Copper-Catalyzed Selective Synthesis of Highly Substituted Pyridones by the Reaction of Enaminones with Alkynes

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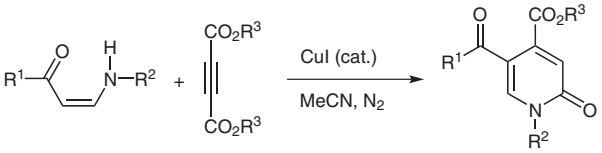
Abstract: An efficient copper-catalyzed selective synthesis of highly functionalized pyridones by the reaction of enaminones with alkynes is reported. The reactions proceed to afford polysubstituted pyridone derivatives in good to high yields using CuI as the catalyst in MeCN under nitrogen.

Key words: copper catalysis, pyridones, regioselective cyclization, enaminones, cascade reactions

Pyridones are important N-containing heterocyclic compounds, which not only represent useful building blocks in the synthesis of natural products but also are key structural units in compounds that exhibit remarkable pharmacological activities.[1] As a result, the development of efficient synthetic methodologies for these heterocycles has become of great interest in organic chemistry.[2] Although many diverse approaches toward pyridone derivatives have been reported,[3] the development of mild, selective, and efficient methods for such compounds is highly desirable. Enaminones are versatile intermediates for the synthesis of heterocycles.[4,5] However, reports concerning the preparation of pyridones starting from enaminones are rare,[6,7] and the substrates employed were those with two substituents at C-3 position. For example, Cacchi et al.[7] reported an effective synthesis of pyridines from enaminones by an intramolecular annulation of *N*-propargylic β-enaminones. There were only two reports on the synthesis of pyridones from the reaction of enaminones and activated alkynes using large excess amount of strong base[6a] or strong acid.[6b] On the other hand, metal-catalyzed methodology for the preparation of pyridones from enaminones has not been disclosed. Furthermore, very little is known about the reactivity of enaminones with a monosubstituent at C-3 position to form heterocycles. During the course of our ongoing study on the development of transition metal-mediated heterocycle-forming protocols using enaminones,[8] we found that pyridones could be selectively prepared from the reaction of C-3 monosubstituted enaminones with alkynes using copper catalyst. Herein, we would like to report these results (Scheme 1).

The reaction of (*Z*)-1-phenyl-3-(phenylamino)prop-2-en-1-one (**1a**) with dimethyl acetylenedicarboxylate (**2a**) was selected as the prototypical case to screen the experimental conditions, and the results are depicted in Table 1. When the reaction was carried out using CuI (20 mol%) as the catalyst in MeCN under nitrogen at 80 °C, the corresponding pyridone **3a** was obtained in 90% isolated yield as the sole product within one hour, and the structure was fully confirmed by X-ray crystal analysis[9] (Table 1, entry 1). Lowering the catalyst loading to 5 mol% resulted in 86% yield, yet the use of 10 mol% of CuI gave a similar result as that of 20 mol% (entries 2, 3). Without the addition of Cu catalyst, **3a** could also be produced; however, much longer reaction time (24 h) was required, and the yield was low (entry 4). Other Cu catalysts gave lower yields or poor selectivity (entries 7–9). Switching to other solvents such as $MeNO_2$, DCE, 1,4-dioxane, toluene, and DMF afforded unsatisfactory results (entries 10–14). It is interesting to note that when the reaction was performed in air, **3a** was obtained in 74% yield, along with 18% yield of pyrrole **4a** (entry 15). Thus, it was clear that the optimized reaction condition for the pyridone formation was to use 10 mol% of CuI as the catalyst and MeCN as the solvent under nitrogen at 80 °C.



