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Construction of 9*H*-Pyrrolo[1,2-*a*]indoles by a Copper-Catalyzed Friedel–Crafts Alkylation/Annulation Cascade Reaction

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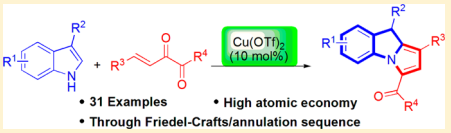
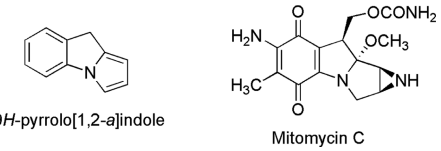
Supporting Information

ABSTRACT: An efficient and concise $Cu(OTf)_2$-catalyzed Friedel–Crafts alkylation/annulation cascade reaction of substituted indoles with 1,2-dicarbonyl-3-enes has been established. This reaction uses readily available starting materials and is operationally simple, thus representing a practical method for the construction of diverse 9*H*-pyrrolo[1,2-*a*]indoles bearing a carbonyl group.

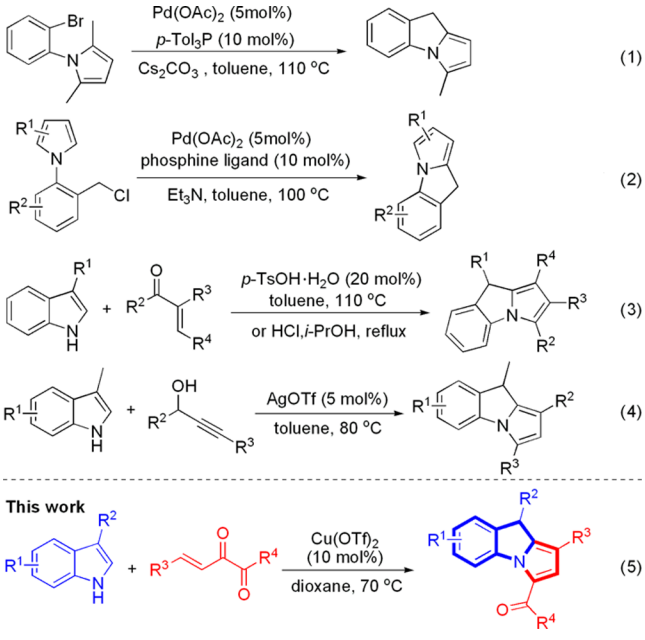


N-Fused heterocyclic compounds have attracted considerable attention both from synthetic and medicinal chemists due to their wide range of applications in numerous organic functional materials and pharmaceutically active molecules.[1] Substrates containing a 9*H*-pyrrolo[1,2-*a*]indole skeleton (Scheme 1) have increasingly been of paramount interest recently due to their considerable antitumor and antibacterial properties.[2] A representative example is mytomycin C, one of the most effective antitumor agents (Scheme 1).[3] Therefore, much effort has been devoted to developing efficient synthetic methods for the construction of these novel 9*H*-pyrrolo[1,2-*a*]indoles.[4] Among these, direct C–H functionalization has been demonstrated to be a powerful tool for the 9*H*-pyrrolo[1,2-*a*]indole synthesis.[5] A major advance in this area has been the Pd-catalyzed chemoselective intramolecular sp^3 C–H activation of the methyl group in 2-bromo-*N*-(2-methylaryl)-pyrroles affording 9*H*-pyrrolo[1,2-*a*]indoles described by Knochel and co-workers (Scheme 2, eq 1).[5a] Subsequently, Chang and co-workers have disclosed an efficient Pd-catalyzed cyclization of *N*-(2-chlorobenzyl)-substituted pyrroles to afford 9*H*-pyrrolo-[1,2-*a*]indoles via tandem activation of a benzylic chloride and an aromatic C–H bond (Scheme 2, eq 2).[5c] However, certain phosphine ligands are necessary in order to improve the reactions' reactivity in these studies. In addition, a tandem Wittig-metathesis strategy uses *N*-allylindole-2-carbaldehyde to generate 9*H*-pyrrolo[1,2-*a*]indoles has been developed by Pérez-Castells.[4c] Moreover, the direct [3 + 2] annulation reactions between indoles and *α,β*-unsaturated ketones under strong acid conditions to provide 9*H*-pyrrolo[1,2-*a*]indoles were reported by Kumar and Zu, respectively (Scheme 2, eq 3).[6] In 2010, a silver-catalyzed cascade Friedel–Crafts reaction/N–C bond formation protocol for the chemoselective assembly of 9*H*-pyrrolo[1,2-*a*]indoles from readily available propargyl alcohols and 3-substituted 1*H*-indoles was reported by Zhan and co-workers (Scheme 2, eq 4).[7]

Scheme 1. 9*H*-Pyrrolo[1,2-*a*]indole Skeleton and the Structure of Mytomycin C



Scheme 2. Synthesis of 9*H*-Pyrrolo[1,2-*a*]indoles



During the course of our recent research on 1,2-dicarbonyl-3-enes synthesis,[8] we envisioned that a Friedel–Crafts/annulation of indoles with 1,2-dicarbonyl-3-enes might occur through a cascade sequence, thus leading to pyrrolo[1,2-*a*]indoles. Herein, we report a copper-catalyzed Friedel–Crafts alkylation/annulation cascade reaction of 3-substituted indoles with 1,2-dicarbonyl-3-enes for ready construction of 9*H*-

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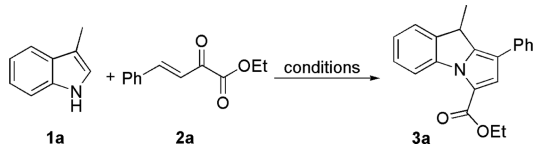
pyrrolo[1,2-*a*]indole derivatives (Scheme 2, eq 4). The current method features advantages including simple and readily available starting materials, mild reaction conditions, and nonhazardous byproducts.

With this hypothesis in mind, we initially chose 3-methyl-1*H*-indole **1a** and ethyl 2-oxo-4-phenylbut-3-enoate **2a** as the model substrates to optimize the reaction conditions (Table 1).

Table 1. Optimization of Reaction Conditions[a]



