JOC The Journal of Organic Chemistry

Article

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Iron-Catalyzed Divergent Tandem Radical Annulation of Aldehydes with Olefins toward Indolines and Dihydropyrans

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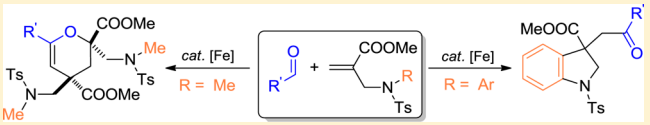
Supporting Information

ABSTRACT: Iron-catalyzed divergent tandem radical annulations of aldehydes with olefins are reported. The new strategy allows the rapid and efficient construction of various multifunctionlized indolines (R = Ar) and dihydropyrans (R = Me), which are significant skeletons in bioactive natural products and pharmaceuticals. The substituents of tertiary amines play vital roles to facilitate the desired transformation. Mechanistic studies on indoline formation disclose that the homolytic cleavage of the carbonyl C−H bond might be involved in the rate-determining step, while dissociation of the aromatic C−H bond was most likely included in the product-determining step.



INTRODUCTION

N-Heterocycle skeletons are significant structural motifs because of their wide existence in a large number of natural alkaloids and pharmaceuticals.[1] Indoles, indolines, and oxindoles are especially attractive due to their impressive bioactivities and drug-like properties (Figure 1).[2−4] For example, lundurine B exhibits remarkable toxicity toward B16 melanoma cells.[5] Aspidophylline A is found to reverse drug resistance in drug-resistant KB cells (IC_{50} = 29.1 μM).[6] These findings suggested that indoline derivatives may serve as promising candidates for new antitumor agents. Moreover, they can also serve as valuable building blocks for the preparation of complex molecules in view of their latent reactive sites and directed functionalization.[7]

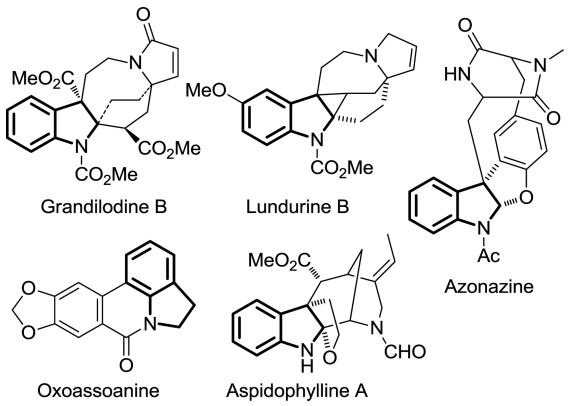
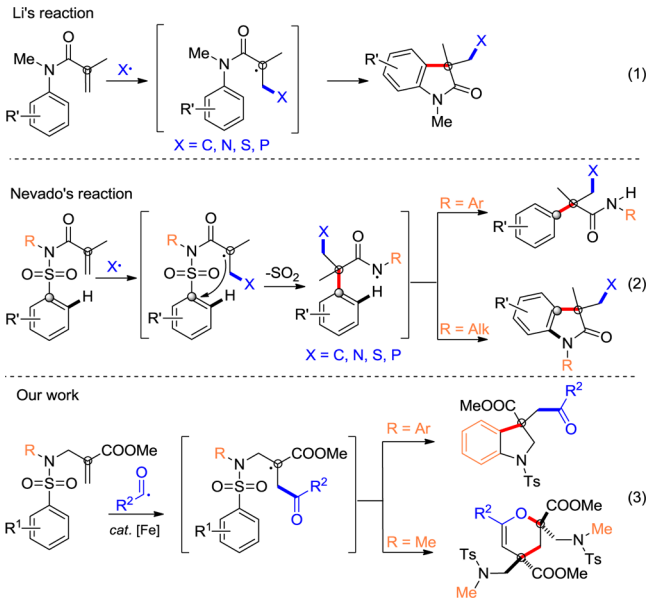


Figure 1. Natural alkaloids and pharmaceuticals containing an indoline moiety.

Radical tandem cyclizations have attracted much attention because of their intrinsic elegance, broad functional group compatibility, and especially the unique and ingenious construction of molecular architectures and polycyclic frameworks in a single step.[8] As a result, the preparation of these biologically active indole derivatives by employing the tandem radical cyclization strategy is highly desirable. For example, Li and co-workers reported the construction of oxindoles through intermolecular addition of carbon radicals to *N*-arylacrylamides and sequential intramolecular radical cyclization (Scheme 1, eq 1).[9] Furthermore, a great variety of synthetically and bio-

Scheme 1. Strategies of Designed Tandem Radical Cyclization of *N*-Allylamides



Received: October 23, 2015
Published: November 18, 2015

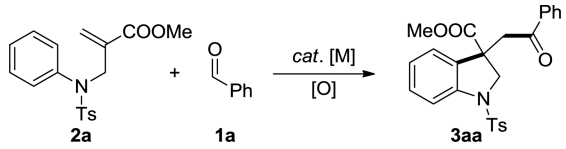
DOI: 10.1021/acs.joc.5b02457
J. Org. Chem. 2015, 80, 12562−12571

logically significant functional groups could be smoothly incorporated into the oxindole scaffold so long as applying different radical precusors.[10] Recently, Nevado et al. reported the formation of *N*-arylamides (R = Ar) and/or oxindoles (R = Alkyl) from *N*-sulfonylacrylamides by an unprecedented radical addition/arylmigration/desulfonylation sequence (Scheme 1, eq 2).[11] Encouraged by these excellent works and connected with our ongoing efforts in the 1,2-difunctionalization of alkenes,[12] we herein wish to report a practical iron-catalyzed[13] cascade acylation−arylation of *N*-allylsulfamides (when R = Ar) with aldehydes and a convergent iron-catalyzed oxidative tandem radical [2 + 2 + 2] cycloaddition[14] (when R = Me) (Scheme 1, eq 3), which allows for the preparation of polyfunctionlized indolines[15] and dihydropyrans.

RESULTS AND DISCUSSION

Initially, the reaction of benzaldehyde **1a** with *N*-allyl-tosyl amide **2a** was chosen as the model to optimize the reaction conditions (Table 1). To our delight, a 74% yield of the

Table 1. Optimization of Reaction Conditions[a]



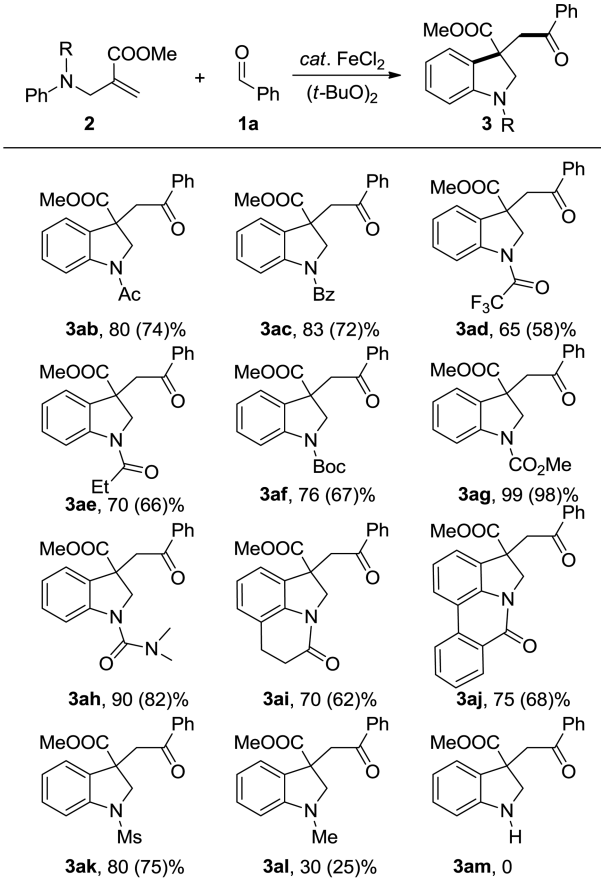
entry	[M]	[O]	yield of **3aa** (%)[b]
1	$FeCl_2$	$(t\text{-BuO})_2$	74[c]
2	$FeCl_2$	$(t\text{-BuO})_2$	85 (80)
3	$FeBr_2$	$(t\text{-BuO})_2$	74
4	$Fe(OAc)_2$	$(t\text{-BuO})_2$	84
5	$Fe_2(CO)_9$	$(t\text{-BuO})_2$	82
6	$Fe(acac)_2$	$(t\text{-BuO})_2$	80
7	$FeCl_3$	$(t\text{-BuO})_2$	83
8	$CuCl_2$	$(t\text{-BuO})_2$	50
9	CuCl	$(t\text{-BuO})_2$	65
10	$CoCl_2$	$(t\text{-BuO})_2$	12
11	$MnCl_2$	$(t\text{-BuO})_2$	11
12	$FeCl_2$	$(t\text{-BuO})_2$	43[d]
13	$FeCl_2$	$(t\text{-BuO})_2$	62[e]
14	$FeCl_2$	*t*-BuOOH	46
15	$FeCl_2$	PhCOOOBu-*t*	67
16	$FeCl_2$	$(PhCOO)_2$	trace
17		$(t\text{-BuO})_2$	trace
18	$FeCl_2$		trace

[a]Reaction conditions: **1a** (1.5 mmol), **2a** (0.3 mmol), [M] (2.5 mol %), [O] (0.75 mmol), PhCl (1.0 mL), 120 °C, 1 h, under N_2 unless other noted. [b]NMR yields were determined by ^{1}H NMR using an internal standard (the yields in parentheses). [c]**1a** (0.9 mmol), **2a** (0.3 mmol). [d]MeCN (1.0 mL) was used as the solvent. [e]DCE (1.0 mL) was used as the solvent.

indoline product **3aa** was obtained with $FeCl_2$ as catalyst and di-*tert*-butyl peroxide as oxidant (entry 1). Increase of the benzaldehyde loading to 1.5 mmol gave **3aa** in a satisfactory yield (entry 2). Subsequent catalyst screening showed that the simple iron salt could efficiently promote the formation of **3aa** (entries 3−7). Copper catalysts led to moderate yields of the desired indolines (entries 8−9), while cobalt and manganese catalyst were less effective compared with iron and copper catalysts (entries 10 and 11). When acetonitrile or dichloroethane was used as the solvent, **3aa** was obtained in moderate yield (entries 12 and 13). Changing the oxidant to *tert*-butyl hydroperoxide, *tert*-butyl peroxybenzoate, or benzoyl peroxide resulted in poor or even no desired transformation (entries 14−16). When no catalyst or oxidant was added, the transformation was dramatically inhibited, and less than 5% yield of **3aa** was detected by ^{1}H NMR analysis of the crude resulting mixture (entries 17 and 18).

With the optimal reaction conditions in hand, we first examined the electronic effect on the nitrogen atom of substrates **2** (Table 2). It was found that the electron-

Table 2. Electronic Effect on the Nitrogen Atom of 2[a]



[a]Reaction conditions: **1a** (1.5 mmol), **2** (0.3 mmol), $FeCl_2$ (2.5 mol %), $(t\text{-BuO})_2$ (0.75 mmol), PhCl (1.0 mL), 120 °C, 1 h, under N_2; NMR yields were determined by ^{1}H NMR using an internal standard, and yields are given in parentheses.