Scheme 1 Selective synthesis of pyridones

Having established an effective catalytic system for the selective cyclization reactions, a variety of enaminones were synthesized next to explore the scope of the pyridone forming reaction under the optimized conditions. The representative results are shown in Table 2. The reaction was applicable to various enaminones. The substituent effect at the nitrogen was studied first. Enaminones with electron-donating (4-OMe, 4-Me) aryl groups at nitrogen reacted smoothly with **2a** to give the corresponding pyridones in high yields (Table 2, entries 2, 3) while electron-withdrawing (4-Cl, 4-NO_2) aryl groups afforded the desired products in good or moderate yields (entries 4, 5). Substituents at nitrogen could also be alkyl groups, such as benzyl, butyl, and *tert*-butyl (entries 6–8). It is noteworthy that when *N*-*t*-Bu enaminone **1h** was employed, pyridone **3h** was produced in 43% yield, along with 20% the corresponding pyrrole (entry 8). The regioselective effect of the substituents on carbonyl carbon was also investigat-

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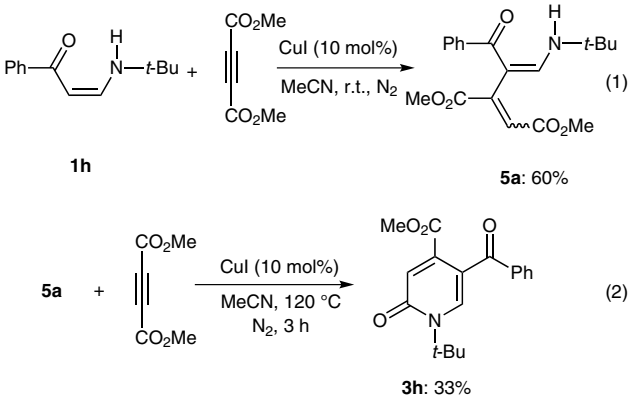
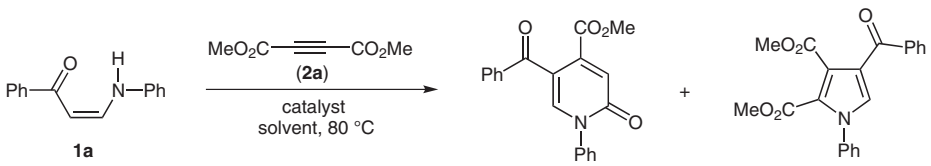
ed. Both the electron-donating (4-OMe, 4-Me) and electron-withdrawing (4-NO_2, 2-Br) aryl groups on carbonyl carbon gave the desired six-membered ring compounds in good to high yields with excellent selectivity (entries 9–12). 1-Naphthyl (**1m**) or 2-thienyl (**1n**) substrates furnished the pyridone derivatives as the only products in high yields (entries 14, 15). Alkyl substituents, such as cyclohexyl and *n*-hexyl, afforded the corresponding **3o** and **3p** in 97% and 85% yield, respectively (entries 15, 16). When diethyl acetylenedicarboxylate (**2b**) was used instead of DMAD to react with **1a**, pyridone **3q** was isolated in 86% yield (entry 17).

To understand the reaction mechanism, the reaction of **1h** with **2a** was carried out using the optimal conditions for pyridone formation at room temperature, and the acyclic intermediate **5a** (*E*/*Z* = 3:5) was produced in 60% yield after 20 hours (Scheme 2, eq. 1). No reaction could be detected even after three hours on treatment of compound **5a** under the standard conditions for pyridone formation. No reaction took place even at a higher reaction temperature of up to 120 °C. Interestingly, when 1.3 equivalents of DMAD were added, compound **5a** was converted into the corresponding **3h** in 33% yield (Scheme 2, eq. 2). This may due to the formation of some active Cu-DMAD species; however, we cannot confirm it at the present stage.



