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Synthesis of Carbamates by Direct C–H Bond Activation of Formamides

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Copper catalysed oxidative coupling reaction of formamides with β-keto esters and 2-carbonyl-substituted phenols successfully proceeded through direct C–H bond activation of formamides. The corresponding carbamates were formed with high stereoselectivity under mild reaction conditions. This protocol was successfully applied to the synthesis of three novel halogenated carbamates and a carbaryl insecticide derivative. Our results suggest the use of 6.0 equiv. TBHP is crucial for this type of reaction.

Introduction

Organic carbamates are important structural motifs in many biologically active natural products, pharmaceutical drugs and agrochemicals (Figure 1).[1] They also play a significant role in organic chemistry as valuable intermediates and protecting groups.[2] Carbamates possess excellent pharmacological activities as neuroprotective, antibacterial, antineoplastic and antifilarial agents as well as acetyl cholinesterase and endocannabinoid hydrolase inhibitors.[3] Carbamates are traditionally prepared from chloroformates or isocyanate by employing phosgene or its substitutes as starting materials.[4] Metal-catalysed reactions as well as the use of carbon dioxide were introduced to replace toxic phosgene.[5] Recently, Hofmann and Curtius rearrangements were applied for carbamate preparation.[6] Despite these reported protocols, an efficient, safe and environmentally benign methodology for carbamate synthesis is lacking.[1a]

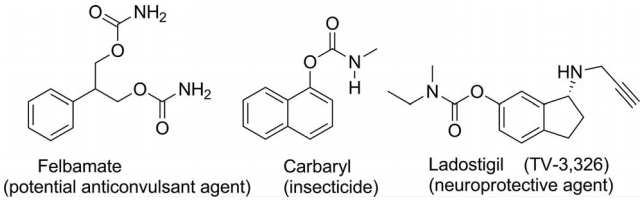

Figure 1. Selected biologically active carbamates.

Chemical transformations using transition-metal-catalysed coupling are now playing a significant role in carbon–carbon and carbon–heteroatom bond formation.[7] They are successfully applied in the synthesis of complex natural products and pharmaceutical drugs.[8] However, traditional coupling reactions suffer from some drawbacks such as the use of expensive transition metals with considerable toxicity, high costs associated with the preparation of starting materials, and poor atom economy. Direct C–H bond activation has emerged as an alternative route in organic synthesis to overcome the drawbacks of traditional coupling reactions.[9,10]

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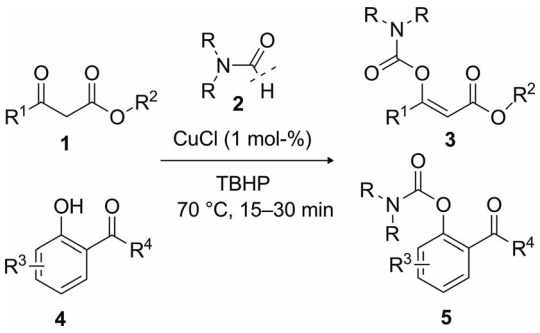
In 2011, the Reddy group reported the synthesis of carbamates using *N*,*N*-dimethylformamide (DMF) and 5 mol-% $CuBr_2$ at 80 °C for 3 h.[11] The developed protocol led to the formation of *O*-(2-carbonylphenyl) carbamates in good to high yields (62–86%) but enol carbamates were prepared in only moderate yields (26–80%).

DMF, with its peculiar nature, is used in organic synthesis as a solvent as well as a source of oxygen, Me_2NCO, Me_2N, CO, carbon, and CN.[12] Recently, direct C–H bond activation of DMF and its derivatives was described.[13] The reaction was proposed to proceed through a radical mechanism.[11,14a] Inspired by these findings, we report herein a high yielding protocol for the synthesis of enol and *O*-(2-carbonylphenyl) carbamates involving oxidative coupling and formamide C–H bond activation (Scheme 1).



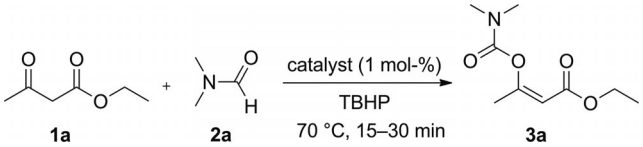
Scheme 1. Synthesis of carbamates by direct C–H bond activation of formamides.

Results and Discussion

Initially, the reaction between ethyl acetoacetate (**1a**), 6.0 equiv. of *tert*-butyl hydroperoxide (TBHP) and DMF (**2a**) was tested under metal-free conditions or by using inexpensive catalysts (1 mol-%) that are known to catalyse radical reactions such as Fe_2O_3, NaI, Bu_4NI, $ZnCl_2$ or I_2.[10d,15] However, the reaction did not proceed and no product was detected (Table 1, entries 1–6). The catalyst utilised in a previous report was also tested, but under our reaction conditions (1 mol-% $CuBr_2$ and 6.0 equiv. TBHP).[11] This reaction was complete within 30 min, the expected enol carbamate **3a** was formed in 80% yield (Table 1, entry 7).

