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Pd/C-Catalyzed Synthesis of Oxamates by Oxidative Cross Double Carbonylation of Amines and Alcohols under Co-catalyst, Base, Dehydrating Agent, and Ligand-Free Conditions

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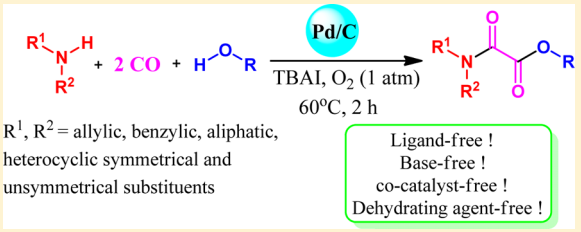
Supporting Information

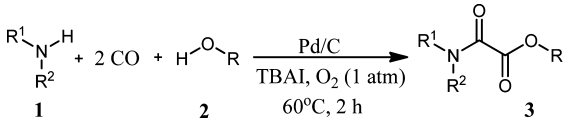
ABSTRACT: This work reports a mild, efficient, and ligand-free Pd/C-catalyzed protocol for the oxidative cross double carbonylation of amines and alcohols. Notably, the reaction does not requires any base, co-catalyst, dehydrating agent, or ligand. Pd/C solves the problem of catalyst recovery, and the catalyst was recycled up to six times.



Oxamates are important functional moieties in the synthesis of numerous organic molecules, biologically active compounds, and natural products.[1] For the synthesis of oxamates various methods such as acylation of the appropriate amine with mono esters of oxalyl chloride[1] or diester of oxalic acid are reported.[2] These methods are stoichiometric and requires the use mono esters of oxalyl chlorides, which are thermally unstable.[3] In addition to this, synthesis of mono esters of oxalyl chlorides requires the combination of equimolar quantities of oxalyl chloride and the appropriate alcohol with a distillation setup for isolation of product from the reaction mixture.[3] Murahashi et al. reported an alternative route for the synthesis of oxamates by carbonylation of amines and alcohols using a stoichiometric amount of a homogeneous $PdCl_2(MeCN)_2$ catalyst system and a mixture of carbon monoxide and oxygen (CO/O_2, 80:5 kg/cm^2). They used CuI as a co-catalyst, a dehydrating agent such as trimethoxy methane, and triethyl amine as a base.[4] The major drawbacks associated with this method are the use of a homogeneous catalyst system along with CuI as co-catalyst, dehydrating agent, high pressure of CO/O_2, reaction time up to 20 h, limited substrate scope, and difficulty in separation of catalyst from product and its reuse. The method for overcoming these drawbacks would involve the use of a heterogeneous palladium catalyst, especially palladium on carbon (Pd/C), which has recently been investigated in a variety of organic chemical fields from sustainable and industrial standpoints due to its easy access, recoverability, reusability, low cost, and avoidance of residual metals in the desired products.[5] On the basis of our research interest in carbonylation reactions,[6] we had reported Pd/C as a ligand-free, heterogeneous catalyst system that worked efficiently for the various carbonylation reactions.[7]

In this paper, we describe an efficient and heterogeneous, ligand-free protocol for Pd/C-catalyzed synthesis of oxamates using oxidative cross double carbonylation of amine and alcohol (Scheme 1). This method avoids use of the base, ligand, co-catalyst, and dehydrating agent, with lower reaction time and ease of recovery of Pd/C from the reaction mixture by simple filtration. The present protocol tolerated a wide range of functional groups, applicable for a variety of substrates such as allylic, benzylic, aliphatic, cyclic, heterocyclic symmetrical and unsymmetrical amines, providing good to excellent yield of desired products.

Scheme 1. Pd/C-Catalyzed Oxidative Cross Double Carbonylation of Amines and Alcohols



We examined the effect of the 10% Pd/C catalyst using piperidine **1a** and ethanol **2a** as substrates in the presence of CO/O_2 (6:1 atm) for the present cross double carbonylation reaction (Table 1). The catalyst loading could be increased to 8 mol % with significant increase in the yield of the product (Table 1, entry 4), while reducing the catalyst loading results in lower yields of the product.