1a 2a 3a

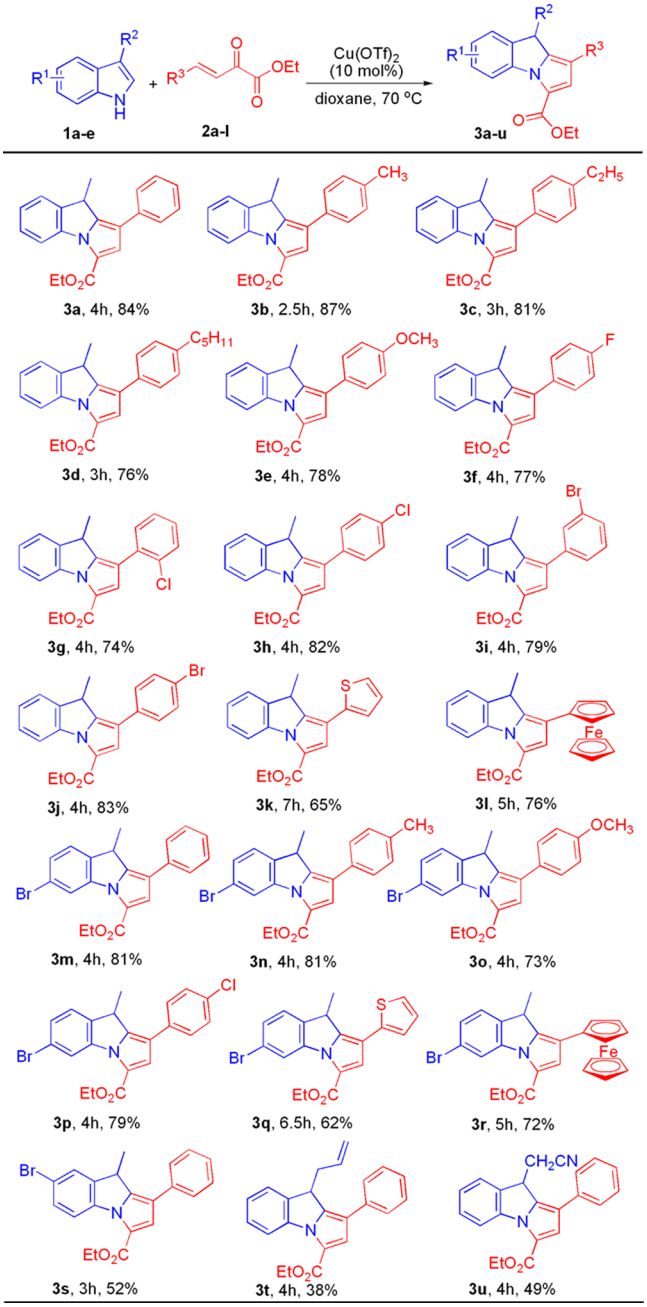
entry	cat. (10 mol %)	solvent	temp (°C)	time (h)	yield (%)[b]
1	AgOTf	dioxane	70	4	52
2	$Zn(OTf)_2$	dioxane	70	4	69
3	$Yb(OTf)_3$	dioxane	70	8	trace
4	$Ce(OTf)_3$	dioxane	70	8	trace
5	$Cu(OTf)_2$	dioxane	70	4	78
6	CuI	dioxane	70	6	27
7	CuBr	dioxane	70	10	15
8	–	dioxane	70	8	0
9	$Cu(OTf)_2$	THF	70	4	55
10	$Cu(OTf)_2$	CH_3CN	70	6	trace
11	$Cu(OTf)_2$	CH_3NO_2	70	6	26
12	$Cu(OTf)_2$	DCE	70	4	21
13	$Cu(OTf)_2$	toluene	70	4	61
14	$Cu(OTf)_2$	dioxane	100	4	77
15[c]	$Cu(OTf)_2$	dioxane	70	4	84
16[d]	$Cu(OTf)_2$	dioxane	70	4	46

[a]All the reactions were carried out with **1a** (0.4 mmol), **2a** (0.8 mmol), and catalyst (0.04 mmol) in 3.0 mL of solvent. [b]Yield of isolated product after chromatography. [c]**1a**/**2a** = 1.0:1.5. [d]**1a**/**2a** = 1.5:1.0.

Gratifyingly, the desired 9*H*-pyrrolo[1,2-*a*]indole **3a** was obtained, with a 52% yield, when the reaction was carried out in the presence of 10 mol % of AgOTf in dioxane at 70 °C for 4 h (entry 1). Motivated by this result, the effect of catalysts was subsequently investigated. It was found that $Zn(OTf)_2$ also exhibited promising catalytic ability, and the yield of **3a** was enhanced to 69% (entry 2). However, only a trace of product **3a** was detected when rare earth metal salts, such as $Yb(OTf)_3$ or $Ce(OTf)_3$, were used as the catalyst (entries 3 and 4). Interestingly, when $Cu(OTf)_2$ was employed as the catalyst in this transformation, **3a** could be obtained in 78% yield, whereas a low yield of **3a** was obtained when CuI and CuBr were employed as catalysts (entries 5–7). No reaction occurred in the absence of a catalyst (entry 8). Subsequently, the effects of solvents were investigated. Compared with THF, CH_3CN, CH_3NO_2, DCE, and toluene, dioxane proved to be the optimal solvent, giving the corresponding product **3a** in a higher yield (entries 9–13). Moreover, it was found that increasing the reaction temperature to 100 °C could not further improve the yield of the product (entry 14). Finally, the ratio of substrates was examined, and it was found that a **1a**/**2a** ratio of 1.0:1.5 led to the highest yield of **3a** (entry 15).

With the optimized reaction conditions in hand, we then proceeded to expand the scope with respect to the substrates with a series of functionalized indoles and *α*-oxo-*β*,*γ*-unsaturated ester derivatives. As illustrated in Scheme 3,

Scheme 3. Scope of Substituted Indoles and *α*-Oxo-*β*,*γ*-unsaturated Ester Derivatives[a]



[a]All the reactions were carried out with indoles **1a**–**e** (0.4 mmol), *α*-oxo-*β*,*γ*-unsaturated esters **2a**–**l** (0.6 mmol), and $Cu(OTf)_2$ (0.04 mmol) in 3.0 mL of dioxane, and isolated yields were reported.

moderate to excellent yields were generally obtained under the optimized reaction conditions. The *α*-oxo-*β*,*γ*-unsaturated ester has shown excellent tolerance to both electron-donating (**3b**–**e**) and electron-withdrawing (**3f**–**j**) groups as aromatic substituents. Moreover, it was noted that this approach was also applicable to the substrate bearing a heteroaromatic ring substituent (**3k**). In addition, the reaction also proceeded smoothly with a ferrocene containing substrate, affording the corresponding product **3l** in 76% isolated yield. Essentially no obvious steric effect was observed in the formation of **3l**. On the other hand, when 6-bromo-3-methyl-1*H*-indole **1b** was

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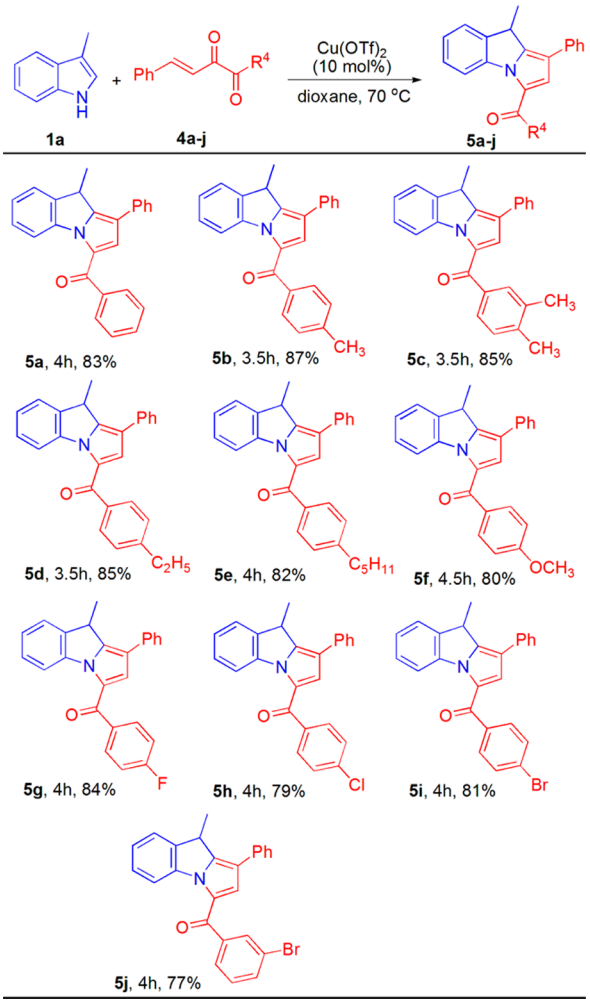
used as the substrate, the reaction also proceeded well and afforded the desired products in good yields with various α-oxo-β,γ-unsaturated esters (**3m**–**r**). To our delight, the procedure could also be applied to 5-substituted indole and afforded the desired product **3s** in moderate yield. Moreover, 3-allyl and 3-cyanomethyl substituted indoles were successfully converted, although in somewhat lower yields (**3t** and **3u**). However, substrates containing a nitro group on the 6-position as well as a formyl or a carboxyl group on the 3-position of the indole ring did not yield any desired 9*H*-pyrrolo[1,2-*a*]indole product.

