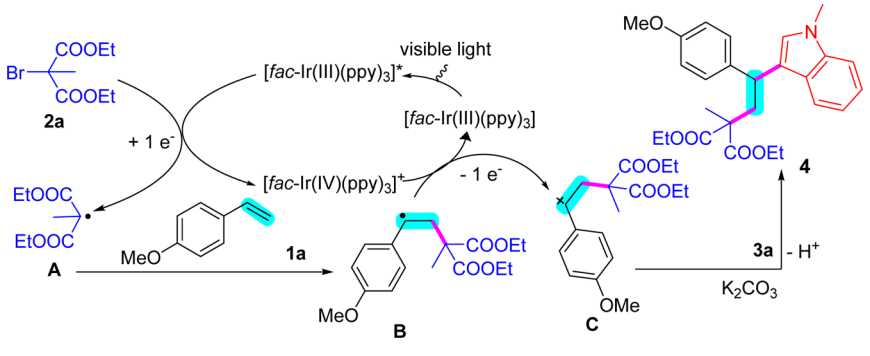
General Considerations. The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solvent on a NMR spectrometer using TMS as internal standard. HRMS was measured on an electrospray ionization (ESI) apparatus using time-of-flight (TOF) mass spectrometry. Melting points are uncorrected.

Typical Experimental Procedure for Visible-Light-Induced 1,2-Alkylarylation of Styrenes with α-Carbonyl Alkyl Bromides and *N*-Heterocyclic Compounds. To a Schlenk tube were added styrenes **1** (0.2 mmol), α-carbonyl alkyl bromides **2** (0.4 mmol), indole **3** (0.4 mmol), [Ir(ppy)$_3$] (1 mol %; 0.002 mmol), K_2CO_3 (2 equiv; 0.4 mmol), and acetonitrile (2 mL). Then the tube was charged with argon, and was stirred at 25 °C (oil bath temperature) under irradiation and argon atmosphere for the indicated time until complete consumption of the starting material as monitored by TLC and/or GC-MS analysis. After the reaction was finished, the reaction mixture was diluted in ethyl acetate and washed with brine. The aqueous phase was re-extracted with ethyl acetate. The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuum, and the resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate) to afford the desired products **4**−**35**.

*Diethyl 2-(2-(4-Methoxyphenyl)-2-(1-methyl-1H-indol-3-yl)ethyl)-2 Methylmalonate (**4**)*[10]. 78.7 mg, 90%; Yellow solid, mp 96.5−97.9 °C (uncorrected); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.54 (d, *J* = 8.0 Hz, 1H), 7.23 (t, *J* = 10.4 Hz, 3H), 7.15 (t, *J* = 8.0 Hz, 1H), 7.02 (t, *J* = 7.2 Hz, 1H), 6.78 (d, *J* = 5.6 Hz, 3H), 4.29 (t, *J* = 6.8 Hz, 1H), 4.0−3.83 (m, 4H), 3.74 (s, 3H), 3.69 (s, 3H), 2.86−2.81 (m, 1H), 2.74−2.69 (m, 1H), 1.42 (s, 3H), 1.13−1.06 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.3, 172.0, 157.8, 137.1, 136.6, 129.0, 126.8, 126.2, 121.5, 119.5, 119.0, 118.7, 113.5, 109.0, 61.0, 60.9, 55.2, 53.3, 40.9, 37.8, 32.6, 20.5, 13.8, 13.7.

*Ethyl 4-(4-Methoxyphenyl)-2,2-dimethyl-4-(1-methyl-1H-indol-3-yl)butanoate (**5**)*.[10] 51.5 mg, 68%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53 (d, *J* = 8.0 Hz, 1H), 7.25−7.21 (m, 3H), 7.16 (t, *J* = 8.0 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.78 (t, *J* = 8.0 Hz,

Scheme 2. Possible Mechanism



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3H), 4.26 (t, J = 6.8 Hz, 1H), 3.74 (s, 3H), 3.69 (s, 3H), 3.64−3.56 (m, 2H), 2.48−2.40 (m, 2H), 1.23 (s, 3H), 1.15 (s, 3H), 1.03 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 177.4, 157.7, 137.2, 137.0, 129.1, 126.9, 126.1, 121.4, 119.5, 119.4, 118.6, 113.5, 109.1, 60.0, 55.2, 46.6, 41.9, 38.7, 32.6, 26.5, 25.7, 13.8.

