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Mechanically Induced Fe(III) Catalysis at Room Temperature: Solvent-Free Cross-Dehydrogenative Coupling of 3-Benzylic Indoles with Methylenes/Indoles

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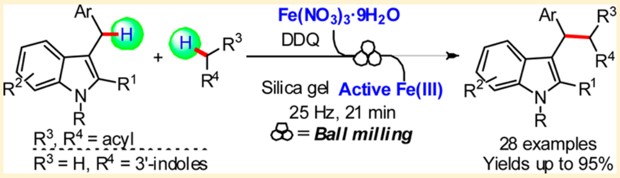
Ⓢ *Supporting Information*

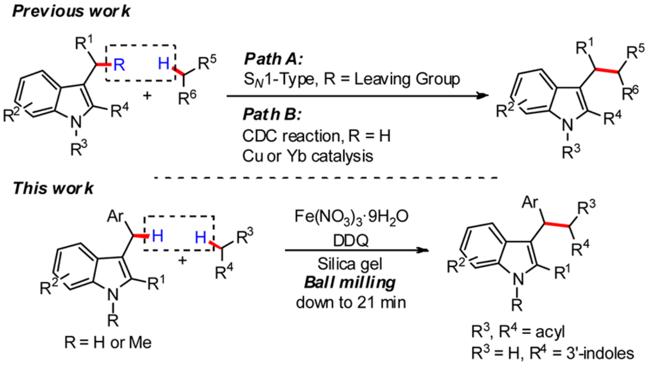
ABSTRACT: An Fe(III)-catalyzed solvent-free cross-dehydrogenative coupling of 3-benzylic indoles and compounds with acidic methylene groups has been achieved under high-speed ball-milling (HSBM) conditions at room temperature. The reactions afford desired 3-arylmethylindole derivatives in moderate to high yields within 21 min of grinding. Besides, both *N*-substituted and *N*-free indoles can take part in this mechanochemical reaction as efficient nucleophiles to give bisindoles with satisfactory results. Remarkably, this protocol displays the possibility to induce high activity when using iron catalysts under HSBM conditions.



Cross-dehydrogenative coupling (CDC) reaction is one of the most powerful tools for covalent bond direct construction and has been extensively studied over the past decade.[1] Besides widely used Cu catalysts, highly active metal catalysts containing Pd, Rh, Ru, and Yb have also been applied in different types of CDC reactions.[2] However, the problems of expense and toxicity are still challenging the chemists for greener and cheaper covalent-bond construction. Recently, iron as an earth-abundant element has received much attention from the catalysis community due to its low cost and nontoxicity.[3] A flurry of iron-catalyzed CDC reactions have arisen since the pioneering investigation by Li and co-workers.[4] Although these findings have revealed iron's catalytic potential, further development of which is plagued by its relatively low activity. Hitherto, how to induce the high activity of iron-catalysts is still one of the most crucial problems in the field of metal-catalyzed synthesis.

High-speed ball-milling (HSBM) is a green mechanical technique which always promotes chemical reactions with high efficiency, energy economy, and sometimes new reactivity.[5] In continuation of our research interest in HSBM promoted CDC reactions,[6] the realization of iron-catalyzed high-efficiency reactions was hypothesized to be induced by mechanochemistry treatment. Initially, the functionalization of the methylene position of 3-benzylic indoles was undertaken for its high utility in pharmaceutical research.[7] Previously, this transformation has been studied successfully by placing a leaving group at the methylene position,[8] especially Xiao and Shao's "on-water" catalysis which represents the state-of-the-art of this transformation.[8f] To the best of our knowledge, the only case of direct coupling of benzylic indoles was reported by Gong *et al.*, which was catalyzed by Cu to give asymmetric products and Yb to afford symmetric ones.[9] Herein, we reported our studies of solvent-free iron-catalyzed CDC reactions of benzylic indoles and compounds with acidic methylene groups as well as indoles (Scheme 1).

Scheme 1. Indoles Synthesis *via* Fe-Catalyzed Mechanical CDC Reactions



At the outset, the reactions between 2-phenyl-3-benzyl-1*H*-indole (**1a**) and diethyl malonate (**2a**) were treated with different combinations of catalysts and oxidants, where silica gel was chosen as a helpful grinding auxiliary for better substrate mixing on the basis of our previous research,[6] and the selected results were summarized in Table 1. To our delight, both Fe(III) and Fe(II) catalysts could afford the desired product **3aa** after 30 min of grinding, where Fe(III) worked much better than Fe(II) (Table 1, entries 1–8). $Fe(NO_3)_3$ and $Fe(NO_3)_3 \cdot 9H_2O$ showed similar high activity (Table 1, entries 3 and 4), and the latter was chosen for its easy handling. Gratifyingly,

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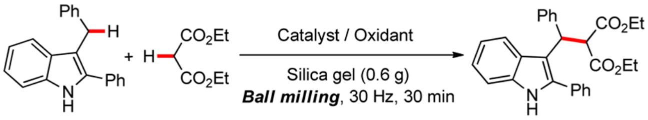
Table 1. Optimization of the Reaction Conditions[a]



1a **2a** **3aa**

entry	catalyst	oxidant	yield (%)[b]
1	$FeCl_3$	DDQ	55
2	$Fe_2(SO_4)_3$	DDQ	43
3	$Fe(NO_3)_3$	DDQ	61
4	$Fe(NO_3)_3·9H_2O$	DDQ	62[c] (58)[d]
5	$FeSO_4$	DDQ	50
6	$FeCl_2$	DDQ	35
7	$FeCl_2·4H_2O$	DDQ	37
8	–	DDQ	n.d.
9	$Fe(NO_3)_3·9H_2O$	TCQ	23
10	$Fe(NO_3)_3·9H_2O$	BQ	14
11	$Fe(NO_3)_3·9H_2O$	Oxone	6
12	$Fe(NO_3)_3·9H_2O$	MnO_2	10
13[e]	$Fe(NO_3)_3·9H_2O$	DDQ	75
14[f]	$Fe(NO_3)_3·9H_2O$	DDQ	83
15[g]	$Fe(NO_3)_3·9H_2O$	DDQ	83
16[h]	$Fe(NO_3)_3·9H_2O$	DDQ	70
17[i]	$Fe(NO_3)_3·9H_2O$	DDQ	trace
18[j]	$Cu(OTf)_2$	DDQ	78

