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Amide/Ester Cross-Coupling via C−N/C−H Bond Cleavage: Synthesis of β-Ketoesters

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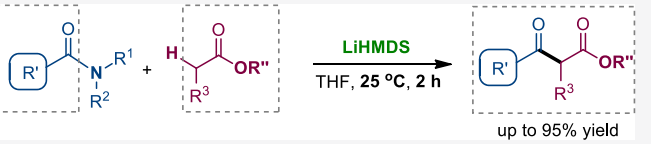
ABSTRACT: Activated primary, secondary, and tertiary amides were coupled with enolizable esters in the presence of LiHMDS to obtain good yields of β-ketoesters at room temperature. Notably, this protocol provides an efficient, mild, and high chemoselectivity method to synthesis of β-alkylketoesters using the cross-coupling between aliphatic amides and esters. Meanwhile, gram-scale secondary and primary amides reacted via in situ generated activated tertiary amides and exhibited good reactivity when coupled with esters.

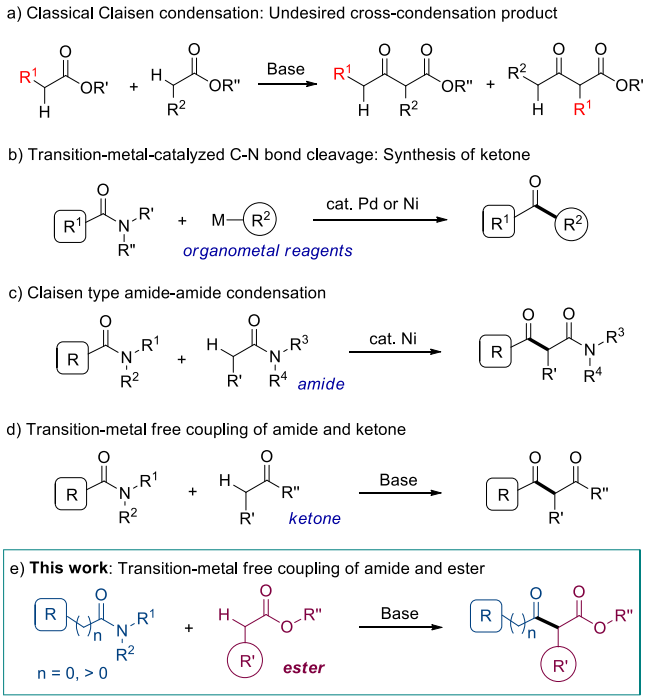


The Claisen condensation reaction, which generates a β-ketoester from the reaction of two esters in the presence of a strong base, is a quintessential carbon−carbon bond-forming methodology utilized extensively in organic synthesis.[1] In addition, Claisen condensation between an ester and an amide bearing an α-proton is a classic and indispensible tool for the synthesis of β-ketoamides.[2]

To the best of our knowledge, a Claisen-type coupling between an amide and an enolizable ester has not been reported, with the exception of Weinreb, acylbenzotriazole, and acylimidazole-type amides.[3] Furthermore, there has been no account of a coupling reaction between an amide and an ester, wherein they both contain α-protons, to yield β-ketoesters, since Claisen condensation was first reported in 1886. One of the reasons for this stems from a practical rationale, wherein the β-ketoester product can be readily obtained from classical Claisen condensation between two different esters. However, one of the drawbacks of Claisen condensation is the undesired cross-condensation product formed when both esters possess α-protons (Scheme 1a). Therefore, the combination of enolizable and nonenolizable esters has generally been employed to obtain various β-ketoesters. Another reason for avoiding the use of an amide as an electrophilic carbonyl species is that C−N bond activation in amides for further transformation has been a long-standing challenge.

Transformations via C−N bond cleavage of amides have received much attention, resulting in the development of numerous synthetic methods over the past decade.[4] For example, reactions between amides and amine nucleophiles afford transamidated products via transition-metal catalysis, as well as under metal-free conditions.[5] The use of alcohols as nucleophiles generates esters.[6] Transition-metal-catalyzed Suzuki, Negishi, and Sonogashira-type reactions entail the reaction of a carbon nucleophile with amides to form corresponding ketones (Scheme 1b).[7] Recently, we reported

Scheme 1. Claisen Condensation and C−N Bond Cleavage of Amides



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the nickel-catalyzed Claisen-type condensation between two different amides and demonstrated that the enolizable amides reacted with the nonenolizable amides to provide good yields of the corresponding β-ketoamides (Scheme 1c).[8] In addition, we have developed a reaction between enolizable ketones and amides to yield 1,3-diketones under transition-metal-catalyst-free conditions (Scheme 1d)[9]

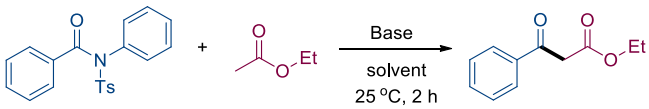
Hartwig and Buchwald independently established that enolizable carbonyl compounds, such as amides,[10] ketones,[11] and esters,[12] can be coupled with aryl halides to obtain the corresponding α-arylated carbonyl compounds in the presence of a palladium catalyst.

On the basis of these studies, we envisaged that a Claisen-type coupling between an amide and an ester can be achieved for the generation of the desired β-ketoester without the formation of undesired cross-coupling products. We conducted numerous trials to achieve our goal. Herein, we report the coupling between amides and esters for the synthesis of β-ketoesters under transition-metal-free conditions (Scheme 1e).

For the optimization of conditions, *N*-phenyl-*N*-tosylbenzamide (**1a**) and ethyl acetate (**2a**) were chosen as standard substrates and allowed to react under various conditions (Table 1). When **1a** and a 2.5-fold excess of equimolar amounts of **2a** and LiHMDS were reacted in THF at 25 °C, 88% yield of the expected β-ketoester **3aa** was obtained (entry 1). When the reactions were conducted in other solvents, such as Et_2O, CH_2Cl_2, 1,4-dioxane, toluene, DMSO, and DMF, lower yields were obtained (entries 2−7). The use of NaHMDS provided trace amounts of the desired product (entry 8). When KHMDS was employed, a 34% yield of **3aa** was obtained. Among the alkoxide bases tested, only KO*t*Bu provided a 20% yield of **3aa**, while other alkoxides, such as LiO*t*Bu, NaO*t*Bu, and NaOEt, yielded no product. The reaction with LDA afforded a 47% yield of **3aa**. Decreasing the amount of LiHMDS to 1.5 equiv and reducing the reaction time simultaneously to 1 h provided 65% and 62% yields of **3aa**, respectively (entries 15 and 16). Based on these results, the optimized standard conditions were as follows: amide (1.0 equiv), ester (2.5 equiv), and LiHMDS (2.5 equiv) reacted in THF at 25 °C for 2 h.

With these optimized conditions, various *N*-phenyl-*N*-tosylbenzamide derivatives were evaluated in the reaction with ethyl acetate (Scheme 2). Alkyl-substituted *N*-phenyl-*N*-tosylbenzamides reacted with ethyl acetate to obtain good yields of the corresponding ethyl-3-oxo-3-(aryl)- propanates, **3ca**, **3da**, and **3ea**. Due to steric hindrance, ortho-substituted *N*-phenyl-*N*-tosylbenzamides exhibited lower yields; thus, **3ba** and **3ha** were obtained in 39% and 46% yields, respectively. 3-Methoxy- and 3-dimethylamino-substituted benzamides **1f** and **1g** provided **3fa** and **3ga** in 81% and 82% yields, respectively.

Table 1. Optimization of Conditions for the Coupling of 1a with 2a[a]

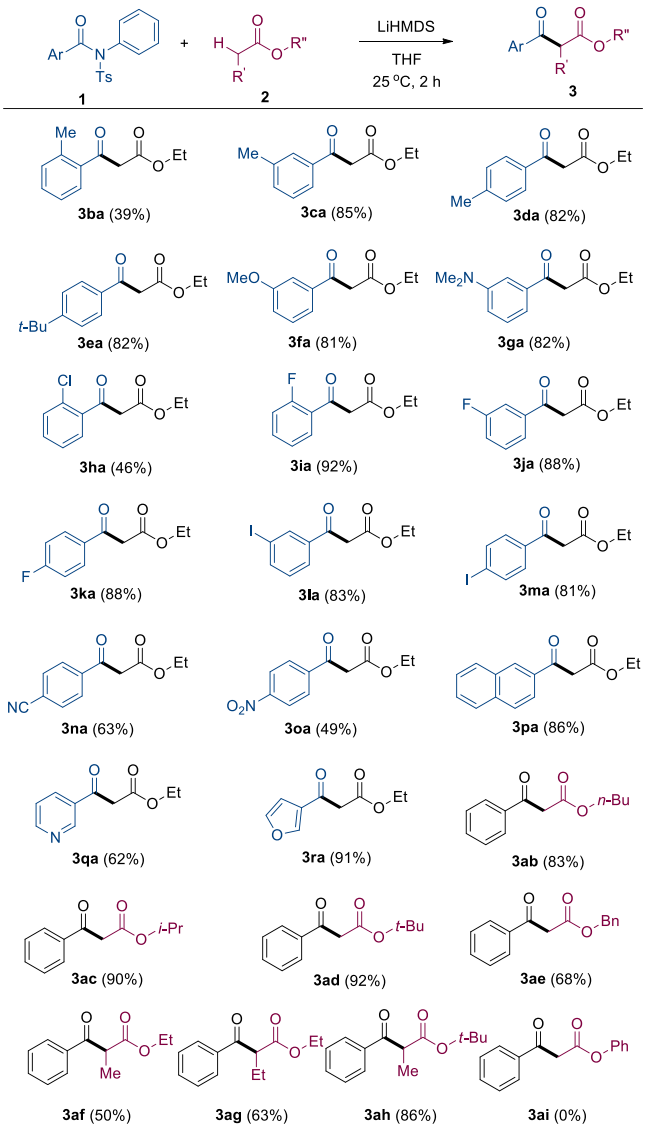


1a 2a 3aa

entry	base	solvent	yield (%)[a]
1	LiHMDS	THF	88
2	LiHMDS	Et_2O	46
3	LiHMDS	CH_2Cl_2	71
4	LiHMDS	1,4-dioxane	55
5	LiHMDS	toluene	66
6	LiHMDS	DMSO	34
7	LiHMDS	DMF	67
8	NaHMDS	THF	trace
9	KHMDS	THF	34
10	LiO*t*Bu	THF	0
11	NaO*t*Bu	THF	0
12	NaOEt	THF	0
13	KO*t*Bu	THF	20
14	LDA	THF	47
15[b]	LiHMDS	THF	65
16[bc]	LiHMDS	THF	62

[a]Reaction conditions: **1a** (0.3 mmol), **2a** (0.75 mmol), base (0.75 mmol), solvent, 25 °C, 2 h. Isolated yields. [b]Using **2a** (0.50 mmol), base (0.75 mmol). [c]The reaction was conducted for 1 h.

Scheme 2. Reaction Scope of Various *N*-Phenyl-*N*-tosylbenzamide Derivatives and Esters[a]



[a]Reaction conditions: Amide **1** (0.3 mmol), ester **2** (0.75 mmol), LiHMDS (0.75 mmol), THF, 25 °C, 2 h. Numbers in parentheses are isolated yields.

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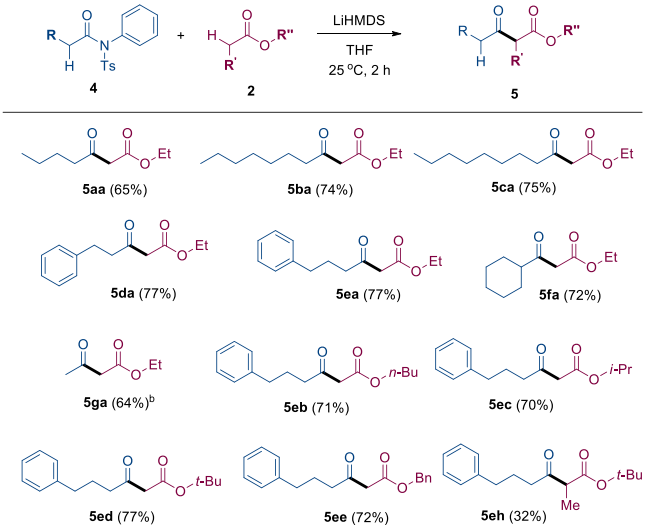
Benzamides bearing fluorine or iodine afforded good yields of the corresponding ethyl-3-oxo-3-(aryl)-propanates. *N*-Phenyl-*N*-tosylbenzamides bearing a cyano or a nitro group gave 63% and 49% yields of **3na** and **3oa**, respectively. *N*-Phenyl-*N*-tosyl-2-naphthamide furnished an 86% yield of **3pa**. *N*-Phenyl-*N*-tosylnicotinamide and *N*-phenyl-*N*-tosylfuran-3-carboxamide provided 62% and 91% yields of **3qa** and **3ra**, respectively. When *n*-butyl-, isopropyl-, and *t*-butyl acetates reacted with *N*-phenyl-*N*-tosylbenzamide instead of ethyl acetate, **3ab**, **3ac**, **3ad**, and **3ae** were isolated in 83%, 90%, 92%, and 68% yields, respectively. When **1a** reacted with ethyl propionate and ethyl butyrate, the corresponding *β*-ketoesters **3af** and **3ag** were obtained in 50% and 63% yields, respectively. The reaction of **1a** and *t*-butyl propionate gave **3ah** in 86% yield. However, the reaction with phenyl acetate did not give the desired product.