*tert-Butyl 4-(4-Methoxyphenyl)-2,2-dimethyl-4-(1-methyl-1H-indol-3-yl)butanoate (**6**).*[10] 58.6 mg, 72%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57 (d, J = 8.0 Hz, 1H), 7.26−7.21 (m, 3H), 7.16 (t, J = 8.0 Hz, 1H), 7.03 (t, J = 7.6 Hz, 1H), 6.78 (t, J = 8.4 Hz, 3H), 4.25 (t, J = 7.2 Hz, 1H), 3.74 (s, 3H), 3.68 (s, 3H), 2.53−2.48 (m, 1H), 2.33−2.78 (m, 1H), 1.31 (s, 9H), 1.11 (s, 3H), 1.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 177.0, 157.7, 137.9, 137.2, 128.9, 127.0, 126.0, 121.4, 119.9, 119.5, 118.6, 113.6, 109.1, 79.7, 55.2, 46.2, 43.1, 38.9, 32.6, 27.8, 26.4, 26.1.

*Methyl 4-(4-Methoxyphenyl)-2-methyl-4-(1-methyl-1H-indol-3-yl)butanoate (**7**).*[10] 52.7 mg, 75%; d.r. = 1.3:1; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.48 (d, J = 8.0 Hz, 0.44H), 7.42 (d, J = 7.6 Hz, 0.57H), 7.25−7.14 (m, 4H), 7.03−6.98 (m, 1H), 6.82−6.79 (m, 3H), 4.21−4.16 (m, 1H), 3.74 (s, 3H), 3.70 (s, 3H), 3.65 (s, 1.29H), 3.57 (s, 1.73H), 2.65−2.58 (m, 0.46H), 2.48−2.41 (m, 1.56H), 2.22−2.17 (m, 0.47H), 2.00−1.93 (m, 0.55H), 1.22 (d, J = 6.0 Hz, 1.68H), 1.16 (d, J = 6.8 Hz, 1.32H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 177.2, 157.9, 157.8, 137.2, 136.6, 136.3, 128.8, 128.7, 127.2, 127.1, 125.8 (2C), 121.5 (2C), 119.5, 119.4, 118.7, 118.6, 118.4 (2C), 113.7, 109.1, 109.0, 55.1, 51.5, 51.4, 40.4, 39.8, 39.7, 39.5, 37.6, 37.5, 32.6, 17.7, 17.0.

*Phenyl 4-(4-Methoxyphenyl)-2-methyl-4-(1-methyl-1H-indol-3-yl)butanoate (**8**).*[10] 54.5 mg, 66%; d.r. = 1.7:1; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53 (d, J = 8.0 Hz, 0.39H), 7.47 (d, J = 8.0 Hz, 0.67H), 7.35 (t, J = 9.6 Hz, 2H), 7.28−7.23 (m, 3H), 7.21−7.16 (m, 2H), 7.06−7.03 (m, 2H), 6.98 (d, J = 8.0 Hz, 1H), 6.86 (d, J = 6.0 Hz, 1.12H), 6.83 (d, J = 8.0 Hz, 1.88H), 4.32 (t, J = 8.0 Hz, 1H), 3.77 (s, 1.11H), 3.76 (s, 1.91H), 3.73 (s, 1.94H), 3.71 (s, 1.06H), 2.78−2.56 (m, 2H), 2.35−2.28 (m, 0.66H), 2.13−2.05 (m, 0.40H), 1.38 (d, J = 6.8 Hz, 1.90H), 1.32 (d, J = 7.2 Hz, 1.12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.2 (2C), 158.0 (2C), 150.8 (2C), 137.3, 137.2, 136.5, 136.3, 129.4, 129.3, 128.8 (2C), 127.2, 127.1, 126.0, 125.9, 125.7, 125.6, 121.6, 121.5 (2C), 119.6, 119.5, 118.8 (2C), 118.3, 118.2, 113.9, 113.8, 109.2, 109.1, 55.2, 40.4, 40.0, 39.8, 39.6, 37.9, 37.8, 32.7, 17.8, 17.2.