Table 1. Effect of Dose of Pd/C on the Reaction[a]

entry	catalyst	catalyst loading (mol %)	yield (%)[b]
1	5% Pd/C	8	78
2	10% Pd/C	4	57
3	10% Pd/C	6	81
4	10% Pd/C	8	98
5	10% Pd/C	10	99

[a]Reaction conditions: **1a** (1 mmol), **2a** (10 mL), TBAI (0.2 mmol), CO/O_2 (6:1 atm), 60 °C, 2 h. [b]GC yield.

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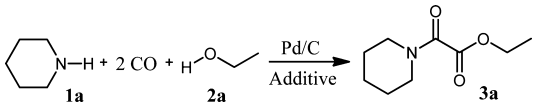
We then investigated the solvent effect on oxidative cross double carbonylation reaction. The reaction hardly took place in THF, 1,4-dioxane, or toluene using equimolar quantities of **1a** and **2a** (Table 2 entries 1−3). The nature of the solvent, such as protic/aprotic, is important for the Pd/C-catalyzed oxidative carbonylation reaction.[8a] The activity of catalyst was found to be significantly higher in polar solvents such as ethanol. The desired product was obtained in excellent yields directly using ethanol as solvent (Table 2, entry 4).

Table 2. Optimization of the Pd/C-Catalyzed Oxidative Cross Double Carbonylation Reaction[a]



entry	solvent	additive (mmol)	temp (°C)	time (h)	yield (%)[b]
		Effect of Solvent			
1	THF	TBAI	60	2	20
2	1,4-dioxane	TBAI	60	2	18
3	toluene	TBAI	60	2	07
4	EtOH	TBAI	60	2	98
		Effect of Additive			
5	EtOH	NaI	60	2	93
6	EtOH	KI	60	2	91
7	EtOH		60	2	
		Effect of Temperature			
8	EtOH	TBAI	50	2	79
9	EtOH	TBAI	70	2	99
		Effect of Time			
10	EtOH	TBAI	60	1	79
11	EtOH	TBAI	60	3	98

[a]Reaction conditions: **1a** (1 mmol), **2a** (10 mL), 10% Pd/C (8 mol %), TBAI (0.2 mmol), CO/O_2 (6:1 atm), 60 °C, 2 h. [b]GC yields.

Pd/C catalyst together with molecular oxygen and iodide additive plays a vital role in oxidative carbonylation reactions.[7a,b,8] The use of KI, NaI, and tetrabutylammoniumiodide (TBAI) was found to be a specifically effective iodide additive (Table 2, entries 5 and 6), while with TBAI excellent yield of the desired products was obtained (Table 2, entry 4). The reaction never proceeded without an iodide source (Table 2, entry 7). The iodide has a "softer" binding nature, so it can be easily adsorbed and desorbed from the catalyst surface.[7b,8a] The temperature of the reaction was also important for the effective progress of the Pd/C-catalyzed cross double carbonylation reaction (Table 2, entries 8 and 9); 60 °C was found to be the optimum temperature, and the target compound **3a** was obtained with 98% yield in 2 h (Table 2, entry 4). Further increase in temperature and time has no profound effect on the yield of the product observed (Table 1, entries 9−11).

Thus, the optimized reaction conditions are **1a** (1 mmol), **2a** (10 mL), Pd/C (8 mol %), TBAI (0.2 mmol), CO/O_2 (6/1 atm) at 60 °C, for a time period of 2 h.