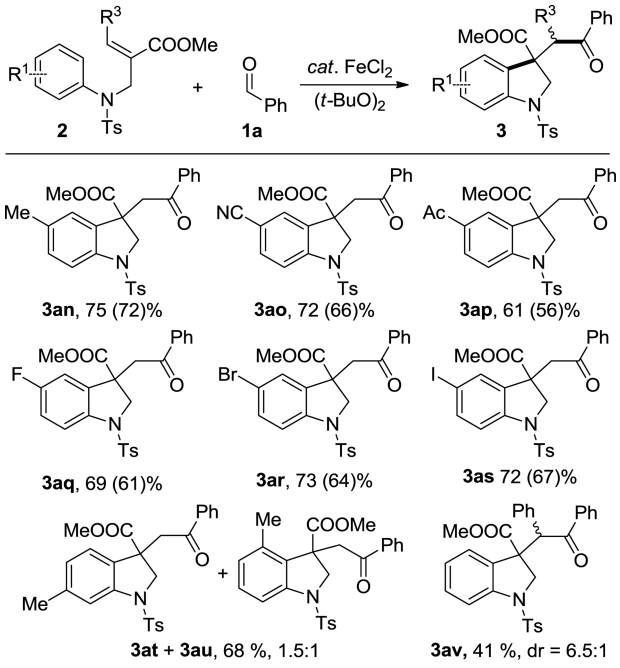
withdrawing *N*-protecting groups play vital roles to facilitate the transformation. For example, *N*-allyl acetamide **2b** and benzamide **2c** reacted smoothly with benzaldehyde **1a** to give the corresponding indolines **3ab** and **3ac** in good yields, yet the strong electron-withdrawing trifluoroacetamide **2d** displayed relatively low reactivity. The *N*-allyl carbamates and urea were successfully applied to this transformation and led to **3af−ah** in moderate to excellent yields. We speculated that the moderate yield of **3af** was due to the existence of the hindered Boc moiety. To our delight, the polycyclic indolines **3ai−aj** were smoothly constructed in good yields under the optimal conditions. In contrast, when the electron-donating methyl group was incorporated onto the nitrogen atom, the efficiency of the reaction was dramatically decreased and the correspond-

DOI: 10.1021/acs.joc.5b02457
J. Org. Chem. 2015, 80, 12562−12571

ing product **3al** was obtained in only 30% yield; also 15% of starting material **2l** was recovered along with some unidentified products. Importantly, the expected *N*-H indoline **3am** was not observed when *N*-H-*N*-allyl aniline **2m** was employed, indicating that tertiary anilines are required for this transformation.

Subsequently, the Ts group was selected as the *N*-protecting group, and the generality of the transformation was investigated (Table 3). The substrate **2** with either electron-donating or

Table 3. Scope of Substrate 2[a]

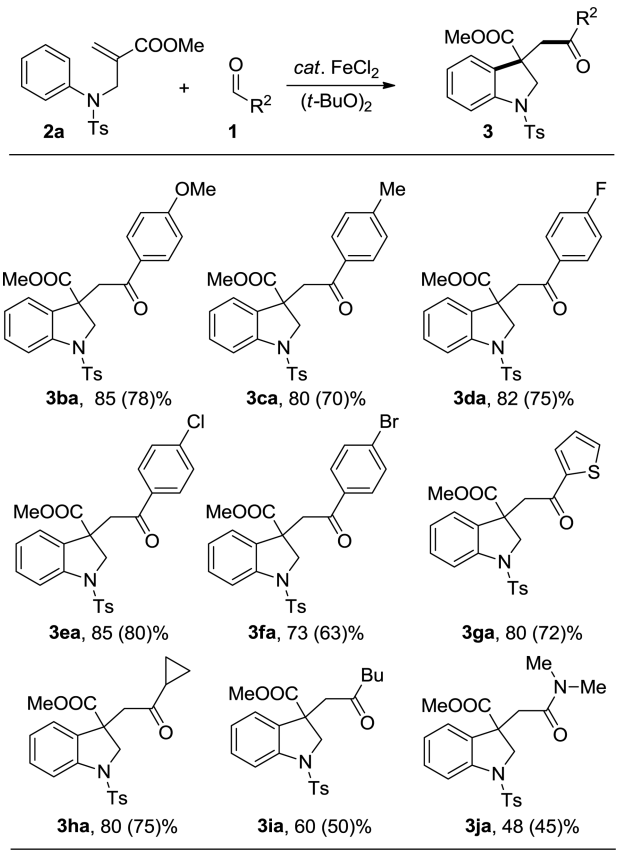


[a]Reaction conditions: **1a** (1.5 mmol), **2** (0.3 mmol), $FeCl_2$ (2.5 mol %), $(t\text{-BuO})_2$ (0.75 mmol), PhCl (1.0 mL), 120 °C, 1 h, under N_2; NMR yields were determined by ^1H NMR using an internal standard, and yields are given in parentheses.

-withdrawing groups on the para position of the aromatic ring could be smoothly converted to the desired indolines **3an**–**ap** in good yields. Gratifyingly, the halide groups were compatible with this protocol, giving the corresponding products **3aq**–**as** in good yields, which allows for further transformation through transition-metal-catalyzed coupling reactions. However, the efficiency of the transformation was dramatically influenced by the steric hindrance. For instance, the tosyl amide with the methyl group on the meta position afforded the combined products **3at** and **3au** in 68% yield with a calculated 1.5:1 ratio, indicating that the steric hindrance influences the regioselectivity of the cyclization. It is noteworthy that the trisubstituted alkene **2v** was also examined to give the desired product **3av** in a 6.5:1 ratio with 18% of starting material **2v** recovered.

Next, the scope of aldehyde **1** was investigated (Table 4). To our delight, a wide range of aromatic aldehydes bearing either electron-donating (**1b** and **1c**) or -withdrawing groups (**1d**–**f**) reacted smoothly with **2a**, thus affording the corresponding indolines **3ba**–**fa** in high yields under the standard conditions. Thiophene-2-carbaldehyde **1g** also gave the indoline **3ga** in good yield. When aliphatic cyclopropanecarbaldehyde **1h** was applied under the standard conditions, the desired product **3ha** was obtained in 80% yield, yet valeraldehyde **1i** retarded the

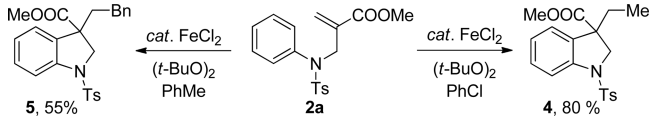
Table 4. Scope of Aldehyde 1[a]



[a]Reaction conditions: **1** (1.5 mmol), **2a** (0.3 mmol), $FeCl_2$ (2.5 mol %), $(t\text{-BuO})_2$ (0.75 mmol), PhCl (1.0 mL), 120 °C, 1 h, under N_2; NMR yields were determined by ^1H NMR using an internal standard, and yields are given in parentheses.

efficiency of the transformation. Gratifyingly, DMF could be utilized as the carbonyl source to undergo such transformation, though a moderate yield of **3ja** was observed. Interestingly, the methyl radical, which was generated by the thermal decomposition of di-*tert*-butyl peroxide,[16] smoothly reacted with **2a** in the absence of aldehyde **1** and gave the desired indoline **4** in 80% yield (Scheme 2). Furthermore, the benzyl-

Scheme 2. Alkyl Radical-Induced Indoline Formation



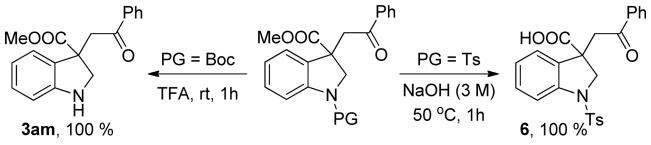
substituted indoline **5** was also obtained in 55% yield in the absence of aldehyde **1** when the reaction was carried out in toluene instead of chlorobenzene (Scheme 2),[17] exhibiting the generality of the transformation.

The obtained indolines could be further manipulated (Scheme 3). For example, the free *N*-H product **3am**, which cannot be synthesized directly (Table 2), was obtained in quantitative yield under acidic condition (PG = Boc). Base hydrolysis of **3aa** gave the carboxylic acid **6** (PG = Ts) with a quaternary carbon in also quantitative yield, which may be applied in the decarboxylative cross-coupling reactions.[18]

When the reactions of *N*-methyl-*N*-allyl sulfamide **7a** with aromatic aldehydes **1** were investigated under the standard

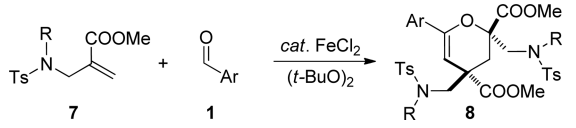
DOI: 10.1021/acs.joc.5b02457
J. Org. Chem. 2015, 80, 12562–12571

Scheme 3. Further Transformation of the Indolines



conditions, 3,4-dihydropyrans **8a–d** were formed in good yields (Table 5, entries 1–4). This transformation presents an

Table 5. Iron-Catalyzed Three-Component Cycloaddition for 3,4-Dihydropyrans[a]



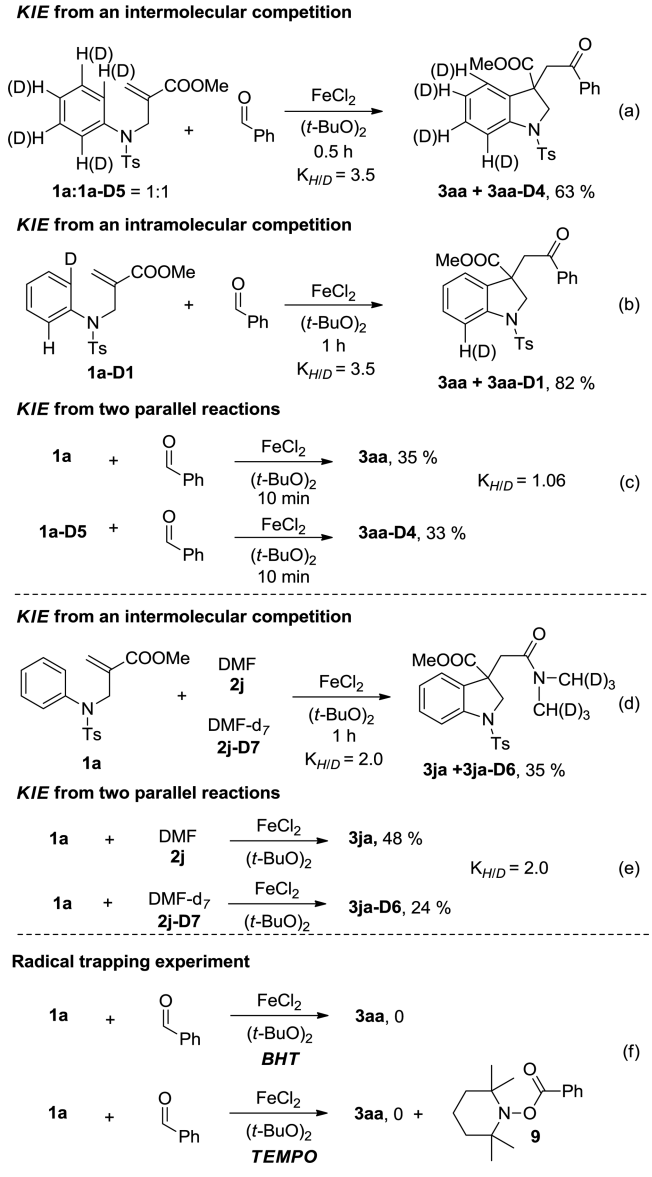
entry	7	1	yield
1	**7a**, R = Me	**1a**, Ar = Ph	**8a**, 70 (68)%, dr =2.2:1
2	**7a**, R = Me	**1c**, Ar = *p*-Me-C_4H_6	**8b**, 53 (50)%, dr =2.0:1
3	**7a**, R = Me	**1e**, Ar = *p*−Cl-C_4H_6	**8c**, 64 (60)%, dr =2.0:1
4	**7a**, R = Me	**1g**, Ar = 1-thiophyl	**8d**, 61 (55)%, dr =1.8:1
5	**7b**, R = Et	**1a**, Ar = Ph	**8e**, 39 (35)%, dr =2.0:1

[a]Reaction conditions: **1** (1.5 mmol), **7** (0.3 mmol), $FeCl_2$ (2.5 mol %), $(t\text{-BuO})_2$ (0.75 mmol), PhCl (1.0 mL), 120 °C, 1 h, under N_2; NMR yields were determined by ^1H NMR using an internal standard, and yields are given in parentheses; diastereomer ratios were determined by ^1H NMR.

oxidative radical [2 + 2 + 2] cycloaddition of one aldehyde **1** with two alkenes **7**. When *N*-ethyl-*N*-allyl sulfamide **7b** was applied, the desired product **8e** was observed in only 39% yield with 40% of starting material remained (entry 5). We speculated that this transformation may be sensitive to the steric hindrance. Importantly, an electron-withdrawing group (such as Ts) on the nitrogen atom is required for this transformation, which is consistent with our recent report.[12a] We hypothesized that iron catalyst might be involved in the cycloaddition step and the electron-deficient tertiary amide would avoid coordination of the nitrogen atom to iron and thus allows the [2 + 2 + 2] cycloaddition process.