Because the alkenyl 1,2-diketone derivatives can be easily obtained using our previous method,[7] we next investigated the scope of the alkenyl 1,2-diketone reactant in this $Cu(OTf)_2$-catalyzed Friedel–Crafts alkylation/annulation cascade reaction. As summarized in Scheme 4, alkenyl 1,2-diketones **4a**–**j** were submitted to this transformation and the corresponding 9*H*-pyrrolo[1,2-*a*]indole products containing various carbonyl groups could be obtained in good yields. It was found that functional groups on the phenyl ring of R^4, regardless of the substitution positions and electronic nature, including electron-rich (**5b**–**f**) and electron-deficient (**5g**–**j**) groups, were well tolerated.

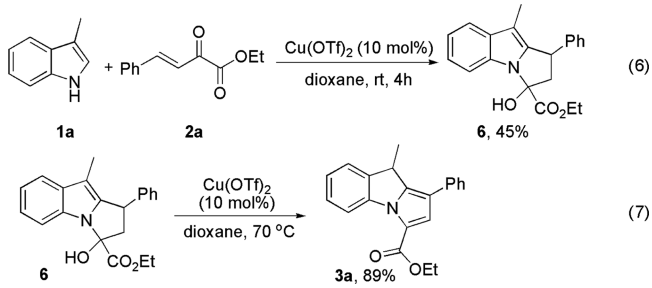
Scheme 4. Scope of Substituted Alkenyl 1,2-Diketone Derivatives[a]



[a]All the reactions were carried out with 3-methyl-1*H*-indole **1a** (0.4 mmol), alkenyl 1,2-diketones **4a**–**j** (0.6 mmol), and $Cu(OTf)_2$ (0.04 mmol) in 3.0 mL of dioxane, and isolated yields were reported.

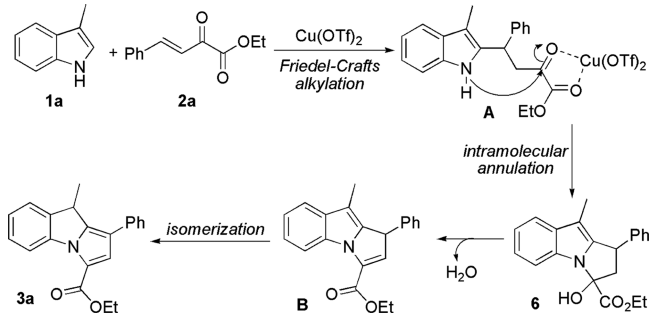
To demonstrate the synthetic potential of this new cascade process, a gram-scale experiment has been carried out under standard reaction conditions. The reaction proceeded smoothly, providing the 9*H*-pyrrolo[1,2-*a*]indole product **3a** in 67% isolated yield.

In order to gain insight into the reaction mechanism, two control experiments were carried out carefully. During the investigation of the reaction conditions, we observed a larger polar intermediate by TLC in some cases. So, we tried to isolate this intermediate first. Fortunately, this intermediate was obtained and further confirmed as 2,3-dihydro-1*H*-pyrrolo-[1,2-*a*]indole **6** in 45% yield when the reaction was carried out at room temperature for 4 h (eq 6).[9] Subsequently, the compound **6** afforded the desired 9*H*-pyrrolo[1,2-*a*]indole product **3a** when it was heated under the standard conditions at 70 °C (eq 7).



On the basis of the above results, a plausible mechanism is proposed as shown in Scheme 5. First, a $Cu(OTf)_2$-catalyzed

Scheme 5. Proposed Mechanism of the Reaction



Friedel–Crafts alkylation reaction of 3-methyl-1*H*-indole **1a** and ethyl 2-oxo-4-phenylbut-3-enoate **2a** occurred, resulting in the formation of intermediate **A**. Subsequently, intermediate **A** undergoes an intramolecular annulation to produce the *N*-fused heterocyclic intermediate **6**. Next, elimination of water from intermediate **6** generates intermediate **B** and releases H_2O. Finally, isomerization of intermediate **B** delivers the 9*H*-pyrrolo[1,2-*a*]indole product **3a**.

In conclusion, we have developed an efficient and concise $Cu(OTf)_2$-catalyzed Friedel–Crafts alkylation/annulation cascade reaction of substituted indoles with 1,2-dicarbonyl-3-enes. This transformation makes possible a rapid and practical construction of diverse 9*H*-pyrrolo[1,2-*a*]indoles from simple components in good yields. The reaction is highly attractive from the synthetic point of view in that the reaction conditions are mild, the scope is broad, and the product incorporates a carbonyl group for further structural elaboration.

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EXPERIMENTAL SECTION

General Information. All commercially available reagents were used directly without purification unless otherwise stated. All solvents were purified following standard procedures. For chromatography, 200−300 mesh silica gel (Qingdao, China) was employed. ^{1}H and ^{13}C NMR spectra were recorded at 500 and 125 MHz, respectively. Chemical shifts are reported in ppm using tetramethylsilane as the internal standard in $CDCl_3$ solvent. IR spectra were recorded on a FT-IR instrument. The HRMS analysis was obtained on a QTOF mass spectrometer. Melting points were determined with a melting point apparatus and are uncorrected.

General Procedure for the Cu(OTf)$_2$-Catalyzed Friedel−Crafts Alkylation/Annulation Cascade Reaction. To a solution of the 3-methyl-1*H*-indole (0.4 mmol) and the 1,2-dicarbonyl-3-ene (0.6 mmol) in dioxane (3.0 mL) was added $Cu(OTf)_2$ (0.04 mmol) under an air atmosphere. The resulting mixture was heated at 70 °C for the indicated time. After completion of the reaction, the mixture was cooled to room temperature. The solvent was removed in a vacuum, and the resulting residue was purified on a silica gel column (petroleum ether/EtOAc = 20:1−10:1) to provide the desired products **3** and **5**.

*Ethyl 9-Methyl-1-phenyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3a**).* Yellow solid; 106 mg, 84% yield; mp: 55−56 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3027, 2985, 2870, 1700, 1608, 1514, 1479, 1389, 754 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (t, J = 7.0 Hz, 3H), 1.46 (d, J = 7.0 Hz, 3H), 4.37 (q, J = 7.0 Hz, 1H), 4.40 (q, J = 7.0 Hz, 2H), 7.17−7.27 (m, 2H), 7.33−7.42 (m, 5H), 7.58−7.60 (m, 2H), 8.63 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.6, 16.7, 36.4, 60.3, 115.7, 118.6, 119.0, 121.3, 124.1, 124.5, 126.2, 126.2, 128.0, 128.8, 134.3, 140.4, 140.4, 144.3, 160.9; HRMS (ESI) calcd for $C_{21}H_{19}NO_2$ $[M + H]^+$ 318.1494, found 318.1486.