In order to study the potential and general applicability of developed methodology, various amines containing different functional groups were investigated (Table 3). Cyclic secondary amines such as piperidine, piperidine-4-carbonitrile, pyrollidine, and morpholine **1a−d** were cross double carbonylated with ethanol to give desired oxamates derivatives **3a−d** in excellent yield (Table 3, entries 1−4). Piperazine possessing either an electron-withdrawing (fluoro group) or an electron-donating functionality (methyl) was found to be a good substrate for cross double carbonylation and was not reported earlier. *N*-Phenyl-, *N*-methyl-, *N*-benzyl-, and 1-(2-fluorophenyl)-piperazines **1e−h** underwent oxidative double carbonylation efficiently with ethanol to afford corresponding oxamates **3e−h** with high yields (Table 3, entries 5−8). As shown in Table 2, the diallyl amine **1i** as well as dibenzyl amine **1j** showed excellent reactivity and selectivity and provided 92% and 93% yield of desired product, respectively (Table 3, entries 9 and 10). Double carbonylation of secondary aliphatic amines such as diethylamine and dibutylamine **1k,l** with ethanol provided the product **3k,l** in good yield (Table 3, entries 11 and 12).

The unsymmetrical amines, such as *N*-methyl-1-phenyl-methanamine, 1,2,3,4-tetrahydroisoquinoline, and *N*-isopropyl-methylamine **1m−o** also smoothly underwent coupling reactions that gave excellent yields (Table 3, entries 13−15). The compounds **3h**, **3j**, **3m**, and **3o** were obtained as 1:1 mixture of *E*/*Z* rotamers around the amide bond as shown by ^1H and ^{13}C NMR spectra, while compound **3n** showed mostly a 2:1 mixture of *E*/*Z* rotamers around the amide bond. No homo double carbonylation product, such as oxamide and oxalate, or cross single carbonylation product could be detected among the products. With primary amines, we observed the formation of carbamate as a major product under such reaction condition.

Next, we examined the scope of Pd/C-catalyzed oxidative double carbonylation of piperidine with various alcohols. Like ethanol, methanol **2b** and *n*-butanol **2c** furnished excellent yield of the corresponding product **3p,q** (Table 3, entries 16 and 17).

The reusability of Pd/C is a great advantage in decreasing environmental pollution and cost reduction in process chemistry. We examined the reuse of Pd/C in the double carbonylation using piperidine and ethanol as substrates in the presence of CO/O_2 (6:1) at 60 °C temperature (Table 4). Pd/C could be reused successfully until the sixth run without significant loss of yield or extension of the reaction time. We also performed the reaction on larger scale (5 mmol of piperidine), and leaching of palladium metal was investigated after the first and sixth recycle runs.

Pd metal was not detected within the limits of the assay (<1 ppm) by analysis with inductively coupled plasma atomic emission spectrometry (ICP-AES).

In conclusion, we have developed a facile, efficient, and environmentally friendly process with widespread application for the synthesis varieties of oxamate derivatives using Pd/C as a heterogeneous catalyst under ligand-free and mild conditions. Simple starting materials, shorter reaction time, low pressure of CO/O_2, and avoidance of the use of any base, co-catalyst, or dehydrating agent adds an additional credit to the present study. The presented reaction demonstrates straightforward Pd/C recovery and the successful reuse of the catalyst until the sixth run without loss in activity and selectivity. The protocol would be practical for use as an economical synthetic method and offers an alternative synthetic strategy for the practical construction of oxamate derivatives.

EXPERIMENTAL SECTION

General. The Pd/C was purchased from Sigma-Aldrich (10 wt % loading; matrix, activated carbon support; Product Number, 205699; Brand, Aldrich). Product was purified by column chromatography on silica gel (100−200) mesh. The product was visualized with a 254 nm UV lamp. The IR spectra were recorded with FT-IR. The ^1H and ^{13}C

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Table 3. Pd/C-Catalyzed Oxidative Cross Double Carbonylation of Amines and Alcohols[a]