[a] Unless otherwise noted, all reactions were carried out with **1a** (1.0 mmol), **2a** (1.0 mmol), catalyst (10 mol %), oxidant (1.0 mmol), and silica gel (0.6 g) at 30 Hz for 30 min, using two stainless steel grinding balls (14 mm diameter) in a 50 mL stainless steel vial (DDQ = 2,3-dicyano-5,6-dichlorobenzoquinone, TCQ = Tetrachlorobenzoquinone, BQ = benzoquinone). [b] Yield based on **1a**. [c] $Fe(NO_3)_3·9H_2O$ was purchased from Sinopharm Chemical Reagent Co. Ltd. (purity ≥98.5%), of which the copper content was determined to be 5.0 ppm (the major contaminant in this sample was calcium [162.8 ppm]). [d] $Fe(NO_3)_3·9H_2O$ was purchased from Aldrich (purity ≥99.95%), of which the copper content was determined to be 0.4 ppm. [e] DDQ was added in two portions during the milling interval [2(15 min + 1 min break)]. [f] DDQ was added in three portions during the milling intervals [3(10 min + 1 min break)]. [g] DDQ was added in four portions during the milling intervals [4(7.5 min + 1 min break)]. [h] 5 mol % of the catalyst was used. [i] Yield of the comparative experiment: **1a** (1.0 mmol), **2a** (1.0 mmol), $Fe(NO_3)_3·9H_2O$ (10 mol %), DDQ (1.0 mmol), and CH_2Cl_2 (30 mL) at room temperature. [j] Yield of the comparative experiment (see ref 9): **1a** (1.0 mmol), **2a** (1.0 mmol), $Cu(OTf)_2$ (10 mol %), DDQ (1.0 equiv), and CH_2Cl_2 (30 mL) at room temperature.

traces of metal impurities in $Fe(NO_3)_3·9H_2O$ had minimal influence on the product yield (Table 1, entry 4). Next, several kinds of oxidants were tested (Table 1, entries 9−12). The reaction with DDQ gave the best result of 62%, while other oxidants involving BQ and TCQ gave lower yields under the same conditions. To further elevate the product yield, we attempted to add DDQ in several portions to avoid the radical polymerization. Gratefully, the strategy worked well giving the best result of 83% yield by adding DDQ in three portions (Table 1, entries 13−15). Decreasing the catalyst loadings to 5 mol % led to erosion in yield (Table 1, entry 16). Furthermore, simple comparison of this protocol with a solvent-based method was conducted (Table 2, entries 17 and 18), and it is interesting to see that though a moderate yield of **3aa** was afforded when using $Cu(OTf)_2$ as the catalyst, the reaction could hardly be promoted by $Fe(NO_3)_3·9H_2O$ at room temperature, which verified our hypothesis that the HSBM may induce high activity when using an Fe catalyst.

Mechanochemistry process parameters usually have a strong influence on the outcomes, which were shown by us and others previously.[6a,d,10] Thus, the combined assessment of the grinding time and vibration frequency was carried out attentively, and the results were summarized in Figure 1. The yields increased sharply when elevating the frequency from 15 to 25 Hz. However, slightly lower yields were obtained when the reactions were performed under 30 Hz. In contrast to the apparent influence of frequency, variation of grinding time did not show any obvious difference at 25 and 30 Hz, where the best result could be obtained by milling at 25 Hz within 21 min (87% yield).[11] However, the gentle growth trend in yields from 15 to 20 Hz might be explained by the insufficient mechanical energy input.

With the optimal conditions in hand, the scopes and limitations of this methodology were then investigated by varying 3-benzylic indoles first. The results were presented in Table 2. To our delight, both electron-withdrawing and -donating aryl groups (involving oxidative sensitive OH group) in **1** were tolerated to give moderate to excellent yields (**3aa**−**3ea**). As expected, electron-rich substrates **1b**−**1e** gave better results than electron-deficient ones **1f**−**1i**. Steric hindrance was found to strongly influence product yields, where *o*-methyl substituted substrate **1j** afforded a low yield of 23%. Moderate to good yields were obtained by replacing the phenyl group with a methyl (**3ka**−**3ma**) or *p*-chlorophenyl (**3na**) group. Further examination of *N*-protected indole substrate **1o** showed that the reaction could also proceed smoothly, but product **3oa** was afforded in a relatively low yield (52%). Besides, 3-thienylmethylindole **1p** provided the desired product **3pa** with an excellent yield of 92%. Then, several compounds with acidic methylene groups were examined to further validate the power of this strategy. Gratifyingly, both of the symmetric and asymmetric methylene compounds proceeded successfully under the optimum conditions, furnishing the desired products **3bb**−**3bg** in moderate to high yields. It was worth mentioning that coupling partners with sensitive groups as malononitrile **2b** and ethyl 4-chloroacetoacetate **2e** were well tolerated under this oxidative condition. However, **2h** and **2i** failed to give the products, which was probably due to the steric hindrance disturbance.

With these positive results, we then turned our attention to indoles as the nucleophile for further expansion of the substrate scope (Scheme 2). We were delighted to find that not only *N*-substituted but also *N*-free indoles could be tolerated under the above-mentioned milling conditions to give the desired bisindole derivatives (**5ba**−**5bd**). However, only a trace amount of **5bb** was obtained when the reaction of **1b** and **4b** was placed under solvent-based conditions,[12] where a high reaction temperature (100 °C) and long reaction time (24 h) were required.[13] The results of electronic effects showed that an indole bearing an electron-donating group (**4d**) gave a much lower yield than that with electron-withdrawing groups (**4a** and **4c**), which was consistent with the finding of Chen's group.[4g]

Further application of this method to large-scale preparation showed that 10.0 mmol of 2-phenyl-3-benzyl-1*H*-indole **1a** were converted into the corresponding **3aa** in a low yield of 55% under the standard conditions, which was probably due to the limited space of the milling vessel which hindered the movement of the milling balls and therefore the energy input was reduced.[10c]