In order to elucidate possible reaction mechanisms for indoline formation, some control experiments were carried out (Scheme 4). Because two C–H bonds, aldehydic C–H and aromatic C–H, are cleaved in the reaction process, kinetic isotope effects (KIEs) had been measured to understand the details of the cleavage of C–H bonds. Large kinetic isotope effects ($k_{H/D}$ = 3.5) were observed from both inter- and intramolecular competition (Scheme 4a and 4b). However, two parallel reactions showed almost no kinetic isotope effect ($k_{H/D}$ = 1.06) (Scheme 4c). The results suggested that dissociation of the aromatic C–H bond cannot occur in the rate-determining step and, instead, most likely is involved in the product-determining step.[19] On the other hand, potential kinetic isotope effects ($k_{H/D}$ = 2.0) were observed in both an intermolecular competition and two parallel reactions by the reactions of *N*-allyl tosyl amide **1a** with DMF and DMF-d_7 (Scheme 4d and 4e), implying that cleavage of the aldehydic C–H bond might be involved in the rate-limiting step.[20] In addition, the present transformation was completely inhibited when the radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) or butylated hydroxytoluene (BHT) was added

Scheme 4. Control Experiments



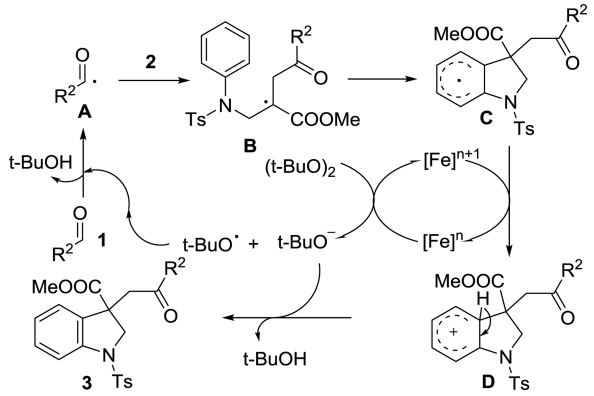
under the standard conditions (Scheme 4f). TEMPO-adduct aldehyde **9** was obtained in the presence of TEMPO, which supported the reaction being initiated by addition of the generated acyl radical.

On the basis of our results and the literature, a proposed mechanism for indoline formation (when R = Ar) was depicted in Scheme 5. Acyl radical **A** is generated by hydrogen abstraction of aldehyde **1**, which most likely occurs in the rate-determining step of the indoline formation. Subsequently, radical addition of **A** to the C=C double bond affords intermediate **B**. Then intramolecular trapping by the aromatic ring gives intermediate **C**, which is irreversibly oxidized by the iron–oxo species to deliver the carbocation intermediate **D**. The reduced iron catalyst reacts with di-*tert*-butylperoxide to give *tert*-butoxyl radical along with *tert*-butanolate. Finally, deprotonation gave the indoline **3**, wherein our kinetic isotope results suggested that C–H bond cleavage might not occur as the rate-determining step.[21]

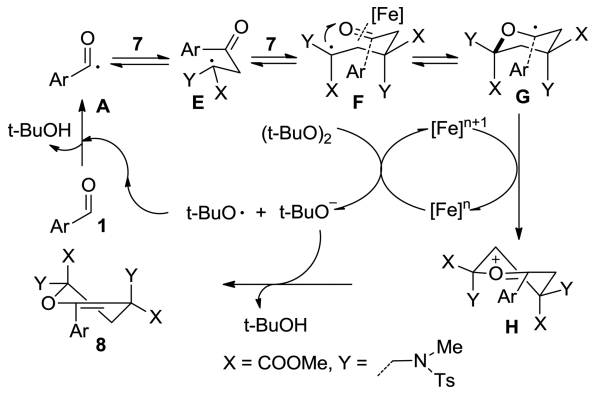
Correspondingly, a tentative mechanism for 3,4-dihydropyran formation (when R = Me) was illustrated in Scheme 6. The

DOI: 10.1021/acs.joc.5b02457
J. Org. Chem. 2015, 80, 12562–12571

Scheme 5. Proposed Reaction Mechanism for Indoline Formation



Scheme 6. Tentative Reaction Mechanism for 3,4-Dihydropyran Formation



sequential acyl radical addition of **A** to two C═C double bonds generated intermediate **F**, which underwent 6-*endo*-*trig* addition to the carbonyls to give intermediate **G**. The irreversible oxidation and deprotonation delivered the final dihydropyran **8**.[12a]

CONCLUSION

We realized a convenient iron-catalyzed divergent tandem radical annulation of aldehydes with olefins. This new method allows the rapid and selective construction of various multifunctionalized indolines (when R = Ar) and dihydropyrans (when R = Me), which are significant structural skeletons in bioactive natural products and pharmaceuticals. Moreover, the preliminary mechanistic studies disclose that the reaction may proceed via a radical pathway, and cleavage of the carbonyl C−H bond might be involved in the rate-determining step, while dissociation of aromatic C−H bond was most likely included in the product-determining step. Further studies on the applications of the tandem radical strategy for the construction of heterocyclic skeletons and the synthesis of natural bioactive products are in progress.

EXPERIMENTAL SECTION

General Information. ^{1}H NMR spectra were recorded on a 400 or 600 MHz spectrometer, and chemical shifts were reported in parts per million (δ) relative to internal standard TMS (0 ppm) for $CDCl_3$. The peak patterns are indicated as follows: s, singlet; d, doublet; dd, doublet of doublet; t, triplet; q, quartet; m, multiplet. The coupling constants, J, are reported in Hertz (Hz). ^{13}C NMR spectra were obtained at 100 or 150 MHz and referenced to the internal solvent signals (central peak is 77.0 ppm in $CDCl_3$, 39.5 ppm in $(CD_3)_2SO$). $CDCl_3$ was used as the NMR solvent. Flash column chromatography was performed over silica gel 200−300. All reagents were weighed and handled in air at room temperature. All reagents were purchased from commercial sources and used without further purification. $FeCl_2$ was purchased from Alfa, and the purity was 99.5% (metals basis). The HRMS measurements were recorded on a FTMS analyzer using an ESI source in the positive mode.

General Procedure for Substrates 2 and 7. Substrates **2** and **7** were prepared according to the reported literatures.[12a]

General Procedure for Products 3 and 8. To a mixture of *N*-allyl amide **1** or **7** (0.3 mmol), aldehyde **2** (1.5 mmol), and $FeCl_2$ (1.0 mg, 2.5 mol %), chlorobenzene (1.0 mL) was added under nitrogen at room temperature. Then pure di-*tert*-butyl peroxide (137 μL, 0.75 mmol) was dropped into the mixture. The resulting mixture was stirred at 120 °C for 1 h. After the mixture was cooled to room temperature, the resulting solution was directly filtered through a pad of silica by EtOAc. The solvent was evaporated in vacuo to give the crude products. NMR yields were determined by ^{1}H NMR using dibromomethane as an internal standard. The residue was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether) to give the pure product **3** or **8**.

*Methyl 3-(2-Oxo-2-phenylethyl)-1-tosylindoline-3-carboxylate (**3aa**).* (108 mg, 80%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.3). IR (neat): ν_{max} 2959, 2901, 1746, 1682, 1598, 1479, 1356, 1306, 1232, 1163, 1086, 1034 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82−7.79 (m, 2H), 7.72 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.2 Hz, 2H), 7.59 (tt, J = 7.5, 1.0 Hz, 1H), 7.47−7.43 (m, 2H), 7.31 (td, J = 7.8, 1.2 Hz, 1H), 7.22 (dd, J = 7.8, 0.8 Hz, 1H), 7.14 (d, J = 8.2 Hz, 2H), 7.04 (td, J = 7.6, 0.8 Hz, 1H), 4.89 (dd, J = 12.0, 0.8 Hz, 1H), 3.88 (d, J = 12.0 Hz, 1H), 3.86 (dd, J = 18.4, 0.8 Hz, 1H), 3.59 (s, 3H), 2.81 (d, J = 18.4 Hz, 1H), 2.30 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 196.7, 172.0, 144.1, 141.4, 135.6, 134.0, 133.6, 132.1, 129.7, 129.6, 128.6, 127.9, 127.2, 123.9, 115.2, 57.7, 52.8, 51.5, 48.3, 21.4. HRMS (ESI) calcd for $C_{25}H_{23}NNaO_5S$ [M + Na$^+$], 472.1189; found: 472.1173. **3aa-D$_4$**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82−7.79 (m, 2H), 7.68 (d, J = 8.2 Hz, 2H), 7.59 (tt, J = 7.5, 1.0 Hz, 1H), 7.47−7.43 (m, 2H), 7.14 (d, J = 8.2 Hz, 2H), 4.89 (dd, J = 12.0, 0.8 Hz, 1H), 3.88 (d, J = 12.0 Hz, 1H), 3.86 (dd, J = 18.4, 0.8 Hz, 1H), 3.59 (s, 3H), 2.81 (d, J = 18.4 Hz, 1H), 2.30 (s, 3H). HRMS (ESI) calcd for $C_{25}H_{19}D_4NNaO_5S$ [M + Na$^+$], 476.1440; found: 476.1421.

*Methyl 1-Acetyl-3-(2-oxo-2-phenylethyl)indoline-3-carboxylate (**3ab**).* Yield: 75 mg, 74%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:2, R_f = 0.6). IR (neat): ν_{max} 2951, 2930, 2916, 1740, 1682, 1667, 1593, 1479, 1404, 1358, 1341, 1283, 1221, 1198, 1167, 1137, 1078 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 8.0 Hz, 1H), 7.97 (d, J = 8.1 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.51−7.47 (m, 2H), 7.35−7.29 (m, 2H), 7.08 (td, J = 7.6, 0.9 Hz, 1H), 5.13 (d, J = 11.4 Hz, 1H), 4.23 (d, J = 18.4 Hz, 1H), 3.83 (d, J = 11.4 Hz, 1H), 3.72 (s, 3H), 3.44 (d, J = 18.4 Hz, 1H), 2.25 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.3, 172.4, 168.7, 142.2, 135.6, 133.8, 131.2, 129.6, 128.7, 128.0, 123.7, 123.2, 117.3, 57.8, 52.9, 51.6, 48.5, 24.1. HRMS (ESI) calcd for $C_{20}H_{19}NNaO_4$ [M + Na$^+$], 360.1206; found: 360.1192.