*Methyl 2-(2-(4-Methoxyphenyl)-2-(1-methyl-1H-indol-3-yl)ethyl)-hexanoate (**9**).*[10] 56.6 mg, 72%; d.r. = 1.3:1; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.48 (d, J = 8.0 Hz, 1H), 7.22−7.14 (m, 4H), 7.02 (t, J = 7.6 Hz, 1H), 6.83 (d, J = 8.8 Hz, 2H), 6.75 (s, 1H), 4.10−4.07 (m, 1H), 3.77 (s, 3H), 3.70 (s, 3H), 3.66 (s, 3H), 2.60−2.52 (m, 1H), 2.36−2.31 (m, 1H), 2.07−2.00 (m, 1H), 1.65−1.58 (m, 1H), 1.50−1.41 (m, 1H), 1.26−1.17 (m, 4H), 0.83 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 176.8, 157.9, 137.2, 136.3, 128.9, 127.1, 125.7, 121.5, 119.5, 119.0, 118.7, 113.7, 109.0, 55.1, 51.3, 43.6, 40.2, 38.8, 32.7, 32.6, 29.3, 22.6, 13.9.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41 (d, J = 7.6 Hz, 1H), 7.23−7.14 (m, 4H), 7.00 (t, J = 7.6 Hz, 1H), 6.84 (s, 1H), 6.79 (d, J = 8.0 Hz, 2H), 4.14 (t, J = 7.6 Hz, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.54 (s, 3H), 2.42−2.35 (m, 2H), 2.29−2.24 (m, 1H), 1.67−1.56 (m, 2H), 1.26−1.22 (m, 4H), 0.85 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 176.8, 157.8, 137.2, 136.7, 128.7, 127.2, 125.9, 121.5, 119.5, 118.6, 118.1, 113.6, 109.1, 55.1, 51.2, 43.8, 40.0, 38.5, 32.6, 32.2, 29.3, 22.6, 13.9.

*Ethyl 4-(4-Methoxyphenyl)-4-(1-methyl-1H-indol-3-yl)butanoate (**10**).*[10] 51.9 mg, 74%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.43 (d, J = 8.0 Hz, 1H), 7.26−7.19 (m, 3H), 7.16 (t, J = 7.6 Hz, 1H), 7.00 (t, J = 7.6 Hz, 1H), 6.86 (s, 1H), 6.81 (d, J = 8.8 Hz, 2H), 4.15−4.06 (m, 3H), 3.75 (s, 3H), 3.72 (s, 3H), 2.52−2.46 (m, 1H), 2.34−2.26 (m, 3H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.7, 157.9, 137.2, 136.5, 128.8, 127.2, 125.8, 121.5, 119.5, 118.7, 118.3, 113.7, 109.1, 60.2, 55.2, 41.4, 32.9, 32.6, 31.2, 14.2.

*Diethyl 2-Methyl-2-(2-(1-methyl-1H-indol-3-yl)-2-phenylethyl)-malonate (**12**).* 35.8 mg, 44%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.55 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 7.6 Hz, 2H), 7.26−7.22 (m, 3H), 7.18−7.11 (m, 2H), 7.03 (t, J = 7.6 Hz, 1H), 6.81 (s, 1H), 4.34 (t, J = 6.8 Hz, 1H), 3.98−3.75 (m, 4H), 3.71 (s, 3H), 2.87−2.83 (m, 1H), 2.79−2.73 (m, 1H), 1.42 (s, 3H), 1.12−1.05 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.3, 172.0, 144.6, 137.1, 128.1 (2C), 126.9, 126.3, 126.1, 121.5, 119.5, 118.7, 118.6, 109.1, 61.0 (2C), 53.3, 40.9, 38.7, 32.6, 20.6, 13.8, 13.7; HRMS m/z (ESI) calcd for $C_{25}H_{30}NO_4$ $[M+H]^+$ 408.2169, found 408.2174.