Next, we evaluated various enolizable alkyl-substituted amides in the reaction with ethyl acetate under optimized conditions (Scheme 3). When *N*-phenyl-*N*-tosylpentamide, *N*-phenyl-*N*-tosyloctamide, and *N*-phenyl-*N*-tosylnonamide reacted with ethyl acetate, the corresponding *β*-ketoesters **5aa**, **5ba**, and **5ca** were formed in 65%, 74%, and 75% yields, respectively. *N*-Phenyl-*N*-tosyl alkylamides **4d**, **4e**, and **4f** reacted with ethyl acetate to give **5da**, **5ea**, and **5fa** in 77%, 77%, and 72% yields, respectively. *N*-Phenyl-*N*-tosyl acetamide **4g** afforded **5ga** in 64% yield. Alkyl amide **4e** reacted with *n*-butyl-, isopropyl-, *t*-butyl-, and benzyl acetates to afford good yields of the corresponding *β*-ketoesters. However, when *t*-butylpropionate reacted with **4e**, **5eh** was obtained in 32% yield. Notably, undesired cross-coupling products, namely, *β*-ketoamides, were not detected in all cases.

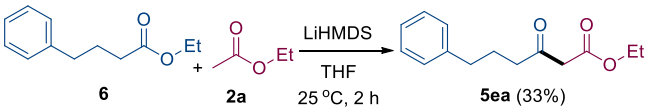
Scheme 3. Reaction Scope of Various Alkyl-Substituted *N*-Phenyl-*N*-tosylbenzamide Derivatives and Esters[a]



[a]Reaction conditions: Amide **4** (0.3 mmol), ester **2** (0.75 mmol), LiHMDS (0.75 mmol), THF, 25 °C, 2 h. Numbers in parentheses are isolated yields. [b]Determined by GC with an internal standard (2-methoxynaphthalene).

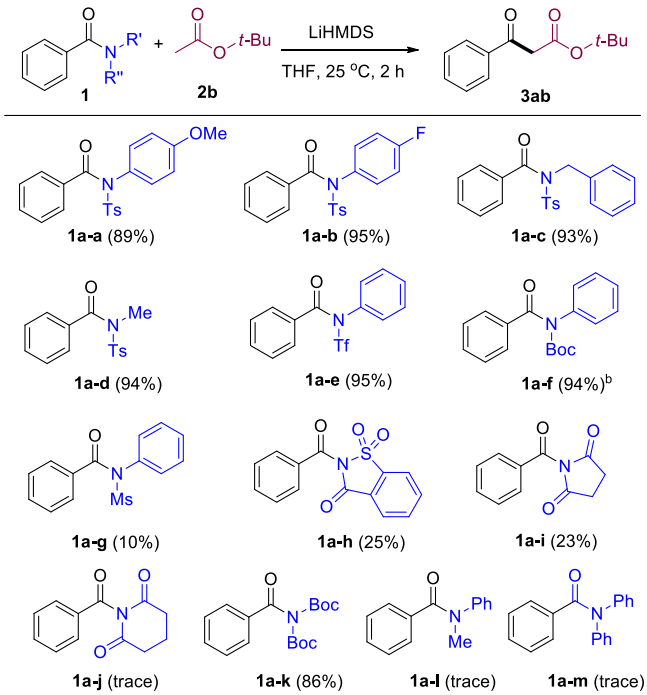
To compare this methodology with classical Claisen condensation, we employed ethyl 4-phenylbutanoate (**6**) instead of the corresponding amide **4e** in the reaction with ethyl acetate. As shown in Scheme 4, the desired Claisen condensation product **5ea** was formed in 33% yield, and an undesired cross-condensation product was detected in the reaction mixture. This result implies that the cross-coupling between an amide and ester provided a higher yield (77% yield in Scheme 3) of the *β*-ketoester than that obtained via classical Claisen condensation.

Scheme 4. Classical Claisen Condensation between 6 and 2a



To evaluate the reactivity of tertiary amides in the reaction with enolizable esters, various tertiary amides were reacted with *t*-butyl acetate under standard conditions (Scheme 5). *N*-4-Methoxyphenyl-, *N*-4-fluorophenyl-, *N*-benzyl-, *N*-methyl-, and *N*-tosylbenzamides, **1a−a**, **1a−b**, **1a−c**, and **1a−d**, respectively, provided **3ab** in good yields. *N*-Phenylbenzamides bearing *N*-protecting groups, such as triflate and Boc, furnished **3ab** in excellent yields. However, *N*-phenyl-*N*-mesitylbenzamide (**1a−g**), *N*-benzoyl-saccharin (**1a−h**), *N*-benzoylsuccinimide (**1a−i**), and *N*-benzoyl-glutarimide (**1a−j**) provided low yields in the formation of **3ab**. *N*,*N*-Di-Boc-protected benzamides **1a−k** gave a good product yield. However, unactivated tertiary amides, such as **1a−l** and **1a−m**, afforded a trace amount of **3ab**. It is noteworthy that the reaction with unactivated alkyl amide such as *N*,*N*-dimethylacetamide and **2a** did not provide the desired product.

Scheme 5. Reaction Scope of a Variety of Amides and *t*-Butyl Acetate[a]



[a]Reaction conditions: amide **1** (0.3 mmol), ester **2b** (0.75 mmol), LiHMDS (0.75 mmol), THF, 25 °C, 2 h. Isolated yield. Numbers in parentheses are isolated yields. [b]Determined by ^{1}H NMR with an internal standard.

To study the reactivity of activated amides, several control experiments were conducted. The competitive reaction between **1d** and **1a−d** afforded **3da** and **3aa** in 52% and 48% yields, respectively (Scheme 6a). This result suggested

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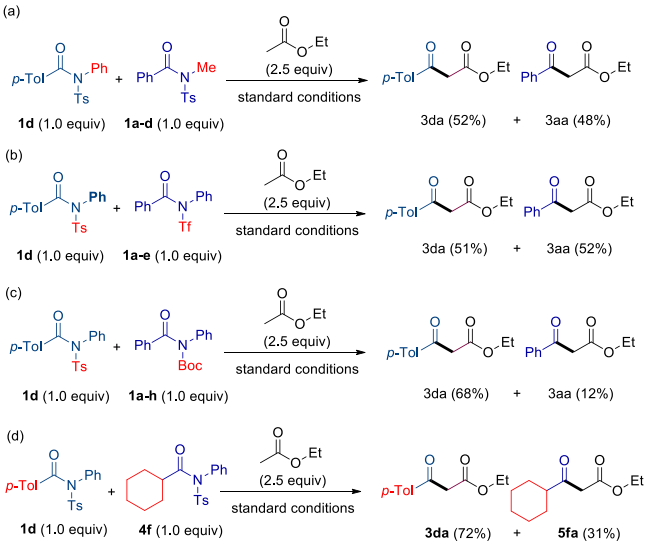
Scheme 6. Control Experiments[a]

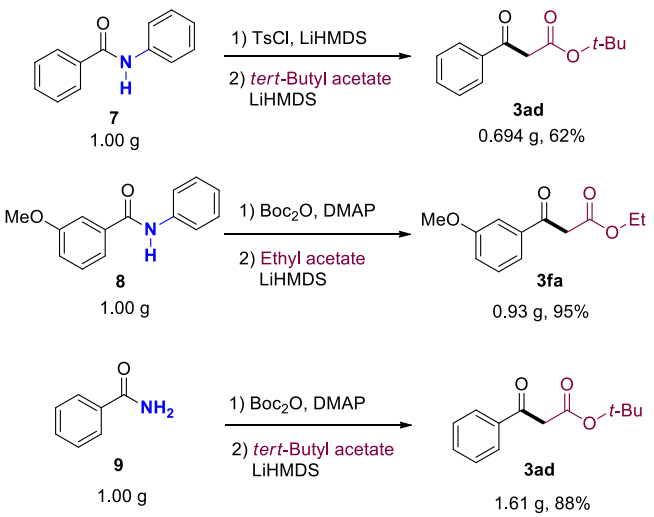


[a]Standard conditions: LiHMDS (2.5 equiv), THF, 25 °C, 2 h.

that *N*-phenyl- and *N*-methyl substituents showed similar reactivity. It was found that **1d** and **1a−e** also showed very similar reactivity (Scheme 6b). However, when the competitive reaction between **1d** and **1a−h** was conducted, **1d** showed higher reactivity than **1a−h** (Scheme 6c). In addition, arylamide such as **1d** showed higher reactivity than alkylamide such as **4f** (Scheme 6d).

Having successfully coupled activated tertiary amides and esters, we then focused on secondary and primary amides. In situ generation of activated amides from secondary and primary amides was conducted prior to reaction with esters under standard conditions. The reactions were all conducted on a gram scale, and the results are summarized in Scheme 7. When *N*-phenylbenzamide (**7**) was treated with TsCl and LiHMDS and then reacted with *tert*-butyl acetate in the presence of additional LiHMDS, the desired *β*-ketoester **3ad** was obtained in 62% yield. The in situ generated Boc-protected secondary benzamide reacted with ethyl acetate in the presence of LiHMDS to give **3fa** in a quantitative yield. Primary amide, benzamide, was treated with Boc_2O and DMAP, and the resulting mixture was reacted with *tert*-butyl acetate to furnish **3ad** in an 88% yield.

Scheme 7. Gram-Scale One-Pot Synthesis of *β*-Ketoesters Using Secondary and Primary Amides



In summary, activated tertiary amides reacted with enolizable esters in the presence of LiHMDS at room temperature to provide the corresponding *β*-ketoesters. The reaction proceeds via a nucleophilic attack by the ester enolate on the amide, resulting in C−N bond cleavage to form the *β*-ketoester and producing a secondary amine. To the best of our knowledge, this is the first example of a Claisen-type reaction between activated secondary amides and esters, although the classical Claisen condensation reaction between esters and amides has been well established. Various substituted tertiary benzamides reacted with enolizable esters to give the desired products in good yields. Enolizable aliphatic amides likewise reacted with esters to give expected *β*-ketoesters in good yields without the formation of undesired cross-coupling products, providing a better alternative to the analogous condensation reaction between two different enolizable esters. Secondary and primary amides reacted with esters to provide the coupling products via in situ generated activated amides.

EXPERIMENTAL SECTION

General Information. All reagents were purchased and used without further purification. ^1H spectra were recorded in $CDCl_3$ on 500 MHz NMR spectrometers, and data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz), and integration. ^{13}C spectra were recorded in $CDCl_3$ on 126 MHz NMR spectrometers, and resonances (δ) are given in ppm. High-resolution mass spectra was recorded on a time-of-flight (TOF) mass spectrometer. ^1H NMR and ^{13}C NMR were recorded on an Agilent Technologics (USA) NMR spectrometer (500 MHz for ^1H).

General Procedure for the Synthesis of Starting Materials. All starting materials of esters were commercially available and used without other purification. Some starting materials of amides were synthesized according to corresponding literature.[13] Citations to the references containing characterization data for these compounds are given: **1a**,[13] **1b**,[13] **1c**,[14] **1d**,[13] **1f**,[14] **1i**,[17] **1k**,[13] **1n**,[13] **1o**,[13] **1p**,[15] **1a−a**,[16] **1a−c**,[14] **1a−d**,[17] **1a−e**,[18] **1a−f**,[17] **1a−g**,[19] **1a−h**,[20] **1a−i**,[14] **1a−j**,[17] **1a−k**,[14] **1a−l**,[21] **1a−m**,[22] **4a**,[23] **4d**,[13] **4c**,[24] **4f**,[13] and **4g**.[23]

General Procedure for the Synthesis of *β*-Ketoester. Amide (0.3 mmol, 1.0 equiv), ester (0.75 mmol, 2.5 equiv), and anhydrous THF (3 mL) were placed in a 20 mL vial, and following flushing with argon gas, LiHMDS (0.75 mL, 2.5 equiv, 1 M in THF) was added using a syringe. The resulting solution was stirred for 2 h. The reaction was then quenched with saturated NH_4Cl (5 mL) and extracted with dichloromethane (25 mL × 2). The combined organic layers were washed with brine (10 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated under a vacuum. The crude product was purified by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1)

Procedure for the Gram-scale Synthesis of *tert*-Butyl 3-oxo-3-phenylpropanoate (3ad) using *N*-Phenylbenzamide (7). For the procedure for the gram-scale synthesis of *tert*-butyl 3-oxo-3-phenylpropanoate (**3ad**) using *N*-phenylbenzamide (**7**), to the solution of *N*-phenylbenzamide (**7**) (1.0 g, 5.07 mmol, 1.0 equiv) in anhydrous THF (15 mL) was added LiHMDS (7.6 mL, 7.6 mmol, 1.5 equiv, 1 M in THF) under argon protection. After the mixture stirred for 1 h at room temperature, TsCl (1.16 g, 6.09 mmol, 1.2 equiv) was added. The resulting solution was stirred for 4 h at room temperature. To the mixture was added *tert*-butyl acetate (1.48 g, 12.7 mmol, 2.5 equiv), anhydrous THF (5 mL), and LiHMDS (12.7 mL, 12.7 mmol, 2.5 equiv, 1 M in THF). The resulting solution was stirred for 2 h under argon protection. The reaction was quenched with saturated NH_4Cl (20 mL) and extracted with dichloromethane (50

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mL × 2). The combined organic layers were washed with brine (20 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated under a vacuum. The crude product was purified by silica gel column chromatography with ethyl acetate in hexane (0−10%) to afford *tert*-butyl 3-oxo-3-phenylpropanoate (**3ad**) (694.4 mg, 3.2 mmol, 62% yield) as a light yellow liquid.