Scheme 2 Formation of intermediate **5a**

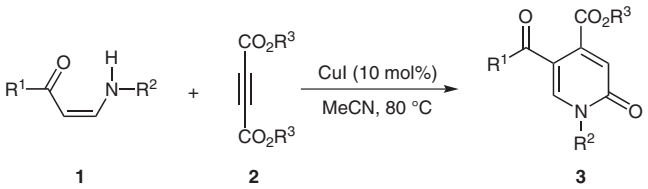
Table 1 Optimization of Reaction Conditions for the Synthesis of **3a**



Entry	Catalyst (mol%)	Solvent	Time (h)	Yield (%)[a] **3a**	Yield (%)[a] **4a**
1	CuI (20)	MeCN	1	90	–
2	CuI (10)	MeCN	1	92	–
3	CuI (5)	MeCN	3	86	–
4	–	MeCN	24	58	–
5	CuI (10)	MeCN	18	–[b]	–
6	CuI (10)	MeCN	6	84[c]	–
7	CuCl (10)	MeCN	4	75	4
8	CuBr (10)	MeCN	3	81	7
9	CuCN (10)	MeCN	7	74	–
10	CuI (10)	$MeNO_2$	24	42	5
11	CuI (10)	DCE	24	72	–
12	CuI (10)	1,4-dioxane	24	70	9
13	CuI (10)	toluene	24	trace	–
14	CuI (10)	DMF	12	49	7
15	CuI (10)	MeCN	6	74[d]	18

[a] Isolated yield. Unless otherwise noted, all reactions were carried out at 80 °C under N_2.
[b] The reaction was carried out at r.t. Product **3a** was not observed.
[c] The reaction temperature was 50 °C.
[d] The reaction was carried out in air.

Table 2 CuI-Catalyzed Selective Synthesis of Pyridones



1 2 3

Entry	1	R^1	R^2	R^3	Time (h)	Yield (%)[a]
1	**1a**	Ph	Ph	Me	3	92 (**3a**)
2	**1b**	Ph	4-$MeOC_6H_4$	Me	4	85 (**3b**)[b]
3	**1c**	Ph	4-MeC_6H_4	Me	4	91 (**3c**)[b]
4	**1d**	Ph	4-ClC_6H_4	Me	12	81 (**3d**)[b]
5	**1e**	Ph	4-$O_2NC_6H_4$	Me	24	52 (**3e**)[b]
6	**1f**	Ph	Bn	Me	6	65 (**3f**)[b]
7	**1g**	Ph	Bu	Me	3	77 (**3g**)[b]
8	**1h**	Ph	*t*-Bu	Me	3	43 (**3h**)[c]
9	**1i**	4-$MeOC_6H_4$	Ph	Me	3	94 (**3i**)[b]
10	**1j**	4-MeC_6H_4	Ph	Me	4	81 (**3j**)[b]
11	**1k**	4-$O_2NC_6H_4$	Ph	Me	12	67 (**3k**)
12	**1l**	2-BrC_6H_4	Ph	Me	24	50 (**3l**)
13	**1m**	1-naphthyl	Ph	Me	2	94 (**3m**)
14	**1n**	2-thienyl	Ph	Me	3	71 (**3n**)
15	**1o**	cyclohexyl	Ph	Me	2	97 (**3o**)
16	**1p**	*n*-hexyl	Ph	Me	3	85 (**3p**)
17	**1a**	Ph	Ph	Et	6	86 (**3q**)

[a] Isolated yield.
[b] Trace amount of pyrrole was isolated.
[c] Along with the corresponding pyrrole in 20% yield.

On the basis of the above results, a plausible reaction mechanism for the pyridone formation is shown in Scheme 3.[10] Enaminone **1** is proposed to be activated via copper complex **6**, which is formed by the replacement of the acidic hydrogen on the amino group. Conjugate addition of **6** with acetylene dicarboxylate affords intermediate **7**, which isomerizes to enaminone **8**. This is followed by intramolecular condensation to deliver the pyridone **3**.

In summary, we have reported an efficient copper-catalyzed synthesis of highly functional pyridones by the reaction of enaminones with alkynes. This methodology provides a facile route for the selective synthesis of substituted pyridones using CuI as the catalyst in MeCN under nitrogen.