*Diethyl 2-Methyl-2-(2-(1-methyl-1H-indol-3-yl)-2-(p-tolyl)ethyl)-malonate (**13**).* 40.4 mg, 48%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.56 (d, J = 8.0 Hz, 1H), 7.22 (d, J = 8.0 Hz, 3H), 7.15 (t, J = 8.4 Hz, 1H), 7.06−7.00 (m, 3H), 6.80 (s, 1H), 4.30 (t, J = 6.8 Hz, 1H), 3.98−3.81 (m, 4H), 3.69 (s, 3H), 2.87−2.82 (m, 1H), 2.76−2.70 (m, 1H), 2.27 (s, 3H), 1.41 (s, 3H), 1.12−1.05 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.3, 172.1, 141.6, 137.1, 135.4, 128.8, 128.0, 126.9, 126.2, 121.5, 119.5, 118.8, 118.7, 109.0, 61.0, 60.9, 53.4, 40.9, 38.2, 32.6, 20.9, 20.6, 13.8, 13.7; HRMS m/z (ESI) calcd for $C_{26}H_{32}NO_4$ $[M+H]^+$ 422.2326, found 422.2333.

*Diethyl 2-(2-(3-Methoxyphenyl)-2-(1-methyl-1H-indol-3-yl)ethyl)-2-methylmalonate (**16**).* 52.4 mg, 60%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57 (d, J = 8.0 Hz, 1H), 7.23 (t, J = 7.6 Hz, 1H), 7.16 (t, J = 8.0 Hz, 2H), 7.03 (t, J = 7.6 Hz, 1H), 6.95 (d, J = 8.0 Hz, 1H), 6.88 (s, 1H), 6.82 (s, 1H), 6.68 (d, J = 8.0 Hz, 1H), 4.32 (t, J = 6.8 Hz, 1H), 4.01−3.80 (m, 4H), 3.75 (s, 3H), 3.70 (s, 3H), 2.87−2.82 (m, 1H), 2.76−2.70 (m, 1H), 1.42 (s, 3H), 1.13−1.06 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.3, 172.0, 159.4, 146.4, 137.1, 129.1, 126.9, 126.3, 121.5, 120.6, 119.5, 118.7, 118.4, 114.2, 111.1, 109.0, 61.0 (2C), 55.1, 53.4, 40.8, 38.7, 32.6, 20.5, 13.8, 13.7; HRMS m/z (ESI) calcd for $C_{26}H_{32}NO_5$ $[M H]^+$ 438.2275, found 438.2280.

*Diethyl 2-(2-(2-Methoxyphenyl)-2-(1-methyl-1H-indol-3-yl)ethyl)-2-methylmalonate (**17**).* 63.8 mg, 73%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.61 (d, J = 8.0 Hz, 1H), 7.27 (d, J = 7.6 Hz, 1H), 7.21 (d, J = 8.0 Hz, 1H), 7.14 (t, J = 7.6 Hz, 1H), 7.09 (t, J = 8.0 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1H), 6.87 (s, 1H), 6.81 (t, J = 7.2 Hz, 2H), 4.89 (t, J = 8.0 Hz, 1H), 3.91−3.88 (m, 1H), 3.87 (s, 3H), 3.86−3.76 (m, 3H), 3.69 (s, 3H), 2.89−2.84 (m, 1H), 2.76−2.70 (m, 1H), 1.48 (s, 3H), 1.11−1.05 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.5, 172.0, 156.6, 136.9, 132.6, 128.8, 127.3, 127.0, 126.4, 121.3, 120.2, 119.7, 118.6 (2C), 110.5, 108.9, 60.8 (2C), 55.3, 53.3, 40.1, 32.6, 29.8, 19.8, 13.8, 13.7; HRMS m/z (ESI) calcd for $C_{26}H_{32}NO_5$ $[M+H]^+$ 438.2275, found 438.2283.