The use of 1 mol-% metal catalyst represents a marked reduction in catalyst loading compared with the reported protocol.[11] Additionally, the short reaction time (15–30 min) and the high yield encouraged us to test other copper catalysts and oxidants with the aim of optimising the new reaction conditions. Catalysts screening established that CuCl was the best catalyst, giving **3a** in 99% yield (Table 1, entry 15). Screening of different organic and inorganic oxidants (Table 2) revealed that TBHP was the most efficient oxidant, providing the highest yield of the target carbamate. Aiming to decrease the amount of oxidant, the reaction was repeated using 1.5, 2.5, 3.5 and 4.5 equiv. of TBHP. Unfortunately, the reaction was not complete even after 6 h using 1–5 mol-% CuCl or $CuBr_2$, suggesting that the use of 6.0 equiv. of TBHP is crucial for reaction completion, in contrast to the previous report in which the use of

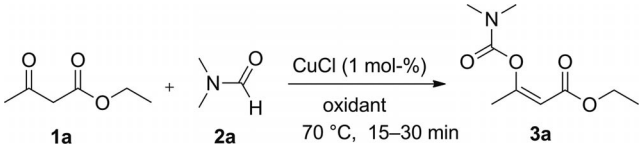
Table 1. Catalyst screening for optimisation of reaction conditions.[a]



Entry	Catalyst	Yield [%][b]
1	–	n.r.[c]
2	Fe_2O_3	n.d.[d]
3	Bu_4NI	n.d.
4	NaI	n.d.
5	$ZnCl_2$	n.d.
6	I_2	n.d.
7	$CuBr_2$	80
8	$CuSO_4·5H_2O$	69
9	$CuCl_2$	82
10	Cu_2O	30
11	$CuCl_2·2H_2O$	62
12	CuBr	60
13	$Cu(NO_3)·2H_2O$	64
14	CuI	40
15	CuCl	99
16	Cu $(OAc)_2$	70
17	$CuSO_4$	67
18	Cu $(OAc)_2·H_2O$	65

[a] Reaction conditions: **1a** (1 equiv.), DMF (2 mL), catalyst (1 mol-%), TBHP (70 wt.-% in water, 6.0 equiv.), 70 °C, 15–30 min. [b] Isolated yield. [c] n.r.: no reaction. [d] n.d.: not detected.

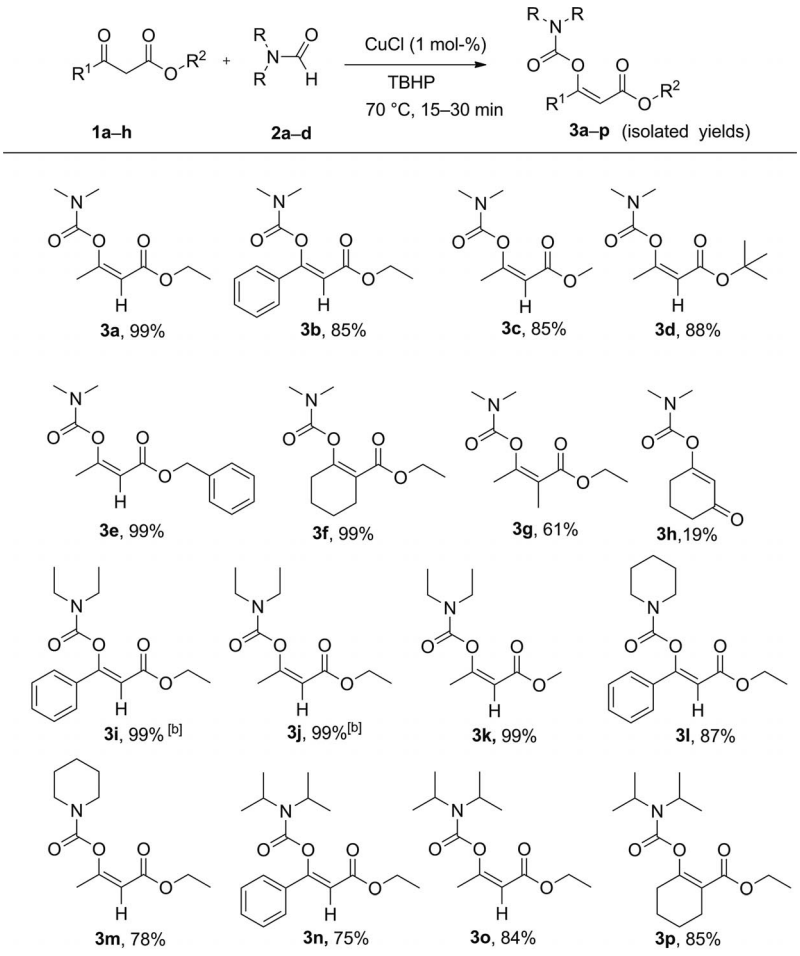
Table 2. Oxidant screening for optimisation of reaction conditions.[a]



Entry	Oxidant	Yield [%][b]
1	*m*-CPBA	20
2	DDQ	n.r.[c]
3	PIFA	n.d.[d]
4	$NaIO_4$	n.d.[e]
5	CAN	n.d.
6	H_2O_2	n.d.
7	benzoquinone	n.r.
8	benzoyl peroxide	n.d.
9	$K_3Fe(CN)_6$	n.d.
10	Oxone	n.d.[f]
11	MnO_2	n.d.
12	*tert*-butyl perbenzoate	n.r.
13	Di-*tert*-butyl peroxide	n.d.
14	TBHP	99
15	–	n.r.