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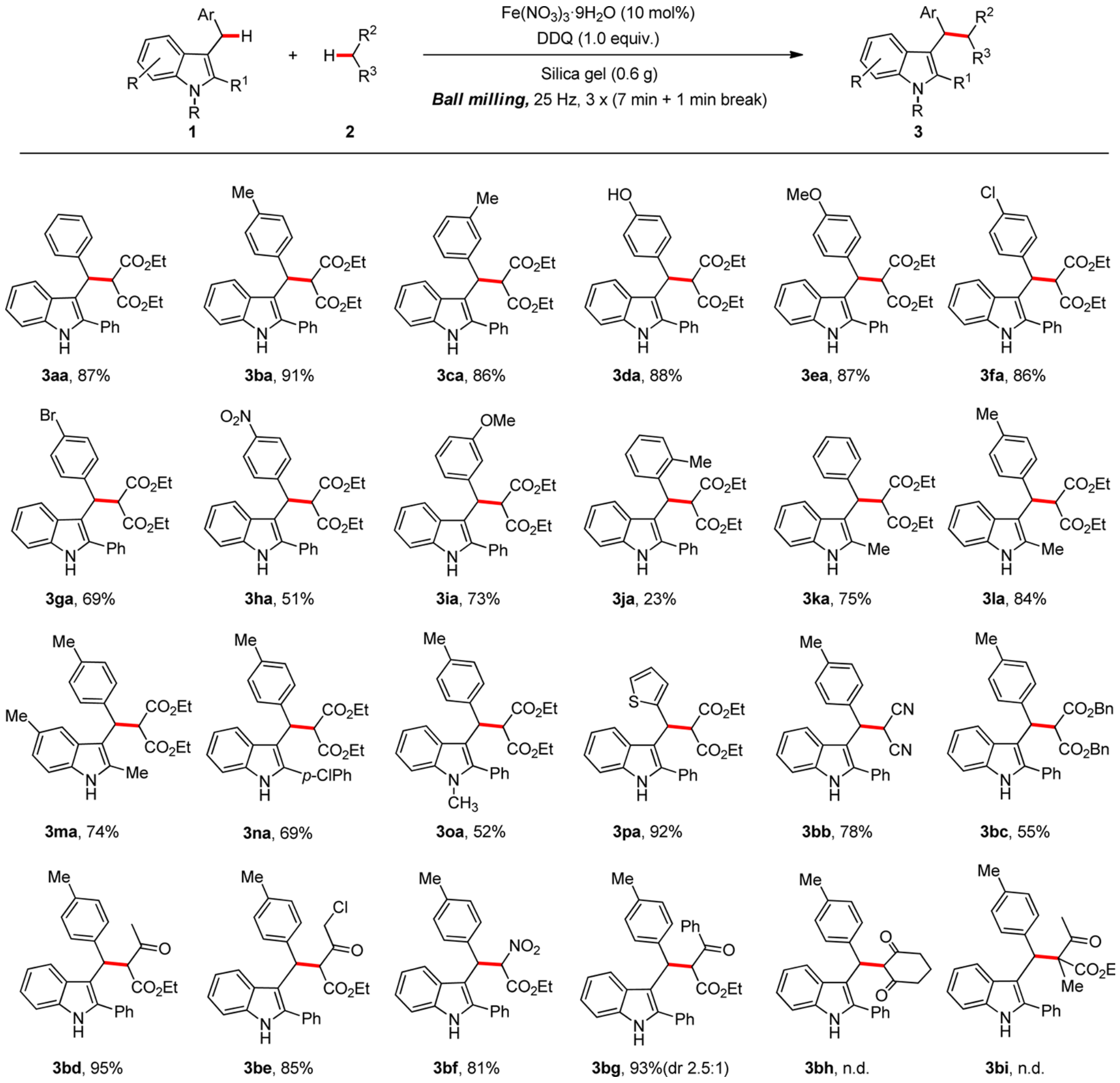
Table 2. Substrate Scope of Fe(III)-Catalyzed CDC Reactions of 3-Benzylic Indoles with Methylenes[a]



[a] Reactions were performed with **1** (1.0 mmol), **2** (1.0 mmol), $Fe(NO_3)_3{\cdot}9H_2O$ (10 mol %), DDQ (1.0 mmol, added in 3 portions during the milling intervals), and silica gel (0.6 g) at 25 Hz in mixer mill [3(7 min + 1 min break)], using two stainless steel grinding balls (14 mm diameter) in 50 mL stainless steel vial. Yield based on **1**.

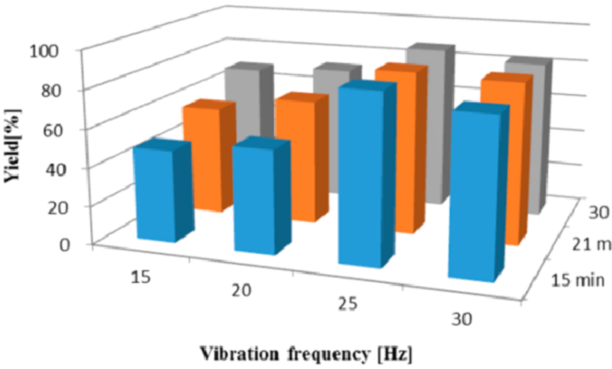
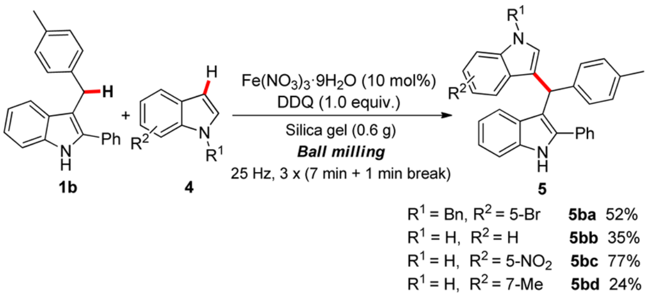


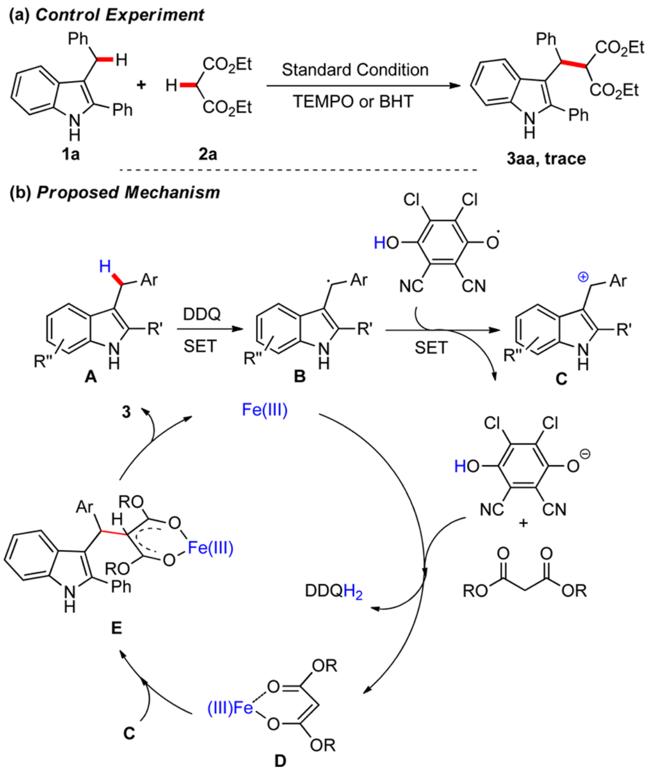
Figure 1. Optimization of mechanochemical parameters for the CDC reaction (all the reactions were proceeded in three milling cycles [3(milling time + 1 min break)]).

Scheme 2. Fe(III)-Catalyzed CDC Reactions of 3-Benzylic Indoles with Indoles



To gain insight into the mechanism, radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and 2,6-di-*tert*-butyl-4-methylphenol (BHT) were added to the reaction mixtures, respectively. Both reactions were inhibited and afforded only trace amounts of the product (Scheme 3a), indicating the reaction may undergo a radical mechanism, which was similar to that in literature reports (Scheme 3b),[4c,g,14] but different from the Cu-catalyzed one.[9]

Scheme 3. Possible Mechanism for the Fe(III)-Catalyzed CDC Reaction



In summary, we have built up a protocol for inducing an iron-catalyzed high-efficiency CDC reaction by using the HSBM technique. The model reaction between benzylic indoles and compounds with acidic methylene groups proceeded smoothly and afforded the desired products in moderate to high yields at room temperature, which could hardly be operated in the solvent environment. Far more important was that not only *N*-substituted indoles but also the *N*-free ones could be tolerated in this mechanical Fe(III) catalyzed CDC (coupling of sp^3 C−H bond and sp^2 C−H bond) reaction to furnish bisindoles in satisfactory yields. The successful development of this protocol showed the potential of HSBM to induce high catalytic activities of low-active iron metals, which provided a complement for HSBM in the field of metal-catalyzed synthesis.