*Diethyl 2-(2-(2,4-Dimethoxyphenyl)-2-(1-methyl-1H-indol-3-yl)-ethyl)-2-methylmalonate (**18**).* 58.8 mg, 63%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.60 (d, J = 8.0 Hz, 1H), 7.21 (d, J = 8.0 Hz, 1H), 7.14 (t, J = 7.6 Hz, 2H), 7.02 (t, J = 7.6 Hz, 1H), 6.85 (s, 1H), 6.40 (s, 1H), 6.36 (d, J = 7.2 Hz, 1H), 4.79−4.76 (m, 1H), 3.92−3.89 (m, 2H), 3.85 (s, 3H), 3.83−3.77 (m, 2H), 3.73 (s, 3H), 3.69 (s, 3H), 2.86−2.81 (m, 1H), 2.72−2.67 (m, 1H), 1.47 (s, 3H), 1.12−1.06 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.5, 172.1, 158.9, 157.6, 137.0, 129.2, 127.3, 126.3, 125.2, 121.3, 119.7, 118.9, 118.5, 108.9, 104.1, 98.2, 60.8 (2C), 55.3, 55.2, 53.3, 40.2, 32.6, 29.5, 19.8, 13.8, 13.7; HRMS m/z (ESI) calcd for $C_{27}H_{34}NO_6$ $[M+H]^+$ 468.2381, found 468.2388.

*Diethyl 2-(2-(4-Methoxy-2-methylphenyl)-2-(1-methyl-1H-indol-3-yl)ethyl)-2-methylmalonate (**19**).* 52.3 mg, 58%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70 (d, J = 8.0 Hz, 1H), 7.36 (d, J = 8.4 Hz, 1H), 7.25−7.16 (m, 2H), 7.08 (t, J = 7.6 Hz, 1H), 6.72 (d, J = 8.4 Hz, 1H), 6.67 (s, 1H), 6.52 (s, 1H), 4.56−4.53 (m, 1H), 4.00−3.90 (m, 2H), 3.88−3.77 (m, 2H), 3.76 (s, 3H), 3.65 (s, 3H), 2.85−2.80 (m, 1H), 2.72−2.66 (m, 1H), 2.31 (s, 3H), 1.42 (s, 3H), 1.15−1.10 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.3, 172.2, 157.5, 137.3, 137.2, 134.2, 128.1, 127.1, 127.0, 121.4, 119.4, 119.0, 118.7, 115.8, 110.8, 109.1, 61.0 (2C), 55.1, 53.4, 40.8, 33.1, 32.6, 21.0, 20.1, 13.8 (2C); HRMS m/z (ESI) calcd for $C_{27}H_{34}NO_5$ $[M+H]^+$ 452.2431, found 452.2437.

*Diethyl 2-Methyl-2-(2-(1-methyl-1H-indol-3-yl)-2-(3-methylthiophen-2-yl)ethyl)malonate (**20**).* 57.2 mg, 67%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66 (d, J = 8.0 Hz, 1H), 7.22 (d, J = 8.0 Hz, 1H), 7.17 (t, J = 7.6 Hz, 1H), 7.06 (t, J = 8.0 Hz, 1H), 7.00 (d, J = 5.2 Hz, 1H), 6.86 (s, 1H), 6.69 (d, J = 4.8 Hz, 1H), 4.67 (t, J = 6.8 Hz, 1H), 4.00−3.91 (m, 2H), 3.84−3.76 (m, 2H), 3.67 (s, 3H)

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2.94−2.89 (m, 1H), 2.72−2.66 (m, 1H), 2.22 (s, 3H), 1.43 (s, 3H), 1.13−1.09 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.0 (2C), 142.9, 136.9, 132.3, 129.7, 126.6, 126.5, 121.5, 121.4, 119.3, 118.8, 118.2, 109.1, 61.1, 61.0, 53.3, 42.7, 32.6, 31.8, 20.4, 14.0, 13.8 (2C); HRMS m/z (ESI) calcd for $C_{24}H_{30}NO_4S$ $[M + H]^+$ 428.1890, found 428.1896.

