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FULL PAPER

Synthesis of Carbamates from Alkyl Bromides and Secondary Amines using Silver Carbonate

Vanitha Acharya,[a], [c] Sanjib Mal,[a] Jagadeesh P. Kilaru,[a] Mark G. Montgomery,[b] Sudhindra H. Deshpande,[a] Ravindra P. Sonawane,[a] Bhanu N. Manjunath,[a] and Sitaram Pal*[a]

Abstract: Synthesis of alkyl carbamates from alkyl bromides and secondary amines using silver carbonate as a carbonate source under mild condition is described. Various secondary amines and bromo derivatives were converted into alkyl carbamate derivatives in 33 to 62% yield.

Introduction

Carbamate functionality received much attention because of their omnipresence in many natural products,[1] pharmaceuticals[2] and agrochemicals. [3] Carbamates are also used as protecting groups in peptide synthesis[4] and as intermediates in numerous organic syntheses. [5]

These carbamate groups are used as protecting groups, toxophores in biologically active molecules or as prodrugs for better biochemical properties.[6] In literature, many methods have been reported for the synthesis of carbamates.[7] These preparations mainly include reacting chloroformates[8] or dialkyl carbonates[9] with amines, and alcohols with isocyanates[10a-d] or isocyanides. [10e], [10f] Carbon monoxide[11] and carbon dioxide [12] have been used as carbonate source for the synthesis of carbamates in the presence of metal catalyst at elevated pressure. Most of these methods suffered from drawbacks including use of toxic phosgene gas or phosgene derivatives, carbon monoxide or carbon dioxide gases at high pressure or temperature where tolerability of sensitive functional group is a concern. [13]

Alkali metal carbonates and bicarbonates were used for the synthesis of carbonates[14a],[14b] and carbamates[14c],[14d] in literature in the presence of CO_2 or with the metal catalyst. Transition metal carbonates like silver carbonate (Ag_2CO_3) has been used in excess amount for the synthesis of carbonate. [15]

Recenltly Yuan's group reported the synthesis of carbamate from propiophenone and secondary amine at 90 °C under 3 Mpa CO_2 pressure in the presence of nBu$_4$NI and oxidant (Scheme 1 a). [12a]

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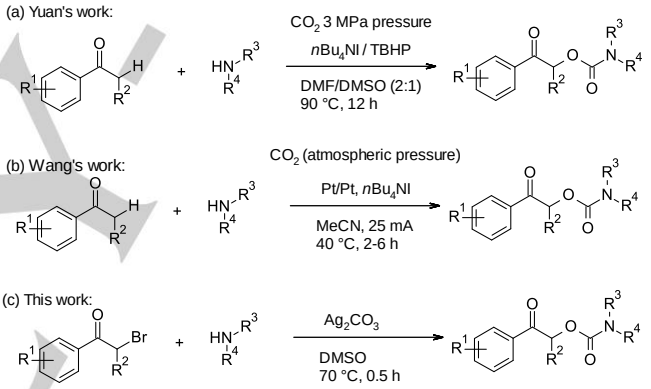
In 2019 Wang's group disclosed the synthesis of carbamates via electrocatalytic fixation of CO_2 with secondary amines and aryl ketones (Scheme 1 b).[12b] However, to the best of our knowledge, there have been no reports for the synthesis of carbamates of α-halopropiophenones using metal carbonates as carbonate source. Herein we report a mild protocol for the synthesis of alkyl carbamates from alkyl halides and secondary amines using Ag_2CO_3, with good functional group tolerance (Scheme 1 c).



Scheme 1. Carbamate synthesis from propiophenone derivatives.

Results and Discussion

For optimization of the reaction α-Bromo propiophenone (**1a**) and morpholine (**2a**) were chosen as the model substrates. The reaction conditions and the results are summarized in Table 1. In the presence of K_2CO_3 in DMF or DMSO at room temperature, 3% of carbamate **3a** was obtained along with major product **4a** (Table 1, entry 1). This finding encouraged us to explore different carbonate sources to increase the carbamate formation. Use of cesium carbonate as base afforded 15% of **3a** along with **4a** as a major product (Table 1, entry 4). When transition metal carbonate-Ag_2CO_3 was tried, **3a** was formed as a major product at room temperature (Table 1, entry 6). At 70 °C, the desired product was obtained in higher ratio (Table 1, entry 7) compared to entry 6 in table 1. Unlike Ag_2CO_3, other transition metal carbonates like manganese carbonate, cobalt carbonate, nickel carbonate, copper carbonate, and zinc carbonate were not useful in this transformation (Table 1, entry 16-20). Other solvents like acetonitrile, acetone, toluene, tetrahydrofuran, 1,2-dichloroethane, ethanol, *N*-methyl-2-pyrrolidone in combination