[a] Reaction conditions: **1a** (1 equiv.), DMF (2 mL), CuCl (1 mol-%), oxidant (6.0 equiv.), 70 °C, 15–30 min. [b] Isolated yield. [c] n.r.: no reaction. [d] 0.75 equiv. of oxidant was used. [e] n.d.: not detected. [f] 1.0 equiv. of oxidant was used.

Table 3. Formation of enol-carbamates.[a]



[a] Reaction conditions: **1a** (1 equiv.), formamide (2 mL), CuCl (1 mol-%), TBHP (70 wt.-% in water, 6.0 equiv.), 70 °C, 15–30 min. [b] Reaction time 45 min.

only 1.5 equiv. of TBHP was sufficient.[11] This finding is also supported by recent research with detailed mechanistic studies showing that the use of 2–6 equiv. of oxidant is essential for similar reactions.[14a,15b,16]

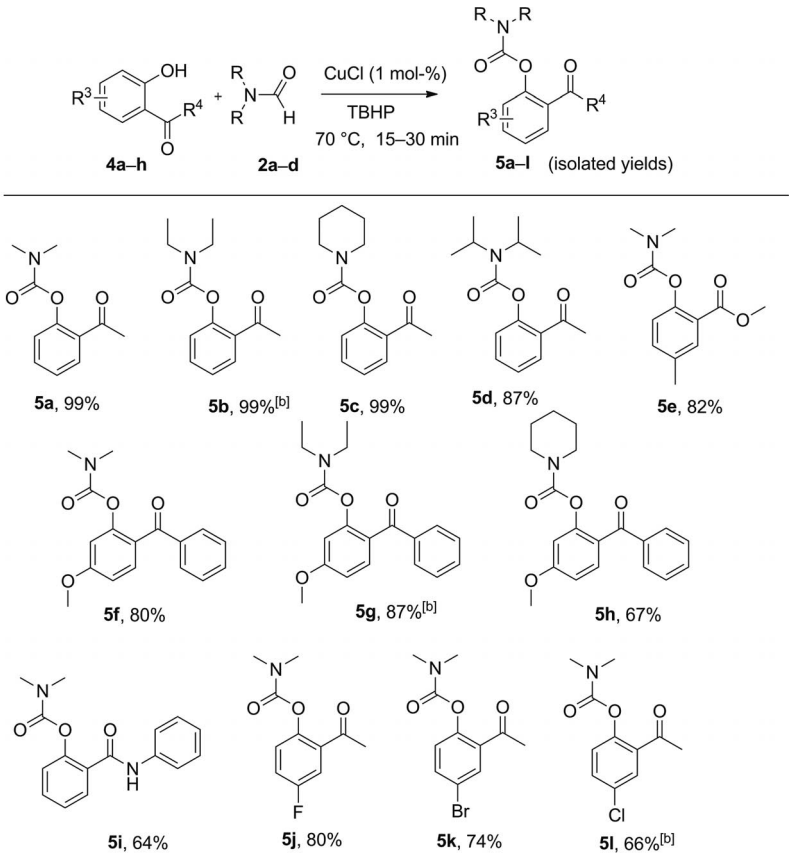
With the optimised conditions in hand, we further investigated the scope of the reaction using different substituted β-keto esters. All substrates were efficiently transformed into their corresponding enol carbamates (Table 3). DMF with various substituted β-keto esters provided carbamates in excellent yields (Table 3, **3a**–**f**). Interestingly, the active methylene group of β-dicarbonyl esters did not participate in the reaction.[17] The lower yield of 1,3-cyclohexadione carbamate (**3h**) may be attributed to the lack of binding capacity of cyclic β-diketones to copper metal in a bidentate fashion.[14b] DMF, with different substituted β-keto esters, rendered carbamates **3i**–**k** in excellent yields. Cyclic and bulky formamides **3l**–**p** provided slightly lower yields, suggesting the negative effect of steric hindrance on the reaction. The reaction exhibited high stereoselectivity, resulting in the formation of the *Z* isomer of the carbamates.[11,14b]

The developed protocol was also applicable to 2-carbonyl-substituted phenols forming the corresponding carbamates (Table 4). Several formamides reacted smoothly with *ortho*-hydroxyacetophenone in excellent yields (for **5a**–**d**). Electron-donating groups on the phenol ring resulted in lower yields compared to *ortho*-hydroxyacetophenone (**5e**–**h**). Salicylinide also participated in the reaction, forming the corresponding carbamate in moderate yield (**5i**).