■ EXPERIMENTAL SECTION

General Information. All reagents were purchased from commercial sources and used without purification, unless otherwise indicated. 3-Benzylic indoles **1** were prepared according to the literature method.[15] A high-energy vibrational ball mill (mix-miller MM 400 from Retsch) was employed. The reaction was performed in a 50 mL stainless steel vial and milled with two stainless steel grinding balls (14 mm diameter). TLC (Thin-Layer Chromatography) analysis was performed using precoated glass plates. Melting points (mp) were obtained on a digital melting point apparatus and uncorrected. ^{1}H and ^{13}C NMR were recorded at 400 (or 500) MHz and 100 (or 125) MHz, respectively, and TMS was used as the internal standard. Mass spectra were measured with an HRMS-ESI-Q-TOF and a low-resolution MS instrument using ESI ionization. Traces of metal impurities in $Fe(NO_3)_3{\cdot}9H_2O$ were determined on an ICP-MS instrument.

Typical Procedure for the Synthesis of Diethyl 2-(Phenyl(2-phenyl-1*H*-indol-3-yl)methyl)malonate (3aa[9]). The following components were added to the screw-capped stainless steel vial: 3-benzyl-2-phenyl-1*H*-indole **1a** (1 mmol, 283 mg), diethyl malonate **2a** (1 mmol, 160 mg), $Fe(NO_3)_3{\cdot}9H_2O$ (0.1 mmol, 40 mg), silica gel (0.6 g), and DDQ (1/3 mmol, 76 mg), along with two stainless steel balls (*d* = 14 mm). Then, the vial was placed in a vibrational micromill (milling cycle: 7 min at 25 Hz, followed by 1 min break, in 3 repetitions); during the next two milling intervals, the other two 1/3 portions of DDQ were added, respectively (total amount of DDQ = 1 mmol). After the reaction was completed, the contents were scratched off the vessel and purified directly by column chromatography on silica gel using PE−EtOAc (15:1) as eluent to give desired products **3aa** as a white solid (384 mg, 87% yield); mp 110−111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.83 (d, *J* = 7.2 Hz, 1H), 7.55 (d, *J* = 6.8 Hz, 2H), 7.45−7.34 (m, 3H), 7.30−7.23 (m, 3H), 7.18−7.04 (m, 5H), 5.24 (d, *J* = 12.0 Hz, 1H), 4.77 (d, *J* = 12.0 Hz, 1H), 4.01 (q, *J* = 7.2 Hz, 2H), 3.87−3.70 (m, 2H), 1.04 (t, *J* = 7.0 Hz, 3H), 0.71 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.0, 167.7, 142.0, 135.9, 135.8, 132.8, 128.9, 128.6, 128.1, 128.0, 127.6, 127.2, 126.2, 121.8, 120.6, 119.7, 112.2, 110.9, 61.4, 61.1, 56.4, 42.6, 13.9, 13.5; HRMS (ESI) *m/z*: calcd for $C_{28}H_{27}NO_4Na$ $[M + Na]^+$ 464.1832, found 464.1836.

*Diethyl 2-((2-Phenyl-1H-indol-3-yl)(p-tolyl)methyl)malonate (**3ba**).* White solid (414 mg, 91% yield); mp 102−103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 6.4 Hz, 1H), 7.46−7.34 (m, 3H), 7.27−7.20 (m, 1H), 7.16 (d, *J* = 7.6 Hz, 2H), 7.13−7.06 (m, 2H), 6.95 (d, *J* = 7.6 Hz, 2H), 5.21 (d, *J* = 12.0 Hz, 1H), 4.75 (d, *J* = 12.0 Hz, 1H), 4.02 (q, *J* = 7.2 Hz, 2H), 3.85−3.70 (m, 2H), 2.21 (s, 3H), 1.07 (t, *J* = 7.2 Hz, 3H), 0.69 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.4, 167.2, 138.6, 135.4, 135.3, 132.4, 128.5, 128.3, 127.7, 127.0, 126.9, 121.5, 120.4, 119.3, 112.1, 110.6, 61.5, 61.2, 56.6, 42.4, 21.4, 14.4, 13.9; HRMS (ESI) *m/z*: calcd for $C_{29}H_{29}NO_4Na$ $[M + Na]^+$ 478.1989, found 478.1984.

*Diethyl 2-((2-Phenyl-1H-indol-3-yl)(m-tolyl)methyl)malonate (**3ca**).* White solid (391 mg, 86% yield); mp 134−135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.54 (d, *J* = 7.2 Hz, 2H), 7.46−7.33 (m, 3H), 7.21−7.19 (m, 1H), 7.13−7.01 (m, 5H), 6.88 (d, *J* = 6.8 Hz, 1H), 5.21 (d, *J* = 12.0 Hz, 1H), 4.74 (d, *J* = 12.0 Hz, 1H), 4.01 (q, *J* = 7.2 Hz, 2H), 3.86−3.68 (m, 2H), 2.19 (s, 3H), 1.06 (t, *J* = 7.2 Hz, 3H), 0.70 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.0, 167.8, 141.8, 137.5, 135.8, 135.7, 132.8, 128.9, 128.5, 128.3, 128.0, 127.3, 127.0, 124.5, 121.7, 120.6, 119.6, 112.2, 110.8, 61.3, 61.4, 56.4, 42.4, 21.6, 14.0, 13.5; HRMS (ESI) *m/z*: calcd for $C_{29}H_{29}NO_4Na$ $[M + Na]^+$ 478.1989, found 478.2005.

*Diethyl 2-((4-Hydroxyphenyl)(2-phenyl-1H-indol-3-yl)methyl)malonate (**3da**).* White solid (402 mg, 88% yield); mp 176−178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 7.2 Hz, 2H), 7.48−7.34 (m, 3H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.17−7.08 (m, 4H), 6.57 (d, *J* = 8.8 Hz, 2H), 5.16 (d, *J* = 12.0 Hz, 1H), 5.04 (brs, 1H), 4.71 (d, *J* = 12.0 Hz, 1H), 4.03 (q, *J* = 7.2 Hz, 2H), 3.87−3.71 (m, 2H), 1.08 (t, *J* = 7.0 Hz, 3H), 0.71 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.2, 167.8, 153.9, 135.7, 134.1, 132.7, 128.80 (2C), 128.75 (2C), 128.6 (2C), 128.1, 127.1, 121.8, 120.6, 119.7, 115.0 (2C), 112.3, 110.9, 61.5, 61.2, 56.7, 41.9, 14.0, 13.5; HRMS (ESI) *m/z*: calcd for $C_{28}H_{27}NO_5Na$ $[M + Na]^+$ 480.1781, found 480.1791.