*Ethyl 9-Methyl-1-p-tolyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3b**).* White solid; 115 mg, 87% yield; mp: 121−123 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3037, 2985, 2870, 1700, 1608, 1460, 1389, 1368, 1168, 754 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (t, J = 7.0 Hz, 3H), 1.46 (d, J = 7.0 Hz, 3H), 2.37 (s, 3H), 4.36 (q, J = 7.0 Hz, 1H), 4.40 (q, J = 7.0 Hz, 2H), 7.16−7.22 (m, 3H), 7.33−7.38 (m, 3H), 7.48 (d, J = 8.0 Hz, 2H), 8.62 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.6, 16.6, 21.2, 36.4, 60.3, 115.7, 118.6, 118.8, 121.2, 124.1, 124.4, 126.1, 127.9, 129.4, 131.4, 135.9, 140.4, 140.5, 144.1, 160.9; HRMS (ESI) calcd for $C_{22}H_{21}NO_2$ $[M]^+$ 331.1572, found 331.1567.

*Ethyl 1-(4-Ethylphenyl)-9-methyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3c**).* Yellow solid; 111 mg, 81% yield; mp: 102−103 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3030, 2977, 2867, 1703, 1609, 1513, 1462, 1364, 1095, 756 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.27 (t, J = 7.5 Hz, 3H), 1.42 (t, J = 7.0 Hz, 3H), 1.46 (d, J = 7.0 Hz, 3H), 2.68 (q, J = 7.5 Hz, 2H), 4.36 (q, J = 3.5 Hz, 1H), 4.39 (q, J = 3.0 Hz, 2H), 7.16−7.20 (m, 1H), 7.22−7.25 (m, 2H), 7.33−7.39 (m, 3H), 7.51 (d, J = 8.0 Hz, 2H), 8.63 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.6, 15.6, 16.7, 28.6, 36.4, 60.3, 115.7, 118.7, 118.7, 118.8, 121.2, 124.1, 124.4, 126.2, 127.9, 128.2, 131.6, 140.5, 142.3, 144.1, 160.9; HRMS (ESI) calcd for $C_{23}H_{23}NO_2$ $[M]^+$ 345.1729, found 345.1723.

*Ethyl 9-Methyl-1-(4-pentylphenyl)-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3d**).* Orange solid; 117 mg, 76% yield; mp: 75−77 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3026, 2974, 2853, 1704, 1610, 1514, 1478, 1389, 1364, 1061, 756 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.91 (t, J = 7.0 Hz, 3H), 1.33−1.37 (m, 4H), 1.42 (t, J = 7.0 Hz, 3H), 1.47 (d, J = 7.0 Hz, 3H), 1.63−1.67 (m, 2H), 2.62 (t, J = 7.0 Hz, 2H) 4.36 (q, J = 7.0 Hz, 1H), 4.40 (q, J = 7.0 Hz, 2H), 7.16−7.25 (m, 3H), 7.30−7.39 (m, 3H), 7.50 (d, J = 3.0 Hz, 2H), 8.63 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 14.6, 16.7, 22.6, 31.2, 31.6, 35.7, 36.4, 60.3, 115.7, 118.6, 118.8, 121.2, 124.1, 124.4, 126.1, 127.9, 128.8, 131.6, 140.4, 140.5, 141.0, 144.1, 160.9; HRMS (ESI) calcd for $C_{26}H_{29}NO_2$ $[M]^+$ 387.2198, found 387.2192.

*Ethyl 1-(4-Methoxyphenyl)-9-methyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3e**).* White solid; 108 mg, 78% yield; mp: 122−123 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3051, 2976, 2870, 1713, 1612, 1513, 1461, 1386, 1368, 759 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (t, J = 7.0 Hz, 3H), 1.46 (d, J = 7.0 Hz, 3H), 3.85 (s, 3H), 4.36 (q, J = 7.0 Hz, 1H), 4.40 (q, J = 7.0 Hz, 2H), 6.95−6.97 (m, 2H), 7.17−7.21 (m, 1H), 7.32−7.40 (m, 3H), 7.50−7.53 (m, 2H), 8.62 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.6, 16.6, 36.3, 55.3, 60.3, 114.2, 115.7, 118.4, 118.7, 121.1, 124.1, 124.3, 126.9, 127.4, 127.9, 140.4, 140.5, 143.7, 158.2, 160.9; HRMS (ESI) calcd for $C_{22}H_{21}NO_3$ $[M]^+$ 347.1521, found 347.1518.

*Ethyl 1-(4-Fluorophenyl)-9-methyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3f**).* White solid; 103 mg, 77% yield; mp: 84−86 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3044, 2959, 2855, 1706, 1607, 1511, 1464, 1389, 750 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (t, J = 7.0 Hz, 3H), 1.43 (d, J = 7.0 Hz, 3H), 4.34 (q, J = 7.0 Hz, 1H), 4.38 (q, J = 7.0 Hz, 2H), 7.07−7.11 (m, 2H), 7.17−7.21 (m, 1H), 7.31 (s, 1H), 7.33−7.38 (m, 2H), 7.50−7.54 (m, 2H), 8.62 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5, 16.6, 36.2, 60.4, 115.5, 115.7, 115.8, 117.7, 120.0 (d, J_{C-F} = 264.8 Hz), 124.1, 124.5, 127.7, 127.8, 128.0, 130.5, 140.2, 140.4, 144.0, 162.4; HRMS (ESI) calcd for $C_{21}H_{18}FNO_2$ $[M]^+$ 335.1322, found 335.1316.

*Ethyl 1-(2-Chlorophenyl)-9-methyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3g**).* Orange solid; 106 mg, 74% yield; mp: 69−70 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3055, 2976, 2869, 1707, 1610, 1463, 1371, 755 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35 (d, J = 7.5 Hz, 3H), 1.42 (t, J = 7.0 Hz, 3H), 4.32−4.41 (m, 3H), 7.14−7.19 (m, 3H), 7.20−7.25 (m, 1H), 7.35−7.39 (m, 3H), 7.52−7.55 (m, 1H), 8.65 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.6, 16.6, 36.9, 60.3, 112.6, 115.8, 115.9, 116.0, 122.8, 122.9, 124.0, 124.3, 124.4, 124.5, 127.9, 129.5, 129.6, 140.5, 140.6, 145.8, 160.9; HRMS (ESI) calcd for $C_{21}H_{18}ClNO_2$ $[M]^+$ 351.1026, found 351.1023.

*Ethyl 1-(4-Chlorophenyl)-9-methyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3h**).* White solid; 115 mg, 82% yield; mp: 115−116 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3049, 2981, 2872, 1713, 1600, 1497, 1465, 1363, 756 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40−1.44 (m, 6H), 4.32−4.39 (m, 3H), 7.17−7.21 (m, 1H), 7.32−7.37 (m, 5H), 7.47−7.50 (m, 2H), 8.62 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5, 16.6, 36.3, 60.4, 115.8, 117.4, 119.2, 121.0, 124.1, 124.6, 127.4, 128.0, 128.9, 131.8, 132.9, 140.2, 140.3, 144.3, 160.8; HRMS (ESI) calcd for $C_{21}H_{18}ClNO_2$ $[M]^+$ 351.1026, found 351.1024.