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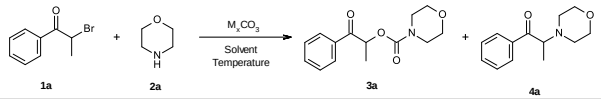
Table 1. Optimization of the reaction condition[a]



Entry	Carbonate source	Solvent[b]	Time (h)	Ratio (%)[c]	
				3a	4a
1	K_2CO_3	DMSO/DMF	16	3	97
2	Na_2CO_3	DMSO	16	2	97
3	$KHCO_3$	DMSO	16	5	95
4	Cs_2CO_3	DMSO	16	15	86
5	$CaCO_3$	DMSO	16	1	99
6	Ag_2CO_3	DMSO	16	75	25
7[b]	**Ag_2CO_3**	**DMSO**	**0.5**	**80**	**20**
8	Ag_2CO_3	DMF	16	76	24
9	Ag_2CO_3	Acetonitrile	16	64	36
10	Ag_2CO_3	Acetone	16	41	59
11	Ag_2CO_3	Toluene	16	23	77
12	Ag_2CO_3	Tetrahydrofuran	16	20	80
13	Ag_2CO_3	1,2-Dichloroethane	16	35	65
14	Ag_2CO_3	Ethanol	16	50	50
15	Ag_2CO_3	*N*-methyl pyrrolidone	16	55	45
16	$MnCO_3$	DMSO	16	0	>95
17	$CoCO_3$	DMSO	16	0	90
18	$NiCO_3$	DMSO	16	0	>95
19	$CuCO_3$	DMSO	16	0	50
20	$ZnCO_3$	DMSO	16	0	80

[a] *α*-Bromopropiophenone **1a** (0.5 mmol), morpholine **2a** (1.5 equiv), and carbonate source (2.5 equiv) were used in 2 mL of solvent at RT for 16 h. [b] heated at 70 °C for 0.5 h. [c] Ratios were determined by ^{1}H NMR.

with Ag_2CO_3 gave poor conversion (entries 9–15). Whereas the conversion in *N,N*-Dimethylformamide as a solvent was comparable to that of dimethylsulfoxide (Table 1, entry 8). Structures of the carbamate products were determined by 1H NMR and 13C NMR analysis. One of the representative carbamate products **3a** was confirmed by single-crystal X-ray analysis (Figure 1).

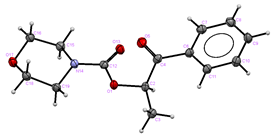
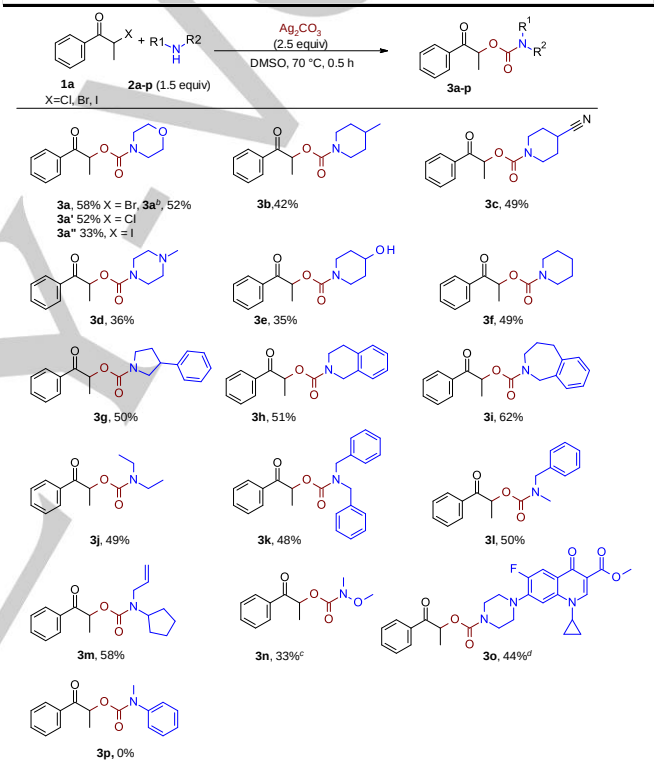


Figure 1. Single crystal of **3a**.

Moiety **3a** was prepared using *α*-bromopropiophenone as well as *α*-chloro and *α*-iodopropiophenones. Low yield (33%) was obtained using *α*-iodopropiophenone. Whereas, both bromo and chloro derivatives resulted in a comparable yield of **3a**. The synthesis of *α*-bromopropiophenone derivatives is more convenient than the *α*-chloro derivatives with better yields. Hence, *α*-bromopropiophenone derivatives were used to study substrate scope variation. A wide range of amines, including symmetric and unsymmetric secondary amines, cyclic and alicyclic secondary amines were treated under the optimized condition (**Table 2**), to furnish the corresponding carbamate derivatives **3a–3o** in moderate to good yields (33**–**62% yield). Primary amines such as benzylamine, aliphatic primary amines and *N*-methylaniline (**2p**) failed to give the desired product (**3p**) under this reaction condition.