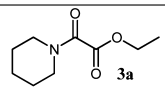
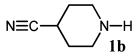
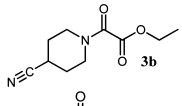
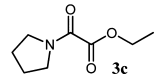
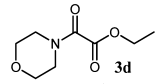
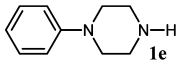
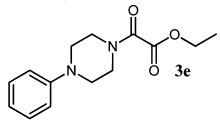
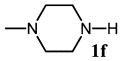
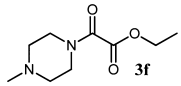
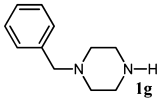
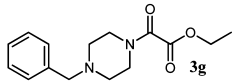
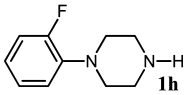
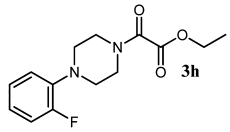
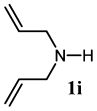
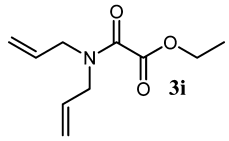
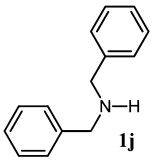
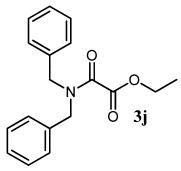
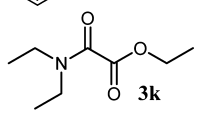
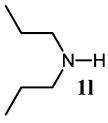
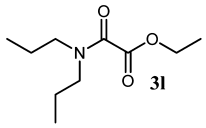
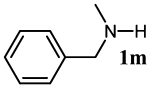
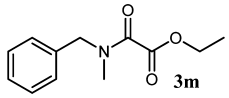
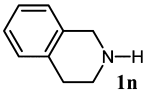
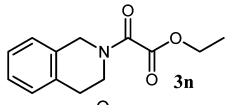
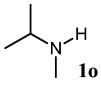
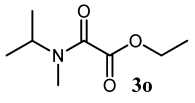
Entry	Amine	Alcohol	Product	Yield [%][b]
1	 1a	 2a	 3a	97
2	 1b	**2a**	 3b	95
3	 1c	**2a**	 3c	93
4	 1d	**2a**	 3d	94
5	 1e	**2a**	 3e	91
6	 1f	**2a**	 3f	95
7	 1g	**2a**	 3g	89
8	 1h	**2a**	 3h	87
9	 1i	**2a**	 3i	92
10	 1j	**2a**	 3j	93
11	 1k	**2a**	 3k	96
12	 1l	**2a**	 3l	97
13	 1m	**2a**	 3m	88
14	 1n	**2a**	 3n	90
15	 1o	**2a**	 3o	94

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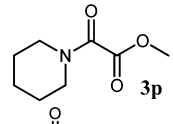
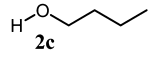
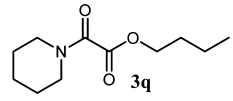
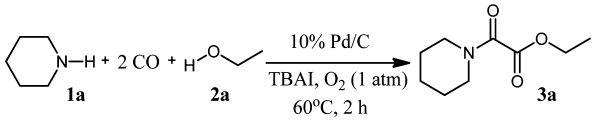
Table 3. continued

Entry	Amine	Alcohol	Product	Yield [%][b]
16	**1a**	 **2b**	 **3p**	93
17	**1a**	 **2c**	 **3q**	94

[a]Reaction conditions: amine (1 mmol), alcohol (10 mL), 10% Pd/C (8 mol %), TBAI (0.2 mmol), CO/O_2 (6:1 atm), 60 °C, 2 h. [b]Isolated yields.

Table 4. Investigation into the Reuse of Pd/C



entry	run	yield (%)[a]
1	1	97
2	2	97
3	3	96
4	4	95
5	5	94
6	6	93

[a]Yields were determined by GC analysis.

NMR spectra were recorded with 300 MHz and 400 MHz FT-NMR spectrometer in $CDCl_3$. HRMS was recorded on a commercial apparatus (ESI Source, ion trap). The chemical shifts are reported in parts per million (δ) relative to tetramethylsilane as an internal standard. J (coupling constant) values are reported in hertz, and splitting patterns of proton are described as s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). The conformation of known compounds was done by comparison with authentic samples on GC and GC–MS. However, new compounds were confirmed by GC–MS, FT-IR, ^1H and ^{13}C NMR, and HR-MS techniques.