*Procedure for the Gram-Scale Synthesis of Ethyl 3-(3-Methoxyphenyl)-3-oxopropanoate (**3fa**) Using 3-Methoxy-N-phenylbenzamide (**8**).* To the solution of 3-methoxy-*N*-phenylbenzamide (**8**) (1.0 g, 4.4 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) were added di-*tert*-butyl dicarbonate (1.44 g, 6.6 mmol, 1.5 equiv) and DMAP (53.8 mg, 0.44 mmol, 0.1 equiv). The resulting solution was stirred for 16 h at room temperature. The dichloromethane was evaporated under a vacuum, and then ethyl acetate (0.97 g, 11.0 mmol, 2.5 equiv), anhydrous THF (20 mL), and LiHMDS (11.0 mL, 11.0 mmol, 2.5 equiv, 1 M in THF) were added. The resulting solution was stirred for 2 h under argon protection. The reaction was quenched with saturated NH_4Cl (20 mL) and extracted with dichloromethane (50 mL × 2). The combined organic layers were washed with brine (20 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated under a vacuum. The crude product was purified by silica gel column chromatography with ethyl acetate in hexane (0−15%) to afford ethyl 3-(3-methoxyphenyl)-3-oxopropanoate as a colorless oil.

*Procedure for the Gram-Scale Synthesis of tert-Butyl 3-Oxo-3-phenylpropanoate (**3ad**) Using benzamide (**9**).* To the solution of benzamide (**9**) (1.0 g, 8.3 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) were added di-*tert*-butyl dicarbonate (4.5 g, 20.6 mmol, 2.5 equiv) and DMAP (101 mg, 0.83 mmol, 0.1 equiv). The resulting solution was stirred for 16 h at room temperature. The dichloromethane was evaporated under a vacuum, and then *tert*-butyl acetate (2.42 g, 20.6 mmol, 2.5 equiv), anhydrous THF (40 mL), and LiHMDS (20.6 mL, 20.6 mmol, 2.5 equiv, 1 M in THF) were added. The resulting solution was stirred for 2 h under argon protection. The reaction was quenched with saturated NH_4Cl (20 mL) and extracted with dichloromethane (50 mL × 2). The combined organic layers were washed with brine (20 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated under a vacuum. The crude product was purified by silica gel column chromatography with ethyl acetate in hexane (0−10%) to afford *tert*-butyl 3-oxo-3-phenylpropanoate (**3ad**) (1.61 g, 7.3 mmol, 88% yield) as a light yellow liquid.

Experiment Data. *4-(tert-Butyl)-N-phenyl-N-tosylbenzamide (**1e**):* white solid; mp 156−158 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 8.3 Hz, 2H), 7.42 (d, J = 8.8 Hz, 2H), 7.34−7.28 (m, 5H), 7.22−7.16 (m, 4H), 2.45 (s, 3H), 1.21 (s, 9H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 169.7, 155.6, 144.6, 137.6, 135.4, 130.5, 130.3, 129.7, 129.4, 129.2, 129.1, 128.9, 125.0, 34.9, 30.9, 21.7; HRMS (FD-TOF) m/z [M]$^+$ calcd for $C_{24}H_{25}NO_3S$ 407.1550, found 407.1549.

*3-(Dimethylamino)-N-phenyl-N-tosylbenzamide (**1g**):* light yellow solid; mp 182−184 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.29−7.26 (m, 3H), 7.22−7.15 (m, 2H), 7.01 (t, J = 8.2 Hz, 1H), 6.85−6.57 (m, 3H), 2.81 (s, 6H), 2.45 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 170.4, 149.6, 144.7, 137.7, 135.4, 134.1, 130.3, 129.4, 129.2, 129.0, 128.9, 128.6, 118.1, 115.9, 113.6, 40.5, 21.7; HRMS (FD-TOF) m/z [M]$^+$ calcd for $C_{22}H_{22}N_2O_3S$ 394.1346, found 394.1344.

*2-Chloro-N-phenyl-N-tosylbenzamide (**1h**):* white solid; mp 165−166 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 8.4 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.28−7.24 (m, 5H), 7.16−7.09 (m, 3H), 7.07−7.02 (m, 1H), 2.49 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.9, 145.2, 135.8, 135.4, 134.8, 130.8, 130.5, 130.0, 129.6, 129.5, 129.4, 129.3, 129.1, 128.4, 126.2, 21.8; HRMS (FD-TOF) m/z [M]$^+$ calcd for $C_{20}H_{16}ClNO_3S$ 385.0534, found 385.0516.

*3-Fluoro-N-phenyl-N-tosylbenzamide (**1j**):* white solid; mp 158−161 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 8.3 Hz, 2H), 7.35−7.28 (m, 5H), 7.22−7.19 (m, 1H), 7.18−7.11 (m, 4H), 7.01−6.96 (m, 1H), 2.47 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.5 (C−F, ^4J = 2.7 Hz), 162.0 (C−F, ^1J = 249.5 Hz), 145.0, 137.0, 135.8 (C−F, ^3J = 7.2 Hz), 135.0, 130.3, 129.7 (C−F, ^3J = 8.8 Hz), 129.5, 129.30, 129.26, 125.1 (C−F, ^4J = 3.2 Hz), 118.8 (C−F, ^2J = 21.4 Hz), 116.4 (C−F, ^2J = 23.9 Hz), 116.3, 21.7; HRMS (FD-TOF) m/z [M]$^+$ calcd for $C_{20}H_{16}FNO_3S$ 369.0829, found 369.0826.

*3-Iodo-N-phenyl-N-tosylbenzamide (**1l**):* white solid; mp 169−172 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 8.4 Hz, 2H), 7.60 (dd, J = 8.0, 0.7 Hz, 1H), 7.38 (d, J = 8.0 Hz, 2H), 7.35−7.30 (m, 2H), 7.29−7.24 (m, 3H), 7.13−7.04 (m, 2H), 6.87−6.83 (m, 1H), 2.48 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.6, 145.2, 140.3, 139.3, 136.1, 135.3, 130.7, 130.2, 129.6, 129.5, 129.4, 129.1, 128.2, 127.2, 92.5, 21.8; HRMS (FD-TOF) m/z [M]$^+$ calcd for $C_{20}H_{16}INO_3S$ 476.9890, found 476.9892.

*4-Iodo-N-phenyl-N-tosylbenzamide (**1m**):* white solid; mp 143−145 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 8.4 Hz, 2H), 7.53 (d, J = 8.6 Hz, 2H), 7.34−7.28 (m, 5H), 7.18−7.13 (m, 4H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 169.1, 145.0, 138.4, 137.3, 137.1, 135.0, 133.1, 131.7, 130.9, 130.3, 129.5, 129.3, 99.3, 21.7; HRMS (FD-TOF) m/z [M]$^+$ calcd for $C_{20}H_{16}INO_3S$ 476.9890, found 476.9884.

*N-Phenyl-N-tosylnicotinamide (**1q**):* white solid; mp 173−175 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, J = 1.4 Hz, 1H), 8.49 (d, J = 3.8 Hz, 1H), 7.84 (d, J = 8.3 Hz, 2H), 7.72 (d, J = 8.0 Hz, 1H), 7.36−7.28 (m, 5H), 7.19−7.12 (m, 3H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 167.5, 151.4, 149.6, 145.3, 137.0, 136.6, 134.8, 130.4, 130.1, 129.7, 129.53, 129.48, 129.4, 123.0, 21.7; HRMS (FD-TOF) m/z [M]$^+$ calcd for $C_{19}H_{16}N_2O_3S$ 352.0876, found 352.0877.

*N-Phenyl-N-tosylfuran-3-carboxamide (**1r**):* white solid; mp 131−132 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, J = 8.4 Hz, 2H), 7.57−7.47 (m, 3H), 7.38−7.32 (m, 4H), 7.16−7.13 (m, 1H), 6.66 (dd, J = 1.3, 0.8 Hz, 1H), 6.21 (dd, J = 1.9, 0.7 Hz, 1H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 162.3, 147.4, 145.0, 142.6, 136.4, 136.0, 130.8, 130.3, 129.7, 129.38, 129.36, 121.3, 110.9, 21.7; HRMS (FD-TOF) m/z [M]$^+$ calcd for $C_{18}H_{15}NO_4S$ 341.0716, found 341.0724.

*N-(4-Fluorophenyl)-N-tosylbenzamide (**1a**−**b**):* white solid; mp 154−156 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 8.3 Hz, 2H), 7.45−7.41 (m, 2H), 7.36−7.29 (m, 3H), 7.20 (t, J = 7.7 Hz, 2H), 7.1−7.11 (m, 2H), 7.00−6.94 (m, 2H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 169.7, 162.5 (C−F, ^1J = 250.7 Hz), 145.0, 134.9, 133.5, 133.4 (C−F, ^4J = 3.8 Hz), 132.11 (C−F, ^3J = 8.8 Hz), 131.9, 129.5, 129.4, 129.3, 128.1, 116.2 (C−F, ^2J = 23.9 Hz), 21.7; HRMS (FD-TOF) m/z [M]$^+$ calcd for $C_{20}H_{16}FNO_3S$ 369.0829, found 369.0824.

*Ethyl 3-Oxo-3-phenylpropanoate (**3aa**).*[25] According to the general procedure, *N*-phenyl-*N*-tosylbenzamide (105.4 mg, 0.3 mmol) afforded ethyl 3-oxo-3-phenylpropanoate (**3aa**) (50.7 mg, 0.26 mmol, 88% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 18% enol tautomer) δ [12.59 (s, 0.18H), 5.76 (s, 0.18 H), 4.00 (s, 1.64H)], [7.95 (d, J = 7.3 Hz, 1.64H), 7.78 (d, J = 7.3 Hz, 0.36H)], 7.63−7.38 (m, 3H), [4.27 (q, J = 7.1 Hz, 0.36H), 4.21 (q, J = 7.1 Hz, 1.64H)], [1.34 (t, J = 7.1 Hz, 0.54H), 1.25 (t, J = 7.1 Hz, 2.46H)]; ^{13}C{^{1}H} NMR (126 MHz, CDCl3, including 18% enol tautomer) δ 192.5, 173.2^{enol}, 171.4^{enol}, 167.5, 136.0, 133.7, 133.4^{enol}, 131.2^{enol}, 128.8, 128.52^{enol},128.49, 126.0^{enol}, 87.4^{enol}, 61.5, 60.3^{enol}, 46.0, 14.3^{enol}, 14.1.

*Ethyl 3-Oxo-3-(o-tolyl)propanoate (**3ba**).*[26] According to the general procedure, 2-methyl-*N*-phenyl-*N*-tosylbenzamide (109.6 mg, 0.3 mmol) afforded ethyl 3-oxo-3-(*o*-tolyl)propanoate (**3ba**) (24.1 mg, 0.12 mmol, 39% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 18% enol tautomer) δ [12.49 (s, 0.18H), 5.29 (s, 0.18H), 3.95 (s, 1.64H)], 7.69−7.19 (m, 4H), [4.27 (q, J = 7.1 Hz, 0.36H), 4.20 (q, J = 7.1 Hz, 1.64H)], [2.55 (s, 2.46H), 2.47 (s, 0.54H)], [1.34 (t, J = 7.1 Hz, 0.54H), 1.24 (t, J = 7.1 Hz, 2.46H)]; ^{13}C{^{1}H} NMR (126 MHz, including 18% enol tautomer) δ 195.6, 174.9^{enol}, 172.9^{enol}, 167.6, 139.4, 136.5^{enol}, 136.2, 134.5^{enol}, 132.2, 132.1, 131.0^{enol}, 130.0^{enol}, 129.1, 128.4^{enol}, 125.78, 125.72^{enol}, 91.6^{enol}, 61.4, 60.3^{enol}, 48.3, 21.5, 20.5^{enol}, 14.3^{enol}, 14.0.

*Ethyl 3-Oxo-3-(m-tolyl)propanoate (**3ca**).*[27] According to the general procedure, 3-methyl-*N*-phenyl-*N*-tosylbenzamide (109.6 mg, 0.3 mmol) afforded ethyl 3-oxo-3-(*m*-tolyl)propanoate (**3ca**) (52.6

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mg, 0.25 mmol, 85% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 18% enol tautomer) δ [12.57 (s, 0.18H), 5.66 (s, 0.18H), 3.98 (s, 1.64H)], [7.81−7.69 (m, 1.64H), 7.62−7.55 (m, 0.36H)], 7.46−7.28 (m, 2H), 4.30−4.25 (m, 2H), [2.42 (s, 2.46H), 2.39 (s, 0.54H)], [1.34 (t, J = 7.1 Hz, 0.54H), 1.26 (t, J = 7.1 Hz, 0.46H)]; ^{13}C{^{1}H} NMR (126 MHz, including 18% enol tautomer)δ 192.7, 173.2^{enol}, 171.6^{enol}, 167.6, 138.6, 138.2^{enol}, 136.0, 134.5, 133.4^{enol}, 132.0^{enol}, 128.9, 128.6, 128.4^{enol}, 126.6^{enol}, 125.8, 123.2^{enol}, 87.3^{enol}, 61.4, 60.3^{enol}, 46.0, 21.4^{enol}, 21.3, 14.3^{enol}, 14.1.