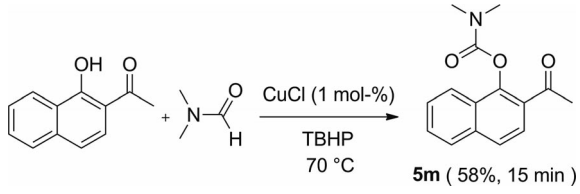
Halogen-substituted 2-carbonylphenols **5j**–**l** reacted smoothly without any dehalogenation, providing novel halogenated carbamates.[1a] Notably, all reactions were performed in open air and were not sensitive to moisture. To test the applicability of our methodology, a carbaryl insecticide derivative was prepared in a single step from 2-acetyl naphthol and DMF (Scheme 2).[18]

Mechanistically, the reaction of simple phenol under the above conditions resulted in no product formation, implying the importance of the adjacent carbonyl group for carbamate formation. This was attributed to the tendency of dicarbonyl compounds to form coordination complex **6** with transition metals (Scheme 3).[14b,17] Copper complex **6** decomposes TBHP to form hydroxyl and *tert*-butoxyl radicals.[14b] The latter can abstract hydrogen from the reacting formamide, generating the corresponding radical, which re-

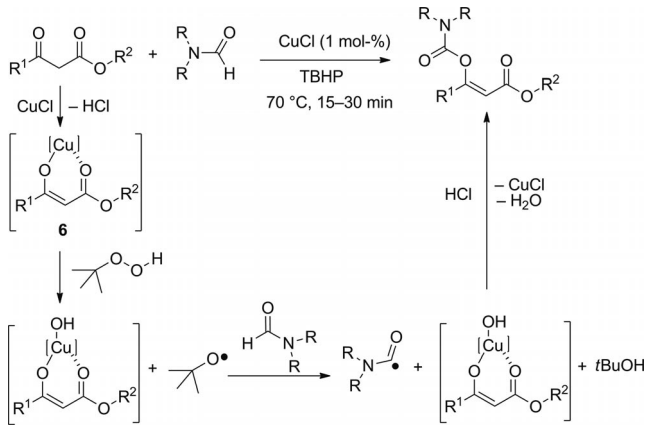
Table 4. Formation of *O*-(2-carbonylphenyl) carbamates.[a]



[a] Reaction conditions: **4a** (1 equiv.), formamide (2 mL), CuCl (1 mol-%), TBHP (70 wt.-% in water, 6.0 equiv.), 70 °C, 15–30 min. [b] Reaction time 45 min.



Scheme 2. Single step synthesis of a carbaryl insecticide derivative.



Scheme 3. Plausible mechanism.

acts with the copper complex affording the desired carbamates.[14a] Furthermore, it was reported that the use of radical scavengers [2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) or 2,6-di-*tert*-butyl-4-methylphenol (BHT)] in metal-catalyzed oxidative reactions with TBHP as an oxidant, prevented C–O coupling, supporting the radical pathway.[11,14b]

Conclusions

A high yielding, efficient, green methodology for the synthesis of carbamates was developed that involves direct C–H bond activation of formamides by oxidative coupling. Compared to other carbamate synthetic protocols, this protocol involves moderate temperature, low catalyst loading, great functional group tolerance, and short reaction time, suggesting its potential application in research and industry.

Experimental Section

General: All chemicals used in this work were purchased from commercial sources. Biotage Flash or Isco Companion systems were used for flash chromatography. Analytical thin-layer chromatography (TLC) was performed on Kieselgel 60, F_{254} (0.20 nm, Merck)

and visualisation was accomplished with UV light (254 and 354 nm). ^{1}H and ^{13}C NMR spectra were recorded with Varian Gemini-2000 (200 MHz FT-NMR) instruments with Me_4Si or solvent resonance as the internal standard (^{1}H NMR: Me_4Si at 0 ppm, $CDCl_3$ at δ = 7.26 ppm; ^{13}C NMR: Me_4Si at 0 ppm, $CDCl_3$ at δ = 77.0 ppm). ^{1}H NMR spectroscopic data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, br. = broad, m = multiplet), coupling constants (Hz), and integration. High-resolution mass measurements (HRESI-MS, ESI-MS) were performed with a Bruker Daltonics APEX II spectrometer.

General Procedures

Synthesis of Enol Carbamates and 2-Carbonyl-Substituted Phenol Carbamates: To a flask charged with a stir bar, β-keto ester **1** or phenol **4** (1 equiv.), copper salt (1 mol-%, CuCl), TBHP (70 wt.-% in water 6.0 equiv.) and formamide (27 equiv.) were mixed at room temperature. The reaction temperature was increased to 70 °C and the reaction mixture was stirred for 30 min. After cooling to room temp., the reaction mixture was extracted with ethyl acetate and dried with anhydrous Na_2SO_4. Removal of the solvent under vacuum yielded the crude product, which was purified by flash chromatography (ethyl acetate/hexane, 2:8) to afford the required product **3** or **5**.