*Methyl 1-Benzoyl-3-(2-oxo-2-phenylethyl)indoline-3-carboxylate (**3ac**).* Yield: 86 mg, 72%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.3). IR (neat): ν_{max} 2961, 2926, 1734, 1680, 1630, 1578, 1481, 1404, 1360, 1283, 1146, 1076, 1003 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28 (br, 1H), 7.91 (d, J = 7.6 Hz, 2H), 7.59−7.57 (m, 3H), 7.47−7.42 (m, 5H), 7.38 (dd, J = 7.6, 0.6 Hz, 1H), 7.32 (br, 1H), 7.11 (br, 1H), 5.14 (d, J = 12.0 Hz, 1H), 4.18 (d, J = 18.2 Hz, 1H), 3.83 (br, 1H), 3.71 (s, 3H), 3.41 (d, J = 18.2 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 196.9, 172.5, 169.1, 142.4, 136.5, 135.8, 133.7, 132.5, 130.5, 129.4, 128.7, 128.6, 128.1, 127.1, 124.3, 123.6, 117.9, 59.5, 52.9, 51.7, 47.9. HRMS (ESI) calcd for $C_{25}H_{21}NNaO_4$ [M + Na$^+$], 422.1363; found: 422.1346.

Methyl 3-(2-Oxo-2-phenylethyl)-1-(2,2,2-trifluoroacetyl)-indoline-3-carboxylate (3ad). Yield: 68 mg, 58%. Isolated by

DOI: 10.1021/acs.joc.5b02457
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flash column chromatography (ethyl acetate/petroleum ether = 1:10, R_f = 0.3). IR (neat): ν_{max} 2955, 2926, 1732, 1694, 1682, 1597, 1485, 1462, 1435, 1353, 1306, 1260, 1202, 1146, 1096, 1080, 1003 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 8.2 Hz, 1H), 7.97 (d, J = 8.2 Hz, 2H), 7.61 (td, J = 7.4, 1.2 Hz, 1H), 7.49 (t, J = 7.8 Hz, 2H), 7.43 (dd, J = 7.6, 0.8 Hz, 1H), 7.39 (td, J = 7.8, 1.2 Hz, 1H), 7.23 (td, J = 7.6, 0.8 Hz, 1H), 5.38 (d, J = 12.0 Hz, 1H), 4.29 (d, J = 18.3 Hz, 1H), 4.04 (d, J = 12.0 Hz, 1H), 3.72 (s, 3H), 3.42 (d, J = 18.3 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.8, 171.9, 154.2 (q, J_{C-F} = 37.8 Hz), 141.1, 135.5, 133.9, 132.1, 129.9, 128.8, 128.1, 126.2, 123.6, 118.4, 115.8 (q, J_{C-F} = 287.2 Hz), 56.8, 53.1, 52.1, 47.9. HRMS (ESI) calcd for $C_{20}H_{16}F_3NNaO_4$ [M + Na^+], 414.0924; found: 414.0905.

*Methyl 3-(2-Oxo-2-phenylethyl)-1-propionylindoline-3-carboxylate (**3ae**).* Yield: 70 mg, 66%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.3). IR (neat): ν_{max} 2951, 2940, 2918, 2882, 1732, 1661, 1651, 1595, 1481, 1402, 1379, 1082, 1003 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 8.1 Hz, 1H), 7.96 (d, J = 8.0 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.8 Hz, 2H), 7.34 (d, J = 7.6 Hz, 1H), 7.30 (t, J = 7.8 Hz, 1H), 7.06 (t, J = 7.3 Hz, 1H), 5.12 (d, J = 11.4 Hz, 1H), 4.23 (d, J = 18.4 Hz, 1H), 3.82 (d, J = 11.4 Hz, 1H), 3.71 (s, 3H), 3.42 (d, J = 18.4 Hz, 1H), 2.60−2.50 (m, 1H), 2.45−2.36 (m, 1H), 1.22 (t, J = 7.3 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.3, 172.4, 172.1, 142.5, 135.7, 133.8, 131.1, 129.6, 128.7, 128.0, 123.6, 123.2, 117.3, 57.0, 52.9, 51.6, 48.6, 29.2, 8.5. HRMS (ESI) calcd for $C_{21}H_{21}NNaO_4$ [M + Na^+], 374.1363; found: 374.1348.

*1-tert-Butyl 3-Methyl 3-(2-oxo-2-phenylethyl)indoline-1,3-dicarboxylate (**3af**).* Yield: 80 mg, 67%. Isolated by flash column chromatography (ethyl acetate/petroleum ether =1:10, R_f = 0.3). IR (neat): ν_{max} 2978, 2953, 2928, 1738, 1703, 1688, 1597, 1485, 1393, 1340, 1146, 1003 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.6 Hz, 2H), 7.93 (br, 1H), 7.58 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.31 (d, J = 7.6 Hz, 1H), 7.27 (t, J = 7.6 Hz, 1H), 6.98 (td, J = 7.6, 0.9 Hz, 1H), 4.98 (d, J = 12.3 Hz, 1H), 4.13 (d, J = 18.3 Hz, 1H), 3.76 (br, 1H), 3.72 (s, 3H), 3.43 (d, J = 18.3 Hz, 1H), 1.55 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.1, 172.8, 152.1, 142.2, 135.9, 133.6, 131.0, 129.5, 128.6, 128.0, 123.4, 122.3, 115.1, 81.0 56.7, 52.8, 51.0, 48.8, 28.3. HRMS (ESI) calcd for $C_{23}H_{25}NNaO_5$ [M + Na^+], 418.1625; found: 418.1613.

*Dimethyl 3-(2-Oxo-2-phenylethyl)indoline-1,3-dicarboxylate (**3ag**).* Yield: 104 mg, 98%. Isolated by flash column chromatography (ethyl acetate/petroleum ether =1:10, R_f = 0.2). IR (neat): ν_{max} 2953, 2857, 1736, 1693, 1682, 1597, 1487, 1393, 1148, 1065, 1003 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.0 Hz, 2H), 7.93 (br, 1H), 7.59 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.8 Hz, 2H), 7.33 (d, J = 7.4 Hz, 1H), 7.30 (t, J = 7.8 Hz, 1H), 7.02 (td, J = 7.5, 0.9 Hz, 1H), 5.04 (d, J = 12.3 Hz, 1H), 4.16 (d, J = 18.3 Hz, 1H), 3.85 (br, 1H), 3.81 (s, 3H), 3.72 (s, 3H), 3.41 (d, J = 18.3 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.0, 172.6, 153.2, 142.1, 135.8, 133.6, 130.9, 129.5, 128.6, 128.0, 123.5, 122.7, 115.1, 56.6, 52.8, 52.5, 51.1, 48.6. HRMS (ESI) calcd for $C_{20}H_{19}NNaO_5$ [M + Na^+], 376.1155; found: 376.1139.

*Methyl 1-(Dimethylcarbamoyl)-3-(2-oxo-2-phenylethyl)indoline-3-carboxylate (**3ah**).* Yield: 90 mg, 82%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:2, R_f = 0.3). IR (neat): ν_{max} 2951, 2884, 2855, 1732, 1694, 1597, 1485, 1360, 1228, 1080, 1003 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.95−7.94 (m, 2H), 7.59 (td, J = 7.4, 1.2 Hz, 1H), 7.47 (t, J = 7.8 Hz, 2H), 7.31 (dd, J = 7.6, 1.2 Hz, 1H), 7.25 (td, J = 7.8, 1.2 Hz, 1H), 7.13 (d, J = 7.9 Hz, 1H), 6.95 (td, J = 7.6, 0.9 Hz, 1H), 4.92 (d, J = 11.2 Hz, 1H), 4.14 (d, J = 18.3 Hz, 1H), 3.76 (d, J = 11.2 Hz, 1H), 3.72 (s, 3H), 3.42 (d, J = 18.3 Hz, 1H), 2.96 (s, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.2, 172.8, 159.9, 144.0, 135.8, 133.5, 131.1, 129.1, 128.6, 128.0, 123.5, 121.7, 114.9, 58.9, 52.7, 51.5, 47.6, 37.9. HRMS (ESI) calcd for $C_{21}H_{22}N_2NaO_4$ [M + Na^+], 389.1472; found: 389.1441.

*Methyl 4-Oxo-1-(2-oxo-2-phenylethyl)-2,4,5,6-tetrahydro-1H-pyrrolo[3,2,1-ij]quinoline-1-carboxylate (**3ai**).* Yield: 65 mg, 62%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:1.5, R_f = 0.2). IR (neat): ν_{max} 2957, 2924, 1734, 1686, 1655, 1630, 1593, 1447, 1395, 1358, 1292, 1225, 1200, 1078 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.1 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.8 Hz, 2H), 7.22 (d, J = 7.6 Hz, 1H), 7.10 (d, J = 7.3 Hz, 1H), 6.98 (t, J = 7.6 Hz, 1H), 5.09 (d, J = 13.0 Hz, 1H), 4.18 (d, J = 18.3 Hz, 1H), 3.88 (d, J = 13.0 Hz, 1H), 3.72 (s, 3H), 3.45 (d, J = 18.3 Hz, 1H), 3.07−2.94 (m, 2H), 2.77−2.63 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.6, 172.4, 167.2, 140.8, 135.7, 133.6, 129.2, 128.6, 127.9, 127.2, 123.5, 122.1, 120.6, 55.1, 52.9, 52.4, 48.4, 31.3, 24.2. HRMS (ESI) calcd for $C_{21}H_{19}NNaO_4$ [M + Na^+], 372.1206; found: 372.1190.

*Methyl 7-Oxo-4-(2-oxo-2-phenylethyl)-5,7-dihydro-4H-pyrrolo-[3,2,1-de]phenanthridine-4-carboxylate (**3aj**).* Yield: 81 mg, 68%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:2, R_f = 0.5). IR (neat): ν_{max} 2951, 2920, 1726, 1676, 1649, 1628, 1604, 1501, 1489, 1437, 1393, 1356, 1294, 1223, 1204, 1179, 1082, 1003 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 8.57 (dd, J = 8.0, 1.0 Hz, 1H), 8.23 (d, J = 8.0 Hz, 1H), 8.04 (d, J = 7.6 Hz, 1H), 7.98−7.96 (m, 2H), 7.78 (td, J = 7.6, 1.2 Hz, 1H), 7.64−7.57 (m, 2H), 7.51−7.45 (m, 3H), 7.30 (t, J = 7.6 Hz, 1H), 5.52 (d, J = 13.6 Hz, 1H), 4.31 (d, J = 18.2 Hz, 1H), 4.30 (d, J = 13.6 Hz, 1H), 3.75 (s, 3H), 3.56 (d, J = 18.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.6, 172.3, 159.7, 139.0, 135.8, 133.8, 133.5, 132.2, 131.3, 128.7, 128.5, 128.2, 128.1, 127.5, 123.7, 123.5, 122.1, 122.0, 117.2, 56.5, 53.2, 52.2, 48.7. HRMS (ESI) calcd for $C_{25}H_{19}NNaO_4$ [M + Na^+], 420.1206; found: 420.1190.

*Methyl 1-(Methylsulfonyl)-3-(2-oxo-2-phenylethyl)indoline-3-carboxylate (**3ak**).* Yield: 84 mg, 75%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:2, R_f = 0.5). IR (neat): ν_{max} 2959, 2930, 1734, 1684, 1477, 1350, 1225, 1159 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.96−7.94 (m, 2H), 7.61 (tt, J = 7.4, 1.2 Hz, 1H), 7.53−7.46 (m, 3H), 7.36 (dd, J = 7.6, 1.2 Hz, 1H), 7.31 (td, J = 7.4, 1.2 Hz, 1H), 7.10 (td, J = 7.6, 0.9 Hz, 1H), 5.02 (d, J = 12.0 Hz, 1H), 4.16 (d, J = 18.2 Hz, 1H), 3.86 (d, J = 12.0 Hz, 1H), 3.73 (s, 3H), 3.48 (d, J = 18.2 Hz, 1H), 3.01 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.8, 172.5, 141.6, 135.6, 133.8, 131.7, 130.1, 128.7, 128.1, 124.3, 124.0, 114.4, 58.9, 53.0, 51.7, 48.1, 35.5. HRMS (ESI) calcd for $C_{19}H_{19}NNaO_5S$ [M + Na^+], 396.0876; found: 396.0867.