*Diethyl 2-((4-Methoxyphenyl)(2-phenyl-1H-indol-3-yl)methyl)malonate (**3ea**).* White solid (410 mg, 87% yield); mp 118−120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 7.2 Hz, 2H), 7.43−7.33 (m, 3H), 7.25−7.18 (m, 3H), 7.14−7.06 (m, 2H), 6.68 (d, *J* = 8.4 Hz, 2H), 5.19 (d, *J* = 12.0 Hz, 1H), 4.72 (d, *J* = 12.0 Hz, 1H), 4.01 (q, *J* = 7.2 Hz, 2H), 3.84−3.71 (m, 2H), 3.67 (s, 3H), 1.06 (t, *J* = 7.2 Hz, 3H), 0.69 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.1, 167.7, 157.8, 135.8, 134.3, 132.8, 128.8, 128.6, 128.0, 127.2, 121.7, 120.6, 119.6, 113.6, 112.4, 110.9, 61.4, 61.0, 56.7, 55.1, 41.9, 14.0, 13.5; HRMS (ESI) m/z: calcd for $C_{29}H_{29}NO_5Na$ [M + Na]$^+$ 494.1938, found 494.1926.

*Diethyl 2-((2-(4-Chlorophenyl)-1H-indol-3-yl)(phenyl)methyl)-malonate (**3fa**).* White solid (409 mg, 86% yield); mp 117−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.79 (d, J = 7.6 Hz, 1H), 7.55 (d, J = 7.2 Hz, 2H), 7.50−7.38 (m, 3H), 7.30 (d, J = 7.2 Hz, 1H), 7.21−7.09 (m, 6H), 5.21 (d, J = 12.0 Hz, 1H), 4.72 (d, J = 12.0 Hz, 1H), 4.05 (q, J = 7.2 Hz, 2H), 3.90−3.72 (m, 2H), 1.10 (t, J = 7.2 Hz, 3H), 0.73 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.2, 166.9, 140.2, 135.7, 135.3, 132.2, 131.6, 128.6, 128.4, 128.0, 126.7, 121.7, 120.1, 119.6, 111.5, 110.7, 61.7, 61.4, 56.4, 42.2, 14.5, 13.9; HRMS (ESI) m/z: calcd for $C_{28}H_{26}ClNO_4Na$ [M + Na]$^+$ 498.1443, found 498.1453.

*Diethyl 2-((4-Bromophenyl)(2-phenyl-1H-indol-3-yl)methyl)-malonate (**3ga**).* Light yellow solid (359 mg, 69% yield); mp 79−82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.78 (d, J = 7.6 Hz, 1H), 7.56−7.36 (m, 5H), 7.30−7.22 (m, 3H), 7.15−7.05 (m, 4H), 5.20 (d, J = 12.0 Hz, 1H), 4.71 (d, J = 12.0 Hz, 1H), 4.04 (q, J = 7.0 Hz, 2H), 3.87−3.71 (m, 2H), 1.09 (t, J = 7.0 Hz, 3H), 0.72 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.8, 167.5, 141.1, 136.1, 135.7, 132.6, 131.2, 129.3, 128.9, 128.7, 128.2, 126.9, 122.0, 120.3, 120.1, 119.8, 111.5, 111.0, 61.6, 61.2, 56.2, 42.0, 14.0, 13.5; HRMS (ESI) m/z: calcd for $C_{28}H_{26}BrNO_4Na$ [M + Na]$^+$ 542.0937, found 542.0911.

*Diethyl 2-((4-Nitrophenyl)(2-phenyl-1H-indol-3-yl)methyl)-malonate (**3ha**).* Light yellow oil (248 mg, 51% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 8.01 (d, J = 8.8 Hz, 2H), 7.99 (d, J = 8.4 Hz, 1H), 7.77 (d, J = 7.6 Hz, 1H), 7.58−7.42 (m, 5H), 7.38−7.30 (m, 3H), 7.20−7.11 (m, 2H), 5.35 (d, J = 12.0 Hz, 1H), 4.78 (d, J = 12.0 Hz, 1H), 4.14−4.01 (m, 2H), 3.94−3.77 (m, 2H), 1.12 (t, J = 7.2 Hz, 3H), 0.76 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 167.8, 167.5, 149.8, 146.4, 136.6, 135.8, 135.6, 132.5, 129.1, 129.0, 128.7, 128.4, 126.8, 123.6 (2C), 122.4, 120.3, 120.1, 111.2, 110.8, 110.7, 61.8, 61.5, 55.6, 42.1, 13.9, 13.4; HRMS (ESI) m/z: calcd for $C_{28}H_{26}N_2O_6Na$ [M + Na]$^+$ 509.1683, found 509.1663.

*Diethyl 2-((3-Methoxyphenyl)(2-phenyl-1H-indol-3-yl)methyl)-malonate (**3ia**).* White solid (344 mg, 73% yield); mp 124−126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.83 (d, J = 6.8 Hz, 1H), 7.54 (d, J = 6.8 Hz, 2H), 7.44−7.32 (m, 3H), 7.26−7.20 (m, 1H), 7.15−7.02 (m, 3H), 6.87 (d, J = 7.6 Hz, 1H), 6.80 (s, 1H), 6.62 (dd, J = 8.0, 1.6 Hz, 1H), 5.22 (d, J = 12.0 Hz, 1H), 4.76 (d, J = 12.0 Hz, 1H), 4.02 (q, J = 7.2 Hz, 2H), 3.84−3.71 (m, 2H), 3.62 (s, 3H), 1.07 (t, J = 7.2 Hz, 3H), 0.70 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.0, 167.7, 159.2, 143.6, 135.9, 135.8, 132.8, 129.1, 128.9, 128.6, 128.0, 127.2, 121.8, 120.5, 119.8, 119.6, 113.5, 112.0, 111.8, 110.9, 61.4, 61.1, 56.3, 55.0, 42.5, 14.0, 13.5; HRMS (ESI) m/z: calcd for $C_{29}H_{29}NO_5Na$ [M + Na]$^+$ 494.1938, found 494.1935.

*Diethyl 2-((2-Phenyl-1H-indol-3-yl)(o-tolyl)methyl)malonate (**3ja**).* White solid (104 mg, 23% yield); mp 138−139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01−7.94 (m, 2H), 7.54 (d, J = 6.4 Hz, 2H), 7.44−7.34 (m, 4H), 7.28−7.23 (m, 1H), 7.16−7.09 (m, 2H), 6.97−6.87 (m, 3H), 5.46 (d, J = 12.0 Hz, 1H), 4.82 (d, J = 12.0 Hz, 1H), 4.01−3.93 (m, 2H), 3.91−3.74 (m, 2H), 1.86 (s, 3H), 1.00 (t, J = 7.2 Hz, 3H), 0.76 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.1, 167.6, 139.6, 136.1, 135.7, 135.2, 133.0, 130.1, 129.0, 128.2, 127.8, 127.2, 126.0, 125.7, 125.1, 121.4, 120.3, 119.3, 111.3, 110.4, 61.0, 60.9, 56.3, 38.0, 19.6, 13.6, 13.2; HRMS (ESI) m/z: calcd for $C_{29}H_{29}NO_4Na$ [M + Na]$^+$ 478.1989, found 478.2004.