Ethyl 3-(Dimethylcarbamoyloxy)but-2-enoate (3a):[11] Yield 99%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.55 (s, 1 H), 4.12 (q, J = 7.2 Hz, 2 H), 3.04 (s, 3 H), 2.98 (s, 3 H), 2.05 (s, 3 H), 1.24 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (50 Hz, $CDCl_3$): δ = 163.9, 160.7, 152.9, 107.9, 59.7, 36.5 (2 C), 22.0, 14.1 ppm. MS (ESI): m/z = 202 [M^+ + H].

Ethyl 3-(Dimethylcarbamoyloxy)-3-phenylacrylate (3b):[11] Yield 85%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.57–7.63 (m, 2 H), 7.37–7.43 (m, 3 H), 6.24 (s, 1 H), 4.19 (q, J = 7.2 Hz, 2 H), 3.17 (s, 3 H), 3.03 (s, 3 H), 1.32 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 164.3, 158.4, 153.3, 134.2, 130.6 (2 C), 128.6 (2 C), 125.9, 106.2, 60.0, 36.6 (2 C), 14.0 ppm. MS (ESI): m/z = 264 [M^+ + H].

Methyl 3-(Dimethylcarbamoyloxy)but-2-enoate (3c):[11] Yield 85%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.56 (s, 1 H), 3.66 (s, 3 H), 3.04 (s, 3 H), 2.98 (s, 3 H), 2.06 (s, 3 H) ppm. ^{13}C NMR (50 MHz $CDCl_3$): δ = 164.4, 161.1, 152.9, 107.3, 50.9, 36.4 (2 C), 22.0 ppm. MS (ESI): m/z = 188 [M^+ + H].

***tert*-Butyl 3-(Dimethylcarbamoyloxy)but-2-enoate (3d):**[11] Yield 88%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.46 (s, 1 H), 3.02 (s, 3 H), 2.98 (s, 3 H), 2.01 (s, 3 H), 1.44 (s, 9 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 163.4, 158.6, 152.9, 109.9, 80.0, 36.4 (2 C), 28.0 (3 C), 21.7 ppm. MS (ESI): m/z = 230 [M^+ + H].

Benzyl 3-(Dimethylcarbamoyloxy)but-2-enoate (3e):[11] Yield 99%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.34 (m, 5 H), 5.60 (s, 1 H), 5.1 (s, 2 H), 2.89 (s, 6 H), 2.05 (s, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 163.8, 161.2, 152.8, 135.8, 128.4 (2 C), 128.2 (2 C), 128.0, 107.7, 65.8, 36.3, 36.2, 22.0 ppm. MS (ESI): m/z = 264 [M^+ + H].

Ethyl 2-(Dimethylcarbamoyloxy)cyclohex-1-ene-carboxylate (3f):[11] Yield 99%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.14 (q, J = 7.2 Hz, 2 H), 2.99 (s, 3 H), 2.96 (s, 3 H), 2.26–2.42 (br. m, 4 H), 1.64–1.74 (br. m, 4 H), 1.24 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 166.1, 155.9, 153.8, 117.6, 60.1, 36.4, 36.3, 29.6, 25.2, 22.0, 21.7, 13.9 ppm. MS (ESI): m/z = 242 [M^+ + H].

Ethyl 3-Dimethylcarbamoyloxy-2-methyl-but-2-enoate (3g):[11] Yield 61%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.16 (q, J = 7.2 Hz, 2 H), 2.97 (s, 6 H), 2.03 (s, 3 H), 1.90 (s, 3 H), 1.25 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 166.7, 153.9, 152.5, 115.8, 60.2, 36.4, 36.1, 19.0, 14.5, 13.9 ppm. MS (ESI): m/z = 216 [M^+ + H].

3-Oxocyclohex-1-enyl Dimethylcarbamate (3h):[11] Yield 19%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.89 (s, 1 H), 3.01 (s, 3 H), 2.98 (s, 3 H), 2.58 (t, J = 6.4 Hz, 2 H), 2.40 (t, J = 6.4 Hz, 2 H), 2.06 (quint, J = 6.4 Hz, 2 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 199.7, 170.6, 152.1, 115.8, 36.6, 36.5, 29.6, 28.4, 21.2 ppm. MS (ESI): m/z = 184 [M^+ + H].

Ethyl 3-(Diethylcarbamoyloxy)-3-phenylacrylate (3i):[11] Yield 99%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.56–7.61 (m, 2 H), 7.37–7.43 (m, 3 H), 6.23 (s, 1 H), 4.19 (q, J = 7.2 Hz, 2 H), 3.52 (q, J = 7.2 Hz, 2 H), 3.39 (q, J = 7.2 Hz, 2 H), 1.17–1.35 (m, 9 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 164.2, 158.1, 152.5, 134.5, 130.5, 128.6 (2 C), 125.9 (2 C), 106.5, 60.0, 42.3, 42.0, 14.1, 13.2 (2 C) ppm. MS (ESI): m/z = 292 [M^+ + H].