All solvents were dried by standard methods and all reactions were carried out under N_2. Unless otherwise noted, all commercial reagents were used without further purification. ^1H and ^{13}C NMR spectra were recorded at 400 MHz, in $CDCl_3$ (with 0.03% TMS) solutions. ^1H NMR spectra were recorded in $CDCl_3$ ($\delta = 7.25$) or with TMS ($\delta = 0.00$) as internal reference; ^{13}C NMR spectra were recorded in $CDCl_3$ ($\delta = 77.00$) or C_6D_6 ($\delta = 128.02$) as internal reference. Mass spectrometric data were obtained by electron ionization (EI, 70 eV), or electrospray ionization (ESI).

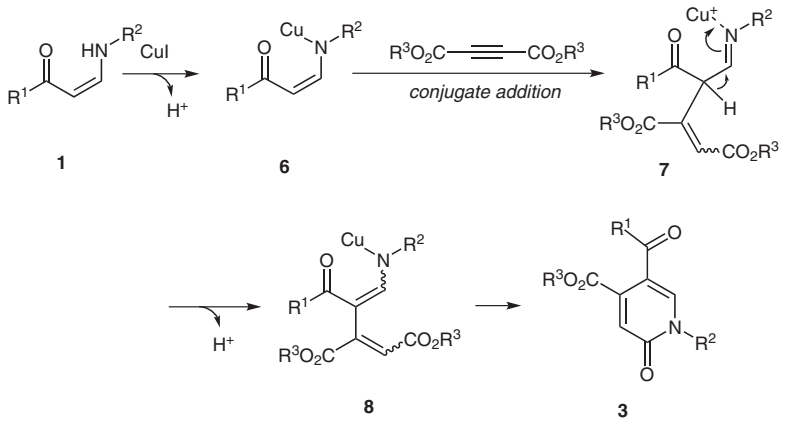
CuI-Catalyzed Synthesis of Pyridones; Methyl 5-Benzoyl-2-oxo-1-phenyl-1,2-dihydropyridine-4-carboxylate (3a); Typical Procedure

(*Z*)-1-Phenyl-3-(phenylamino)prop-2-en-1-one (**1a**; 0.5 mmol), MeCN (5 mL), dimethyl acetylenedicarboxylate (**2a**; 0.65 mmol), and CuI (10 mg, 0.05 mmol) were added successively to a Schlenk tube under N_2. The mixture was stirred and heated to 80 °C for 1 h. After cooling to r.t., the mixture was quenched with H_2O (20 mL) and extracted with EtOAc (3 × 15 mL). The combined organic extracts were washed with brine (15 mL) and dried (Na_2SO_4). The solvent was evaporated under vacuo and the residue was purified by chromatography on silica gel to afford 153 mg (92%) of the pyridone derivative **3a** as a yellow solid; mp 113–114 °C.

^1H NMR ($CDCl_3$/TMS): $\delta = 3.58$ (s, 3 H), 6.89 (s, 1 H), 7.27–7.33 (m, 2 H), 7.34–7.45 (m, 5 H), 7.46–7.53 (m, 1 H), 7.67–7.73 (m, 3 H).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 52.75$, 116.85, 122.06, 126.17, 126.68, 129.04, 129.21, 129.53, 133.02, 136.94, 139.46, 142.88, 143.08, 160.97, 165.64, 191.06.

HMRS: *m*/*z* calcd for $C_{20}H_{15}NO_4$: 333.1001; found: 333.1002.



1 6 7 8 3

Scheme 3 Proposed reaction mechanism

Methyl 5-Benzoyl-1-(4-methoxyphenyl)-2-oxo-1,2-dihydropyridine-4-carboxylate (3b)
Yield: 0.154 g (85%); yellow solid; mp 135–136 °C.