*Ethyl 3-Oxo-3-(p-tolyl)propanoate (**3da**).*[25] According to the general procedure, 4-methyl-*N*-phenyl-*N*-tosylbenzamide (109.6 mg, 0.3 mmol) afforded ethyl 3-oxo-3-(*p*-tolyl)propanoate (**3ca**) (50.7 mg, 0.25 mmol, 82% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1); ^{1}H NMR (500 MHz, $CDCl_3$, including 16% enol tautomer) δ [12.59 (s, 0.16H), 5.63 (s, 0.16H), 3.96 (s, 1.68H)], [7.84 (d, J = 8.2 Hz, 1.68H), 7.67 (d, J = 8.2 Hz, 0.32H)], [7.27 (d, J = 8.2 Hz, 1.68H), 7.22 (d, J = 8.2 Hz, 0.32H)], 4.28−4.17 (m, 2H), [2.42 (s, 2.52H), 2.39 (s, 0.48H)], [1.33 (t, J = 7.1 Hz, 0.48H), 1.25 (t, J = 7.1 Hz, 2.52H)]; ^{13}C{^{1}H} NMR (126 MHz, including 16% enol tautomer)δ 192.1, 173.3^{enol}, 171.6^{enol}, 167.7, 144.7, 141.7^{enol}, 133.5^{enol}, 130.6^{enol}, 129.4, 129.2, 128.6, 126.0^{enol}, 86.6^{enol}, 61.4, 60.2^{enol}, 45.9, 21.7, 21.5^{enol}, 14.3^{enol}, 14.1;

*Ethyl 3-(4-(tert-Butyl)phenyl)-3-oxopropanoate (**3ea**).*[28] According to the general procedure, 4-(*tert*-butyl)-*N*-phenyl-*N*-tosylbenzamide (122.3 mg, 0.3 mmol) afforded ethyl 3-(4-(*tert*-butyl)phenyl)-3-oxopropanoate (**3ea**) (61.1 mg, 0.25 mmol, 82%) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 15% enol tautomer) δ [12.58 (s, 0.15H), 5.64 (s, 0.15H), 3.97 (s, 1.7H)], [7.89 (d, J = 8.6 Hz, 1.7H), 7.71 (d, J = 8.6 Hz, 0.3H)], [7.49 (d, J = 8.6 Hz, 1.7H), 7.44 (d, J = 8.6 Hz, 0.3H)], 4.29−4.18 (m, 2H), 1.38−1.23 (m, 12H); ^{13}C{^{1}H} NMR (126 MHz, including 15% enol tautomer) δ 192.13, 173.3^{enol}, 171.6^{enol}, 167.7, 157.6, 154.8^{enol}, 133.5, 130.6^{enol}, 128.5, 125.8^{enol}, 125.7, 125.5^{enol}, 86.7^{enol}, 61.4, 60.2^{enol}, 45.9, 35.2, 34.9 ^{enol}, 31.1^{enol}, 31.0, 14.32^{enol}, 14.1.

*Ethyl 3-(3-Methoxyphenyl)-3-oxopropanoate (**3fa**).*[28] According to the general procedure, 3-methoxy-*N*-phenyl-*N*-tosylbenzamide (114.4 mg, 0.3 mmol) afforded ethyl 3-(3-methoxyphenyl)-3-oxopropanoate (**3fa**) (54.0 mg, 0.24 mmol, 81%) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 17% enol tautomer) δ [12.58 (s, 0.17H), 5.65 (s, 0.17H), 3.97 (s, 1.66H)], 7.54−7.29 (m, 3H), [7.16−7.11 (m, 0.83H), 7.02−6.98 (m, 0.17H)], 4.29−4.17 (m, 2H), [3.85 (s, 2.49H), 3.84 (s, 0.51H)], [1.33 (t, J = 7.1 Hz, 0.51H), 1.25 (t, J = 7.1 Hz, 2.49H)]; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, including 17% enol tautomer) δ 192.4, 173.2^{enol}, 171.2^{enol}, 167.5, 159.9, 159.7^{enol}, 137.3, 134.8^{enol}, 129.7, 129.5^{enol}, 121.2, 120.3, 118.4^{enol}, 117.2^{enol}, 112.5, 111.1^{enol}, 87.6^{enol}, 61.5, 60.4^{enol}, 55.4, 55.3^{enol}, 46.1, 14.3^{enol}, 14.1.

*Ethyl 3-(3-(Dimethylamino)phenyl)-3-oxopropanoate (**3ga**).*[29] According to the general procedure, 3-(dimethylamino)-*N*-phenyl-*N*-tosylbenzamide (118.4 mg, 0.3 mmol) afforded ethyl 3-(3-(dimethylamino)phenyl)-3-oxopropanoate (**3ga**) (57.9 mg, 0.25 mmol, 82%) as yellow liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 17% enol tautomer) δ [12.60 (s, 0.17H), 5.65 (s, 0.17H), 3.97 (s, 1.66H)], 7.37−7.09 (m, 3H), 6.98−6.84 (m, 1H), [4.26 (q, J = 7.1 Hz, 0.34H), 4.21 (q, J = 7.1 Hz, 1.66H)], 2.99 (s, 6H), [1.33 (t, J = 7.1 Hz, 0.51H), 1.26 (t, J = 7.1 Hz, 2.49H)]; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, including 17% enol tautomer) δ 193.2, 173.2^{enol}, 167.7, 150.6, 136.8, 129.3, 129.2^{enol}, 117.6, 116.8, 111.4, 87.3^{enol}, 61.3, 60.2^{enol}, 46.2, 40.5, 14.3^{enol}, 14.1.

*Ethyl 3-(2-Chlorophenyl)-3-oxopropanoate (**3ha**).*[25] According to the general procedure, 2-chloro-*N*-phenyl-*N*-tosylbenzamide (115.8 mg, 0.3 mmol) afforded ethyl 3-(2-chlorophenyl)-3-oxopropanoate (**3ha**) (31.3 mg, 0.14 mmol, 46%) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 30% enol tautomer) δ [12.49 (s, 0.3H), 5.56 (s, 0.3H), 4.04 (s, 1.4H)], 7.64−7.56 (m, 1H), 7.47−7.28 (m, 3H), [4.28 (q, J = 7.1 Hz, 0.6H), 4.19 (q, J = 7.1 Hz, 1.4H)], [1.34 (t, J = 7.1 Hz, 0.9H), 1.24 (t, J = 7.1 Hz, 2.1H)]; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, including 30% enol tautomer) δ 194.7, 172.7^{enol}, 170.4^{enol}, 166.9, 137.6, 133.5^{enol}, 132.6, 132.1^{enol}, 131.5^{enol}, 131.0, 130.7, 130.6^{enol}, 130.1^{enol}, 130.0, 127.0, 126.8^{enol}, 93.3^{enol}, 61.5, 60.5^{enol}, 49.2, 14.3^{enol}, 14.0.

*Ethyl 3-(2-Fluorophenyl)-3-oxopropanoate (**3ia**).*[25] According to the general procedure, 2-fluoro-*N*-phenyl-*N*-tosylbenzamide (110.8 mg, 0.3 mmol) afforded ethyl 3-(2-fluorophenyl)-3-oxopropanoate (**3ia**) (58.0 mg, 0.28 mmol, 92%) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 20% enol tautomer) δ [12.68 (s, 0.2H), 5.84 (s, 0.2H), 3.98 (d, J = 3.5 Hz, 1.6H)], 7.99−7.83 (m, 1H), [7.59−7.52 (m, 0.8H), 7.44−7.38 (m, 0.2H)], 7.30−7.07 (m, 2H), [4.27 (q, J = 7.1 Hz, 0.4H), 4.21 (q, J = 7.1 Hz, 1.6H)], 1.33 (t, J = 7.1 Hz, 0.6H), 1.25 (t, J = 7.1 Hz, 2.4H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, including 20% enol tautomer) δ 190.3 (C−F, $^3J_{C-F}$ = 3.3 Hz), 173.3^{enol}, 167.4 (C−F, $^5J_{C-F}$ = 2.5 Hz), 166.3 (C−F, $^5J_{C-F}$ = 3.8 Hz), 162.1 (C−F, $^1J_{C-F}$ = 255.8 Hz), 160.7 (C−F, $^1J_{C-F}$ = 255.8 Hz)^{enol}, 135.4 (C−F, $^3J_{C-F}$ = 9.3 Hz), 132.3 (C−F, $^3J_{C-F}$ = 9.2 Hz)^{enol}, 130.9 (C−F, $^4J_{C-F}$ = 2.1 Hz), 129.2 (C−F, $^4J_{C-F}$ = 1.9 Hz)^{enol}, 124.6 (C−F, $^3J_{C-F}$ = 3.8 Hz), 124.5 (C−F, $^2J_{C-F}$ = 12.6 Hz), 124.3 (C−F, $^3J_{C-F}$ 3.8 Hz)^{enol}, 121.6 (C−F, $^2J_{C-F}$ = 9.6 Hz)^{enol}, 116.6 (C−F, $^2J_{C-F}$ = 23.9 Hz), 116.4 (C−F, $^2J_{C-F}$ = 22.7 Hz)^{enol}, 92.58 (C−F, $^4J_{C-F}$ = 14.3 Hz)^{enol}, 61.3, 60.5^{enol}, 49.87 (C−F, $^4J_{C-F}$ = 7.9 Hz), 14.2^{enol}, 14.0.

*Ethyl 3-(3-Fluorophenyl)-3-oxopropanoate (**3ja**).*[29] According to the general procedure, 3-fluoro-*N*-phenyl-*N*-tosylbenzamide (110.8 mg, 0.3 mmol) afforded ethyl 3-(3-fluorophenyl)-3-oxopropanoate (**3ja**) (55.5 mg, 0.26 mmol, 88%) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 25% enol tautomer) δ [12.55 (s, 0.25H), 5.65 (s, 0.25H), 3.97 (s, 1.5H),], 7.74−7.34 (m, 3H), [7.32−7.26 (m, 0.75H), 7.17−7.12 (m, 0.25H)], [4.27 (q, J = 7.1 Hz, 0.5H), 4.21 (q, J = 7.1 Hz, 1.5H)], [1.33 (t, J = 7.1 Hz, 0.75H), 1.25 (t, J = 7.1 Hz, 2.25H)]; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, including 25% enol tautomer) δ 191.3 (C−F, $^4J_{C-F}$ = 2.2 Hz), 173.0^{enol}, 169.8 (C−F, $^6J_{C-F}$ = 2.6 Hz)^{enol}, 167.1, 162.8 (C−F, $^1J_{C-F}$ = 248.2 Hz), 162.8 (C−F, $^1J_{C-F}$ = 247.0 Hz)^{enol}, 138.0 (C−F, $^3J_{C-F}$ = 6.3 Hz), 135.7 (C−F, $^3J_{C-F}$ = 7.9 Hz)^{enol}, 130.5 (C−F, $^3J_{C-F}$ = 7.6 Hz), 130.1 (C−F, $^3J_{C-F}$ = 8.1 Hz)^{enol}, 124.3 (C−F, $^4J_{C-F}$ = 3.0 Hz), 121.6 (C−F, $^4J_{C-F}$ = 3.0 Hz)^{enol}, 120.8 (C−F, $^2J_{C-F}$ = 21.4 Hz), 118.0 (C−F, $^2J_{C-F}$ = 21.4 Hz)^{enol}, 115.2 (C−F, $^2J_{C-F}$ = 22.7 Hz), 113.1 (C−F, $^2J_{C-F}$ = 23.9 Hz)^{enol}, 88.2^{enol}, 61.6, 60.5^{enol}, 46.0, 14.2^{enol}, 14.02.

*Ethyl 3-(4-Fluorophenyl)-3-oxopropanoate (**3ka**).*[25] According to the general procedure, 4-fluoro-*N*-phenyl-*N*-tosylbenzamide (110.8 mg, 0.3 mmol) afforded ethyl 3-(4-fluorophenyl)-3-oxopropanoate (**3ka**) (55.5 mg, 0.26 mmol, 88%) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 16% enol tautomer) δ [12.61 (s, 0.16H), 5.60 (s, 0.16H), 3.96 (s, 1.68H)], [7.97 (dd, J = 8.8, 5.4 Hz, 1.68H), 7.76 (dd, J = 8.8, 5.4 Hz, 0.32H)], [7.14 (t, J = 8.6 Hz, 1.68H), 7.09 (t, J = 8.6 Hz, 0.32H)], [4.26 (q, J = 7.1 Hz, 0.32H), 4.20 (q, J = 7.1 Hz, 1.68H)], [1.32 (t, J = 7.1 Hz, 0.48H), 1.24 (t, J = 7.1 Hz, 2.52H)]; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, including 16% enol tautomer) δ 190.9, 173.1^{enol}, 170.3^{enol}, 167.3, 166.0 (C−F, $^1J_{C-F}$ = 255.8 Hz), 164.0 (C−F, $^1J_{C-F}$ = 252.0 Hz)^{enol}, 132.5 (C−F, $^4J_{C-F}$, J = 3.0 Hz), 131.2 (C−F, $^2J_{C-F}$ = 9.5 Hz), 129.6 (C−F, $^4J_{C-F}$ = 3.1 Hz)^{enol}, 128.2 (C−F, $^3J_{C-F}$ = 8.8 Hz)^{enol}, 115.9 (C−F, $^2J_{C-F}$ = 22.7 Hz), 115.6 (C−F, $^2J_{C-F}$ = 21.4 Hz)^{enol}, 87.1^{enol}, 61.5, 60.4^{enol}, 45.9, 14.3^{enol}, 14.0.