*Methyl 1-Methyl-3-(2-oxo-2-phenylethyl)indoline-3-carboxylate (**3al**).* Yield: 23 mg, 25%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:10, R_f = 0.3). IR (neat): ν_{max} 2951, 2924, 2853, 1738, 1732, 1694, 1682, 1595, 1537, 1495, 1487, 1454, 1225 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.95−7.93 (m, 2H), 7.57 (td, J = 7.4, 1.2 Hz, 1H), 7.45 (t, J = 7.8 Hz, 2H), 7.21 (dd, J = 7.6, 0.8 Hz, 1H), 7.18 (td, J = 7.6, 1.2 Hz, 1H), 6.70 (td, J = 7.4, 0.9 Hz, 1H), 6.52 (d, J = 7.8 Hz, 1H), 4.22 (dd, J = 10.0, 0.8 Hz, 1H), 3.97 (dd, J = 18.3, 0.8 Hz, 1H), 3.75 (s, 3H), 3.49 (d, J = 18.3 Hz, 1H), 3.31 (d, J = 10.0 Hz, 1H), 2.80 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.7, 173.1, 152.1, 136.2, 133.4, 130.1, 129.3, 128.6, 128.0, 123.4, 117.7, 107.6, 63.2, 52.5, 51.8, 47.3, 35.3. HRMS (ESI) calcd for $C_{19}H_{19}NNaO_3$ [M + Na^+], 332.1257; found: 332.1235.

*Methyl 5-Methyl-3-(2-oxo-2-phenylethyl)-1-tosylindoline-3-carboxylate (**3an**).* Yield: 100 mg, 72%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.4). IR (neat): ν_{max} 2951, 2928, 1734, 1684, 1597, 1489, 1449, 1398, 1354, 1213, 1165, 1092 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72−7.70 (m, 2H), 7.57 (d, J = 8.2 Hz, 2H), 7.52 (d, J = 8.3 Hz, 1H), 7.51−7.48 (m, 1H), 7.37−7.34 (m, 2H), 7.03 (d, J = 8.2 Hz, 2H), 7.02 (d, J = 8.3 Hz, 1H), 6.93 (s, 1H), 4.79 (dd, J = 12.2, 0.8 Hz, 1H), 3.78 (d, J = 12.2 Hz, 1H), 3.76 (d, J = 18.2 Hz, 1H), 3.50 (s, 3H), 2.62 (d, J = 18.2 Hz, 1H), 2.21 (s, 3H), 2.20 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.8, 172.1, 144.0, 139.0, 135.6, 134.0, 133.8, 133.6, 132.2, 130.3, 129.6, 128.6, 127.9, 127.2, 124.3, 115.2, 57.9, 52.8, 51.5, 48.4, 21.4, 20.9. HRMS (ESI) calcd for $C_{26}H_{25}NNaO_5S$ [M + Na^+], 486.1346; found: 486.1325.

*Methyl 5-Cyano-3-(2-oxo-2-phenylethyl)-1-tosylindoline-3-carboxylate (**3ao**).* Yield: 94 mg, 66%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.3). IR (neat): ν_{max} 2951, 2920, 2222, 1738, 1732, 1682, 1601, 1485, 1435, 1360, 1090 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ 7.85−7.84 (m, 2H), 7.75 (d, J = 8.4 Hz, 1H), 7.72 (d, J = 8.2 Hz, 2H), 7.62−7.58 (m, 2H), 7.52 (d, J = 1.5 Hz, 1H), 7.48−7.46 (m, 2H), 7.24 (d, J = 8.2 Hz, 2H), 4.92 (d, J = 11.8 Hz, 1H), 3.93 (d, J = 11.8 Hz, 1H), 3.91 (d, J = 18.0

DOI: 10.1021/acs.joc.5b02457
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Hz, 1H), 3.62 (s, 3H), 3.07 (d, J = 18.0 Hz, 1H), 2.35 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 196.1, 171.1, 145.3, 145.0, 135.4, 134.4, 134.0, 133.8, 133.0, 130.0, 128.7, 128.2, 128.0, 127.2, 118.5, 114.8, 106.7, 58.2, 53.2, 51.1, 48.1, 21.5. HRMS (ESI) calcd for $C_{26}H_{22}N_2NaO_5S$ [M + Na^+], 497.1142; found: 497.1122.

*Methyl 5-Acetyl-3-(2-oxo-2-phenylethyl)-1-tosylindoline-3-carboxylate (**3ap**).* Yield: 83 mg, 56%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:2, R_f = 0.3). IR (neat): ν_{max} 2951, 2916, 2849, 1736, 1682, 1595, 1470, 1356, 1294, 1246, 1213, 1169, 1117, 1043 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, J = 8.6, 1.8 Hz, 1H), 7.86−7.84 (m, 3H), 7.75−7.73 (m, 3H), 7.62−7.58 (m, 1H), 7.49−7.45 (m, 2H), 7.21 (d, J = 8.1 Hz, 2H), 4.97 (d, J = 11.8 Hz, 1H), 4.01 (d, J = 18.2 Hz, 1H), 3.93 (d, J = 11.8 Hz, 1H), 3.59 (s, 3H), 3.00 (d, J = 18.2 Hz, 1H), 2.56 (s, 3H), 2.34 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.5, 196.3, 171.6, 145.6, 144.7, 135.5, 134.0, 133.8, 133.0, 132.5, 131.3, 129.8, 128.7, 128.0, 127.2, 124.2, 113.9, 58.5, 53.1, 51.1, 48.2, 26.5, 21.5. HRMS (ESI) calcd for $C_{27}H_{25}NNaO_6S$ [M + Na^+], 514.1295; found: 514.1279.

*Methyl 5-Fluoro-3-(2-oxo-2-phenylethyl)-1-tosylindoline-3-carboxylate (**3aq**).* Yield: 86 mg, 61%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.5). IR (neat): ν_{max} 2954, 2920, 1740, 1728, 1684, 1676, 1628, 1597, 1477, 1400, 1356, 1294, 1167, 1090, 1001 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.79−7.77 (m, 2H), 7.68 (dd, J = 8.9, 4.5 Hz, 1H), 7.64 (d, J = 8.2 Hz, 2H), 7.62−7.58 (m, 1H), 7.48−7.44 (m, 2H), 7.14 (d, J = 8.2 Hz, 2H), 7.00 (td, J = 8.9, 2.7 Hz, 1H), 6.94 (dd, J = 8.0, 2.7 Hz, 1H), 4.88 (dd, J = 12.2, 1.0 Hz, 1H), 3.90 (d, J = 12.2 Hz, 1H), 3.78 (dd, J = 18.2, 0.6 Hz, 1H), 3.62 (s, 3H), 2.72 (d, J = 18.2 Hz, 1H), 2.30 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.3, 171.5, 159.6 (d, J_{C-F} = 242.1 Hz), 144.3, 137.5, 135.4, 133.8, 129.7, 128.6, 128.0, 127.2, 116.5, 116.4 (d, J_{C-F} = 17.6 Hz), 111.3 (d, J_{C-F} = 24.7 Hz), 58.0, 53.0, 51.6, 48.2, 21.5. HRMS (ESI) calcd for $C_{25}H_{22}FNNaO_5S$ [M + Na^+], 490.1095; found: 490.1075.

*Methyl 5-Bromo-3-(2-oxo-2-phenylethyl)-1-tosylindoline-3-carboxylate (**3ar**).* Yield: 102 mg, 64%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.3). IR (neat): ν_{max} 2953, 2924, 2853, 1748, 1684, 1597, 1450, 1362, 1001 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.82−7.79 (m, 2H), 7.67 (d, J = 8.2 Hz, 2H), 7.62−7.58 (m, 1H), 7.60 (d, J = 8.7 Hz, 1H), 7.48−7.44 (m, 2H), 7.42 (dd, J = 8.7, 2.0 Hz, 1H), 7.33 (d, J = 2.0 Hz, 1H), 7.17 (d, J = 8.2 Hz, 2H), 4.88 (dd, J = 12.2, 0.8 Hz, 1H), 3.87 (d, J = 12.2 Hz, 1H), 3.83 (dd, J = 18.2, 0.6 Hz, 1H), 3.60 (s, 3H), 2.82 (d, J = 18.2 Hz, 1H), 2.32 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.4, 171.5, 144.4, 140.7, 135.4, 134.2, 133.8, 132.7, 129.8, 128.6, 128.0, 127.2, 127.1, 116.6, 116.4, 57.9, 53.1, 51.4, 48.3, 21.5. HRMS (ESI) calcd for $C_{25}H_{22}BrNNaO_5S$ [M + Na^+], 550.0294; found: 550.0277.

*Methyl 5-Iodo-3-(2-oxo-2-phenylethyl)-1-tosylindoline-3-carboxylate (**3as**).* Yield: 116 mg, 67%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.5). IR (neat): ν_{max} 3063, 2951, 2918, 1744, 1734, 1684, 1597, 1582, 1472, 1449, 1398, 1356, 1292, 1227, 1165, 1115, 1090, 1001 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.83−7.80 (m, 2H), 7.67 (d, J = 8.2 Hz, 2H), 7.62−7.58 (m, 2H), 7.50−7.46 (m, 4H), 7.17 (d, J = 8.2 Hz, 2H), 4.86 (dd, J = 12.0, 0.8 Hz, 1H), 3.85 (d, J = 12.0 Hz, 1H), 3.84 (dd, J = 18.4, 0.8 Hz, 1H), 3.60 (s, 3H), 2.83 (d, J = 18.4 Hz, 1H), 2.32 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.4, 171.5, 144.4, 141.4, 138.6, 135.4, 134.4, 133.8, 133.7, 132.8, 129.8, 128.6, 128.0, 127.2, 117.0, 86.5, 57.8, 53.1, 51.2, 48.3, 21.5. HRMS (ESI) calcd for $C_{25}H_{22}INNaO_5S$ [M + Na^+], 598.0156; found: 598.0128.

*Methyl 6(7)-Methyl-3-(2-oxo-2-phenylethyl)-1-tosylindoline-3-carboxylate (**3at** + **3au**).* Yield: 95 mg, 68%, **3at**:**3au** = 1.5:1. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.5). IR (neat): ν_{max} 2951, 2926, 1734, 1684, 1653, 1647, 1597, 1578, 1458, 1356, 1220, 1167, 1092, 1001 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) **3at+3au**: δ 7.81−7.79 (m, 2H), 7.70−7.65 (m, 2H), 7.65−7.55 (m, 2H), 7.48−7.43 (m, 2H), 7.21−7.08 (m, 3H), 6.85 (d, J = 7.6 Hz, 0.6H), 6.81 (d, J = 7.6 Hz, 0.4H), 4.87 (dd, J = 12.0, 0.9 Hz, 0.6H), 4.77 (dd, J = 12.2, 1.2 Hz, 0.4H), 4.13 (d, J = 12.2 Hz, 0.4H), 4.00 (dd, J = 18.2, 0.9 Hz, 0.4H), 3.87 (d, J = 12.0 Hz, 0.6H), 3.85 (d, J = 18.2 Hz, 0.6H), 3.58 (s, 1.8H), 3.56 (s, 1.2H), 2.79 (d, J = 18.2 Hz, 0.6H), 2.47 (d, J = 18.2 Hz, 0.4H), 2.39 (s, 1.8H), 2.30 (s, 1.8H), 2.25 (s, 1.2H), 2.22 (s, 1.2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) **3at**: δ 196.8, 172.1, 144.0, 141.5, 140.1, 135.6, 134.1, 133.6, 129.6, 128.6, 128.0, 127.2, 127.0, 124.8, 123.5, 115.7, 58.0, 52.8, 51.2, 48.3, 21.7, 21.4. **3au**: δ 196.5, 172.4, 144.0, 142.0, 136.1, 135.1, 134.4, 133.4, 130.3, 129.6, 129.3, 129.2, 128.5, 127.8, 127.1, 113.2, 58.7, 52.6, 52.4, 43.8, 21.4, 18.3. HRMS (ESI) calcd for $C_{26}H_{25}NNaO_5S$ [M + Na^+], 486.1346; found: 486.1325.