Ethyl 3-(Diethylcarbamoyloxy)but-2-enoate (3j):[11] Yield 99%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.54 (s, 1 H), 4.09 (q, J = 7.2 Hz, 2 H), 3.30–3.43 (m, 4 H), 2.05 (s, 3 H), 1.18–1.31 (m, 9 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 163.9, 160.3, 152.2, 108.0, 59.7, 42.0, 41.8, 21.9, 14.1, 13.9, 13.2 ppm. MS (ESI): m/z = 230 [M^+ + H].

Methyl 3-(Diethylcarbamoyloxy)but-2-enoate (3k):[11] Yield 99%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.56 (s, 1 H), 3.66 (s, 3 H), 3.30–3.43 (m, 4 H), 2.06 (s, 3 H), 1.15–1.25 (m, 6 H) ppm. ^{13}C NMR (50 MHz $CDCl_3$): δ = 164.9, 161.3, 152.8, 108.1, 51.6, 42.6, 42.4, 22.5, 14.4, 13.8 ppm. MS (ESI): m/z = 216 [M^+ + H].

2-Ethoxycarbonyl-1-phenylvinyl Piperidine-1-carboxylate (3l):[11] Yield 87%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.57–7.61 (m, 2 H), 7.37–7.41 (m, 3 H), 6.23 (s, 1 H), 4.21 (q, J = 7.2 Hz, 2 H), 3.67 (br. m, 2 H), 3.51 (br. m, 2 H), 1.67 (m, 6 H), 1.28 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 163.6, 157.7, 151.4, 133.7, 129.9 (2 C), 127.9 (2 C), 125.2, 105.7, 59.4, 45.1, 44.6, 25.7, 24.9, 23.6, 13.5 ppm. MS (ESI): m/z = 304 [M^+ + H].

2-Ethoxycarbonyl-1-methylvinyl Piperidine-1-carboxylate (3m):[11] Yield 78%; colourless liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.54 (s, 1 H), 4.14 (q, J = 7.2 Hz, 2 H), 3.50 (br. m, 4 H), 2.05 (s, 3 H), 1.62 (br., 6 H), 1.24 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 163.9, 160.5, 151.7, 107.8, 59.7, 45.5, 44.9, 29.6, 25.4, 24.2, 21.9, 14.1 ppm. MS (ESI): m/z = 242 [M^+ + H].

Ethyl 3-(Diisopropylcarbamoyloxy)-3-phenylacrylate (3n):[11] Yield 75%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.56–7.60 (m, 2 H), 7.27–7.43 (m, 3 H), 6.21 (s, 1 H), 4.14–4.24 (m, 3 H), 4.94 (m, 1 H), 1.17–1.39 (m, 15 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 164.8, 158.4, 152.1, 135.5, 131.0 (2 C), 129.3 (2 C), 128.5, 107.3, 60.6, 47.7, 47.1, 21.9 (2 C), 21.1 (2 C), 14.9 ppm. MS (ESI): m/z = 320 [M^+ + H].

Ethyl 3-(Diisopropylcarbamoyloxy)but-2-enoate (3o):[11] Yield 84%; colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.53 (s, 1 H), 4.11 (q, J = 7.2 Hz, 2 H), 3.96 (m, 2 H), 2.04 (s, 3 H), 1.20–1.30 (m, 15 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 163.9, 159.7, 151.3, 107.9, 59.6, 46.5 (2 C), 21.8 (2 C), 21.2 (2 C), 20.4, 14.2 ppm. MS (ESI): m/z = 258 [M^+ + H].

Ethyl 2-(Diisopropylcarbamoyloxy)cyclohex-1-ene-1-carboxylate (3p):[11] Yield 85%; yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.15 (q, J = 7.2 Hz, 2 H), 3.91–3.98 (m, 2 H), 2.40 (br. m, 2 H), 2.28 (br. m, 2 H), 1.71 (br., 4 H), 1.20–1.30 (m, 15 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 166.5, 154.6, 152.2, 117.7, 60.1, 46.3,

29.3, 25.3, 23.4, 23.3, 22.0, 21.7, 21.2, 20.4, 20.1, 14.1 ppm. MS (ESI): *m*/*z* = 298 [M$^+$ + H].

2-Acetylphenyl Dimethylcarbamate (5a):[11] Yield 99%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.77 (dd, *J* = 8.0, 1.8 Hz, 1 H), 7.55 (td, *J* = 8.0, 1.8 Hz, 1 H), 7.28 (td, *J* = 8.0, 1.8 Hz, 1 H), 7.14 (dd, *J* = 8.0, 1.8 Hz, 1 H), 3.15 (s, 3 H), 3.03 (s, 3 H), 2.56 (s, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 197.9, 154.3, 149.8, 133.0, 131.4, 129.7, 125.2, 123.8, 36.6, 36.4, 29.4 ppm. MS (ESI): *m*/*z* = 230 [M$^+$ + Na].