General Experimental Procedure for Oxidative Cross Double Carbonylation of Amines and Alcohols. Amine (1 mmol), alcohol (10 mL), 10% Pd/C (8 mol %), and TBAI (0.2 mmol) were added to a 100-mL stainless steel autoclave, and the autoclave was closed and pressurized with oxygen (1 atm) and CO (6 atm) without flushing. The reaction mixture was stirred with a mechanical stirrer (525 rpm) at 60 °C for 2 h. After cooling to room temperature, the pressure was carefully released. The reactor vessel was washed with ethyl acetate (3 × 5 mL) to remove traces of product and catalyst if present. The filtrate was washed with a saturated solution of sodium thiosulphate (3 × 5 mL), dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography (silica gel 100–200 mesh, petroleum ether/ethyl acetate) to give the corresponding oxamate compounds. The compounds were confirmed by GC, GC–MS, FT-IR, ^1H and ^{13}C NMR, and HR-MS techniques.

Typical Procedure for Reuse of Pd/C. After the reaction mixture was passed through a filter paper, crude Pd/C was washed with distilled water (5 × 2.5 mL) and methanol (5 × 2.5 mL) to remove trace amounts of organic material if present. The resulting Pd/C was dried in vacuo and used for catalyst recyclability experiments.

Ethyl 2-(4-Cyanopiperidin-1-yl)-2-oxoacetate (3b). Yellowish liquid; 199 mg, yield 95%; IR (neat) 2242, 1729, 1666 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.35 (q, J = 7.16 Hz, 2H), 3.79–3.67 (m, 2H), 3.64–3.58 (m, 1H), 3,47–3.40 (m, 1H), 3.00–2.94 (m, 1H), 2.03–1.91 (m, 4H), 1.37 (t, J = 7.16 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.5, 160.1, 120.3, 62.4, 44.1, 39.2, 28.8, 27.8, 26.2, 14.0; GC–MS (EI, 70 eV) m/z (%) 210 (14, M^+), 181 (9), 137 (100), 109 (12), 94 (20), 67 (29), 56 (35), 42 (21); HRMS (ESI-ion trap) m/z calcd for $[(C_{10}H_{14}O_3N_2)Na]^+$ 233.0897, found 233.0898.

Ethyl 2-Oxo-2-(4-phenylpiperazin-1-yl)acetate (3e). Yellowish liquid; 238 mg, yield 91%; IR (neat) 1738, 1668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31–7.26 (m, 2H), 6.94–6.91 (m, 3H), 4.36 (q, J = 7.16 Hz, 2H), 3.80 (t, J = 5.12 Hz, 2H), 3.61 (t, J = 5 Hz, 2H), 3.22 (t, 4H), 1.40 (t, J = 7.16 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.6, 160.1, 150.7, 129.3, 121.0, 117.0, 62.3, 49.9, 49.3, 46.0, 41.4, 14.0; GC–MS (EI, 70 eV) m/z (%) 262 (66, M^+), 189 (24), 161 (65), 132 (100), 119 (32), 104 (29), 91 (18), 77 (31), 56 (51), 42 (18); HRMS (ESI-ion trap) m/z calcd for $[(C_{14}H_{18}O_3N_2)H]^+$ 263.1390, found 263.1389.

Ethyl 2-(4-Benzylpiperazin-1-yl)-2-oxoacetate (3g). Yellowish liquid; 245 mg, yield 89%; IR (neat) 1739, 1667 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.25 (m, 5H), 4.35–4.29 (q, 2H), 3.64 (t, 2H), 3.54 (s, 2H), 3.43 (t, 2H), 2.50–2.46 (m, 4H), 1.35 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.8, 160.2, 137.3, 129.1, 128.4, 127.4, 62.8, 62.1, 52.8, 52.2, 46.1, 41.4, 14.0; GC–MS (EI, 70 eV) m/z (%) 276 (6, M^+), 247 (2), 203 (9), 199 (4), 185 (5), 175 (19), 146 (20), 132 (11), 111 (3), 91 (100); HRMS (ESI-ion trap) m/z calcd for $[(C_{15}H_{20}O_3N_2)H]^+$ 277.1547, found 277.1548.