*Methyl 3-(2-Oxo-1,2-diphenylethyl)-1-tosylindoline-3-carboxylate (**3av**).* Yield: 65 mg, 41%, dr = 6:1. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.2). IR (neat): ν_{max} 2959, 1710, 1676, 1597, 1477, 1450, 1356, 1273, 1230, 1167, 1105, 1090, 1056, 1036 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) Major and Minor: δ 7.83−7.73 (m, 2H), 7.61−7.55 (m, 2H), 7.46−7.42 (m, 2H), 7.39−7.37 (m, 1H), 7.33−7.27 (m, 2H), 7.24−6.93 (m, 7H), 6.83−6.73 (m, 2H), 5.57 (s, 0.86H), 5.25 (s, 0.14H), 4.88 (d, J = 11.8 Hz, 0.86H), 4.44 (d, J = 11.0 Hz, 0.14H), 4.37 (d, J = 11.0 Hz, 0.14H), 4.32 (d, J = 11.8 Hz, 0.86H), 3.58 (s, 0.4H), 3.49 (s, 2.6H), 2.37 (s, 0.4H), 2.35 (s, 2.6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) Major: δ 199.3, 172.6, 143.6, 142.5, 135.4, 134.2, 133.2, 132.9, 130.2, 129.8, 129.5, 129.4, 128.9, 128.6, 128.4, 127.7, 127.1, 124.3, 122.8, 113.8, 60.3, 57.0, 53.9, 52.9, 21.4. Minor: δ 197.2, 171.8, 144.0, 142.1, 136.0, 134.1, 134.0, 133.1, 130.1, 129.8, 129.6, 129.4, 128.9, 128.7, 128.4, 127.9, 127.4, 126.3, 122.8, 113.8, 59.3, 57.2, 56.6, 52.5, 21.4. HRMS (ESI) calcd for $C_{31}H_{27}NNaO_5S$ [M + Na^+], 548.1502; found: 548.1494.

*Methyl 3-(2-(4-Methoxyphenyl)-2-oxoethyl)-1-tosylindoline-3-carboxylate (**3ba**).* Yield: 112 mg, 78%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.2). IR (neat): ν_{max} 2953, 2924, 2841, 1739, 1670, 1601, 1574, 1512, 1352, 1108, cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.9 Hz, 2H), 7.72−7.70 (m, 1H), 7.69 (d, J = 8.1 Hz, 2H), 7.30 (td, J = 7.8, 1.2 Hz, 1H), 7.22 (dd, J = 7.6, 0.8 Hz, 1H), 7.16 (d, J = 8.1 Hz, 2H), 7.03 (td, J = 7.6, 0.9 Hz, 1H), 6.91 (d, J = 8.9 Hz, 2H), 4.87 (dd, J = 12.0, 0.8 Hz, 1H), 3.88 (d, J = 12.0 Hz, 1H), 3.87 (s, 3H), 3.82 (d, J = 18.1 Hz, 1H), 3.58 (s, 3H), 2.83 (d, J = 18.1 Hz, 1H), 2.32 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 195.1, 172.1, 163.8, 144.1, 141.4, 134.1, 132.2, 130.3, 129.6, 128.7, 127.2, 124.0, 123.8, 115.1, 113.7, 57.8, 55.5, 52.8, 51.5, 48.1, 21.5. HRMS (ESI) calcd for $C_{26}H_{25}NNaO_6S$ [M + Na^+], 502.1295; found: 502.1279.

*Methyl 3-(2-Oxo-2-(lp-tolyl)ethyl)-1-tosylindoline-3-carboxylate (**3ca**).* Yield: 98 mg, 70%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.2). IR (neat): ν_{max} 2953, 2920, 1734, 1676, 1607, 1477, 1356, 1238, 1167, 1107, 1047 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72−7.68 (m, 5H), 7.30 (td, J = 7.8, 1.2 Hz, 1H), 7.23 (d, J = 7.8 Hz, 2H), 7.23−7.21 (m, 1H), 7.15 (d, J = 8.2 Hz, 2H), 7.03 (td, J = 7.6, 0.9 Hz, 1H), 4.88 (dd, J = 12.0, 0.8 Hz, 1H), 3.88 (d, J = 12.0, 1H), 3.84 (d, J = 18.3 Hz, 1H), 3.59 (s, 3H), 2.82 (d, J = 18.3 Hz, 1H), 2.42 (s, 3H), 2.31 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.3, 172.0, 144.6, 144.1, 141.4, 134.1, 133.2, 132.1, 129.6, 129.2, 128.1, 127.2, 123.9, 123.8, 115.1, 57.8, 52.8, 51.5, 48.3, 21.6, 21.4. HRMS (ESI) calcd for $C_{26}H_{25}NNaO_5S$ [M + Na^+], 486.1346; found: 486.1328.

*Methyl 3-(2-(4-Fluorophenyl)-2-oxoethyl)-1-tosylindoline-3-carboxylate (**3da**).* Yield: 105 mg, 75%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.2). IR (neat): ν_{max} 2953, 2928, 2857, 1734, 1684, 1597, 1508, 1477, 1142, 1358, 1300, 1230, 1169, 1092, 1001 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 5.4 Hz, 1H), 7.83 (d, J = 5.4 Hz, 1H), 7.72−7.68 (m, 3H), 7.30 (td, J = 7.8, 1.0 Hz, 1H), 7.22 (d, J = 7.4 Hz, 1H), 7.16 (d, J = 8.1 Hz, 2H), 7.11 (t, J = 8.5 Hz, 2H), 7.03 (t, J = 7.6 Hz, 1H), 4.87 (d, J = 12.0 Hz, 1H), 3.88 (d, J = 12.0 Hz, 1H), 3.86 (d, J = 18.2 Hz, 1H), 3.58 (s, 3H), 2.83 (d, J = 18.2 Hz, 1H), 2.31 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 195.1, 171.9, 166.0 (d, J_{C-F} = 255.6 Hz), 144.1, 141.4, 134.0, 132.1, 131.9, 130.7 (d, J_{C-F} = 9.3 Hz), 129.7, 129.6, 127.2, 123.9, 115.7 (d, J_{C-F} = 21.7 Hz), 115.1, 57.7, 52.8, 51.5, 48.1, 21.4. HRMS (ESI) calcd for $C_{25}H_{22}FNNaO_5S$ [M + Na^+], 490.1095; found: 490.1074.

DOI: 10.1021/acs.joc.5b02457
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*Methyl 3-(2-(4-Chlorophenyl)-2-oxoethyl)-1-tosylindoline-3-carboxylate (**3ea**).* Yield: 116 mg, 80%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.3). IR (neat): ν_{max} 3090, 3074, 3042, 2955, 2916, 1738, 1680, 1589, 1570, 1447, 1435, 1400, 1358, 1340, 1294, 1282, 1228, 1217, 1168, 1089, 1078, 1050, 1030 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.6 Hz, 2H), 7.72−7.67 (m, 1H), 7.69 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 8.6 Hz, 2H), 7.30 (td, J = 7.8, 1.3 Hz, 1H), 7.21 (dd, J = 7.6, 0.8 Hz, 1H), 7.16 (d, J = 8.0 Hz, 2H), 7.03 (td, J = 7.6, 0.8 Hz, 1H), 4.84 (dd, J = 12.0, 0.9 Hz, 1H), 3.87 (d, J = 12.0 Hz, 1H), 3.83 (dd, J = 18.3, 0.9 Hz, 1H), 3.58 (s, 3H), 2.82 (d, J = 18.3 Hz, 1H), 2.32 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 195.6, 171.9, 144.1, 141.4, 140.2, 134.2, 134.0, 131.9, 129.8, 129.7, 129.4, 128.9, 127.3, 123.9, 123.8, 115.1, 57.7, 52.9, 51.5, 48.2, 21.5. HRMS (ESI) calcd for $C_{25}H_{22}ClNNaO_5S$ [M + Na^+], 506.0799; found: 506.0792.

*Methyl 3-(2-(4-Bromophenyl)-2-oxoethyl)-1-tosylindoline-3-carboxylate (**3fa**).* Yield: 100 mg, 63%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.4). IR (neat): ν_{max} 2953, 2920, 2851, 1746, 1732, 1715, 1694, 1585, 1435, 1393, 1354, 1238, 1165, 997 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72−7.66 (m, 5H), 7.59 (d, J = 8.6 Hz, 2H), 7.31 (td, J = 7.8, 1.2 Hz, 1H), 7.21 (dd, J = 7.6, 0.8 Hz, 1H), 7.16 (d, J = 8.1 Hz, 2H), 7.03 (td, J = 7.6, 0.8 Hz, 1H), 4.85 (dd, J = 12.0, 0.6 Hz, 1H), 3.87 (d, J = 12.0 Hz, 1H), 3.83 (d, J = 18.3 Hz, 1H), 3.58 (s, 3H), 2.81 (d, J = 18.3 Hz, 1H), 2.32 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 195.8, 171.9, 144.2, 141.4, 134.4, 134.1, 132.0, 131.9, 129.8, 129.7, 129.5, 129.0, 127.3, 123.9, 123.8, 115.2, 57.7, 52.9, 51.5, 48.2, 21.5. HRMS (ESI) calcd for $C_{25}H_{22}BrNNaO_5S$ [M + Na^+], 550.0294; found: 550.0275.

*Methyl 3-(2-Oxo-2-(thiophen-2-yl)ethyl)-1-tosylindoline-3-carboxylate (**3ga**).* Yield: 98 mg, 72%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.2). IR (neat): ν_{max} 2984, 2953, 2922, 1732, 1651, 1595, 1518, 1477, 1462, 1416, 1360, 1304, 1238, 1169, 1107, 1089, 1059, 1045 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72−7.70 (m, 3H), 7.67 (d, J = 4.8 Hz, 1H), 7.55 (d, J = 3.4 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.22 (d, J = 7.8 Hz, 1H), 7.19 (d, J = 8.0 Hz, 2H), 7.12 (t, J = 4.4 Hz, 1H), 7.03 (t, J = 7.6 Hz, 1H), 4.82 (d, J = 12.0 Hz, 1H), 3.93 (d, J = 12.0 Hz, 1H), 3.81 (d, J = 18.0 Hz, 1H), 3.59 (s, 3H), 2.85 (d, J = 18.0 Hz, 1H), 2.33 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 189.5, 171.8, 144.2, 142.5, 141.3, 134.2, 134.0, 132.3, 131.8, 129.7, 129.6, 128.1, 127.2, 123.9, 123.8, 115.0, 57.6, 52.8, 51.4, 48.3, 21.4. HRMS (ESI) calcd for $C_{23}H_{21}NNaO_5S_2$ [M + Na^+], 478.0753; found: 478.0739.

*Methyl 3-(2-Cyclopropyl-2-oxoethyl)-1-tosylindoline-3-carboxylate (**3ha**).* Yield: 93 mg, 75%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.3). IR (neat): ν_{max} 2955, 2922, 2849, 1738, 1693, 1643, 1470, 1358, 1167, 1026 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.2 Hz, 2H), 7.67 (J = 8.1 Hz, 1H), 7.29−7.26 (m, 1H), 7.25 (d, J = 8.2 Hz, 2H), 7.16 (dd, J = 7.8, 0.8 Hz, 1H), 6.98 (td, J = 7.6, 0.8 Hz, 1H), 4.71 (dd, J = 11.8, 0.9 Hz, 1H), 3.77 (d, J = 11.8 Hz, 1H), 3.52 (s, 3H), 3.50 (d, J = 18.3 Hz, 1H), 2.59 (d, J = 18.3 Hz, 1H), 2.83 (s, 3H), 1.81−1.75 (m, 1H), 1.04−1.01 (m, 2H), 0.92−0.88 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 207.4, 171.8, 144.1, 141.3, 134.0, 131.8, 129.6, 127.3, 123.8, 123.7, 114.7, 57.7, 52.6, 52.1, 51.2, 21.4, 20.2, 11.1, 11.0. HRMS (ESI) calcd for $C_{22}H_{23}NNaO_5S$ [M + Na^+], 436.1189; found: 436.1178.