2-Acetylphenyl Diethylcarbamate (5b):[11] Yield 99%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.75 (dd, *J* = 7.8, 1.8, Hz, 1 H), 7.51 (td, *J* = 8.0, 1.8, Hz, 1 H), 7.27 (td, *J* = 7.6, 1.2, Hz, 1 H), 7.13 (d, *J* = 8.0 Hz, 1 H), 3.34–3.55 (m, 4 H), 2.55 (s, 3 H), 1.15–1.36 (m, 6 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 198.2, 153.7, 149.8, 132.9, 131.9, 129.6, 125.2, 123.7, 42.2, 41.9, 29.5, 14.1, 13.2 ppm. MS (ESI): *m*/*z* = 236 [M$^+$ + H].

2-Acetylphenyl Piperidine-1-carboxylate (5c):[11] Yield 99%; colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 7.8 Hz, 1 H), 7.48 (t, *J* = 8.0 Hz, 1 H), 7.27 (d, *J* = 7.4 Hz, 1 H), 7.13 (d, *J* = 8.0 Hz, 1 H), 3.65 (br. m, 2 H), 3.52 (br. m, 2 H), 2.56 (s, 3 H), 1.61 (br., 6 H) ppm. ^{13}C MR (50 MHz, $CDCl_3$): δ = 198.0, 153.1, 149.9, 133, 131.6, 129.7, 125.3, 123.9, 45.6, 45.2, 29.7, 25.8, 25.6, 24.2 ppm. MS (ESI): *m*/*z* = 248 [M$^+$ + H].

2-Acetylphenyl Diisopropylcarbamate (5d):[11] Yield 87%; colourless crystalline solid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 7.6 Hz, 1 H), 7.49 (t, *J* = 7.4 Hz, 1 H), 7.26 (t, *J* = 7.4 Hz, 1 H), 7.12 (d, *J* = 7.0 Hz, 1 H), 4.21 (m, 1 H), 3.90 (m, 1 H), 2.54 (s, 3 H), 1.33 (t, *J* = 6.6 Hz, 12 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 198.3, 152.8, 149.6, 132.8, 132.3, 129.4, 125.1, 123.7, 46.9, 46.5, 29.6, 29.5, 21.2, 20.9, 20.4 ppm. MS (ESI): *m*/*z* = 264 [M$^+$ + H].

Methyl 2-(Dimethylcarbamoyloxy)-5-methylbenzoate (5e):[11] Yield 82%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 1.6, Hz 1 H), 7.32 (dd, *J* = 7.8, 1.6 Hz 1 H), 7.05 (d, *J* = 8.2 Hz, 1 H), 3.88 (s, 3 H), 3.13 (s, 3 H), 3.08 (s, 3 H), 2.36 (s, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 165.3, 154.9, 149.1, 135.0, 134.1, 131.7, 123.8, 123.0, 119.6, 51.8, 36.6, 20.5 ppm. MS (ESI): *m*/*z* = 238 [M$^+$ + H].

2-Benzoyl-5-methoxyphenyl Dimethylcarbamate (5f):[11] Yield 80%; colourless crystalline solid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.22–7.77 (m, 2 H), 7.42–7.56 (m, 4 H), 6.76–6.85 (m, 2 H), 3.86 (s, 3 H), 2.8 (s, 3 H), 2.63 (s, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 194.5, 162.9, 153.6, 151.5, 138.7, 132.2, 132.1, 129.4 (2 C), 128.0 (2 C), 124.1, 111.1, 108.8, 55.6, 36.4, 35.8 ppm. MS (ESI): *m*/*z* = 300 [M$^+$ + H].

2-Benzoyl-5-methoxyphenyl Diethylcarbamate (5g):[11] Yield 87%; yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.71–7.79 (m, 2 H), 7.41–7.52 (m, 4 H), 6.78–6.84 (m, 2 H), 3.86 (s, 3 H), 3.21 (q, *J* = 7.0 Hz, 2 H), 3.03 (q, *J* = 7.0 Hz, 2 H), 1.0–1.13 (m, 6 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 194.5, 162.7, 152.9, 151.3, 138.5, 132.3, 131.9, 129.6 (2 C), 128.1 (2 C), 124.4, 110.9, 108.6, 55.5, 41.9, 41.4, 13.7, 13.0 ppm. MS (ESI): *m*/*z* = 328.

2-Benzoyl-5-methoxyphenyl Piperidine-1-carboxylate (5h):[11] Yield 67%; colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.74–7.78 (m, 2 H), 7.42–7.54 (m, 4 H), 6.76–6.85 (m, 2 H), 3.86 (s, 3 H), 3.29 (br. m, 2 H), 3.1 (br. m, 2 H), 1.46–1.56 (m, 6 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 194.5, 189.8, 162.8, 152.4, 151.3, 138.7, 132.3, 132.0, 129.5 (2 C), 128.1 (2 C), 124.3, 111.3, 108.6, 55.6, 44.9, 29.6, 25.3, 24.0 ppm. MS (ESI): *m*/*z* = 340 [M$^+$ + Na].