*Diethyl 2-((2-Methyl-1H-indol-3-yl)(phenyl)methyl)malonate (**3ka**).* White solid (284 mg, 75% yield); mp 144−145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.67−7.63 (m, 1H), 7.37 (d, J = 7.6 Hz, 2H), 7.24−7.15 (m, 3H), 7.11 (t, J = 7.2 Hz, 1H), 7.06−6.99 (m, 2H), 5.04 (d, J = 12.0 Hz, 1H), 4.68 (d, J = 12.0 Hz, 1H), 4.09 (q, J = 7.2 Hz, 2H), 3.88−3.77 (m, 2H), 2.46 (s, 3H), 1.11 (t, J = 7.2 Hz, 3H), 0.78 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.0, 167.8, 141.6, 135.0, 131.9, 128.2 (2C), 127.4 (2C), 127.2, 126.2, 120.7, 119.2, 119.0, 111.3, 110.1, 61.5, 61.2, 55.8, 42.5, 14.0, 13.6, 12.5; HRMS (ESI) m/z: calcd for $C_{23}H_{25}NO_4Na$ [M + Na]$^+$ 402.1676, found 402.1670.

*Diethyl 2-((2-Methyl-1H-indol-3-yl)(p-tolyl)methyl)malonate (**3la**).* Pale red solid (330 mg, 84% yield); mp 112−113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.66−7.60 (m, 1H), 7.24 (d, J = 7.6 Hz, 2H), 7.14−7.08 (m, 1H), 6.99 (d, J = 8.4 Hz, 4H), 5.00 (d, J = 12.0 Hz, 1H), 4.66 (d, J = 12.0 Hz, 1H), 4.08 (q, J = 7.0 Hz, 2H), 3.85−3.72 (m, 2H), 2.36 (s, 3H), 2.22 (s, 3H), 1.11 (t, J = 7.0 Hz, 3H), 0.74 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 167.9, 138.7, 135.5, 135.1, 131.8, 128.8, 127.2, 120.5, 119.1, 119.0, 111.3, 110.2, 61.4, 61.1, 55.9, 42.1, 21.0, 14.0, 13.5, 12.3; HRMS (ESI) m/z: calcd for $C_{24}H_{27}NO_4Na$ [M + Na]$^+$ 416.1832, found 416.1844.

*Diethyl 2-((2,5-Dimethyl-1H-indol-3-yl)(p-tolyl)methyl)malonate (**3ma**).* Light yellow solid (301 mg, 74% yield); mp 138−139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.42 (s, 1H), 7.23 (d, J = 7.6 Hz, 2H), 6.99 (d, J = 8.0 Hz, 3H), 6.82 (d, J = 8.0 Hz, 1H), 4.97 (d, J = 12.0 Hz, 1H), 4.65 (d, J = 12.0 Hz, 1H), 4.08 (q, J = 7.2 Hz, 2H), 3.87−3.72 (m, 2H), 2.40 (s, 3H), 2.32 (s, 3H), 2.22 (s, 3H), 1.11 (t, J = 7.2 Hz, 3H), 0.77 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.2, 167.8, 138.9, 135.5, 133.5, 131.9, 128.8, 128.1, 127.7, 127.3, 122.1, 118.8, 111.1, 109.8, 61.4, 61.0, 56.1, 42.1, 21.7, 21.0, 14.0, 13.5, 12.5; HRMS (ESI) m/z: calcd for $C_{25}H_{29}NO_4Na$ [M + Na]$^+$ 430.1989, found 430.2007.

*Diethyl 2-((2-(4-Chlorophenyl)-1H-indol-3-yl)(p-tolyl)methyl)-malonate (**3na**).* White solid (337 mg, 69% yield); mp 123−125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.0 (s, 1H), 7.83 (d, J = 7.2 Hz, 1H), 7.49 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 7.2 Hz, 1H), 7.16−7.08 (m, 4H), 6.96 (d, J = 8.0 Hz, 2H), 5.13 (d, J = 12.0 Hz, 1H), 4.73 (d, J = 12.0 Hz, 1H), 4.03 (q, J = 7.2 Hz, 2H), 3.85−3.71 (m, 2H), 2.22 (s, 3H), 1.08 (t, J = 7.0 Hz, 3H), 0.71 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.9, 167.8, 138.7, 135.8 (2C), 134.5, 134.0, 131.2, 130.1 (2C), 128.92 (2C), 128.86 (2C), 127.3 (2C), 127.0, 122.0, 120.7, 119.8, 112.7, 110.9, 61.5, 61.2, 56.3, 42.2, 21.1, 14.0, 13.5; HRMS (ESI) m/z: calcd for $C_{29}H_{28}ClNO_4Na$ [M + Na]$^+$ 512.1599, found 512.1612.

*Diethyl 2-((1-Methyl-2-phenyl-1H-indol-3-yl)(p-tolyl)methyl)-malonate (**3oa**).* Yellow oil (244 mg, 52% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 6.0 Hz, 1H), 7.59−7.45 (m, 4H), 7.35−7.17 (m, 4H), 7.11 (d, J = 6.4 Hz, 2H), 6.98 (d, J = 6.0 Hz, 2H), 5.00 (d, J = 10.0 Hz, 1H), 4.74 (d, J = 10.0 Hz, 1H), 4.08−4.01 (m, 2H), 3.97−3.83 (m, 2H), 3.48 (s, 1H), 2.26 (s, 1H), 1.08 (t, J = 6.0 Hz, 3H), 0.83 (t, J = 6.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 168.2, 168.1, 139.4, 138.8, 137.1, 135.5, 131.8, 131.0 (2C), 128.8 (4C), 128.4, 128.3, 127.4 (3C), 126.2, 121.3, 120.3, 119.3, 61.2, 61.0, 56.3, 42.5, 30.6, 20.9, 13.8, 13.4; HRMS (ESI) m/z: calcd for $C_{30}H_{31}NO_4Na$ [M + Na]$^+$ 492.2145, found 492.2161.

*Diethyl 2-((2-Phenyl-1H-indol-3-yl)(thiophen-2-yl)methyl)-malonate (**3pa**).* White solid (411 mg, 92% yield); mp 107−108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.76 (d, J = 7.6 Hz, 1H), 7.55 (d, J = 7.2 Hz, 2H), 7.47−7.31 (m, 3H), 7.24 (d, J = 7.6 Hz, 1H), 7.15−7.01 (m, 3H), 6.87 (brs, 1H), 6.82−6.76 (m, 1H), 5.49 (d, J = 11.6 Hz, 1H), 4.68 (d, J = 11.6 Hz, 1H), 4.15−4.05 (m, 2H), 3.79−3.62 (m, 2H), 1.14 (t, J = 7.0 Hz, 3H), 0.63 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.8, 167.0, 146.0, 136.1, 135.9, 132.6, 128.8, 128.7, 128.1, 127.0, 126.2, 124.5, 123.9, 122.0, 120.8, 119.7, 111.8, 110.9, 61.6, 61.1, 57.9, 38.2, 14.0, 13.4; HRMS (ESI) m/z: calcd for $C_{26}H_{25}NSO_4Na$ [M + Na]$^+$ 470.1397, found 470.1418.