Ethyl 2-(4-(2-Fluorophenyl)piperazine-1-yl)-2-oxoacetate (3h). Yellowish liquid; 243 mg, yield 87%; IR (neat) 1739, 1668 cm^{-1}; (^1H and ^{13}C NMR spectra are described for both rotamers about the amide bond) ^1H NMR (400 MHz, $CDCl_3$) δ 7.10–6.91 (m, 4H), 4.35 (q, 2H), 3.81 (t, 2H), 3.61 (t, 2H), 3.15–3.11 (m, 4H), 1.38 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.6, 160.2, 157.4, 154.2, 139.3, 139.2, 124.7, 124.6, 123.6, 123.5, 119.4, 119.4, 116.5, 116.2, 62.3, 50.8, 50.8, 50.1, 50.1, 46.3, 41.5, 14.0; GC–MS (EI, 70 eV) m/z (%) 280 (43, M^+), 251 (3), 207 (35), 179 (46), 150 (100), 137 (41), 122 (36), 109 (18), 95 (12), 70 (16), 56 (62), 42 (22); HRMS (ESI-ion trap) m/z calcd for $[(C_{14}H_{17}O_3N_2F)H]^+$ 281.1296, found 281.1295.

Ethyl 2-(Diallylamino)-2-oxoacetate (3i).[1c] Yellowish liquid; 181 mg, yield 92%; IR (neat) 1739, 1667 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.83–5.71 (m, 2H), 5.27–5.18 (m, 4H), 4.33 (q, J = 7.16 Hz, 2H), 4.01–4.00 (m, 2H), 3.88–3.85 (m, 2H), 1.36 (t, J = 7.16 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.8, 161.7, 132.3, 131.5, 119.0, 118.7, 62.1, 49.6, 46.3, 14.0; GC–MS (EI, 70 eV) m/z (%) 197 (1, M^+), 156 (7), 124 (35), 96 (5), 81 (10), 56 (7), 41 (100).

Ethyl 2-(Dibenzylamino)-2-oxoacetate (3j).[1c] Yellowish solid; 276 mg, yield 93%; IR (KBr) 1732, 1661 cm^{-1}; (^1H and ^{13}C NMR spectra are described for both rotamers about the amide bond) ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.16 (m, 10H), 4.54 (s, 2H), 4.49 (s, 2H), 4.38 (s, 2H), 4.33 (s, 2H), 4.33(q, 2H), 1.32 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 163.1, 162.4, 135.9, 135.5, 135.2, 134.9, 128.9, 128.9, 128.8, 128.6, 128.5, 128.3, 128.3, 128.0, 127.9, 127.8, 62.3, 50.3, 46.2, 46.0, 14.0; GC–MS (EI, 70 eV) m/z (%) 206 (58, M^+), 178 (4), 132 (17), 106 (11), 91 (100), 65 (13).

Ethyl 2-(Benzyl(methyl)amino)-2-oxoacetate (3m). Yellowish liquid; 194 mg, yield 88%; IR (neat) 1736, 1655 cm^{-1}; (^1H and ^{13}C NMR spectra are described for both rotamers about the amide bond) ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.26 (m, 5H), 4.60 (s, 2H), 4.45 (s, 2H), 4.39–4.31 (m, 2H), 2.90 (s, 3H), 2.87 (s, 3H), 1.38 (t, 3H), 1.33 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1, 163.0, 162.1,

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162.0, 135.5, 135.1, 128.9, 128.8, 128.3, 127.9, 127.7, 62.2, 62.1, 53.7, 49.9, 34.6, 31.6, 14.0, 14.0; GC−MS (EI, 70 eV) *m*/*z* (%) 221 (2, M^+), 192 (2), 147 (16), 118 (9), 119 (10), 91 (100), 65 (12); HRMS (ESI-ion trap) *m*/*z* calcd for $[(C_{12}H_{15}O_3N)Na]^+$ 244.0944, found 244.0944.