^{1}H NMR ($CDCl_3$/TMS): δ = 3.57 (s, 3 H), 3.74 (s, 3 H), 6.85–6.92 (m, 3 H), 7.17–7.23 (m, 2 H), 7.35–7.42 (m, 2 H), 7.45–7.52 (m, 1 H), 7.66–7.72 (m, 3 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 52.71, 55.48, 114.65, 116.68, 121.83, 127.27, 128.64, 129.01, 132.17, 132.97, 136.95, 142.97, 143.24, 159.88, 161.24, 165.68, 191.08.

HRMS: *m*/*z* calcd for $C_{21}H_{17}NO_5$: 363.1107; found: 363.1109.

Methyl 5-Benzoyl-2-oxo-1-*p*-tolyl-1,2-dihydropyridine-4-carboxylate (3c)
Yield: 0.158 g (91%); pale yellow solid; mp 182–183 °C.

^{1}H NMR ($CDCl_3$/TMS): δ = 2.31 (s, 3 H), 3.58 (s, 3 H), 6.88 (s, 1 H), 7.14–7.24 (m, 4 H), 7.35–7.42 (m, 2 H), 7.45–7.51 (m, 1 H), 7.66–7.72 (m, 3 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 21.05, 52.73, 116.72, 121.93, 125.88, 128.67, 129.04, 130.10, 132.98, 136.93, 136.97, 139.41, 143.03, 143.12, 161.12, 165.71, 191.10.

HRMS: *m*/*z* calcd for $C_{21}H_{17}NO_4$: 347.1158; found: 347.1161.

Methyl 5-Benzoyl-1-(4-chlorophenyl)-2-oxo-1,2-dihydropyridine-4-carboxylate (3d)
Yield: 0.149 g (81%); pale yellow solid; mp 142–143 °C.

^{1}H NMR ($CDCl_3$/TMS): δ = 3.55 (s, 3 H), 6.85 (s, 1 H), 7.21–7.27 (m, 2 H), 7.33–7.42 (m, 4 H), 7.45–7.53 (m, 1 H), 7.62–7.70 (m, 3 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 52.71, 117.05, 121.98, 127.55, 128.65, 128.95, 129.62, 133.06, 135.11, 136.75, 137.73, 142.36, 143.08, 160.72, 165.39, 190.87.

HRMS: *m*/*z* calcd for $C_{20}H_{14}ClNO_4$: 367.0611; found: 367.0613.

Methyl 5-Benzoyl-1-(4-nitrophenyl)-2-oxo-1,2-dihydropyridine-4-carboxylate (3e)
Yield: 0.098 g (52%); pale yellow solid; mp 183–184 °C.

^{1}H NMR ($CDCl_3$/TMS): δ = 3.57 (s, 3 H), 6.94 (s, 1 H), 7.37–7.46 (m, 2 H), 7.50–7.59 (m, 3 H), 7.65–7.74 (m, 3 H), 8.26–8.31 (m, 2 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 52.93, 117.90, 122.50, 124.91, 127.53, 128.84, 129.03, 133.38, 136.72, 141.24, 143.38, 144.33, 147.72, 160.47, 165.16, 190.85.

HRMS: *m*/*z* calcd for $C_{20}H_{14}N_2O_6$: 378.0852; found: 378.0847.

Methyl 5-Benzoyl-1-benzyl-2-oxo-1,2-dihydropyridine-4-carboxylate (3f)
Yield: 0.112 g (65%); yellow solid; mp 122–123 °C.

^{1}H NMR ($CDCl_3$/TMS): δ = 3.52 (s, 3 H), 5.04 (s, 2 H), 6.78 (s, 1H), 7.16–7.27 (m, 5 H), 7.28–7.36 (m, 2 H), 7.42–7.48 (m, 1 H), 7.52–7.58 (m, 2 H), 7.65 (s, 1 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 52.39, 52.58, 116.58, 121.05, 128.18, 128.42, 128.50, 128.93, 128.97, 132.84, 134.88, 136.84, 142.52, 142.68, 161.16, 165.72, 190.86.

HRMS: *m*/*z* calcd for $C_{21}H_{17}NO_4$: 347.1158; found: 347.1159.