*2-((2-Phenyl-1H-indol-3-yl)(p-tolyl)methyl)malononitrile (**3bb**).* White solid (282 mg, 78% yield); mp 183−184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.45 (brs, 4H), 7.36 (d, J = 8.0 Hz, 3H), 7.24−7.19 (m, 1H), 7.18−7.10 (m, 4H), 4.93 (d, J = 10.8 Hz, 1H), 4.67 (d, J = 10.8 Hz, 1H), 2.32 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 137.9, 137.7, 136.0, 134.5, 131.4, 129.6, 129.1, 129.0, 128.1, 128.1, 127.5, 127.2, 122.7, 120.6, 119.4, 112.5, 112.2, 111.7, 44.5, 28.6, 21.2; HRMS (ESI) m/z: calcd for $C_{25}H_{19}N_3Na$ [M + Na]$^+$ 384.1471, found 384.1453.

*Dibenzyl 2-((2-Phenyl-1H-indol-3-yl)(p-tolyl)methyl)malonate (**3bc**[9]).* White solid (318 mg, 55% yield); mp 125−126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.80 (d, J = 7.6 Hz, 1H), 7.45 (d, J = 6.8 Hz, 2H), 7.36 (d, J = 6.8 Hz, 3H), 7.27−7.19 (m, 4H), 7.16−7.02 (m, 9H), 6.90 (d, J = 7.2 Hz, 2H), 6.68 (d, J = 7.2 Hz, 2H), 5.23 (d, J = 12.0 Hz, 1H), 4.96 (brs, 2H), 4.90 (d, J = 12.0 Hz, 1H), 4.78–4.70 (m, 2H), 2.20 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 167.8, 167.6, 138.7, 135.9, 135.8, 135.7, 135.1, 135.0, 132.6, 129.0, 128.9, 128.6, 128.2, 128.0, 127.9, 127.6, 127.6, 127.3, 127.0, 121.8, 120.6, 119.8, 112.0, 111.0, 67.1, 66.9, 56.3, 42.5, 21.1; HRMS (ESI) *m*/*z*: calcd for $C_{39}H_{33}NO_4Na$ [M + Na]$^+$ 602.2302, found 602.2287.

*Ethyl 3-Oxo-2-((2-phenyl-1H-indol-3-yl)(p-tolyl)methyl)-butanoate (**3bd**).* White solid (403 mg, 95% yield). The ratio of isolated diastereoisomers is 7.8; mp 156−157 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.03 (s, 1H), 7.84 (d, *J* = 5.2 Hz, 1H), 7.56 (d, *J* = 6.8 Hz, 2H), 7.46−7.36 (m, 3H), 7.25−7.21 (m, 1H), 7.14−7.08 (m, 4H), 6.95 (d, *J* = 7.6 Hz, 2H), [5.21 major, 5.12 minor] (d, *J* = 12.0 Hz, *J* = 12.4 Hz 1H), 4.94 (d, *J* = 12.0 Hz, 1H), [(4.03−3.95) minor, (3.83−3.70) major] (m, 2H), [2.23 minor, 2.20 major] (s, 3H), [2.12 minor, 2.11 major] (s, 3H), 0.70 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 202.1, 167.8, 138.9, 135.8, 135.7, 132.8, 129.1, 128.9, 128.6, 128.0, 127.4, 127.1, 121.9, 121.8, 120.6, 119.6, 112.6, 110.9, 64.2 major, 63.7 minor, 61.3 minor, 61.1 major, 42.0, 30.0 major, 21.0 minor, 13.5; HRMS (ESI) *m*/*z*: calcd for $C_{28}H_{27}NO_3Na$ [M + Na]$^+$ 448.1883, found 448.1888.

*Ethyl 4-Chloro-3-oxo-2-((2-phenyl-1H-indol-3-yl)(p-tolyl)methyl)-butanoate (**3be**).* Yellow solid (391 mg, 85% yield); mp 152−154 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.11 (s, 1H), 7.77 (d, *J* = 7.2 Hz, 1H), 7.50 (d, *J* = 7.6 Hz, 2H), 7.46−7.35 (m, 3H), 7.26 (d, *J* = 7.6 Hz, 1H), 7.22−7.18 (m, 2H), 7.16−7.06 (m, 2H), 6.99 (d, *J* = 7.6 Hz, 2H), 5.16 (d, *J* = 12.0 Hz, 1H), 5.09 (d, *J* = 12.0 Hz, 1H), 4.03−3.89 (m, 3H, including3.93 [d, *J* = 16.4 Hz, 1H]), 3.73 (d, *J* = 16.4 Hz, 1H), 2.23 (s, 3H), 1.04 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 195.1, 167.1, 138.5, 136.1, 135.9, 132.2, 129.0, 128.8, 128.7, 128.3, 127.3, 126.5, 122.2, 120.1, 119.8, 111.5, 111.1, 61.7, 60.3, 48.6, 42.4, 21.0, 13.9; HRMS (ESI) *m*/*z*: calcd for $C_{28}H_{26}NClO_3Na$ [M + Na]$^+$ 482.1493, found 482.1502.

*Ethyl 2-Nitro-3-(2-phenyl-1H-indol-3-yl)-3-p-tolylpropanoate (**3bf**).* Yellow solid (347 mg, 81% yield); mp 148−149 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.08 (s, 1H), 7.87 (s, 1H), 7.41 (brs, 5H), 7.31−7.12 (m, 5H), 7.08−6.99 (m, 2H), 6.36 (brm, 1H), 5.36 (brm, 1H), 4.11−3.92 (m, 2H), 2.26 (s, 3H), 1.02 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 163.5, 137.1, 136.9, 135.8, 135.4, 132.1, 129.3, 128.9, 128.7, 128.5, 128.0, 126.4, 122.2, 120.3, 119.7, 111.4, 109.1, 90.5, 62.8, 44.6, 21.1, 13.7; HRMS (ESI) *m*/*z*: calcd for $C_{26}H_{24}N_2O_4Na$ [M + Na]$^+$ 451.1628, found 451.1634.