*Ethyl 1-(3-Bromophenyl)-9-methyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3i**).* White solid; 125 mg, 79% yield; mp: 79−81 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3507, 2975, 2870, 1707, 1597, 1463, 1389, 757 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (t, J = 7.0 Hz, 3H), 1.47 (d, J = 7.0 Hz, 3H), 4.37 (q, J = 7.0 Hz, 1H), 4.40 (q, J = 7.0 Hz, 2H), 7.19−7.23 (m, 1H), 7.24−7.28 (m, 1H), 7.35−7.41 (m, 4H), 7.50 (d, J = 3.0 Hz, 1H), 7.72 (t, J = 2.0 Hz, 1H), 8.63 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5, 16.6, 36.4, 60.4, 115.8, 117.1, 119.3, 121.0, 123.0, 124.1, 124.6, 124.7, 128.1, 129.1, 129.2, 130.3, 136.6, 140.2, 140.3, 144.5, 160.8; HRMS (ESI) calcd for $C_{21}H_{18}BrNO_2$ $[M + H]^+$ 396.0599, found 396.0595.

*Ethyl 1-(4-Bromophenyl)-9-methyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3j**).* Orange solid; 131 mg, 83% yield; mp: 129−130 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3049, 2981, 2871, 1713, 1612, 1464, 1383, 1164, 755 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37−1.42 (m, 6H), 4.26 (q, J = 7.5 Hz, 1H), 4.35 (q, J = 7.0 Hz, 2H), 7.16−7.17 (m, 1H), 7.30−7.40 (m, 5H), 7.46−7.48 (m, 2H), 8.61 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.6, 16.5, 36.3, 60.4, 115.8, 117.4, 119.2, 119.8, 120.9, 124.1, 124.6, 131.8, 133.3, 140.2, 140.3, 144.3, 160.7; HRMS (ESI) calcd for $C_{21}H_{18}BrNO_2$ $[M]^+$ 395.0521, found 395.0518.

*Ethyl 9-Methyl-1-(thiophen-2-yl)-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3k**).* Gray solid; 84 mg, 65% yield; mp: 162−163 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3072, 2977, 2851, 1692, 1606, 1513, 1478, 1384, 1165, 761 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (d, J = 7.0

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Hz, 3H), 1.58 (t, J = 7.5 Hz, 3H), 4.28 (q, J = 7.0 Hz, 1H), 4.38 (q, J = 7.0 Hz, 2H), 7.07 (t, J = 4.0 Hz, 1H), 7.16 (d, J = 3.0 Hz, 1H), 7.20−7.22 (m, 2H), 7.32 (s, 1H), 7.33−7.41 (m, 2H), 8.62 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5, 16.7, 36.1, 60.4, 112.8, 115.8, 118.9, 121.1, 122.8, 123.0, 124.2, 124.6, 127.5, 127.8, 137.0, 140.3, 140.5, 143.9, 160.8; HRMS (ESI) calcd for $C_{19}H_{17}NO_2S[M]^+$ 323.0980, found 323.0977.

*Ethyl 1-Ferrocenyl-9-methyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3l**).* Gray solid; 129 mg, 76% yield; mp: 78−80 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3052, 2975, 2871, 1704, 1612, 1475, 1385, 1155, 754 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.45 (t, J = 7.0 Hz, 3H), 1.58 (d, J = 7.0 Hz, 3H), 4.07 (s, 5H), 4.38 (q, J = 7.0 Hz, 1H), 4.42 (s, 2H), 4.53 (q, J = 7.0 Hz, 2H), 4.55 (s, 2H), 7.18 (t, J = 7.5 Hz, 1H), 7.24 (s, 1H), 7.33−7.40 (m, 2H), 8.59 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.6, 17.7, 35.9, 60.3, 66.3, 66.7, 67.8, 67.9, 69.4, 79.6, 115.5, 115.7, 118.6, 121.3, 124.1, 124.2, 128.0, 140.4, 140.6, 143.6, 160.9; HRMS (ESI) calcd for $C_{25}H_{23}FeNO_2$ $[M]^+$ 425.1078, found 425.1075.

*Ethyl 6-Bromo-9-methyl-1-phenyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3m**).* White solid; 128 mg, 81% yield; mp: 104−105 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 2984, 2971, 2868, 1708, 1602, 1469, 1325, 1162, 758 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (t, J = 7.0 Hz, 3H), 1.45 (d, J = 7.0 Hz, 3H), 4.32−4.40 (m, 3H), 7.26 (t, J = 3.0 Hz, 1H), 7.37−7.42 (m, 3H), 7.44−7.49 (m, 2H), 7.56 (d, J = 7.5 Hz, 2H), 8.53 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5, 16.6, 36.4, 60.5, 117.2, 117.5, 118.9, 119.1, 121.5, 126.3, 126.4, 127.3, 128.8, 130.9, 134.0, 139.5, 142.6, 143.7, 160.8; HRMS (ESI) calcd for $C_{21}H_{18}BrNO_2$ $[M]^+$ 395.0521, found 395.0518.

*Ethyl 6-Bromo-9-methyl-1-p-tolyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3n**).* Yellow solid; 133 mg, 81% yield; mp: 114−115 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3080, 2980, 2871, 1703, 1606, 1565, 1477, 1390, 1163, 761 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (t, J = 7.0 Hz, 3H), 1.45 (d, J = 7.5 Hz, 3H), 2.38 (s, 3H), 4.34−4.40 (m, 3H), 7.22 (d, J = 7.5 Hz, 2H), 7.35 (s, 1H), 7.44−7.47 (m, 3H), 7.49−7.50 (m, 1H), 8.52 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5, 16.5, 21.2, 36.4, 60.4, 117.2, 117.5, 118.9, 119.0, 121.4, 126.2, 127.3, 129.5, 130.9, 131.0, 136.1, 139.5, 142.6, 143.5, 160.8; HRMS (ESI) calcd for $C_{22}H_{20}BrNO_2$ $[M]^+$ 409.0677, found 409.0675.

*Ethyl 6-Bromo-1-(4-methoxyphenyl)-9-methyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3o**).* Yellow solid; 124 mg, 73% yield; mp: 122−123 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3034, 2978, 2833, 1699, 1613, 1511, 1478, 1389, 1173, 760 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39−1.43 (m, 6H), 3.84 (s, 3H), 4.31−4.38 (m, 3H), 6.95 (d, J = 8.5 Hz, 2H), 7.31 (s, 1H), 7.44−7.48 (m, 4H), 8.51 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5, 16.5, 36.3, 55.3, 60.4, 114.2, 117.2, 117.4, 118.6, 118.9, 121.3, 126.5, 127.3, 127.4, 130.8, 139.5, 142.6, 143.1, 158.3, 160.8; HRMS (ESI) calcd for $C_{22}H_{20}BrNO_3$ $[M]^+$ 425.0627, found 425.0625.

*Ethyl 6-Bromo-1-(4-chlorophenyl)-9-methyl-9H-pyrolo[1,2-a]indole-3-carboylate (**3p**).* White solid; 135 mg, 79% yield; mp: 125−127 °C (petroleum ether and ethyl acetate at room temperature); IR (KBr) 3068, 2982, 2872, 1698, 1598, 1514, 1471, 1384, 1172, 760 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39−1.44 (m, 6H), 4.32−4.39 (m, 3H), 7.32 (s, 1H), 7.35−7.38 (m, 2H), 7.44−7.48 (m, 4H), 8.52 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5, 16.5, 36.3, 60.5, 117.3, 117.7, 119.3, 121.2, 127.3, 127.4, 129.0, 131.0, 132.0, 132.5, 139.4, 142.4, 143.7, 160.7; HRMS (ESI) calcd for $C_{21}H_{17}BrClNO_2$ $[M]^+$ 429.0131, found 429.0128.