*Diethyl 2-(1-(4-Methoxyphenyl)-1-(1-methyl-1H-indol-3-yl)-propan-2-yl)-2-methylmalonate (**21**).* 52.3 mg, 58%; d.r. > 20:1; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 1H), 7.16 (t, J = 8.0 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 6.98 (s, 1H), 6.74 (d, J = 8.4 Hz, 2H), 4.49 (d, J = 6.8 Hz, 1H), 4.07−4.01 (m, 2H), 3.90−3.82 (m, 2H), 3.74 (s, 3H), 3.72 (s, 3H), 3.36−3.29 (m, 1H), 1.33 (s, 3H), 1.18 (t, J = 7.2 Hz, 3H), 1.11 (t, J = 7.2 Hz, 3H), 1.05 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.8, 171.7, 157.6, 136.7, 136.5, 129.8, 128.1, 126.8, 121.4, 119.3, 118.7, 116.7, 113.2, 108.9, 61.1, 61.0, 58.1, 55.2, 43.1, 42.7, 32.7, 16.8, 14.7, 13.9, 13.8; HRMS m/z (ESI) calcd for $C_{27}H_{34}NO_5$ $[M + H]^+$ 452.2431, found 452.2435.

*Diethyl 2-(2-(4-Methoxyphenyl)-2-(1-methyl-1H-indol-3-yl)-propyl)-2-methylmalonate (**22**).* 36.1 mg, 40%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.29 (d, J = 7.6 Hz, 2H), 7.23 (d, J = 8.4 Hz, 1H), 7.11 (t, J = 8.0 Hz, 2H), 6.88−6.84 (m, 2H), 6.78 (d, J = 7.6 Hz, 2H), 4.07−3.96 (m, 3H), 3.91−3.79 (m, 1H), 3.77 (s, 3H), 3.74 (s, 3H), 3.24 (d, J = 14.4 Hz, 1H), 3.01 (d, J = 14.8 Hz, 1H), 1.73 (s, 3H), 1.20−1.13 (m, 6H), 1.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.0, 172.7, 157.5, 140.8, 137.6, 128.2, 126.4, 126.1, 124.1, 121.4, 121.1, 118.4, 113.1, 109.0, 61.1, 60.9, 55.1, 53.5, 44.0, 41.1, 32.6, 26.8, 20.4, 13.9, 13.8; HRMS m/z (ESI) calcd for $C_{27}H_{34}NO_5$ $[M+H]^+$ 452.2431, found 452. 2437.

*Diethyl 2-(2-(1-Benzyl-1H-indol-3-yl)-2-(4-methoxyphenyl)ethyl)-2-methylmalonate (**26**).*[10] 72.9 mg, 71%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.54 (d, J = 8.0 Hz, 1H), 7.29−7.22 (m, 5H), 7.16 (d, J = 8.0 Hz, 1H), 7.09−7.06 (m, 3H), 7.00 (t, J = 7.6 Hz, 1H), 6.92 (s, 1H), 6.78 (d, J = 8.4 Hz, 2H), 5.23 (s, 2H), 4.32 (t, J = 7.2 Hz, 1H), 3.99−3.88 (m, 3H), 3.73 (s, 3H), 3.67−3.63 (m, 1H), 2.87−2.75(m, 1H), 2.73−2.69 (m, 1H), 1.42 (s, 3H), 1.12−1.05 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.3, 172.0, 157.8, 137.6, 136.8, 136.6, 129.1, 128.6, 127.4, 127.2, 126.6, 125.6, 121.7, 119.6, 119.5, 118.9, 113.5, 109.6, 61.0, 60.9, 55.1, 53.3, 49.9, 40.9, 37.9, 20.5, 13.8, 13.7.

*Diethyl 2-(2-(1,5-Dimethyl-1H-indol-3-yl)-2-(4-methoxyphenyl)-ethyl)-2-methylmalonate (**28**).*[10] 66.8 mg, 74%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.30 (s, 1H), 7.25 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 8.4 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 6.77 (t, J = 10.0 Hz, 3H), 4.27−4.23 (m, 1H), 4.01−3.82 (m, 4H), 3.74 (s, 3H), 3.67 (s, 3H), 2.83−2.78 (m, 1H), 2.73−2.68 (m, 1H), 2.40 (s, 3H), 1.41 (s, 3H), 1.14−1.07 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.3, 172.0, 157.8, 136.8, 135.6, 129.0, 127.8, 127.0, 126.3, 123.1, 119.0, 118.3, 113.5, 108.7, 61.0, 60.9, 55.2, 53.3, 41.0, 37.7, 32.6, 21.5, 20.5, 13.8, 13.7.