*Ethyl 2-Benzoyl-3-(2-phenyl-1H-indol-3-yl)-3-(p-tolyl)propanoate (**3bg**).* Light yellow solid (453 mg, 93% yield). The ratio of isolated diastereoisomers is 2.3; mp 156−157 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ [8.05 major, 8.03 minor] (s, 1H), 7.89−7.80 (m, 2H), [7.74 major, 7.65 minor] (d, *J* = 7.6, *J* = 7.2 Hz, 2H), 7.54 (d, *J* = 6.8 Hz, 2H), 7.50−7.34 (m, 5H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.22−7.19 (m, 1H), 7.16−7.12 (m, 1H), 7.08−6.99 (m, 3H, including 7.02 major [d, *J* = 8.0 Hz]), 6.86 minor (d, *J* = 8.0 Hz, 0.70H), [5.80 minor, 5.78 major] (d, *J* = 11.2, *J* = 11.6 Hz, 1H), [5.63 minor, 5.42 major] (d, *J* = 11.2, *J* = 11.6 Hz, 1H), 3.94 major (q, *J* = 7.2 Hz, 1.78H), (3.78−3.60) minor (m, 0.85H), [2.25 major, 2.14 minor] (s, 3H), [0.97 major, 0.56 minor] (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 193.2, 168.1 major, 167.7 minor, 139.6, 136.7, 135.9, 135.7, 135.6, 133.1, 132.5, 129.1, 128.8, 128.5, 128.2, 128.0 (3C), 127.8, 127.5 major, 127.3 minor, 121.6, 120.3, 119.6, 112.8 minor, 112.7 major, 110.9, 61.3, 58.4, 42.4, 21.0, 14.3 minor, 13.9 major; HRMS (ESI) *m*/*z*: calcd for $C_{33}H_{29}NO_3Na$ [M + Na]$^+$ 510.2040, found 510.2046.

Typical Procedure for the Synthesis of 1-Benzyl-5-bromo-3-((2-phenyl-1*H*-indol-3-yl)(*p*-tolyl)methyl)-1*H*-indole (5ba). The following components were added to the screw-capped stainless steel vial: 3-(4-methylbenzyl)-2-phenyl-1*H*-indole **1b** (1 mmol, 297 mg), 1-benzyl-5-bromo-1*H*-indole **4a** (1 mmol, 286 mg), $Fe(NO_3)_3{\cdot}9H_2O$ (0.1 mmol, 40 mg), silica gel (0.6 g), DDQ (1/3 mmol, 76 mg), along with two stainless steel balls (d = 14 mm). Then, the vial was placed in a vibrational micromill (milling cycle: 7 min at 25 Hz, followed by 1 min break, in 3 repetitions); during the next two milling intervals, the other two 1/3 portions of DDQ were added, respectively (total amount of DDQ = 1 mmol). After the reaction was completed, the contents were scratched off the vessel and purified directly by column chromatography on silica gel using PE-EtOAc (15:1) as eluent to give desired products **5ba** in a light yellow solid (302 mg, 52% yield); mp 192−193 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.04 (s, 1H), 7.46 (d, *J* = 6.8 Hz, 2H), 7.42−7.34 (m, 3H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.27−7.15 (m, 8H, including CDCl$_3$), 7.13−7.05 (m, 2H), 7.05−6.90 (m, 5H), 6.83 (dd, J_1 = 7.6 Hz, J_2 = 7.6 Hz, 1H), 6.78 (s, 1H), 5.92 (s, 1H), [5.15, 5.14] (s, 2H), 2.29 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 140.3, 137.3, 136.1, 135.3, 134.9, 132.8, 129.6, 129.0, 128.8, 128.6, 128.5, 128.3, 128.2, 128.0, 127.4, 126.0, 124.3, 122.3, 121.7, 121.2, 119.3, 118.5, 114.7, 112.3, 111.1, 110.7, 50.1, 38.9, 21.2; HRMS (ESI) *m*/*z*: calcd for $C_{37}H_{29}BrN_2Na$ [M + Na]$^+$ 603.1406, found 603.1379.

*3-((1H-indol-3-yl)(p-tolyl)methyl)-2-phenyl-1H-indole (**5bb**).* Yellow oil (144 mg, 35% yield); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.94 (s, 1H), 7.79 (s, 1H), 7.46−7.42 (m, 1H), 7.38−7.24 (m, 5H), 7.18−6.77 (m, 11H), 6.73 (s, 1H), [5.95 major, 6.05 minor] (s, 1H), [2.26 major, 2.33 minor] (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 140.9, 136.6, 136.3, 135.0, 133.1, 128.9, 128.8, 128.6, 128.4, 128.2, 128.1, 127.7, 127.5, 127.2, 125.1, 123.8, 121.8, 121.4, 119.8, 119.3, 119.2, 110.8, 110.6, 110.4, 39.3, 21.1; HRMS (ESI) *m*/*z*: calcd for $C_{30}H_{24}N_2Na$ [M + Na]$^+$ 435.1831, found 435.1847.

*5-Nitro-3-((2-phenyl-1H-indol-3-yl)(p-tolyl)methyl)-1H-indole (**5bc**).* Yellow solid (352 mg, 77% yield); mp 163−164 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.25 (s, 1H), 8.11 (s, 1H), 8.02−7.93 (m, 2H), 7.50−7.31 (m, 6H), 7.25−7.18 (m, 4H), 7.11−7.02 (m, 3H), 6.92−6.82 (m, 2H), 5.96 (s, 1H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 141.6, 139.9, 139.4, 136.3, 135.7, 135.5, 132.8, 128.9, 128.8, 128.6, 128.5, 128.2, 128.1, 126.9, 126.2, 122.8, 121.9, 120.9, 119.5, 117.6, 117.0, 114.4, 110.9, 110.7, 39.3, 21.1; HRMS (ESI) *m*/*z*: calcd for $C_{30}H_{23}N_3O_2Na$ [M + Na]$^+$ 480.1682, found 480.1676.

*7-Methyl-3-((2-phenyl-1H-indol-3-yl)(p-tolyl)methyl)-1H-indole (**5bd**).* White solid (102 mg, 24% yield); mp 121−123 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.83 (s, 1H), 7.63 (s, 1H), 7.42−7.38 (m, 2H), 7.33−7.25 (m, 4H), 7.11−6.99 (m, 5H), 6.97−6.91 (m, 3H), 6.87 (t, *J* = 7.6 Hz, 2H), 6.67 (s, 1H), 5.93 (s, 1H), 2.45 (s, 3H), 2.25 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 140.3, 135.7, 135.5, 134.5, 134.3, 132.4, 128.2, 128.1, 128.0, 127.8, 127.7, 127.3, 126.9 126.4, 123.4, 121.9, 121.3, 121.2, 119.7, 119.0, 118.8, 117.2, 115.4, 113.8, 110.5, 39.1, 21.5, 17.1; HRMS (ESI) *m*/*z*: calcd for $C_{31}H_{26}N_2Na$ [M + Na]$^+$ 449.1988, found 449.2006.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02197.

Optimization of mechanochemical parameters for CDC reaction; copies of ^{1}H and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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(11) For the detailed results, see Table S1 in the Supporting Information.

(12) Comparative experiment (solvent-based reaction): the reaction was performed with **1b** (1.0 mmol), **4b** (1.0 mmol), $Fe(NO_3)_3\cdot 9H_2O$ (0.1 mmol), DDQ (1.0 mmol), and dichloroethane (1 mL) in an oven-dried Schlenk tube with a magnetic stirring bar under nitrogen, and the reaction mixture was stirred at 100 °C for 24 h.

(13) For the reaction conditions of the solvent-based iron-catalyzed CDC reaction between indoles and benzylic C−H bonds, see ref 4g.

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