Methyl 5-Benzoyl-1-butyl-2-oxo-1,2-dihydropyridine-4-carboxylate (3g)
Yield: 0.12 g (77%); pale yellow solid; mp 63–64 °C.

^{1}H NMR ($CDCl_3$/TMS): δ = 0.87 (t, *J* = 7.3 Hz, 3 H), 1.24–1.34 (m, 2 H), 1.60–1.71 (m, 2 H), 3.52 (s, 3 H), 3.88 (t, *J* = 7.3 Hz, 2 H), 6.76 (s, 1 H), 7.36–7.44 (m, 2 H), 7.47–7.55 (m, 1 H), 7.62–7.68 (m, 3 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 13.44, 19.62, 30.95, 50.09, 52.55, 116.43, 120.96, 128.58, 128.90, 132.85, 137.13, 142.52, 142.66, 161.15, 165.77, 191.14.

HRMS: *m*/*z* calcd for $C_{18}H_{19}NO_4$: 313.1314; found: 313.1317.

Methyl 5-Benzoyl-1-*tert*-butyl-2-oxo-1,2-dihydropyridine-4-carboxylate (3h)
Yield: 0.067 g (43%); pale yellow solid; mp 121–122 °C.

^{1}H NMR ($CDCl_3$/TMS): δ = 1.60 (s, 9 H), 3.51 (s, 3 H), 6.70 (s, 1 H), 7.35–7.56 (m, 3 H), 7.61–7.69 (m, 2 H), 7.93 (s, 1 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 28.16, 52.59, 63.07, 115.78, 122.62, 128.65, 128.93, 132.79, 137.53, 140.13, 141.59, 162.56, 166.07, 191.77.

HRMS: *m*/*z* calcd for $C_{18}H_{19}NO_4$: 313.1314; found: 313.1310.

Methyl 5-(4-Methoxybenzoyl)-2-oxo-1-phenyl-1,2-dihydropyridine-4-carboxylate (3i)
Yield: 0.171 g (94%); yellow solid; mp 130–131 °C.

^{1}H NMR ($CDCl_3$/TMS): δ = 3.60 (s, 3 H), 3.76 (s, 3 H), 6.82–6.89 (m, 3 H), 7.25–7.42 (m, 5 H), 7.61–7.73 (m, 3 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 52.71, 55.38, 113.84, 117.12, 122.04, 126.09, 129.04, 129.40, 129.45, 131.41, 139.42, 142.05, 143.01, 160.91, 163.50, 165.58, 189.71.

HRMS: *m*/*z* calcd for $C_{21}H_{17}NO_5$: 363.1107; found: 363.1104.

Methyl 5-(4-Methylbenzoyl)-2-oxo-1-phenyl-1,2-dihydropyridine-4-carboxylate (3j)
Yield: 0.14 g (81%); yellow solid; mp 182–183 °C.

^{1}H NMR ($CDCl_3$/TMS): δ = 2.31 (s, 3 H), 3.58 (s, 3 H), 6.86 (s, 1 H), 7.14–7.20 (m, 2 H), 7.24–7.30 (m, 2 H), 7.31–7.42 (m, 3 H), 7.57–7.67 (m, 3 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 21.46, 52.65, 116.93, 121.89, 126.08, 129.05, 129.16, 129.26, 129.39, 134.14, 139.39, 142.58, 143.05, 143.91, 160.88, 165.61, 190.65.

HRMS: *m*/*z* calcd for $C_{21}H_{17}NO_4$: 347.1158; found: 347.1156.

Methyl 5-(4-Nitrobenzoyl)-2-oxo-1-phenyl-1,2-dihydropyridine-4-carboxylate (3k)
Yield: 0.127 g (67%); yellow solid; mp 172–173 °C.