*Methyl 3-(2-Oxohexyl)-1-tosylindoline-3-carboxylate (**3ia**).* Yield: 65 mg, 50%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.5). IR (neat): ν_{max} 2957, 2926, 2872, 1732, 1713, 1597, 1479, 1462, 1435, 1398, 1352, 1220, 1165, 1092, 1030, 953 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.2 Hz, 2H), 7.67 (J = 8.1 Hz, 1H), 7.28−7.26 (m, 1H), 7.25 (d, J = 8.2 Hz, 2H), 7.13 (dd, J = 7.8, 0.9 Hz, 1H), 6.98 (td, J = 7.6, 0.8 Hz, 1H), 4.74 (d, J = 11.8 Hz, 1H), 3.77 (d, J = 11.8 Hz, 1H), 3.53 (s, 3H), 3.35 (d, J = 18.4 Hz, 1H), 2.43 (d, J = 18.4 Hz, 1H), 2.38 (s, 3H), 2.37−2.24 (m, 2H), 1.56−1.48 (m, 2H), 1.34−1.24 (m, 2H), 0.90 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 208.1, 172.0, 144.1, 141.3, 134.1, 131.8, 129.6, 127.3, 123.8, 123.7, 114.7, 57.8, 52.7, 51.6, 51.2, 41.9, 25.7, 22.2, 21.4, 13.7. HRMS (ESI) calcd for $C_{23}H_{27}NNaO_5S$ [M + Na^+], 452.1502; found: 452.1487.

*Methyl 3-(2-(Dimethylamino)-2-oxoethyl)-1-tosylindoline-3-carboxylate (**3ja**).* Yield: 56 mg, 45%. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 2:1, R_f = 0.4). IR (neat): ν_{max} 2983, 2949, 2926, 1726, 1634, 1597, 1479, 1416, 1350, 1234, 1163, 1057 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.3 Hz, 2H), 7.68 (d, J = 8.1 Hz, 1H), 7.27 (td, J = 7.8, 1.3 Hz, 1H), 7.25 (d, J = 8.3 Hz, 2H), 7.20 (dd, J = 7.7, 1.0 Hz, 1H), 6.98 (td, J = 7.7, 1.0 Hz, 1H), 4.76 (dd, J = 11.8, 1.0 Hz, 1H), 3.91 (d, J = 11.8 Hz, 1H), 3.54 (s, 3H), 3.25 (d, J = 16.7 Hz, 1H), 2.92 (s, 3H), 2.87 (s, 3H), 2.39 (d, J = 16.7 Hz, 1H), 2.38 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 172.2, 169.3, 144.0, 141.5, 134.1, 131.8, 129.6, 129.5, 127.4, 124.0, 123.5, 114.6, 58.0, 52.7, 52.1, 43.4, 36.8, 35.2, 21.5. HRMS (ESI) calcd for $C_{21}H_{24}N_2NaO_5S$ [M + Na^+], 439.1298; found: 439.1280. **3ja-D6**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.3 Hz, 2H), 7.68 (d, J = 8.1 Hz, 1H), 7.27 (td, J = 7.8, 1.3 Hz, 1H), 7.25 (d, J = 8.3 Hz, 2H), 7.20 (dd, J = 7.7, 1.0 Hz, 1H), 6.98 (td, J = 7.7, 1.0 Hz, 1H), 4.76 (dd, J = 11.8, 1.0 Hz, 1H), 3.91 (d, J = 11.8 Hz, 1H), 3.54 (s, 3H), 3.25 (d, J = 16.7 Hz, 1H), 2.39 (d, J = 16.7 Hz, 1H), 2.38 (s, 3H). HRMS (ESI) calcd for $C_{21}H_{18}D_6N_2NaO_5S$ [M + Na^+], 445.1675; found: 445.1658.

*Methyl 3-Ethyl-1-tosylindoline-3-carboxylate (**4**).* Yield: 86 mg, 80%. The procedure is similair to the synthesis of product **3** unless no aldehyde was added. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.4). IR (neat): ν_{max} 2967, 2953, 2936, 1734, 1597, 1477, 1460, 1358, 1308, 1227, 1169, 1092 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.2 Hz, 2H), 7.64 (d, J = 8.0 Hz, 1H), 7.32 (dd, J = 7.6, 1.0 Hz, 1H), 7.27−7.23 (m, 3H), 7.00 (td, J = 7.6, 1.0 Hz, 1H), 4.47 (d, J = 11.0 Hz, 1H), 3.82 (d, J = 11.0 Hz, 1H), 3.61 (s, 3H), 2.36 (s, 3H), 2.02−1.93 (m, 1H), 1.62−1.53 (m, 1H), 0.75 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 172.7, 144.1, 141.2, 133.8, 132.5, 129.6, 129.1, 127.3, 125.0, 123.5, 114.3, 55.9, 55.1, 52.5, 31.8, 21.4, 8.9. HRMS (ESI) calcd for $C_{19}H_{21}NNaO_4S$ [M + Na^+], 382.1083; found: 382.1059.

*Methyl 3-Phenethyl-1-tosylindoline-3-carboxylate (**5**).* Yield: 72 mg, 55%. The procedure is similair to the synthesis of product **3** unless the solvent changed to toluene. Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.4). IR (neat): ν_{max} 3057, 2953, 2918, 2847, 1730, 1690, 1610, 1493, 1470, 1449, 1371, 1352, 1242, 1120, 1086 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.3 Hz, 2H), 7.68 (d, J = 8.1 Hz, 1H), 7.324(dd, J = 7.7, 1.0 Hz, 1H), 7.29−7.20 (m, 5H), 7.17 (td, J = 7.6, 1.3 Hz, 1H), 7.04−7.00 (m, 3H), 4.56 (d, J = 11.3 Hz, 1H), 3.90 (d, J = 11.0 Hz, 1H), 3.62 (s, 3H), 2.39−2.35 (m, 2H), 2.32 (s, 3H), 2.25−2.17 (m, 1H), 1.79−7.71 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 172.5, 144.2, 141.2, 140.4, 133.8, 132.4, 129.6, 129.3, 128.3, 128.1, 127.2, 126.1, 124.9, 123.7, 114.5, 56.2, 54.6, 52.6, 40.6, 30.9, 21.4. HRMS (ESI) calcd for $C_{25}H_{25}NNaO_4S$ [M + Na^+], 458.1397; found: 458.1389.

*Methyl 3-(2-Oxo-2-phenylethyl)indoline-3-carboxylate (**3am**).* Yield: 59 mg, 100%. To a stirred solution of **3af** (80 mg, 0.2 mmol) in CH_2Cl_2 (1.0 mL) at room temperature, TFA (1.0 mL) was added dropwise. The resulting mixture was stirred at room temperatue for 3 h. After the reaction was completed, the mixture was concentrated in vacuo to remove excess TFA. The residue was dissolved with EtOAc and washed with saturated Na_2CO_3 solution and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give the pure product **3am** (ethyl acetate/petroleum ether = 1:2, R_f = 0.3). IR (neat): ν_{max} 2947, 1707, 1684, 1609, 1489, 1466, 1449, 1435, 1394, 1356, 1294, 1219, 1165, 1142, 1074, 1032, 1001, 970 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.94−7.92 (m, 2H), 7.58−7.54 (m, 1H), 7.46−7.42 (m, 2H), 7.24 (dd, J = 7.4, 0.8 Hz, 1H), 7.11 (td, J = 7.8, 1.2 Hz, 1H), 6.75 (td, J = 7.4, 0.8 Hz, 1H), 6.67 (d, J = 7.8 Hz, 1H), 4.52 (d, J = 10.2 Hz, 1H), 4.00 (d, J = 18.4 Hz, 1H), 3.88 (br, 1H), 3.73 (s, 3H), 3.49 (d, J = 18.4 Hz, 1H), 3.44 (d, J = 10.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.6, 173.4, 150.7, 136.2, 133.4, 129.5, 129.2, 128.6, 128.0, 123.8, 118.8, 110.2, 55.2, 53.3, 52.6, 47.5. HRMS (ESI) calcd for $C_{18}H_{17}NNaO_3$ [M + Na^+], 318.1101; found: 318.1091.

*3-(2-Oxo-2-phenylethyl)-1-tosylindoline-3-carboxylic Acid (**6**).* Yield: 87 mg, 100%. To a stirred solution of **3aa** (90 mg, 0.2 mmol) in a mixed solvent (2.0 mL, MeOH/THF = 1:1) at room

DOI: 10.1021/acs.joc.5b02457
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temperature, NaOH (3M, 2.0 mL) was added dropwise. The resulting mixture was stirred at 50 °C for 1 h. After the reaction was completed, EtOAc was added. The mixture was washed with 5% HCl and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give the pure product **6** (methanol/dichloromethane = 1:20, R_f = 0.5). IR (neat): ν_{max} 2928, 2882, 1735, 1632, 1582, 1043, 1022 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ 12.9 (br, 1H), 7.92−7.90 (m, 2H), 7.71 (d, J = 8.2 Hz, 2H), 7.66−7.63 (m, 1H), 7.53−7.49 (m, 3H), 7.36 (d, J = 7.4 Hz, 1H), 7.31 (td, J = 7.6, 1.2 Hz, 1H), 7.26 (d, J = 8.2 Hz, 2H), 7.06 (td, J = 7.6, 0.3 Hz, 1H), 4.38 (d, J = 11.4 Hz, 1H), 4.08 (d, J = 18.4 Hz, 1H), 3.85 (d, J = 11.4 Hz, 1H), 3.01 (d, J = 18.4 Hz, 1H), 2.25 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 198.5, 174.0, 145.3, 141.7, 136.6, 134.5, 134.4, 133.6, 130.8, 130.4, 129.6, 129.0, 128.1, 125.5, 124.6, 114.8, 59.0, 51.9, 48.5, 22.0. HRMS (ESI) calcd for $C_{24}H_{21}NNaO_5S$ [M + Na^+], 458.1033; found: 458.1016.

*Dimethyl 2,4-Bis((N,4-dimethylphenylsulfonamido)methyl)-6-phenyl-3,4-dihydro-2H-pyran-2,4-dicarboxylate (**8a**).* Yield: 68 mg, 68%, dr = 2.2:1. **Major:** Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:2, R_f = 0.35). IR (neat): ν_{max} 2984, 2953, 2926, 1734, 1653, 1599, 1495, 1447, 1344, 1248, 1163, 1092, 1045 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.67−7.61 (m, 6H), 7.37−7.26 (m, 7H), 5.56 (s, 1H), 3.81 (s, 3H), 3.78 (d, J = 14.0 Hz, 1H), 3.77 (s, 3H), 3.30 (d, J = 14.0 Hz, 1H), 3.25 (d, J = 14.0 Hz, 1H), 3.08 (d, J = 14.0 Hz, 1H), 2.87 (s, 3H), 2.69 (s, 3H), 2.54 (d, J = 14.8 Hz, 1H), 2.49 (d, J = 14.8 Hz, 1H), 2.42 (s, 3H), 2.40 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.0, 170.8, 151.3, 143.7, 143.6, 134.7, 134.2, 134.1, 129.8, 129.7, 128.9, 128.2, 127.5, 125.7, 97.7, 81.4, 58.1, 56.3, 52.9, 52.8, 44.3, 37.6, 37.4, 33.5, 21.5. **Minor:** Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:2, R_f = 0.3). IR (neat): ν_{max} 2951, 2926, 1734, 1452, 1342, 1244, 1211, 1161, 1092 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.69−7.66 (m, 6H), 7.35−7.32 (m, 7H), 5.55 (d, J = 1.4 Hz, 1H), 3.71 (s, 3H), 3.69 (s, 3H), 3.55 (d, J = 14.3 Hz, 1H), 3.50 (d, J = 13.8 Hz, 1H), 3.44 (d, J = 14.3 Hz, 1H), 3.17 (d, J = 14.0 Hz, 1H), 2.99 (dd, J = 14.3, 1.4 Hz, 1H), 2.92 (s, 3H), 2.77 (s, 3H), 2.43 (s, 6H), 2.18 (d, J = 14.3 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.9, 170.5, 151.8, 143.7, 143.6, 135.0, 134.2, 129.8, 128.8, 128.2, 127.5, 127.4, 125.7, 98.1, 81.3, 59.4, 56.6, 52.7, 52.6, 44.8, 38.1, 37.9, 33.8, 21.5. HRMS (ESI) calcd for $C_{33}H_{39}N_2O_9S_2$ [M + H^+], 671.2091; found: 671.2098.