*Ethyl 6-Bromo-9-methyl-1-(thiophen-2-yl)-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3q**).* Gray solid; 99 mg, 62% yield; mp: 170−171 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3075, 2977, 2851, 1693, 1606, 1513, 1478, 1389, 1165, 761 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (d, J = 7.0 Hz, 3H), 1.57 (t, J = 7.0 Hz, 3H), 4.28 (q, J = 7.0 Hz, 1H), 4.37 (q, J = 7.0 Hz, 2H), 7.07 (t, J = 4.0 Hz, 1H), 7.15 (d, J = 3.0 Hz, 1H), 7.22−7.24 (m, 1H), 7.32 (s, 1H), 7.45−7.51 (m, 2H), 8.52 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5, 16.9, 36.1, 60.5, 113.1, 117.3, 117.7, 119.1, 121.4, 123.0, 123.2, 127.4, 127.6, 130.9, 136.6, 139.4, 142.7, 143.3, 160.7; HRMS (ESI) calcd for $C_{19}H_{16}BrNO_2S$ $[M]^+$ 401.0085, found 401.0083.

*Ethyl 6-Bromo-1-ferrocenyl-9-methyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3r**).* Gray solid; 145 mg, 72% yield; mp: 81−82 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3096, 2959, 2870, 1703, 1609, 1492, 1474, 1364, 1064, 731 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.45 (t, J = 7.0 Hz, 3H), 1.57 (d, J = 7.0 Hz, 3H), 4.07 (s, 5H), 4.14 (q, J = 7.0 Hz, 1H), 4.27 (s, 2H), 4.39 (q, J = 7.0 Hz, 2H), 4.52 (s, 2H), 7.23 (s, 1H), 7.44−7.50 (m, 2H), 8.49 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.6, 17.6, 35.9, 60.4, 66.3, 66.7, 67.9, 68.0, 69.4, 79.1, 116.1, 117.0, 117.2, 118.7, 121.6, 127.4, 130.8, 139.5, 142.7, 143.0, 160.8; HRMS (ESI) calcd for $C_{25}H_{22}FeBrNO_2$ $[M]^+$ 503.0183, found 503.0185.

*Ethyl 7-Bromo-9-methyl-1-phenyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3s**).* Yellow solid; 83 mg, 52% yield; mp: 98−100 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 2973, 2923, 2864, 1704, 1601, 1474, 1442, 1257, 1162, 818, 753, 691 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39−1.44 (m, 6H), 4.33−4.93 (m, 3H), 7.24−7.27 (m, 1H), 7.37−7.41 (m, 3H), 7.44−7.47 (m, 2H), 7.50 (d, J = 7.0 Hz, 2H), 8.51 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5, 16.5, 36.4, 60.5, 117.2, 117.5, 118.9, 119.0, 121.5, 126.2, 126.4, 127.3, 128.8, 130.9, 134.0, 139.5, 142.6, 143.7, 160.8; HRMS (ESI) calcd for $C_{21}H_{18}BrNO_2Na$ $[M + Na]^+$ 420.0395, found 420.0398.

*Ethyl 9-Allyl-1-phenyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3t**).* Yellow solid; 52 mg, 38% yield; mp: 75−77 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 2976, 2920, 2849, 1706, 1601, 1477, 1460, 1262, 1162, 756, 694 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (t, J = 7.5 Hz, 3H), 2.55−2.61 (m, 1H), 2.78−2.83 (m, 1H), 4.36−4.40 (m, 2H), 4.49−4.51 (dd, J_1 = 6.5 Hz, J_2 = 4.0 Hz, 1H), 4.74−4.81 (m, 2H), 5.35−5.44 (m, 1H), 7.17−7.20 (m, 1H), 7.26 (t, J = 7.5 Hz, 1H), 7.34−7.44 (m, 5H), 7.58 (d, J = 7.0 Hz, 2H), 8.63 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5, 34.7, 41.1, 60.3, 115.6, 118.0, 119.0, 119.1, 121.3, 124.2, 124.7, 126.3, 128.1, 128.8, 133.6, 134.4, 138.1, 141.1, 142.2, 160.8; HRMS (ESI) calcd for $C_{23}H_{21}NO_2Na$ $[M + Na]^+$ 366.1465, found 366.1454.

*Ethyl 9-(Cyanomethyl)-1-phenyl-9H-pyrrolo[1,2-a]indole-3-carboxylate (**3u**).* Yellow solid; 67 mg, 49% yield; mp: 173−175 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3055, 2979, 2964, 2926, 2243, 1701, 1601, 1480, 1463, 1439, 1271, 1257, 1162, 753 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (t, J = 7.5 Hz, 3H), 2.50 (q, J = 9.0 Hz, 1H), 3.07−3.12 (dd, J_1 = 17.0 Hz, J_2 = 4.0 Hz, 1H), 4.36−4.41 (m, 2H), 4.63−4.65 (dd, J_1 = 12.5 Hz, J_2 = 3.5 Hz, 1H), 7.24−7.34 (m, 3H), 7.42−7.53 (m, 5H), 7.70 (d, J = 7.5 Hz, 1H), 8.66 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5, 19.9, 37.2, 60.6, 116.2, 117.4, 119.9, 120.3, 121.3, 124.8, 125.1, 126.1, 127.0, 129.2, 129.5, 133.5, 138.4, 140.8, 160.6; HRMS (ESI) calcd for $C_{22}H_{18}N_2O_2Na$ $[M + Na]^+$ 365.1260, found 365.1252.

*(9-Methyl-1-phenyl-9H-pyrrolo[1,2-a]indol-3-yl)(phenyl)methanone (**5a**).* White solid; 116 mg, 83% yield; mp: 96−97 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3032, 2971, 2869, 1630, 1601, 1460, 1327, 900, 648 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.52 (d, J = 7.0 Hz, 3H), 4.48 (q, J = 7.5 Hz, 1H), 7.11 (s, 1H), 7.22−7.26 (m, 2H), 7.38−7.42 (m, 4H), 7.50−7.57 (m, 5H), 7.93−7.96 (m, 2H), 8.49 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.5, 36.7, 116.1, 119.1, 124.1, 124.8, 126.1, 126.3, 126.5, 127.3, 128.1, 128.3, 128.8, 129.5, 131.8, 134.0, 139.7, 140.3, 140.5, 146.3, 185.0; HRMS (ESI) calcd for $C_{25}H_{19}NO$ $[M]^+$ 349.1467, found 349.1465.

*(9-Methyl-1-phenyl-9H-pyrrolo[1,2-a]indol-3-yl)(p-tolyl)methanone (**5b**).* White solid; 126 mg, 87% yield; mp: 163−164 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3056, 2968, 2867, 1630, 1605, 1563, 1461, 1177, 903, 752 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.52 (d, J = 7.0 Hz, 3H), 2.46 (s, 3H), 4.48 (q, J = 7.5 Hz, 1H), 7.11 (s, 1H), 7.21−7.24 (m, 2H), 7.31 (d, J = 7.5 Hz, 2H), 7.36−7.43 (m, 4H), 7.55 (d, J

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= 7.5 Hz, 2H), 7.87 (d, J = 8.0 Hz, 2H), 8.44 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.5, 21.7, 36.7, 116.0, 119.0, 124.0, 124.7, 125.7, 126.3, 126.4, 127.4, 128.1, 128.8, 129.0, 129.7, 134.1, 136.9, 140.3, 140.5, 142.5, 146.0, 184.9; HRMS (ESI) calcd for $C_{26}H_{21}NO$ $[M]^+$ 363.1623, found 363.1622.