*Ethyl 3-(3-Iodophenyl)-3-oxopropanoate (**3la**).*[30] According to the general procedure, 3-iodo-*N*-phenyl-*N*-tosylbenzamide (143.2 mg, 0.3 mmol) afforded ethyl 3-(3-iodophenyl)-3-oxopropanoate (**3la**) (79.2 mg, 0.25 mmol, 83%) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 26% enol tautomer) δ [12.52 (s, 0.26H), 5.62 (s, 0.26H), 3.94 (s, 1.48H),], [8.26 (s, 0.74H), 8.10 (s, 0.26H)], [7.93−7.85 (m, 1.48H), 7.79−7.69 (m, 0.52H)], [7.22 (t, J = 7.8 Hz, 0.74H), 7.14 (t, J = 7.9 Hz, 0.26H)], [4.26 (q, J = 7.1 Hz, 0.52H),

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4.21 (q, J = 7.1 Hz, 1.48H)], [1.33 (t, J = 7.1 Hz, 0.78H), 1.25 (t, J = 7.1 Hz, 1.22H)]; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, including 26% enol tautomer) δ 191.1, 172.9^{enol}, 169.5^{enol}, 167.0, 142.4, 139.9^{enol}, 137.7^{enol}, 137.4, 135.4^{enol}, 135.0, 130.4, 130.2^{enol}, 127.6, 125.2^{enol}, 94.5, 94.2^{enol}, 88.2^{enol}, 61.6, 60.5^{enol}, 45.8, 14.3^{enol}, 14.1.

*Ethyl 3-(4-Iodophenyl)-3-oxopropanoate (**3ma**).*[29] According to the general procedure, 4-iodo-*N*-phenyl-*N*-tosylbenzamide (143.2 mg, 0.3 mmol) afforded ethyl 3-(4-iodophenyl)-3-oxopropanoate (**3ma**) (77.3 mg, 0.24 mmol, 81%) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^1H NMR (500 MHz, $CDCl_3$, including 24% enol tautomer) δ [12.54 (s, 0.24H), 5.64 (s, 0.24H), 3.94 (s, 1.52H)], [7.84 (d, J = 8.6 Hz, 1.52H), 7.75 (d, J = 8.6 Hz, 0.48H)], [7.64 (d, J = 8.6 Hz, 1.52H), 7.48 (d, J = 8.6 Hz, 0.48H)], [4.26 (q, J = 7.1 Hz, 0.48H), 4.20 (q, J = 7.1 Hz, 1.52H)], [1.33 (t, J = 7.1 Hz, 0.72H), 1.25 (t, J = 7.1 Hz, 2.28H)]; $^{13}C\{^1H\}$ NMR (126 MHz, including 24% enol tautomer) δ 191.8, 173.0^{enol}, 170.3^{enol}, 167.1, 138.1, 137.7^{enol}, 135.2, 132.9^{enol}, 129.8, 127.5^{enol}, 102.0, 97.9^{enol}, 87.7^{enol}, 61.6, 60.5^{enol}, 45.8, 14.3^{enol}, 14.1.

*Ethyl 3-(4-Cyanophenyl)-3-oxopropanoate (**3na**).*[29] According to the general procedure, 4-cyano-*N*-phenyl-*N*-tosylbenzamide (112.9 mg, 0.3 mmol) afforded ethyl 3-(4-cyanophenyl)-3-oxopropanoate (**3na**) (41.1 mg, 0.19 mmol, 63%) as a white solid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): mp 65−66 °C; ^1H NMR (500 MHz, $CDCl_3$, including 46% enol tautomer) δ [12.55 (s, 0.46H), 5.72 (s, 0.46H), 4.00 (s, 1.08H)], [8.04 (d, J = 8.6 Hz, 1.08H), 7.86 (d, J = 8.7 Hz, 0.92H)], [7.79 (d, J = 8.6 Hz, 1.08H), 7.71 (d, J = 8.6 Hz, 0.92H)], [4.28 (q, J = 7.1 Hz, 0.92H), 4.21 (q, J = 7.1 Hz, 1.08H)], [1.34 (t, J = 7.1 Hz, 1.38H), 1.25 (t, J = 7.1 Hz, 1.62H)]; ^{13}C NMR (126 MHz, including 46% enol tautomer) δ $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, including 46% enol tautomer) δ 191.3, 172.7^{enol}, 168.6^{enol}, 166.7, 138.9, 137.6^{enol}, 132.6, 132.3^{enol}, 128.9, 126.5^{enol}, 118.2^{enol}, 117.7, 117.0, 114.4^{enol}, 89.7^{enol}, 61.8, 60.8^{enol}, 46.0, 14.2^{enol}, 14.0.

*Ethyl 3-(4-Nitrophenyl)-3-oxopropanoate (**3oa**).*[31] According to the general procedure, 4-nitro-*N*-phenyl-*N*-tosylbenzamide (118.9 mg, 0.3 mmol) afforded ethyl 3-(4-nitrophenyl)-3-oxopropanoate (**3oa**) (34.9 mg, 0.15 mmol, 49%) as a yellow solid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): mp 69−70 °C; ^1H NMR (500 MHz, $CDCl_3$, including 53% enol tautomer) δ [12.56 (s, 0.53H), 5.76 (s, 0.53H), 4.04 (s, 0.94H)], [8.33 (d, J = 8.9 Hz, 0.94H), 8.27 (d, J = 8.9 Hz, 1.06H)], [8.11 (d, J = 8.9 Hz, 0.94H), 7.93 (d, J = 9.0 Hz, 1.06H)], [4.30 (q, J = 7.1 Hz, 1.06H), 4.22 (q, J = 7.1 Hz, 0.94H)], [1.35 (t, J = 7.1 Hz, 1.59H), 1.26 (t, J = 7.1 Hz, 1.41H)]; $^{13}C\{^1H\}$ NMR (126 MHz, including 53% enol tautomer) δ 191.1, 172.6^{enol}, 168.3^{enol}, 166.7, 150.6, 149.2^{enol}, 140.3, 139.3^{enol}, 129.6, 126.9^{enol}, 124.0, 123.7^{enol}, 90.2^{enol}, 61.8, 60.9^{enol}, 46.2, 14.2^{enol}, 14.0.

*Ethyl 3-(Naphthalen-2-yl)-3-oxopropanoate (**3pa**).*[32] According to the general procedure, *N*-phenyl-*N*-tosyl-2-naphthamide (120.5 mg, 0.3 mmol) afforded ethyl 3-(naphthalen-2-yl)-3-oxopropanoate (**3pa**) (62.5 mg, 0.26 mmol, 86%) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^1H NMR (500 MHz, $CDCl_3$, including 20% enol tautomer) δ [12.71 (s, 0.2H), 5.81 (s, 0.2H), 4.12 (s, 1.6H)], [8.45 (s, 0.8H), 8.36 (s, 0.2H)], 8.05−7.75 (m, 4H), 7.64−7.49 (m, 2H), 5.81 (s, 1H), [4.30 (q, J = 7.1 Hz, 0.4H), 4.24 (q, J = 7.1 Hz, 1.6H)], [1.36 (t, J = 7.1 Hz, 0.6H), 1.27 (t, J = 7.1 Hz, 2.4H)]; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, including 20% enol tautomer) δ 192.5, 173.2^{enol}, 171.2^{enol}, 167.6, 135.8, 134.6^{enol}, 133.4, 132.8^{enol}, 132.4, 130.6, 129.7, 129.0^{enol}, 128.9, 128.7, 128.2^{enol}, 127.8, 127.7^{enol}, 127.6^{enol}, 127.0, 126.69^{enol}, 126.66^{enol}, 123.8, 122.5^{enol}, 87.9^{enol}, 61.5, 60.4^{enol}, 46.1, 14.3^{enol}, 14.1.

*Ethyl 3-Oxo-3-(pyridin-3-yl)propanoate (**3qa**).*[28] According to the general procedure, *N*-phenyl-*N*-tosylnicotinamide (105.7 mg, 0.3 mmol) afforded ethyl 3-(naphthalen-2-yl)-3-oxopropanoate (**3qa**) (35.9 mg, 0.19 mmol, 62%) as a yellow liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^1H NMR (500 MHz, $CDCl_3$, including 34% enol tautomer) δ [12.54 (s, 0.34H), 5.68 (s, 0.34H), 3.99 (s, 1.32H)], [9.13 (d, J = 1.5 Hz, 0.66H), 8.97 (d, J = 1.4 Hz, 0.34H)], [8.79 (dd, J = 4.8, 1.5 Hz, 0.66H), 8.66 (dd, J = 4.8, 1.4 Hz, 0.34H)], [8.25−8.19 (m, 0.66H), 8.06−8.01 (m, 0.34H)], [7.46−7.40 (m, 0.66H), 7.38−7.32 (m, 0.34H)], [4.26 (q, J = 7.1 Hz, 0.68H), 4.20 (q, J = 7.1 Hz, 1.32H)], [1.32 (t, J = 7.1 Hz, 1.02H), 1.24 (t, J = 7.1 Hz, 1.98H)]; $^{13}C\{^1H\}$ NMR (126 MHz, including 34% enol tautomer) δ 191.4, 172.7^{enol}, 168.7^{enol}, 166.8, 154.0, 151.8^{enol}, 149.9, 147.4^{enol}, 135.8, 133.4^{enol}, 131.4, 129.3^{enol}, 123.7, 123.3^{enol}, 88.6^{enol}, 61.7, 60.6^{enol}, 46.0, 14.2^{enol}, 14.0.

*Ethyl 3-(Furan-3-yl)-3-oxopropanoate (**3ra**).*[30] According to the general procedure, *N*-phenyl-*N*-tosylfuran-3-carboxamide (102.4 mg, 0.3 mmol) afforded ethyl 3-(furan-3-yl)-3-oxopropanoate (**3ra**) (49.7 mg, 0.27 mmol, 91%) as a brown liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^1H NMR (500 MHz, $CDCl_3$, including 12% enol tautomer) δ [12.20 (s, 0.12H), 5.35 (s, 0.12H), 3.75 (s, 1.76H)], [8.10−8.06 (m, 0.88H), 7.90−7.87 (m, 0.12H)], [7.47−7.44 (m, 0.88H), 7.43−7.41 (m, 0.12H)], [6.80−6.76 (m, 0.88H), 6.56−6.55 (m, 0.8 Hz, 0.12H)], 4.26−4.16 (m, 2H), [1.31 (t, J = 7.1 Hz, 0.36H), 1.25 (t, J = 7.1 Hz, 2.64H)]; $^{13}C\{^1H\}$ NMR (126 MHz, including 12% enol tautomer) δ 186.4, 172.8^{enol}, 166.9^{enol}, 166.2, 148.1, 144.5, 143.9^{enol}, 143.5^{enol}, 127.2, 121.8^{enol}, 108.7, 107.4^{enol}, 87.4^{enol}, 61.6, 60.2^{enol}, 47.6, 14.3^{enol}, 14.0.

*Butyl 3-Oxo-3-phenylpropanoate (**3ab**).*[33] According to the general procedure, *N*-phenyl-*N*-tosylbenzamide (105.4 mg, 0.3 mmol) afforded butyl 3-oxo-3-phenylpropanoate (**3ab**) (54.9 mg, 0.25 mmol, 83% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^1H NMR (500 MHz, $CDCl_3$, including 19% enol tautomer) δ [12.59 (s, 0.19H), 5.67 (s, 0.19H), 3.99 (s, 1.62H)], [7.94 (d, J = 7.4 Hz, 1.62H), 7.78 (d, J = 7.2 Hz, 0.38H)], 7.63−7.39 (m, 3H), [4.21 (t, J = 6.7 Hz, 0.38H), 4.15 (t, J = 6.7 Hz, 1.62H)], 1.72−1.55 (m, 2H), 1.47−1.27 (m, 2H), [0.96 (t, J = 7.4 Hz, 0.57H), 0.88 (t, J = 7.4 Hz, 2.43H)]; $^{13}C\{^1H\}$ NMR (126 MHz, including 19% enol tautomer) δ 192.5, 173.3^{enol}, 171.4^{enol}, 167.6, 136.0, 133.7, 133.4^{enol}, 131.2^{enol}, 128.7, 128.50^{enol}, 128.48, 126.0^{enol}, 87.4^{enol}, 65.3, 64.2^{enol}, 46.0, 30.7^{enol}, 30.5, 19.1^{enol}, 19.0, 13.7^{enol}, 13.6.