*Dimethyl 2,4-Bis((N,4-dimethylphenylsulfonamido)methyl)-6-(p-tolyl)-3,4-dihydro-2H-pyran-2,4-dicarboxylate (**8b**).* Yield: 51 mg, 50%, dr = 2.0:1. **Major:** Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:2, R_f = 0.4). IR (neat): ν_{max} 2949, 2920, 1732, 1643, 1445, 1344, 1251, 1163, 1089 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.3 Hz, 2H), 7.61 (d, J = 8.3 Hz, 2H), 7.54 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 5.49 (s, 1H), 3.81 (s, 3H), 3.78 (d, J = 13.8 Hz, 1H), 3.76 (s, 3H), 3.29 (d, J = 14.0 Hz, 1H), 3.23 (d, J = 14.0 Hz, 1H), 3.06 (d, J = 14.0 Hz, 1H), 2.86 (s, 3H), 2.69 (s, 3H), 2.54 (d, J = 14.8 Hz, 1H), 2.47 (d, J = 14.8 Hz, 1H), 2.42 (s, 3H), 2.40 (s, 3H), 2.35 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.0, 170.8, 151.3, 143.6, 143.5, 138.9, 134.2, 134.1, 131.9, 129.7, 129.6, 128.9, 127.4, 125.5, 96.9, 81.3, 58.2, 56.2, 52.9, 52.8, 44.3, 37.6, 37.4, 33.4, 21.5. **Minor**: Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:2, R_f = 0.35). IR (neat): ν_{max} 2951, 2922, 1732, 1597, 1445, 1342, 1161, 1092 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.3 Hz, 4H), 7.55 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 8.0 Hz, 4H), 7.15 (d, J = 8.0 Hz, 2H), 5.47 (d, J = 1.4 Hz, 1H), 3.70 (s, 3H), 3.68 (s, 3H), 3.55 (d, J = 14.2 Hz, 1H), 3.50 (d, J = 13.8 Hz, 1H), 3.43 (d, J = 14.2 Hz, 1H), 3.15 (d, J = 13.8 Hz, 1H), 2.98 (dd, J = 14.2, 1.4 Hz, 1H), 2.91 (s, 3H), 2.76 (s, 3H), 2.44 (s, 6H), 2.35 (s, 3H), 2.18 (d, J = 13.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.0, 170.6, 151.9, 143.7, 138.8, 134.3, 132.3, 129.8, 128.9, 127.5, 127.4, 125.6, 97.3, 91.3, 59.4, 56.6, 52.7, 52.6, 44.8, 38.1, 38.0, 33.8, 21.5, 21.3. HRMS (ESI) calcd for $C_{34}H_{40}N_2NaO_9S_2$ [M + Na^+], 707.2067; found: 707.2042.

*Dimethyl 6-(4-Chlorophenyl)-2,4-bis((N,4-dimethylphenylsulfonamido)methyl)-3,4-dihydro-2H-pyran-2,4-dicarboxylate (**8c**).* Yield: 63 mg, 60%, dr = 2.0:1. **Major:** Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:2, R_f = 0.35). IR (neat): ν_{max} 2953, 2926, 1732, 1661, 1597, 1491, 1445, 1344, 1251, 1163, 1092 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.2 Hz, 2H), 7.62−7.58 (m, 4H), 7.32 (d, J = 8.6 Hz, 4H), 7.27 (d, J = 8.0 Hz, 2H), 5.55 (s, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 3.73 (d, J = 14.2 Hz, 1H), 3.28 (s, 2H), 3.12 (d, J = 14.2 Hz, 1H), 2.85 (s, 3H), 2.68 (s, 3H), 2.51 (d, J = 15.0 Hz, 1H), 2.47 (d, J = 15.0 Hz, 1H), 2.43 (s, 3H), 2.41 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.9, 170.8, 150.3, 143.7, 143.6, 134.7, 134.1, 134.0, 133.2, 129.7, 129.6, 128.4, 127.4, 127.0, 98.3, 81.5, 58.0, 56.2, 53.0, 52.9, 44.2, 37.6, 37.3, 33.4, 21.5. **Minor**: Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:2, R_f = 0.3). IR (neat): ν_{max} 2951, 2924, 1732, 1597, 1492, 1445, 1343, 1161, 1091 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.3 Hz, 4H), 7.62 (d, J = 8.6 Hz, 2H), 7.34 (d, J = 8.3 Hz, 4H), 7.32 (d, J = 8.6 Hz, 2H), 5.57 (d, J = 1.4 Hz, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 3.51 (d, J = 14.4 Hz, 1H), 3.48 (d, J = 13.8 Hz, 1H), 3.46 (d, J = 14.4 Hz, 1H), 3.19 (d, J = 13.8 Hz, 1H), 2.98 (dd, J = 14.4, 1.4 Hz, 1H), 2.89 (s, 3H), 2.75 (s, 3H), 2.44 (s, 6H), 2.16 (d, J = 14.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.8, 170.5, 150.8, 143.7, 134.6, 134.2, 133.6, 129.8, 128.5, 127.5, 127.4, 127.1, 98.7, 81.4, 59.4, 56.5, 52.8, 52.6, 44.8, 38.1, 37.9, 33.8, 21.5. HRMS (ESI) calcd for $C_{33}H_{37}ClN_2NaO_9S_2$ [M + Na^+], 727.1521; found: 727.1502.

*Dimethyl 2,4-Bis((N,4-dimethylphenylsulfonamido)methyl)-6-(thiophen-2-yl)-3,4-dihydro-2H-pyran-2,4-dicarboxylate (**8d**).* Yield: 56 mg, 55%, dr = 1.8:1. **Major**: Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:2, R_f = 0.3). IR (neat): ν_{max} 2965, 2926, 1732, 1643, 1597, 1453, 1344, 1250, 1163, 1090 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.3 Hz, 2H), 7.63 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 7.32−7.25 (m, 4H), 7.00 (dd, J = 5.0, 3.6 Hz, 1H), 5.52 (s, 1H), 3.81 (s, 3H), 3.80 (d, J = 14.0 Hz, 1H), 3.76 (s, 3H), 3.28 (d, J = 14.2 Hz, 1H), 3.22 (d, J = 14.2 Hz, 1H), 3.03 (d, J = 14.0 Hz, 1H), 2.91 (s, 3H), 2.70 (s, 3H), 2.56 (d, J = 14.8 Hz, 1H), 2.46 (d, J = 14.8 Hz, 1H), 2.43 (s, 3H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.7, 170.4, 146.7, 143.7, 143.6, 138.2, 134.1, 129.7, 127.4, 127.3, 125.8, 124.5, 96.6, 81.7, 58.1, 55.9, 53.0, 52.9, 44.3, 37.5, 33.4, 21.5. **Minor**: Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:2, R_f = 0.25). IR (neat): ν_{max} 2951, 2924, 1732, 1659, 1597, 1441, 1343, 1269, 1213, 1161, 1090, 1020 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 2H), 7.67 (d, J = 8.2 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.30 (dd, J = 3.6, 1.2 Hz, 1H), 7.25 (dd, J = 5.0, 1.2 Hz, 1H), 7.00 (dd, J = 5.0, 3.6 Hz, 1H), 5.49 (d, J = 1.4 Hz, 1H), 3.71 (s, 3H), 3.70 (s, 3H), 3.58 (d, J = 14.2 Hz, 1H), 3.50 (d, J = 13.8 Hz, 1H), 3.41 (d, J = 14.2 Hz, 1H), 3.12 (d, J = 13.8 Hz, 1H), 2.98 (dd, J = 14.4, 1.6 Hz, 1H), 2.95 (s, 3H), 2.76 (s, 3H), 2.44 (s, 6H), 2.21 (d, J = 14.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.5, 170.1, 147.3, 143.6, 138.4, 134.2, 129.8, 127.5, 127.4, 127.3, 125.6, 124.4, 96.8, 81.5, 59.2, 56.4, 52.7, 52.6, 44.9, 38.0, 33.6, 21.5. HRMS (ESI) calcd for $C_{31}H_{36}N_2NaO_9S_3$ [M + Na^+], 699.1475; found: 699.1452.

*Dimethyl 2,4-Bis((N-ethyl-4-methylphenylsulfonamido)methyl)-6-phenyl-3,4-dihydro-2H-pyran-2,4-dicarboxylate (**8e**).* Yield: 37 mg, 35%, dr = 2.0:1. **Major**: Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.4). IR (neat): ν_{max} 3028, 2978, 2953, 2928, 2874, 2855, 1732, 1663, 1599, 1493, 1450, 1389, 1244, 1159, 1092 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.3 Hz, 2H), 7.63 (d, J = 8.3 Hz, 2H), 7.63−7.60 (m, 2H), 7.35−7.33 (m, 3H), 7.29 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 8.1 Hz, 2H), 5.50 (s, 1H), 3.83 (d, J = 14.6 Hz, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 3.59 (d, J = 14.6 Hz, 1H), 3.46−3.40 (m, 2H), 3.38−3.30 (m, 2H), 3.24−3.17 (m, 1H), 3.13−3.04 (m, 1H), 2.48 (d, J = 14.9 Hz, 1H), 2.42 (d, J = 14.9 Hz, 1H), 2.42 (s, 3H), 2.36 (s, 3H), 0.97 (t, J = 7.1 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.4, 171.1, 151.1, 143.4, 143.2, 136.8, 136.7, 134.8, 129.7, 129.5, 128.8, 128.1, 127.3, 125.6, 97.9, 81.4, 54.5, 53.1, 52.9, 52.8, 44.5, 44.1, 44.0, 33.9, 21.5, 12.8, 12.7. HRMS (ESI) calcd for $C_{35}H_{43}N_2O_9S_2$ [M + H^+], 699.2404; found: 699.2392.

*2,2,6,6-Tetramethylpiperidin-1-yl Benzoate (**9**).*[12d] ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.0 Hz, 2H), 7.57 (t, J = 7.2 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 1.82−1.57 (m, 5H), 1.46 (d, J = 12.4 Hz, 1H), 1.28

DOI: 10.1021/acs.joc.5b02457
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(s, 6H), 1.13 (s, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.3, 132.8, 129.7, 129.5, 128.4, 60.3, 39.0, 31.9, 20.8, 16.9.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02457.

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

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support by State Key Laboratory of Heavy Oil Processing, the National Science Foundation of China (21272267), the Fundamental Research Funds for the Central Universities, the Research Funds of Renmin University of China (10XNL017), and Beijing National Laboratory for Molecular Sciences (BNLMS).

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DOI: 10.1021/acs.joc.5b02457
J. Org. Chem. 2015, 80, 12562−12571