*Diethyl 2-(2-(5-Bromo-1-methyl-1H-indol-3-yl)-2-(4-methoxyphenyl)ethyl)-2-methylmalonate (**29**).*[10] 63.9 mg, 62%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.64 (s, 1H), 7.22 (d, J = 8.8 Hz, 3H), 7.08 (d, J = 8.4 Hz, 1H), 6.80 (t, J = 4.2 Hz, 3H), 4.22 (t, J = 7.2 Hz, 1H), 4.01−3.82 (m, 3H), 3.76 (s, 3H), 3.74−3.68 (m, 1H), 3.68 (s, 3H), 2.79−2.74 (m, 1H), 2.71−2.66 (m, 1H), 1.39 (s, 3H), 1.16−1.08 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.2, 172.0, 157.9, 136.2, 135.8, 128.9, 128.5, 127.4, 124.3, 121.9, 118.5, 113.6, 112.2, 110.6, 61.1, 61.0, 55.2, 53.3, 40.9, 37.7, 32.8, 20.6, 13.8, 13.7.

*Diethyl 2-(2-(5-Cyano-1-methyl-1H-indol-3-yl)-2-(4-methoxyphenyl)ethyl)-2-methylmalonate (**30**).*[10] 61.9 mg, 67%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.88 (s, 1H), 7.37 (d, J = 8.8 Hz, 1H), 7.27−7.20 (m, 3H), 6.94 (s, 1H), 6.81 (d, J = 8.4 Hz, 2H), 4.29 (t, J = 7.2 Hz, 1H), 4.01−3.84 (m, 4H), 3.76 (s, 3H), 3.74 (s, 3H), 2.80−2.67 (m, 2H), 1.40 (s, 3H), 1.16−1.08 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.0, 171.8, 158.1, 138.5, 135.6, 128.8, 128.3, 126.6, 125.1, 124.5, 120.9, 120.3, 113.7, 109.9, 101.7, 61.1, 61.0, 55.1, 53.1, 40.8, 37.6, 32.8, 20.6, 13.8, 13.7.

*Diethyl 2-(2-(1,2-Dimethyl-1H-indol-3-yl)-2-(4-methoxyphenyl)-ethyl)-2-methylmalonate (**31**).*[10] 71.3 mg, 79%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.58 (d, J = 8.0 Hz, 1H), 7.28 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.4 Hz, 1H), 7.08 (t, J = 8.0 Hz, 1H), 6.98 (t, J = 7.8 Hz, 1H), 6.76 (d, J = 8.4 Hz, 2H), 4.28−4.24 (m, 1H), 4.04−3.95 (m, 2H), 3.72 (s, 3H), 3.61 (s, 3H), 3.59−3.55 (m, 1H), 3.17−3.11 (m, 1H), 3.05−2.97 (m, 1H), 2.85−2.80 (m, 1H), 2.38 (s, 3H), 1.41 (s, 3H), 1.13 (t, J = 7.2 Hz, 3H), 0.79 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.6, 171.6, 157.5, 137.7, 136.9, 133.4, 128.4, 126.6, 120.2, 119.9, 118.6, 113.5, 112.8, 108.4, 61.0, 60.4, 55.2, 53.3, 39.5, 36.7, 29.5, 19.9, 13.9, 13.4, 10.8.

*Diethyl 2-(2-(1,3-Dimethyl-1H-indol-2-yl)-2-(4-methoxyphenyl)-ethyl)-2-methylmalonate (**32**).*[10] 35.2 mg, 39%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.51 (d, J = 7.6 Hz, 1H), 7.18−7.12 (m, 4H), 7.06 (t, J = 7.6 Hz, 1H), 6.78 (d, J = 8.4 Hz, 2H), 4.53−4.50 (m, 1H), 4.02−3.97 (m, 2H), 3.74 (s, 3H), 3.68−3.64 (m, 1H), 3.48 (s, 3H), 3.47−3.42 (m, 1H), 3.00−2.94 (m, 1H), 2.90−2.85 (m, 1H), 2.37 (s, 3H), 1.43 (s, 3H), 1.16 (t, J = 7.2 Hz, 3H), 0.98 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.2, 171.4, 157.9, 136.9, 136.4, 134.3, 128.4, 128.3, 121.0, 118.5, 118.1, 113.7, 108.4, 108.2, 61.3, 61.1, 55.2, 38.3, 35.6, 30.5, 20.2, 13.8, 13.6, 9.8.