*Isopropyl 3-Oxo-3-phenylpropanoate (**3ac**).*[34] According to the general procedure, *N*-phenyl-*N*-tosylbenzamide (105.4 mg, 0.3 mmol) afforded isopropyl 3-oxo-3-phenylpropanoate (**3ac**) (55.7 mg, 0.27 mmol, 90% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^1H NMR (500 MHz, $CDCl_3$, including 17% enol tautomer) δ [12.66 (s, 0.17H), 5.63 (s, 0.17H), 3.95 (s, 1.66H)], [7.94 (d, J = 7.2 Hz, 1.66H), 7.77 (d, J = 7.0 Hz, 0.34H)], 7.62−7.37 (m, 3H), 5.18−5.03 (m, 1H), [1.31 (d, J = 6.3 Hz, 1.02H), 1.22 (d, J = 6.3 Hz, 4.98H); $^{13}C\{^1H\}$ NMR (126 MHz, including 17% enol tautomer) δ 192.6, 172.8^{enol}, 171.3^{enol}, 167.0, 136.1, 133.6, 133.5^{enol}, 131.1^{enol}, 128.7, 128.5^{enol}, 128.4, 126.0^{enol}, 87.8^{enol}, 69.0, 67.8^{enol}, 46.3, 21.9^{enol}, 21.6.

*tert-Butyl 3-Oxo-3-phenylpropanoate (**3ad**).*[34] According to the general procedure, *N*-phenyl-*N*-tosylbenzamide (105.4 mg, 0.3 mmol) afforded *tert*-butyl 3-oxo-3-phenylpropanoate (**3ad**) (60.8 mg, 0.28 mmol, 92% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^1H NMR (500 MHz, $CDCl_3$, including 13% enol tautomer) δ [12.73 (s, 0.13H), 5.58 (s, 0.13H), 3.89 (s, 1.74H)], [7.94 (d, J = 7.4 Hz, 1.74H), 7.75 (d, J = 7.1 Hz, 0.26H)], 7.61−7.37 (m, 3H), [1.54 (s, 1.17H), 1.43 (s, 7.83H)]; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, including 13% enol tautomer) δ 193.0, 173.1^{enol}, 170.8^{enol}, 166.7, 136.2, 133.7^{enol}, 133.5, 130.9^{enol}, 128.7, 128.4, 125.9^{enol}, 88.9, 82.0^{enol}, 81.1^{enol}, 47.4, 28.3^{enol}, 27.9.

*Benzyl 3-Oxo-3-phenylpropanoate (**3ae**).*[33] According to the general procedure, *N*-phenyl-*N*-tosylbenzamide (105.4 mg, 0.3 mmol) afforded benzyl 3-oxo-3-phenylpropanoate (**3ae**) (51.9 mg, 0.20 mmol, 68% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^1H NMR (500 MHz, $CDCl_3$, including 20% enol tautomer) δ [12.53 (s, 0.2H), 5.76 (s, 0.2H), 4.06 (s, 1.6H)], [7.94 (d, J = 7.2 Hz, 1.6H), 7.80 (d, J = 7.2 Hz, 0.4H)], 7.63−7.30 (m, 8H), [5.27 (s, 0.4H), 5.21 (s, 1.6H)]; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, including 20% enol tautomer) δ 192.3, 172.9^{enol}, 171.8^{enol}, 167.3, 136.0, 135.8^{enol}, 135.4, 133.8, 133.3^{enol}, 131.4^{enol}, 128.8, 128.64^{enol}, 128.56, 128.50, 128.4, 128.3, 128.2^{enol}, 126.1^{enol}, 87.2^{enol}, 67.2, 66.1^{enol}, 45.9.

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*Ethyl 2-Methyl-3-oxo-3-phenylpropanoate (**3af**).*[35] According to the general procedure, *N*-phenyl-*N*-tosylbenzamide (105.4 mg, 0.3 mmol) afforded ethyl 2-methyl-3-oxo-3-phenylpropanoate (**3af**) (30.9 mg, 0.15 mmol, 50% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 7.3 Hz, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.48 (q, J = 7.5 Hz, 2H), 4.38 (q, J = 7.1 Hz, 1H), 4.15 (q, J = 7.1 Hz, 2H), 1.50 (d, J = 7.1 Hz, 3H), 1.17 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 195.9, 170.9, 135.9, 133.4, 128.7, 128.6, 61.4, 48.4, 13.9, 13.7.

*Ethyl 2-Benzoylbutanoate (**3ag**).*[35] According to the general procedure, *N*-phenyl-*N*-tosylbenzamide (105.4 mg, 0.3 mmol) afforded ethyl 2-benzoylbutanoate (**3ag**) (41.6 mg, 0.19 mmol, 63% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 7.3 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.3 Hz, 2H), 4.22 (t, J = 7.2 Hz, 1H), 4.18−4.12 (m, 2H), 2.09−2.00 (m, 2H), 1.17 (t, J = 7.1 Hz, 3H), 1.00 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 195.2, 170.0, 136.4, 133.4, 128.7, 128.5, 61.3, 55.9, 22.4, 14.0, 12.1.

*tert-Butyl 2-Methyl-3-oxo-3-phenylpropanoate (**3ah**).*[39] According to the general procedure, *N*-phenyl-*N*-tosylbenzamide (105.4 mg, 0.3 mmol) afforded *tert*-butyl 2-methyl-3-oxo-3-phenylpropanoate (**3ah**) (60.4 mg, 0.26 mmol, 86% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 4.25 (q, J = 7.0 Hz, 1H), 1.44 (d, J = 7.1 Hz, 3H), 1.33 (s, 9H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 196.1, 170.0, 136.2, 133.2, 128.6, 128.5, 81.7, 49.5, 27.7, 13.4.

*Ethyl 3-Oxoheptanoate (**5aa**).*[36] According to the general procedure, *N*-phenyl-*N*-tosylpentanamide (99.4 mg, 0.3 mmol) afforded ethyl 3-oxoheptanoate (**5aa**) (33.6 mg, 0.20 mmol, 65% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 12% enol tautomer) δ [12.09 (s, 0.12H), 4.96 (s, 0.12H), 3.42 (s, 1.76H)], 4.22−4.15 (m, 2H), [2.53 (t, J = 7.4 Hz, 1.76H), 2.19 (t, J = 7.4 Hz, 0.24H)], 1.63−1.52 (m, 2H), 1.39−1.22 (m, 5H), 0.96−0.85 (m, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, including 12% enol tautomer) δ 202.9, 191.8^{enol}, 179.0^{enol}, 167.2, 88.9^{enol}, 61.3, 59.9^{enol}, 49.3, 42.7, 34.7^{enol}, 28.3^{enol}, 25.5, 22.13^{enol}, 22.10, 14.2^{enol}, 14.1, 13.8, 13.7^{enol}.

*Ethyl 3-Oxodecanoate (**5ba**).*[36] According to the general procedure, *N*-phenyl-*N*-tosyloctanamide (112.1 mg, 0.3 mmol) afforded ethyl 3-oxodecanoate (**5ba**) (47.6 mg, 0.22 mmol, 74% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 10% enol tautomer) δ [12.09 (s, 0.1H), 4.96 (s, 0.1H), 3.42 (s, 1.8H)], 4.19 (q, J = 7.1 Hz, 2H), [2.52 (t, J = 7.4 Hz, 1.8H), 2.18 (t, J = 7.4 Hz, 0.2H), 1.66−1.50 (m, 2H), 1.34−1.18 (m, 11H), 0.87 (t, J = 6.9 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 203.0, 167.2, 61.3, 49.3, 43.0, 31.6, 29.0, 28.9, 23.4, 22.6, 14.1, 14.0.

*Ethyl 3-Oxoundecanoate (**5ca**).*[36] According to the general procedure, *N*-phenyl-*N*-tosylnonanamide (116.3 mg, 0.3 mmol) afforded ethyl 3-oxoundecanoate (**5ca**) (56.5 mg, 0.25 mmol, 75% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 10% enol tautomer) δ [12.09 (s, 0.1H), 4.96 (s, 0.1H), 3.42 (s, 1.8H)], 4.19 (q, J = 7.1 Hz, 2H), [2.52 (t, J = 7.4 Hz, 1.8H), 2.18 (t, J = 7.4 Hz, 0.2H)], 1.64−1.51 (m, 2H), 1.40−1.14 (m, 13H), 0.87 (t, J = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, including 10% enol tautomer) δ 203.0, 179.0^{enol},172.7^{enol}, 167.2, 88.9^{enol}, 61.3, 59.9^{enol}, 49.3, 43.0, 35.0^{enol}, 31.8, 29.3, 29.2^{enol}, 29.11^{enol}, 29.07, 29.03^{enol}, 28.99, 26.2^{enol}, 23.4, 22.6, 14.2^{enol}, 14.1, 14.0.

*Ethyl 3-Oxo-5-phenylpentanoate (**5da**).*[31] According to the general procedure, *N*,3-diphenyl-*N*-tosylpropanamide (113.9 mg, 0.3 mmol) afforded ethyl 3-oxo-5-phenylpentanoate (**5da**) (50.9 mg, 0.23 mmol, 77% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 10% enol tautomer) δ [12.17 (s, 0.1H), 4.98 (s, 0.1H), 3.43 (s, 1.8H)], 7.32−7.27 (m, J = 7.4 Hz, 2H), 7.24−7.16 (m, 3H), 4.19 (q, J = 7.1 Hz, 2H), 2.99−2.84 (m, 4H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$,) δ 201.8, 167.1, 140.5, 128.5, 128.3, 126.2, 61.4, 49.4, 44.5, 29.4, 14.1.

*Ethyl 3-Oxo-6-phenylhexanoate (**5ea**).*[37] According to the general procedure, *N*,4-Diphenyl-*N*-tosylbutanamide (118.1 mg, 0.3 mmol) afforded ethyl 3-oxo-6-phenylhexanoate (**5ea**) (54.1 mg, 0.23 mmol, 77% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1); ethyl 4-phenylbutanoate (57.7 mg, 0.30 mmol) afforded **5ea** (23.4 mg, 0.10 mmol, 33% yield) as a colorless liquid: ^{1}H NMR (500 MHz, $CDCl_3$, including 10% enol tautomer) δ [12.15 (s, 0.1H), 5.00 (s, 0.1H), 3.41 (s, 1.8H)], 7.34−7.25 (m, 2H), 7.23−7.13 (m, 3H), 4.19 (q, J = 7.1 Hz, 2H), 2.64 (t, J = 7.6 Hz, 2H), [2.56 (t, J = 7.3 Hz, 1.8H), 2.23 (t, J = 7.3 Hz, 0.2H)], 2.00−1.88 (m, 2H), 1.33−1.23 (m, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 202.5, 167.2, 141.3, 128.44, 128.41, 126.0, 61.3, 49.3, 42.1, 34.8, 24.9, 14.1.

*Ethyl 3-Cyclohexyl-3-oxopropanoate (**5fa**).*[31] According to the general procedure, *N*-phenyl-*N*-tosylcyclohexanecarboxamide (107.3 mg, 0.3 mmol) afforded ethyl 3-cyclohexyl-3-oxopropanoate (**5fa**) (42.8 mg, 0.22 mmol, 72% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 13% enol tautomer) δ [12.13 (s, 0.13H), 4.94 (s, 0.13H), 3.46 (s, 1.74H)], 4.18 (q, J = 7.1 Hz, 2H), 2.50−2.40 (m, 1H), 1.92−1.61 (m, 5H), 1.41−1.13 (m, 8H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, including 13% enol tautomer) δ 205.9, 182.7^{enol}, 173.1^{enol}, 167.4, 86.9^{enol}, 61.2, 59.9^{enol}, 50.9, 47.3, 43.5^{enol}, 29.9^{enol}, 28.2, 25.9^{enol}, 25.7, 25.5, 14.3^{enol}, 14.1.

*Butyl 3-Oxo-6-phenylhexanoate (**5eb**).* According to the general procedure, *N*,4-diphenyl-*N*-tosylbutanamide (118.1 mg, 0.3 mmol) afforded butyl 3-oxo-6-phenylhexanoate (**5eb**) (55.9 mg, 0.21 mmol, 71% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 9% enol tautomer) δ [12.15 (s, 0.09H), 5.00 (s, 0.09H), 3.42 (s, 1.82H)], 7.33−7.27 (m, 2H), 7.23−7.15 (m, 3H), 4.14 (t, J = 6.7 Hz, 2H), 2.65 (t, J = 7.6 Hz, 2H), [2.56 (t, J = 7.3 Hz, 1.82H), 2.24 (t, J = 7.3 Hz, 0.18H)], 1.99−1.90 (m, 2H), 1.68−1.59 (m, 2H), 1.44−1.33 (m, 2H), 0.94 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 202.5, 167.3, 141.3, 128.45, 128.41, 126.0, 65.2, 49.3, 42.1, 34.8, 30.5, 24.9, 19.0, 13.7; HRMS (FD-TOF) m/z [M]$^+$ calcd for $C_{16}H_{22}O_3$ 262.1563, found 262.1563.