*(3,4-Dimethylphenyl)(9-methyl-1-phenyl-9H-pyrrolo[1,2-a]indol-3-yl)methanone (**5c**).* Orange solid; 128 mg, 85% yield; mp: 81−82 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3031, 2970, 2869, 1630, 1603, 1565, 1459, 1395, 1072, 902, 756 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.49 (d, J = 7.0 Hz, 3H), 2.34 (s, 6H), 4.42 (q, J = 7.0 Hz, 1H), 7.12 (s, 1H), 7.16−7.25 (m, 3H), 7.32−7.39 (m, 4H), 7.53 (d, J = 7.5 Hz, 2H), 7.69−7.75 (m, 2H), 8.45 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.5, 19.9, 20.1, 36.7, 116.1, 118.9, 124.1, 124.7, 125.6, 126.3, 126.4, 127.4, 127.5, 128.1, 128.8, 129.5, 130.7, 134.2, 136.7, 137.4, 140.4, 140.5, 141.3, 145.9, 185.1; HRMS (ESI) calcd for $C_{27}H_{23}NO$ $[M + H]^+$ 378.1858, found 378.1849.

*(4-Ethylphenyl)(9-methyl-1-phenyl-9H-pyrrolo[1,2-a]indol-3-yl)-methanone (**5d**).* Yellow solid; 128 mg, 85% yield; mp: 63−65 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3024, 2966, 2871, 1631, 1575, 1477, 1109, 901, 828, 791 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.26 (t, J = 7.5 Hz, 3H), 1.52 (d, J = 7.0 Hz, 3H), 2.66 (q, J = 7.0 Hz, 2H), 4.46 (q, J = 7.5 Hz, 1H), 7.09 (s, 1H), 7.21−7.25 (m, 2H), 7.35−7.42 (m, 2H), 7.46−7.52 (m, 5H), 7.58 (t, J = 7.5 Hz, 1H), 7.94 (d, J = 7.0 Hz, 2H), 8.49 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.6, 16.5, 28.6, 36.7, 116.1, 119.2, 124.1, 124.7, 126.1, 126.2, 127.2, 128.1, 128.2, 128.3, 129.5, 131.3, 131.8, 139.8, 140.4, 140.5, 142.6, 146.1, 185.0; HRMS (ESI) calcd for $C_{27}H_{23}NO$ $[M]^+$ 377.1787, found 377.1780.

*(9-Methyl-1-phenyl-9H-pyrrolo[1,2-a]indol-3-yl)(4-pentylphenyl)-methanone (**5e**).* White solid; 137 mg, 82% yield; mp: 66−67 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3024, 2955, 2855, 1632, 1511, 1457, 1076, 901, 752 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.96 (t, J = 7.0 Hz, 3H), 1.38−1.41 (m, 4H), 1.57 (d, J = 7.0 Hz, 3H), 1.67−1.71 (m, 2H), 2.67 (t, J = 7.5 Hz, 2H), 4.50 (q, J = 7.5 Hz, 1H), 7.15 (s, 1H), 7.24−7.29 (m, 3H), 7.40−7.47 (m, 2H), 7.50−7.57 (m, 4H), 7.63 (t, J = 7.5 Hz, 1H), 8.00 (d, J = 7.0 Hz, 2H), 8.56 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 16.5, 22.6, 31.2, 31.6, 35.7, 36.7, 116.1, 119.2, 124.1, 124.7, 126.1, 126.2, 127.2, 128.1, 128.2, 128.9, 129.5, 131.3, 131.8, 139.8, 140.4, 140.5, 141.3, 146.1, 185.0; HRMS (ESI) calcd for $C_{30}H_{29}NO$ $[M + H]^+$ 420.2327, found 420.2318.

*(4-Methoxyphenyl)(9-methyl-1-phenyl-9H-pyrrolo[1,2-a]indol-3-yl)methanone (**5f**).* Yellow solid; 121 mg, 80% yield; mp: 61−62 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3054, 2970, 2838, 1627, 1600, 1509, 1459, 1108, 903, 734 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.52 (d, J = 7.5 Hz, 3H), 3.90 (s, 3H), 4.47 (q, J = 7.5 Hz, 1H), 7.00 (d, J = 9.0 Hz, 2H), 7.11 (s, 1H), 7.21−7.27 (m, 2H), 7.35−7.42 (m, 4H), 7.57 (d, J = 7.5 Hz, 2H), 7.98 (d, J = 8.5 Hz, 2H), 8.37 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.5, 36.7, 55.5, 113.6, 115.9, 118.8, 124.0, 124.7, 125.1, 126.3, 126.4, 127.3, 128.0, 128.8, 131.8, 132.1, 134.2, 140.4, 140.5, 145.7, 162.8, 184.0; HRMS (ESI) calcd for $C_{26}H_{21}NO_2$ $[M]^+$ 379.1572, found 379.1570.

*(4-Fluorophenyl)(9-methyl-1-phenyl-9H-pyrrolo[1,2-a]indol-3-yl)-methanone (**5g**).* White solid; 123 mg, 84% yield; mp: 70−71 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); R_f = 0.52 (petroleum ether/ethyl acetate = 5:1); IR (KBr) 3055, 2972, 2870, 1672, 1631, 1509, 1458, 1094, 901, 751 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.47 (d, J = 7.5 Hz, 3H), 4.38 (q, J = 7.5 Hz, 1H), 7.03 (s, 1H), 7.04−7.09 (m, 2H), 7.20 (t, J = 7.5 Hz, 1H), 7.34−7.40 (m, 2H), 7.47−7.57 (m, 5H), 7.93 (d, J = 6.5 Hz, 2H), 8.49 (d, J = 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.4, 36.6, 115.6, 115.8, 116.1, 118.2, 124.1, 124.9, 125.8, 127.3, 127.8, 127.9 (d, J_{C-F} = 256.4 Hz), 128.1, 128.3, 129.5, 131.9, 139.6, 140.2, 140.4, 146.0, 185.0; HRMS (ESI) calcd for $C_{25}H_{18}FNO$ $[M]^+$ 367.1372, found 367.1370.

*(4-Chlorophenyl)(9-methyl-1-phenyl-9H-pyrrolo[1,2-a]indol-3-yl)methanone (**5h**).* White solid; 121 mg, 79% yield; mp: 162−163 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3058, 2982, 2862, 1624, 1596, 1456, 1089, 900, 757 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.50 (d, J = 7.5 Hz, 3H), 4.43 (q, J = 7.5 Hz, 1H), 7.05 (s, 1H), 7.23 (t, J = 7.5 Hz, 1H), 7.34−7.42 (m, 4H), 7.46−7.53 (m, 4H), 7.59 (t, J = 7.5 Hz, 1H), 7.93 (d, J = 7.5 Hz, 2H), 8.47 (d, J = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.4, 36.7, 116.1, 118.0, 124.1, 124.9, 125.7, 127.4, 127.5, 128.2, 128.3, 129.0, 129.5, 131.9, 132.1, 132.6, 139.6, 140.2, 140.4, 146.2, 185.0; HRMS (ESI) calcd for $C_{25}H_{18}ClNO$ $[M + H]^+$ 384.1155, found 384.1178.