^{1}H NMR ($CDCl_3$/TMS): δ = 3.71 (s, 3 H), 6.99 (s, 1 H), 7.35–7.42 (m, 2 H), 7.44–7.55 (m, 3 H), 7.79 (s, 1 H), 7.94 (d, *J* = 8.7 Hz, 3 H), 8.30 (d, *J* = 8.5 Hz, 2 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 52.94, 115.91, 122.43, 123.82, 126.07, 129.39, 129.59, 129.77, 139.16, 141.95, 142.19, 143.38, 149.99, 160.74, 165.20, 189.36.

HRMS: *m*/*z* calcd for $C_{20}H_{14}N_2O_6$: 378.0852; found: 378.0851.

Methyl 5-(2-Bromobenzoyl)-2-oxo-1-phenyl-1,2-dihydropyridine-4-carboxylate (3l)
Yield: 0.103 g (50%); yellow liquid.

^{1}H NMR ($CDCl_3$/TMS): δ = 3.87 (s, 3 H), 6.80 (s, 1 H), 7.30–7.53 (m, 8 H), 7.61–7.67 (m, 2 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 53.02, 115.73, 120.10, 120.92, 126.21, 127.56, 129.34, 129.59, 129.92, 132.18, 133.73, 138.43, 139.26, 143.36, 145.78, 160.86, 166.37, 189.68.

HRMS: *m*/*z* calcd for $C_{20}H_{14}BrNO_4$: 411.0106; found: 411.0110.

Methyl 5-(1-Naphthoyl)-2-oxo-1-phenyl-1,2-dihydropyridine-4-carboxylate (3m)
Yield: 0.18 g (94%); yellow solid; mp 156–157 °C.

^{1}H NMR ($CDCl_3$/TMS): δ = 3.58 (s, 3 H), 6.88 (s, 1 H), 7.25–7.31 (m, 2 H), 7.37–7.49 (m, 4 H), 7.52–7.59 (m, 2 H), 7.66 (d, *J* = 7.1 Hz, 1 H), 7.77 (s, 1 H), 7.87 (d, *J* = 7.8 Hz, 1 H), 7.97 (d, *J* = 8.3 Hz, 1 H), 8.38 (d, *J* = 8.3 Hz, 1 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 52.70, 118.00, 121.14, 124.07, 125.26, 126.01, 126.66, 127.72, 128.19, 128.28, 129.06, 129.35, 130.55, 132.43, 133.62, 134.41, 139.16, 143.48, 144.48, 160.85, 166.13, 191.79.

HRMS: *m*/*z* calcd for $C_{24}H_{17}NO_4$: 383.1158; found: 383.1157.

Methyl 2-Oxo-1-phenyl-5-(thiophene-2-carbonyl)-1,2-dihydropyridine-4-carboxylate (3n)
Yield: 0.12 g (71%); yellow solid; mp 161–162 °C.

^{1}H NMR ($CDCl_3$/TMS): δ = 3.77 (s, 3 H), 7.01 (s, 1 H), 7.12–7.17 (m, 1 H), 7.38–7.42 (m, 2 H), 7.43–7.56 (m, 3 H), 7.59 (d, *J* = 3.2 Hz, 1 H), 7.72 (d, *J* = 4.4 Hz, 1 H), 7.89 (s, 1 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 52.99, 117.09, 122.64, 126.22, 128.21, 129.31, 129.63, 133.62, 134.69, 139.49, 141.87, 142.66, 142.95, 161.01, 165.50, 182.73.

HRMS: *m*/*z* calcd for $C_{18}H_{13}NO_4S$: 339.0565; found: 339.0566.

Methyl 5-(Cyclohexanecarbonyl)-2-oxo-1-phenyl-1,2-dihydropyridine-4-carboxylate (3o)
Yield: 0.164 g (97%); yellow solid; mp 166–167 °C.

^{1}H NMR ($CDCl_3$/TMS): δ = 1.19–1.31 (m, 3 H), 1.43–1.55 (m, 2 H), 1.58–1.73 (m, 1 H), 1.75–1.84 (m, 4 H), 2.76–2.85 (m, 1 H), 3.91 (s, 3 H), 6.70 (s, 1 H), 7.34–7.39 (m, 2 H), 7.46–7.57 (m, 3 H), 7.94 (s, 1 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 25.33, 25.49, 29.06, 45.87, 52.80, 116.03, 120.90, 126.24, 129.20, 129.52, 139.54, 141.42, 143.59, 160.84, 166.72, 199.02.