*Isopropyl 3-Oxo-6-phenylhexanoate (**5ec**).* According to the general procedure, *N*,4-diphenyl-*N*-tosylbutanamide (118.1 mg, 0.3 mmol) afforded isopropyl 3-oxo-6-phenylhexanoate (**5ec**) (52.1 mg, 0.21 mmol, 70% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 9% enol tautomer) δ [12.22 (s, 0.09H), 4.96 (s, 0.09H), 3.38 (s, 1.82H)], 7.32−7.26 (m, 2H), 7.23−7.15 (m, 3H), 5.11−5.00 (m, 1H), 2.64 (t, J = 7.6 Hz, 2H), [2.55 (t, J = 7.3 Hz, 1.82H), 2.23 (t, 0.18H)], 2.00−1.89 (m, 2H), 1.31−1.20 (m, 6H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 202.7, 166.7, 141.4, 128.44, 128.40, 126.0, 69.0, 49.7, 42.1, 34.8, 24.8, 21.7; HRMS (FD-TOF) m/z [M]$^+$ calcd for $C_{15}H_{20}O_3$ 248.1407, found 248.1399.

*tert-Butyl 3-Oxo-6-phenylhexanoate (**5ed**).*[38] According to the general procedure, *N*,4-diphenyl-*N*-tosylbutanamide (118.1 mg, 0.3 mmol) afforded *tert*-butyl 3-oxo-6-phenylhexanoate (**5ed**) (60.6 mg, 0.23 mmol, 77% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 6% enol tautomer) δ [12.28 (s, 0.06H), 4.91 (s, 0.06H), 3.32 (s, 1.88H)], 7.29 (t, J = 7.5 Hz, 2H), 7.22−7.16 (m, 3H), 2.64 (t, J = 7.6 Hz, 2H), 2.54 (t, J = 7.3 Hz, 2H), 1.98−1.90 (m, 2H), 1.46 (s, 9H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 203.0, 166.4, 141.4, 128.45, 128.40, 126.0, 81.9, 50.7, 42.0, 34.9, 27.9, 24.9.

*Benzyl 3-Oxo-6-phenylhexanoate (**5ee**).* According to the general procedure, *N*,4-diphenyl-*N*-tosylbutanamide (118.1 mg, 0.3 mmol) afforded benzyl 3-oxo-6-phenylhexanoate (**5ee**) (64.0 mg, 0.22 mmol, 72% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^{1}H NMR (500 MHz, $CDCl_3$, including 9% enol tautomer) δ [12.08 (s, 0.09H), 5.08 (s, 0.09H), 3.48 (s, 1.82H)], 7.42−7.33 (m, 5H), 7.32−7.26 (m, 2H), 7.24−7.15 (m, 3H), [2.19 (s, 0.18H), 5.20 (s, 1.82H), [2.68 (t, J = 7.6 Hz,

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0.18H)2.62 (t, J = 7.6 Hz, 1.82H), [2.54 (t, J = 7.3 Hz, 1.82H), 2.27−2.23 (t, J = 7.3 Hz, 0.18H)], 1.99−1.89 (m, 2H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 202.3, 167.0, 141.3, 135.3, 128.6, 128.5, 128.45, 128.42, 128.40, 126.0, 67.1, 49.3, 42.2, 34.8, 24.8; HRMS (FD-TOF) m/z $[M]^+$ calcd for $C_{19}H_{20}O_3$ 296.1407, found 296.1407.

*tert-Butyl 2-Methyl-3-oxo-6-phenylhexanoate (**5eh**).* According to the general procedure, *N*,4-diphenyl-*N*-tosylbutanamide (118.1 mg, 0.3 mmol) afforded *tert*-butyl 2-methyl-3-oxo-6-phenylhexanoate (**5eh**) (26.5 mg, 0.10 mmol, 32% yield) as a colorless liquid by silica gel column chromatography (eluent: *n*-hexane/EtOAc = 9:1): ^1H NMR (500 MHz, $CDCl_3$) δ 7.34−7.27 (m, 2H), 7.22−7.15 (m, 3H), 3.40 (q, J = 7.1 Hz, 1H), 2.67−2.45 (m, 4H), 1.98−1.90 (m, 2H), 1.43 (s, 9H), 1.28 (d, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 206.0, 169.7, 141.4, 128.4, 128.3, 125.9, 81.6, 53.9, 40.4, 34.9, 27.8, 25.0, 12.6; HRMS (FD-TOF) m/z $[M]^+$ calcd for $C_{17}H_{24}O_3$ 276.1720, found 276.1723.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02868.

^1H and ^{13}C NMR spectra for all products (PDF)

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Notes

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■ REFERENCES

(1) (a) Claisen, L.; Claparĕde, A. A. Condensationen von Ketonen mit Aldehyden. *Ber. Dtsch. Chem. Ges.* **1881**, *20*, 651−654. (b) Bartmess, J. E.; Hays, R. L.; Caldwell, G. The Addition of Carbanions to the Carbonyl Group in the Gas Phase. *J. Am. Chem. Soc.* **1981**, *103*, 1338−1344. (c) Li, J. J. *Name Reactions*; Springer: Berlin, Heidelberg, 2003. (d) Kim, S.-H.; Bae, S.; Ko, E. B.; Park, G. Y.; Lee, E.; Hwang, H. J.; Im, C. Y.; Song, M. Silica Gel-mediated Synthesis of β-Enamino Esters and its Application for the Synthesis of Indeno 4-Hydroxypyridin-2(1H)-Ones. *Bull. Korean Chem. Soc.* **2019**, *40*, 262−269.

(2) (a) Morris, J.; Wishka, D. G.; Fang, Y. A Cyclodehydration Route to 2-Aminochromones. *Synth. Commun.* **1994**, *24*, 849−858. (b) Yang, D.; Lian, C.-Y.; Yang, H.-F.; Yu, J.-D.; Zhang, D.-W.; Gao, X. Synthesis of γ-Butyrolactams by Photoinduced PhSe Group Transfer Radical Cyclization and Formal Synthesis of (±)-Isocynometrine with Diphenyldiselenide as Promoter. *J. Org. Chem.* **2009**, *74*, 8610−8615. (c) Kobayashi, K.; Kanbe, Y.; Horiuchi, M. Concise synthesis of 3-acetoxy-N,N-dialkylbenzo[b]thiophene-2-carboxamides from 2-ethylsulfanylbenzoates. *Synthesis* **2011**, *21*, 3429−3434. (d) Lou, Y.; Hu, Y.; Lu, J.; Guan, F.; Gong, G.; Yin, Q.; Zhang, X. Dynamic Kinetic Asymmetric Reductive Amination: Synthesis of Chiral Primary β -Amino Lactams. *Angew. Chem., Int. Ed.* **2018**, *57*, 14193−14197.

(3) (a) Turner, J. A.; Jacks, W. S. Acylation of Ester Enolates by *N*-Methoxy-*N*-methylamides: An Effective Synthesis of β-Keto Esters. *J. Org. Chem.* **1989**, *54*, 4229−4231. (b) Inoue, S.; Sato, Y. Reaction of Ethyl (Trimethylgermyl)acetate with Carboxylic Acid Derivatives. *Organometallics* **1990**, *9*, 1325−1326. (c) Katritzky, A. R.; Wang, Z.; Wang, M.; Wilkerson, C. R.; Hall, C. D.; Akhmedov, N. G. Preparation of β-Keto Esters and β-Diketones by C-Acylation/Deacetylation of Acetoacetic Esters and Acetonyl Ketones with 1-Acylbenzotriazoles. *J. Org. Chem.* **2004**, *69*, 6617−6622.

(4) For selected examples, see: (a) Dander, J. E.; Garg, N. K. Breaking Amides using Nickel Catalysis. *ACS Catal.* **2017**, *7*, 1413−1423. (b) Kaiser, D.; Bauer, A.; Lemmerer, M.; Maulide, N. Amide activation: an emerging tool for chemoselective synthesis. *Chem. Soc. Rev.* **2018**, *47*, 7899−7925. (c) Kovács, E.; Rózsa, B.; Csomos, A.; Csizmadia, I. G.; Mucsi, Z. Amide Activation in Ground and Excited States. *Molecules* **2018**, *23*, 2859−2889. (d) Liu, C.; Szostak, M. Decarbonylative cross-coupling of amides. *Org. Biomol. Chem.* **2018**, *16*, 7998−8010. (e) Guo, L.; Rueping, M. Decarbonylative Cross-Couplings: Nickel Catalyzed Functional Group Interconversion Strategies for the Construction of Complex Organic Molecules. *Acc. Chem. Res.* **2018**, *51*, 1185−1195. (f) Kaiser, D.; Bauer, A.; Lemmerer, M.; Maulide, N. Amide activation: an emerging tool for chemoselective synthesis. *Chem. Soc. Rev.* **2018**, *47*, 7899−7925. (g) Sato, T.; Yoritate, M.; Tajima, H.; Chida, N. Total synthesis of complex alkaloids by nucleophilic addition to amides. *Org. Biomol. Chem.* **2018**, *16*, 3864−3875. (h) Huang, P.-Q. Direct Transformations of Amides: Tactics and Recent Progress. *Huaxue Xuebao* **2018**, *76*, 357−365. (i) Bourne-Branchu, Y.; Gosmini, C.; Danoun, G. *N*-Boc-Amides in Cross-Coupling Reactions. *Chem. - Eur. J.* **2019**, *25*, 2663−2674.

(5) For selected examples, see: (a) Ghosh, S. C.; Li, C. C.; Zeng, H. C.; Ngiam, J. S. Y.; Seayad, A. M.; Chen, A. Mesoporous Niobium Oxide Spheres as an Effective Catalyst for the Transamidation of Primary Amides with Amines. *Adv. Synth. Catal.* **2014**, *356*, 475−484. (b) Wu, J.-W.; Wu, Y.-D.; Dai, J.-J.; Xu, H.-J. Benzoic Acid-Catalyzed Transamidation Reactions of Carboxamides, Phthalimide, Ureas and Thioamide with Amines. *Adv. Synth. Catal.* **2014**, *356*, 2429−2436. (c) Nageswara Rao, S.; Chandra Mohan, D.; Adimurthy, S. Chitosan: an efficient recyclable catalyst for transamidation of carboxamides with amines under neat conditions. *Green Chem.* **2014**, *16*, 4122−4126. (d) Liu, Y.; Meng, G.; Liu, R.; Szostak, M. Sterically-controlled intermolecular Friedel-Crafts acylation with twisted amides *via* selective N-C cleavage under mild conditions. *Chem. Commun.* **2016**, *52*, 6841−6844. (e) Baker, E. L.; Yamano, M. M.; Zhou, Y.; Anthony, S. M.; Garg, N. K. A two-step approach to achieve secondary amide transamidation enabled by nickel catalysis. *Nat. Commun.* **2016**, *7*, 11554−11558. (f) Liu, Y.; Shi, S.; Achtenhagen, M.; Liu, R.; Szostak, M. Metal-Free Transamidation of Secondary Amides via Selective N-C Cleavage under Mild Conditions. *Org. Lett.* **2017**, *19*, 1614−1617. (g) Verho, O.; Lati, M. P.; Oschmann, M. A Two-Step Procedure for the Overall Transamidation of 8-Aminoquinoline Amides Proceeding via the Intermediate *N*-Acyl-Boc-Carbamates. *J. Org. Chem.* **2018**, *83*, 4464−4476. (h) Chen, J.; Xia, Y.; Lee, S. Transamidation for the Synthesis of Primary Amides at Room Temperature. *Org. Lett.* **2020**, *22*, 3504−3508. (i) Guo, W.; Huang, J.; Wu, H.; Liu, T.; Luo, Z.; Jian, J.; Zeng, Z. One-pot