*(4-Bromophenyl)(9-methyl-1-phenyl-9H-pyrrolo[1,2-a]indol-3-yl)methanone (**5i**).* Gray solid; 138 mg, 81% yield; mp: 156−157 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3042, 2957, 2855, 1631, 1602, 1563, 1459, 1106, 899, 753 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (d, J = 7.0 Hz, 3H), 4.47 (q, J = 7.0 Hz, 1H), 7.07 (s, 1H), 7.21−7.28 (m, 2H), 7.38−7.43 (m, 4H), 7.55 (d, J = 7.5 Hz, 2H), 7.64 (d, J = 8.0 Hz, 2H), 7.81 (d, J = 8.0 Hz, 2H), 8.46 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.4, 36.8, 116.0, 119.3, 124.1, 124.9, 126.0, 126.3, 126.6, 126.9, 128.1, 128.9, 131.0, 131.5, 133.8, 138.5, 140.3, 140.4, 146.7, 183.7; HRMS (ESI) calcd for $C_{25}H_{18}BrNO$ $[M]^+$ 427.0572, found 427.0571.

*(3-Bromophenyl)(9-methyl-1-phenyl-9H-pyrrolo[1,2-a]indol-3-yl)methanone (**5j**).* Yellow solid; 131 mg, 77% yield; mp: 68−69 °C (recrystallized from petroleum ether and ethyl acetate at room temperature); IR (KBr) 3044, 2977, 2865, 1674, 1630, 1511, 1470, 1089, 903, 754 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (d, J = 7.0 Hz, 3H), 4.44 (q, J = 7.0 Hz, 1H), 7.06 (s, 1H), 7.21−7.26 (m, 2H), 7.35−7.48 (m, 4H), 7.51 (t, J = 7.5 Hz, 2H), 7.59 (t, J = 7.5 Hz, 1H), 7.67 (s, 1H), 7.93 (d, J = 7.0 Hz, 2H), 8.47 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.5, 36.7, 116.2, 117.6, 123.0, 124.1, 124.8, 125.0, 125.7, 127.5, 128.2, 128.4, 129.2, 129.3, 129.5, 130.3, 132.0, 136.3, 139.5, 140.2, 140.3, 146.4, 185.0; HRMS (ESI) calcd for $C_{25}H_{18}BrNO$ $[M + H]^+$ 428.0650, found 428.0649.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02143.

Copies of ^{1}H and ^{13}C NMR spectra for all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Eicher, T.; Hauptmann, S. *The Chemistry of Heterocycles*; Wiley-VCH: Weinheim, 2003. (b) Veh, V. S. C.; Iyengar, R. In *Comprehensive Heterocyclic Chemistry III*, Vol. 4; Katritzky, A. R., Ramsden, C. A., Scriven, E. F. V., Taylor, R. J. K., Eds.; Pergamon: Oxford, U.K., 2008. (c) Sanda, F.; Nakai, T.; Kobayashi, N.; Masuda, T. *Macromolecules* **2004**, *37*, 2703−2708. (d) Häussler, M.; Liu, J.; Zheng, R.; Lam, J. W. Y.; Qin, A.; Tang, B. Z. *Macromolecules* **2007**, *40*, 1914−1925. (e) Martins, M. A. P.; Frizzo, C. P.; Moreira, D. N.; Buriol, L.; Machado, P. *Chem. Rev.* **2009**, *109*, 4140−4182.

(2) (a) Franck, R. W.; Bernady, K. F. *J. Org. Chem.* **1968**, 33, 3050−3055. (b) Tanaka, M.; Sagawa, S.; Hoshi, J.; Shimoma, F.; Yasue, K.; Ubukata, M.; Ikemoto, T.; Hase, Y.; Takahashi, M.; Sasase, T.; Ueda,

DOI: 10.1021/acs.joc.6b02143
J. Org. Chem. 2016, 81, 11987−11993

N.; Matsushita, M.; Inaba, T. *Bioorg. Med. Chem.* **2006**, *14*, 5781−5794. (c) Kakadiya, R.; Dong, H.; Lee, P.; Kapuriya, N.; Zhang, X.; Chou, T.; Lee, T.; Kapuriya, K.; Shah, A.; Su, T. *Bioorg. Med. Chem.* **2009**, *17*, 5614−5626.

(3) (a) Wakaki, S.; Marumo, H.; Tomioka, K.; Shimizu, G.; Kato, E.; Kamada, H.; Kudo, S.; Fujimoto, Y. *Antiobiot. Chemother.* **1958**, *8*, 288−240. (b) Galm, U.; Hager, M. H.; Van Lanen, S. G.; Ju, J.; Thorson, J. S.; Shen, B. *Chem. Rev.* **2005**, *105*, 739−758.

(4) (a) Beccalli, E. M.; Broggini, G.; La Rosa, C.; Passarella, D.; Pilati, T.; Terraneo, A.; Zecchi, G. *J. Org. Chem.* **2000**, *65*, 8924−8932. (b) Yavari, I.; Adib, M.; Sayahi, M. H. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1517−1519. (c) González-Pérez, P.; Pérez-Serrano, L.; Casarrubios, L.; Domínguez, G.; Pérez-Castells, J. *Tetrahedron Lett.* **2002**, *43*, 4765−4767. (d) Siebeneicher, H.; Bytschkov, I.; Doye, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 3042−3044. (e) Pérez-Serrano, L.; Domínguez, G.; Pérez-Castells, J. *J. Org. Chem.* **2004**, *69*, 5413−5418. (f) Prajapati, D.; Gadhwal, S. *Tetrahedron* **2004**, *60*, 4909−4913. (g) Borah, H. N.; Deb, M. L.; Boruah, R. C.; Bhuyan, P. J. *Tetrahedron Lett.* **2005**, *46*, 3391−3393. (h) Abbiati, G.; Casoni, A.; Canevari, V.; Nava, D.; Rossi, E. *Org. Lett.* **2006**, *8*, 4839−4842.

(5) (a) Ren, H.; Knochel, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 3462−3465. (b) Ren, H.; Li, Z.; Knochel, P. *Chem. - Asian J.* **2007**, *2*, 416−433. (c) Hwang, S. J.; Cho, S. H.; Chang, S. *J. Am. Chem. Soc.* **2008**, *130*, 16158−16159.

(6) (a) Wood, K.; Black, D. S.; Kumar, N. *Tetrahedron Lett.* **2009**, *50*, 574−576. (b) Li, H.; Wang, Z.; Zu, L. *RSC Adv.* **2015**, *5*, 60962−60965.

(7) Hao, L.; Pan, Y.; Wang, T.; Lin, M.; Chen, L.; Zhan, Z. *Adv. Synth. Catal.* **2010**, *352*, 3215−3222.

(8) Chen, S.; Li, X.; Zhao, H.; Li, B. *J. Org. Chem.* **2014**, *79*, 4137−4141.

(9) (a) Zeng, M.; Zhang, W.; You, S. *Chin. J. Chem.* **2012**, *30*, 2615−2623. (b) Cheng, H.; Lu, L.; Wang, T.; Yang, Q.; Liu, X.; Li, Y.; Deng, Q.; Chen, J.; Xiao, W. *Angew. Chem., Int. Ed.* **2013**, *52*, 3250−3254. (c) Zhang, Y.; Liu, X.; Zhao, X.; Zhang, J.; Zhou, L.; Lin, L.; Feng, X. *Chem. Commun.* **2013**, *49*, 11311−11313. (d) Ma, H.; Li, J.; Sun, L.; Hou, X.; Zhang, Z.; Fu, B. *Tetrahedron* **2015**, *71*, 3625−3631.

DOI: 10.1021/acs.joc.6b02143
J. Org. Chem. 2016, 81, 11987−11993