*Diethyl 2-(2-(5,6-Dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1-yl)-2-(4-methoxyphenyl)ethyl)-2-methylmalonate (**33**).*[10] 51.9 mg, 56%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35 (d, J = 7.6 Hz, 1H), 7.25 (d, J = 8.4 Hz, 2H), 6.92 (t, J = 7.6 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 6.79 (d, J = 7.6 Hz, 3H), 4.28−4.24 (m, 1H), 4.04 (t, J = 6.0 Hz, 2H), 4.00−3.82 (m, 3H), 3.74 (s, 3H), 3.72−3.68 (m, 1H), 2.92 (t, J = 6.4 Hz, 2H), 2.89−2.84 (m, 1H), 2.75−2.70 (m, 1H), 2.16 (t, J = 6.0 Hz, 2H), 1.41 (s, 3H), 1.13−1.07 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.3, 172.0, 157.8, 136.8, 134.6, 129.1, 124.3, 123.4, 121.5, 119.2, 119.1, 118.3, 117.1, 113.4, 61.0, 60.9, 55.2, 53.3, 43.8, 40.8, 38.3, 24.6, 22.8, 20.4, 13.8, 13.7.

*Diethyl 2-(2-(4-Acetyl-1,3,5-trimethyl-1H-pyrrol-2-yl)-2-(4-methoxyphenyl)ethyl)-2-methylmalonate (**34**).* 70.4 mg, 77%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.10 (d, J = 8.4 Hz, 2H), 6.82 (d, J = 8.4 Hz, 2H), 4.37−4.33 (m, 1H), 4.12−4.06 (m, 2H), 3.90−3.83 (m, 1H), 3.77 (s, 3H), 3.74−3.68 (m, 1H), 3.18 (s, 3H), 2.85−2.77(m, 2H), 2.44 (s, 3H), 2.40 (s, 3H), 2.27 (s, 3H), 1.44 (s, 3H), 1.22 (t, J = 7.2 Hz, 3H), 1.12 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 195.8, 172.3, 171.3, 157.8, 135.5, 134.3, 129.2, 128.0, 121.2, 116.6, 113.7, 61.4, 61.2, 55.2, 53.1, 37.6, 34.1, 31.4, 31.3, 20.0, 13.9, 13.7, 13.1, 12.3; HRMS m/z (ESI) calcd for $C_{26}H_{36}NO_6$ $[M+H]^+$ 458.2537, found 458.2543.

*Diethyl 2-(2-(4-Acetyl-1-benzyl-3,5-dimethyl-1H-pyrrol-2-yl)-2-(4-methoxyphenyl)ethyl)-2-methylmalonate (**35**).* 73.6 mg, 69%; Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.13 (d, J = 6.4 Hz, 3H), 6.97 (d, J = 8.4 Hz, 2H), 6.69−6.68 (m, 2H), 6.62 (d, J = 8.4 Hz, 2H), 5.07−4.95 (m, 2H), 4.25−4.17 (m, 1H), 4.01−3.78 (m, 4H), 3.68 (s, 3H), 2.77−2.66 (m, 2H), 2.46 (s, 3H), 2.38 (s, 3H), 2.32 (s, 3H), 1.29 (s, 3H), 1.17−1.10 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 196.1, 172.0, 171.7, 157.7, 136.7, 135.0, 134.2, 131.1, 128.5, 128.3, 126.8, 125.5, 122.2, 116.1, 113.4, 61.2, 55.1, 53.2, 47.3, 39.1, 35.6, 31.6, 20.0, 13.8 (2C), 13.3, 12.5; HRMS m/z (ESI) calcd for $C_{32}H_{40}NO_6$ $[M+H]^+$ 534.2850, found 534.2858.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01002.

Copies of ^{1}H and ^{13}C spectra (PDF)

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Notes

The authors declare no competing financial interest.

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