transition-metal free transamidation to sterically hindered amides. *Org. Chem. Front.* **2018**, *5*, 2950−2954.
(6) (a) Kita, Y.; Nishii, Y.; Onoue, A.; Mashima, K. Combined Catalytic System of Scandium Triflate and Boronic Ester for Amide Bond Cleavage. *Adv. Synth. Catal.* **2013**, *355*, 3391−3395. (b) Bourne-Branchu, Y.; Gosmini, C.; Danoun, G. Cobalt-Catalyzed Esterification of Amides. *Chem. - Eur. J.* **2017**, *23*, 10043−10047. (c) Wybon, C. C. D.; Mensch, C.; Hollanders, K.; Gadais, C.; Herrebout, W. A.; Ballet, S.; Maes, B. U. W. Zn-Catalyzed *tert*-Butyl Nicotinate-Directed Amide Cleavage as a Biomimic of Metallo-Exopeptidase Activity. *ACS Catal.* **2018**, *8*, 203−218. (d) Wu, H.; Guo, W.; Daniel, S.; Li, Y.; Liu, C.; Zeng, Z. Fluoride-Catalyzed Esterification of Amides. *Chem. - Eur. J.* **2018**, *24*, 3444−3447. (e) Li, G.; Lei, P.; Szostak, M. Transition-Metal-Free Esterification of Amides via Selective N-C Cleavage under Mild Conditions. *Org. Lett.* **2018**, *20*, 5622−5625. (f) Chen, X.; Hu, S.; Chen, R.; Wang, J.; Wu, M.; Guo, H.; Sun, S. Fe-catalyzed esterification of amides *via* C-N bond activation. *RSC Adv.* **2018**, *8*, 4571−4576. (g) Nagae, H.; Hirai, T.; Kato, D.; Soma, S.; Akebi, S.-Y.; Mashima, K. Dinuclear manganese alkoxide complexes as catalysts for C-N bond cleavage of simple tertiary *N*,*N*-dialkylamides to give esters. *Chem. Sci.* **2019**, *10*, 2860−2868. (h) Ye, D.; Liu, Z.; Chen, H.; Sessler, J. L.; Lei, C. Cesium Carbonate Catalyzed Esterification of *N*-Benzyl-*N*-Boc-amides under Ambient Conditions. *Org. Lett.* **2019**, *21*, 6888−6892.
(7) (a) Meng, G.; Szostak, R.; Szostak, M. Suzuki-Miyaura Cross-Coupling of *N*-Acylpyrroles and Pyrazoles: Planar, Electronically Activated Amides in Catalytic N-C Cleavage. *Org. Lett.* **2017**, *19*, 3596−3599. (b) Gao, Y.; Ji, C.-L.; Hong, X. Ni-mediated C-N activation of amides and derived catalytic transformations. *Sci. China: Chem.* **2017**, *60*, 1413−1424. (c) Liu, X.; Hsiao, C.-C.; Guo, L.; Rueping, M. Cross-Coupling of Amides with Alkylboranes via Nickel-Catalyzed C-N Bond Cleavage. *Org. Lett.* **2018**, *20*, 2976−2979. (d) Boit, T.; Weires, N. A.; Kim, J.; Garg, N. K. Nickel-Catalyzed Suzuki-Miyaura Coupling of Aliphatic Amides. *ACS Catal.* **2018**, *8*, 1003−1008. (e) Wang, S.-R.; Huang, P.-Q. Cross-Coupling of Secondary Amides with Tertiary Amides: The Use of Tertiary Amides as Surrogates of Alkyl Carbanions for Ketone Synthesis. *Chin. J. Chem.* **2019**, *37*, 887−891. (f) Wang, H.; Zhang, S.-Q.; Hong, X. Computational studies on Ni-catalyzed amide C-N bond activation. *Chem. Commun.* **2019**, *55*, 11330−11341. (g) Mehta, M. M.; Boit, T. B.; Dander, J. E.; Garg, N. K. Ni-Catalyzed Suzuki-Miyaura Cross-Coupling of Aliphatic Amides on the Benchtop. *Org. Lett.* **2020**, *22*, 1−5. (h) Buchspies, J.; Rahman, M. M.; Szostak, R.; Szostak, M. *N*-Acylcarbazoles and *N*-Acylindoles: Electronically Activated Amides for N-C(O) Cross-Coupling by N_{lp} to Ar Conjugation Switch. *Org. Lett.* **2020**, *22*, 4703−4709. (i) Xiong, L.; Deng, R.; Liu, T.; Luo, Z.; Wang, Z.; Zhu, X.-F.; Wang, H.; Zeng, Z. Selective C-N Bond Cleavage of *N*-Acylisatins: Towards High Performance Acylation/Arylation/Transamination Reagents. *Adv. Synth. Catal.* **2019**, *361*, 5383−5391.
(8) Chen, J.; Xu, M.; Yu, S.; Xia, Y.; Lee, S. Nickel-Catalyzed Claisen Condensation Reaction between Two Different Amides. *Org. Lett.* **2020**, *22*, 2287−2292.
(9) Chen, J.; Xia, Y.; Lee, S. Coupling of amides with ketones *via* C-N/C-H bond cleavage: a mild synthesis of 1,3-diketones. *Org. Chem. Front.* **2020**, *7*, 2931−2937.
(10) Hama, T.; Culkin, D. A.; Hartwig, J. F. Palladium-Catalyzed Intermolecular α-Arylation of Zinc Amide Enolates under Mild Conditions. *J. Am. Chem. Soc.* **2006**, *128*, 4976−4985.
(11) (a) Palucki, M.; Buchwald, S. L. Palladium-Catalyzed α-Arylation of Ketones. *J. Am. Chem. Soc.* **1997**, *119*, 11108−11109. (b) Fox, J. M.; Huang, X.; Chieffi, A.; Buchwald, S. L. Highly Active and Selective Catalysts for the Formation of α-Aryl Ketones. *J. Am. Chem. Soc.* **2000**, *122*, 1360−1370. (c) Marelli, E.; Renault, Y.; Sharma, S. V.; Nolan, S. P.; Goss, R. J. M. Mild, aqueous α-arylation of ketones: towards new diversification tools for halogenated metabolites and drug molecules. *Chem. - Eur. J.* **2017**, *23*, 3832−3836.
(12) (a) Lee, S.; Beare, N. A.; Hartwig, J. F. Palladium-Catalyzed α-Arylation of Esters and Protected Amino Acids. *J. Am. Chem. Soc.* **2001**, *123*, 8410−8411. (b) Moradi, W. A.; Buchwald, S. L. Palladium-Catalyzed α-Arylation of Esters. *J. Am. Chem. Soc.* **2001**, *123*, 7996−8002. (c) Jørgensen, M.; Lee, S.; Liu, X.; Wolkowski, J. P.; Hartwig, J. F. Efficient Synthesis of α-Aryl Esters by Room-Temperature Palladium-Catalyzed Coupling of Aryl Halides with Ester Enolates. *J. Am. Chem. Soc.* **2002**, *124*, 12557−1265. (d) Hama, T.; Hartwig, J. F. α -Arylation of Esters Catalyzed by the Pd(I) Dimer $\{[P(^tBu)_3]PdBr\}_2$. *Org. Lett.* **2008**, *10*, 1545−1548. (e) Hama, T.; Ge, S.; Hartwig, J. F. Palladium-Catalyzed alpha-Arylation of Zinc Enolates of Esters: Reaction Conditions and Substrate Scope. *J. Org. Chem.* **2013**, *78*, 8250−8266.
(13) Li, X.; Zou, G. Acylative Suzuki coupling of amides: acyl-nitrogen activation via synergy of independently modifiable activating groups. *Chem. Commun.* **2015**, *51*, 5089−5092.
(14) Li, Y.; Wu, H.; Zeng, Z. Palladium-Catalyzed Aerobic Oxidative Coupling of Amides with Arylboronic Acids by Cooperative Catalysis. *Eur. J. Org. Chem.* **2019**, *2019*, 4357−4361.
(15) Luo, Z.; Wu, H.; Li, Y.; Chen, Y.; Nie, J.; Lu, S.; Zhu, Y.; Zeng, Z. Cesium Fluoride and Copper-Catalyzed One-Pot Synthesis of Benzoxazoles via a Site-Selective Amide C-N Bond Cleavage. *Adv. Synth. Catal.* **2019**, *361*, 4117−4125.
(16) Massah, A. R.; Azadi, D.; Aliyan, H.; Momeni, A. R.; Naghash, H. J.; Kazemi, F. An Effifficient Method for the Synthesis of *N*-Acylsulfonamides: One-pot Sulfonylation and Acylation of Primary Arylamines under Solvent-Free Conditions. *Monatsh. Chem.* **2008**, *139*, 233−240.
(17) Lei, P.; Meng, G.; Szostak, M. General Method for the Suzuki-Miyaura Cross-Coupling of Amides Using Commercially Available, Air- and Moisture-Stable Palladium/ NHC (NHC = N-Heterocyclic Carbene) Complexes. *ACS Catal.* **2017**, *7*, 1960−1965.
(18) Shi, S.; Lalancette, R.; Szostak, R.; Szostak, M. Triflamides: Highly Reactive, Electronically Activated *N*-Sulfonyl Amides in Catalytic N-C(O) Amide Cross-Coupling. *Org. Lett.* **2019**, *21*, 1253−1257.
(19) Liu, C.; Liu, Y.; Liu, R.; Lalancette, R.; Szostak, R.; Szostak, M. Palladium-Catalyzed Suzuki-Miyaura Cross-Coupling of N-Mesylamides by N-C Cleavage: Electronic Effffect of the Mesyl Group. *Org. Lett.* **2017**, *19*, 1434−1437.
(20) Cui, M.; Wu, H.; Jian, J.; Wang, H.; Liu, C.; Daniel, S.; Zeng, Z. Palladium-Catalyzed Sonogashira Coupling of Amides: Access to Ynones *via* C-N Bond Cleavage. *Chem. Commun.* **2016**, *52*, 12076−12079.
(21) Shi, S.; Meng, G.; Szostak, M. Synthesis of Biaryls through Nickel-Catalyzed Suzuki-Miyaura Coupling of Amides by Carbon-Nitrogen Bond Cleavage. *Angew. Chem., Int. Ed.* **2016**, *55*, 6959−6963.
(22) Rezayee, N. M.; Samblanet, D. C.; Sanford, M. S. Iron-Catalyzed Hydrogenation of Amides to Alcohols and Amines. *ACS Catal.* **2016**, *6*, 6377−6383.
(23) Massah, A. R.; Asadi, B.; Hoseinpour, M.; Molseghi, A.; Kalbasi, R. J.; Javaherian Naghash, H. A novel and effifficient solvent-free and heterogeneous method for the synthesis of primary, secondary and bis-*N*-acylsulfonamides using metal hydrogen sulfate catalysts. *Tetrahedron* **2009**, *65*, 7696−7705.
(24) Wu, H.; Guo, W.; Daniel, S.; Li, Y.; Liu, C.; Zeng, Z. Fluoride-Catalyzed Esterification of Amides. *Chem. - Eur. J.* **2018**, *24*, 3444−3447.
(25) Chen, S.; Yuan, F.; Zhao, H.; Li, B. *tert*-BuOK-Catalyzed condensation of ethyl diazoacetate to aldehydes and palladium-catalyzed 1,2-hydrogen migration for the synthesis of β-ketoesters under solvent-free conditions. *RSC Adv.* **2013**, *3*, 12616−12620.
(26) Liao, M.; Wang, J. $CuSO_4$-catalyzed diazo decomposition in water: a practical synthesis of β-keto esters. *Tetrahedron Lett.* **2006**, *47*, 8859−8861.
(27) Tarigopula, C.; Thota, G. K.; Balamurugan, R. Efficient Synthesis of Functionalized β-Keto Esters and β-Diketones through Regioselective Hydration of Alkynyl Esters and Alkynyl Ketones by Use of a Cationic NHC-AuI Catalyst. *Eur. J. Org. Chem.* **2016**, *2016*, 5855−5861.

https://dx.doi.org/10.1021/acs.joc.0c02868
J. Org. Chem. 2021, 86, 5943−5953

(28) Baburajan, P.; Elango, K. P. One pot direct synthesis of β-keto esters via carbonylation of aryl halides using cobalt carbon. *Tetrahedron Lett.* **2014**, *55*, 3525−3528.
(29) Song, Z.-L.; Bai, F.; Zhang, B.; Fang, J. Synthesis of Dithiolethiones and Identification of Potential Neuroprotective Agents via Activation of Nrf_2-Driven Antioxidant Enzymes. *J. Agric. Food Chem.* **2020**, *68*, 2214−2231.
(30) Wierenga, W.; Skulnick, H. I. General, efficient, one-step synthesis of β-keto esters. *J. Org. Chem.* **1979**, *44*, 310−311.
(31) Balaji, B. S.; Chanda, B. M. Simple and high yielding syntheses of β-keto esters catalyzed by zeolit. *Tetrahedron* **1998**, *54*, 13237−13252.
(32) Yadav, J.S.; Subba Reddy, B.V.; Eeshwaraiah, B.; Reddy, P.N. Niobium(V) chloride-catalyzed C-H insertion reactions of β-diazoesters: synthesis of β-keto esters. *Tetrahedron* **2005**, *61*, 875−878.
(33) Solhy, A.; Clark, J. H.; Tahir, R.; Sebti, S.; Larzek, M. Transesterifications catalysed by solid, reusable apatite-zinc chloride catalysts. *Green Chem.* **2006**, *8*, 871−874.
(34) McDonald, S. L.; Wang, Q. Selective α-amination and α-acylation of esters and amides via dual reactivity of O-acylhydroxylamines toward zinc enolat. *Chem. Commun.* **2014**, *50*, 2535−2538.
(35) Shneider, O. S.; Pisarevsky, E.; Fristrup, P.; Szpilman, A. M. Oxidative Umpolung α-Alkylation of Ketones. *Org. Lett.* **2015**, *17*, 282−285.
(36) Ganeshapillai, D.; Woo, L. W. L.; Thomas, M. P.; Purohit, A.; Potter, B. V. L. C-3- and C-4-Substituted Bicyclic Coumarin Sulfamates as Potent Steroid Sulfatase Inhibitors. *ACS Omega* **2018**, *3*, 10748−10772.
(37) Liu, H.; Feng, W.; Kee, C. W.; Leow, D.; Loh, W.-T.; Tan, C.-H. Brønsted Base-Catalyzed Tandem Isomerization-Michael Reactions of Alkynes: Synthesis of Oxacycles and Azacycles. *Adv. Synth. Catal.* **2010**, *352*, 3373−3379.
(38) Fleming, I.; Ramarao, C. Decarboxylative elimination of enol triflates as a general synthesis of acetylenes. *Org. Biomol. Chem.* **2004**, *2*, 1504−1510.
(39) Zhang, Z.; Liu, Y.; Gong, M.; Zhao, X.; Zhang, Y.; Wang, J. Palladium-Catalyzed Carbonylation/Acyl Migratory Insertion Sequence. *Angew. Chem., Int. Ed.* **2010**, *49*, 1139−1142.

https://dx.doi.org/10.1021/acs.joc.0c02868
J. Org. Chem. 2021, 86, 5943−5953