HRMS: *m*/*z* calcd for $C_{20}H_{21}NO_4$: 339.1471; found: 339.1474.

Methyl 5-Heptanoyl-2-oxo-1-phenyl-1,2-dihydropyridine-4-carboxylate (3p)
Yield: 0.145 g (85%); yellow solid; mp 88–89 °C.

^{1}H NMR ($CDCl_3$/TMS): δ = 0.87 (t, *J* = 6.6 Hz, 3 H), 1.25–1.30 (m, 6 H), 1.61–1.66 (m, 2 H), 2.68 (t, *J* = 7.3 Hz, 2 H), 3.91 (s, 3 H), 6.60 (s, 1 H), 7.28-7.39 (m, 2 H), 7.45–7.55 (m, 3 H), 8.03 (s, 1 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 13.76, 22.21, 23.87, 28.51, 31.29, 37.80, 52.73, 116.16, 120.12, 126.17, 129.15, 129.43, 139.45, 142.47, 143.40, 160.75, 166.89, 194.99.

HRMS: *m*/*z* calcd for $C_{20}H_{23}NO_4$: 341.1627; found: 341.1626.

Ethyl 5-Benzoyl-2-oxo-1-phenyl-1,2-dihydropyridine-4-carboxylate (3q)
Yield: 0.149 g (86%); yellow solid; mp 167–168 °C.

^{1}H NMR ($CDCl_3$/TMS): δ = 1.17 (t, *J* = 9.2 Hz, 3 H), 4.12 (q, *J* = 9.2 Hz, 2 H), 7.00 (s, 1 H), 7.35–7.61 (m, 8 H), 7.75–7.83 (m, 3 H).

^{13}C NMR ($CDCl_3$/TMS): δ = 13.55, 62.13, 116.90, 121.93, 126.11, 128.62, 129.03, 129.13, 129.46, 133.01, 136.88, 139.38, 142.57, 143.22, 160.99, 165.03, 191.04.

HRMS: *m*/*z* calcd for $C_{21}H_{17}NO_4$: 347.1158; found: 347.1153.

Dimethyl (*Z*)-2-[1-(*tert*-Butylamino)-3-oxo-3-phenylprop-1-en-2-yl]but-2-enedioate (5a)
Yield: 0.104 g (60%); yellow solid; two isomers in a ratio of 3:5.

Major Isomer
^{1}H NMR ($CDCl_3$/TMS): δ = 1.31 (s, 9 H), 3.56 (s, 3 H), 3.57 (s, 3 H), 5.37 (s, 1 H), 7.20–7.40 (m, 5 H), 7.48–7.52 (m, 1 H), 10.84 (d, *J* = 14.2 Hz, 1 H).

^{13}C NMR (400 MHz, $CDCl_3$/TMS): δ = 29.61, 51.33, 52.13, 53.25, 102.87, 115.63, 127.88, 128.07, 130.33, 140.29, 148.13, 151.61, 165.88, 169.05, 193.74.

Minor Isomer
^{1}H NMR: δ = 1.34 (s, 9 H), 3.24 (s, 3 H), 3.68 (s, 3 H), 6.37 (s, 1 H), 11.03 (d, *J* = 12.7Hz, 1 H); other peaks were overlapped with the major isomer.

^{13}C NMR: δ = 29.78, 51.49, 52.07, 52.99, 99.88, 120.32, 127.41, 127.75, 129.92, 141.76, 146.47, 154.85, 166.65, 168.37, 192.78.

HRMS: *m*/*z* calcd for $C_{19}H_{24}NO_5$ $[M + H]^+$: 346.1654; found: 346.1653.

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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