Ethyl 2-(3,4-Dihydroisoquinoline-2(1*H*)-yl)-2-oxoacetate (3n). Yellowish liquid; 209 mg, yield 90%; IR (neat) 1739, 1660 cm^{-1}; (^1H and ^{13}C NMR spectra are described for both rotamers about the amide bond) ^1H NMR (400 MHz, $CDCl_3$) δ 7.26−7.06 (m, 4H), 4.75 (s, 2H), 4.63 (s, 2H), 4.38 (q, *J* = 7.16 Hz, 2H), 3.86 (t, 2H), 3.68 (t, 2H), 2.96−2.90 (m, 2H), 1.41 (t, 3H), 1.38 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.8, 162.7, 160.8, 160.4, 134.3, 133.5, 131.7, 131.6, 129.0, 128.7, 127.3, 126.9, 126.8, 126.7, 126.1, 62.2, 47.5, 43.8, 43.7, 39.6, 29.7, 29.3, 28.0, 14.1; GC−MS (EI, 70 eV) *m*/*z* (%) 233 (41, M^+), 204 (9), 160 (59), 159 (24), 142 (53), 131 (100), 117 (36), 115 (23), 104 (30), 91 (13), 77 (19); HRMS (ESI-ion trap) *m*/*z* calcd for $[(C_{13}H_{15}O_3N)Na]^+$ 256.0944, found 256.0943.

Ethyl 2-(Isopropyl(methyl)amino)-2-oxoacetate (3o). Yellowish liquid; 162 mg, yield 94%; IR (neat) 1736, 1655 cm^{-1}. (^1H and ^{13}C NMR spectra are described for both rotamers about the amide bond) ^1H NMR (400 MHz, $CDCl_3$) δ 4.74 (m, 1H), 4.33 (q, *J* = 7.16 Hz, 2H), 3.83 (m, 1H), 2.84 (s, 3H), 1.36 (t, *J* = 7.16 Hz, 3H), 1.24 (d, *J* = 6.64 Hz, 3H), 1.17 (d, *J* = 6.80 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.5, 163.3, 161.8, 161.6, 61.9, 49.6, 44.1, 28.6, 24.9, 20.2, 18.9, 14.0; GC−MS (EI, 70 eV) *m*/*z* (%) 173 (4, M^+), 144 (15), 130 (9), 100 (44), 58 (60), 43 (100); HRMS (ESI-ion trap) *m*/*z* calcd for $[(C_8H_{15}O_3N)H]^+$ 174.1125, found 174.1124.

Methyl 2-Oxo-2-(piperidine-1-yl)acetate (3p).[4b] Yellowish liquid; 159 mg, yield 93%; IR (neat) 1742, 1660 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.87 (s, 3H), 3.57 (t, *J* = 5.76 Hz, 2H), 3.34 (t, *J* = 5.6 Hz, 2H), 1.72−1.59 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.6, 160.0, 52.5, 47.3, 42.3, 26.2, 25.1, 24.3; GC−MS (EI, 70 eV) *m*/*z* (%) 171 (23, M^+), 112 (89), 83 (14), 69 (100), 56 (20), 41 (74).

Butyl 2-Oxo-2-(piperidine-1-yl)acetate (3q).[4b] Yellowish liquid; 200 mg, yield 94%; IR (neat) 1739, 1661 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.27 (t, *J* = 6.68 Hz, 2H), 3.56 (t, *J* = 5.76 Hz, 2H), 3.33 (t, *J* = 5.6 Hz, 2H), 1.74−1.61 (m, 8H), 1.47−1.37 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.4, 160.4, 65.7, 47.3, 42.1, 30.4, 26.2, 25.1, 24.4, 19.0, 13.6; GC−MS (EI, 70 eV) *m*/*z* (%) 213 (10, M^+), 156 (7), 112 (100), 83 (9), 69 (70), 56 (11), 41 (46).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^1H and ^{13}C NMR of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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