2-Phenylcarbamoylphenyl Dimethylcarbamate (5i):[11] Yield 64%; yellow amorphous solid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.59 (br., 1 H), 7.77 (dd, *J* = 1.8, 7.8 Hz, 1 H), 7.51–7.63 (m, 2 H), 7.29–7.48 (m, 4 H), 7.09–7.16 (m, 2 H), 3.10 (s, 3 H), 3.01 (s, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 164.2, 155.2, 148.0, 138.1, 131.7, 130.4, 129.9 (2 C), 129.0 (2 C), 126.2, 124.3, 123.2, 119.6, 36.8, 36.6 ppm. MS (ESI): *m*/*z* = 285 [M$^+$ + H].

2-Acetyl-4-flurophenyl Dimethylcarbamate (5j): Yield 80%; yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.44 (dd, *J* = 8.7, 3 Hz, 1 H), 7.12–7.21 (m, 2 H), 3.14 (s, 3 H), 3.03 (s, 3 H), 2.55 (s, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 197.2, 162.5, 154.8, 146.4, 133.1, 126.1, 120.3, 116.9, 37.4, 37.0, 30.1 ppm. FTIR (KBr pellet): $\tilde{\nu}$ = 2933, 1727, 1691, 1618, 1585, 1483, 1389, 1265, 1159, 1007, 815, 750, 558 cm^{-1}. UV (MeOH): λ_{max} (logε) = 206 (4.20), 235 (4.25), 289 (4.34) nm. MS (ESI): *m*/*z* = 225 [M$^+$ + H]. HRMS (ESI): *m*/*z* [M$^+$ + Na] calcd. for $C_{11}H_{12}FNO_3Na$ 248.0699; found 248.0701.

2-Acetyl-4-bromophenyl Dimethylcarbamate (5k): Yield 74%; colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 2.4 Hz, 1 H), 7.60 (dd, *J* = 2.4, 1.2 Hz, 1 H), 7.04 (d, *J* = 8.6 Hz, 1 H), 3.13 (s, 3 H), 3.02 (s, 3 H), 2.54 (s, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 196.5, 153.8, 148.8, 135.7, 132.9, 132.4, 125.6, 118.3, 36.7, 36.4, 29.4 ppm. FTIR (KBr pellet): $\tilde{\nu}$ = 2928, 1727, 1690, 1591, 1565, 1472, 1384, 1213, 1160, 1067, 864, 752, 657, 509 cm^{-1}. UV (MeOH): λ_{max} (logε) = 238 (4.40), 291 (4.49), 367 (4.59) nm. MS (ESI): *m*/*z* = 285 [M$^+$ + H]. HRMS (ESI): *m*/*z* [M$^+$ + Na] calcd. for $C_{11}H_{12}BrNO_3Na$ 307.9898; found 307.9896.

2-Acetyl-4-chlorophenyl Dimethylcarbamate (5l): Yield 66%; colourless crystalline solid; m.p. 62–64 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 2.6 Hz, 1 H), 7.45 (dd, *J* = 2.6, 0.6 Hz, 1 H), 7.09 (d, *J* = 8.6 Hz, 1 H), 3.13 (s, 3 H), 3.02 (s, 3 H), 2.54 (s, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 196.6, 153.9, 148.3, 132.7, 132.6, 130.8, 129.4, 125.3, 36.7, 36.4, 29.4 ppm. FTIR (KBr pellet): $\tilde{\nu}$ = 2928, 1728, 1692, 1570, 1592, 1474, 1386, 1206, 1160, 1098, 865, 749, 669, 513 cm^{-1}. UV (MeOH): λ_{max} (logε) = 211 (4.25), 235 (4.30), 292 (4.39) nm. MS (ESI): *m*/*z* = 242 [M$^+$ + H]. HRMS (ESI): *m*/*z* [M$^+$ + Na] calcd. for $C_{11}H_{12}ClNO_3Na$ 264.0403; found 264.0402.

2-Acetylnaphthyl Dimethylcarbamate (5m): Yield 58%; yellow amorphous solid; m.p. 86–88 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.0–8.05 (m, 1 H), 7.70–7.84 (m, 3 H), 7.53–7.60 (m, 2 H), 3.31 (s, 3 H), 3.0 (s, 3 H), 2.65 (s, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 198.0, 169.9, 154.1, 146.9, 136.1, 128.2, 127.8, 127.6, 127.0, 125.3, 124.9, 122.8, 36.9, 36.7, 29.8 ppm. FTIR (KBr pellet): $\tilde{\nu}$ = 2923, 1728, 1682, 1627, 1598, 1465, 1364, 1273, 1148, 1070, 817, 751, 681, 551 cm^{-1}. UV (MeOH): λ_{max} (logε) = 210 (4.29), 243 (4.35), 284 (4.42), 333 (4.49) nm. MS (ESI): *m*/*z* = 258 [M$^+$ + H]. HRMS (ESI): *m*/*z* [M$^+$ + Na] calcd. for $C_{15}H_{15}NO_3Na$ 280.0950; found 280.0948.

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H and ^{13}C NMR spectra for all reaction products.

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