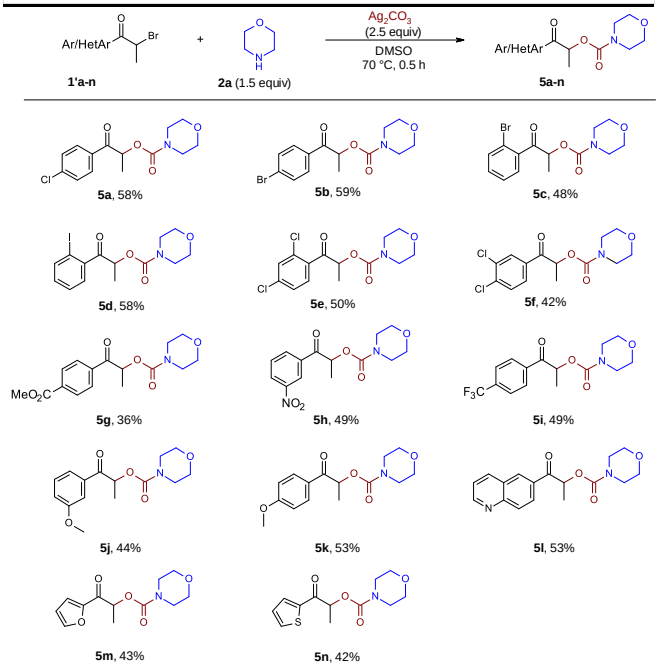
Table 2. Substrate Scope of Various Secondary Amines[a]



[a] Reaction condition: *α*-Bromopropiophenone **1a** (1.0 mmol), **2a–p** (1.5 equiv), and silver carbonate (2.5 equiv) in 3.5 ml DMSO, isolated yields. [b] The reaction performed in 10 mmol scale. [c] HCl salt of **2n** and 3.5 equiv of Ag_2CO_3 were used. [d] 1.2 equiv of **2o** was used.

Ciprofloxacin, an antibiotic, was converted into its methyl ester **2o**. This methyl ester **2o** was successfully converted into its

Table 3. Substrate Scope of Various Aryl/Heteroaryls[a]

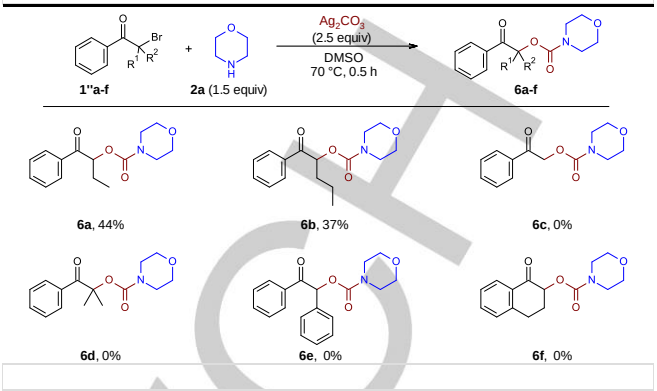


[a] Reaction condition: *α*-bromoethyl aryl(heteroaryl) ketones **1'a–1'n** (1 mmol), morpholine **2a** (1.5 equiv), and Ag_2CO_3 (2.5equiv) in 3.5 mL of DMSO at 70 °C for 0.5 h, isolated yields based on **1'a-n**.

carbamate **3o** in 44% yield. A wide range of functional groups like nitrile, hydroxyl, allylic groups as well as *N,O*-dimethylhydroxylamine group and ester group are well tolerated under this optimized reaction condition (**3c**, **3e**, **3m, 3n**, **3o**).

To further study the scope of this protocol, a variety of *α*-bromoketones, derived from aryl and heteroaryl substrates were examined (Table 3). To our delight, various propiophenone derivatives bearing electron-donating groups or electron-withdrawing groups such as methoxy, trifluoromethyl, methyl ester, nitro, halides (Cl, Br, I) at *ortho*, *meta* and *para*-positions of the benzene ring afforded the desired products **5a–5k** in 42**–**59% yields. Notably, the heteroaryl *α*-bromoketones containing quinoline (**1l**), furan (**1m**) and thiophene (**1n**) delivered the desired products **5l**–**5n** in 42**–**53% yields.

Table 4. Substrate scope for side chain variation[a]

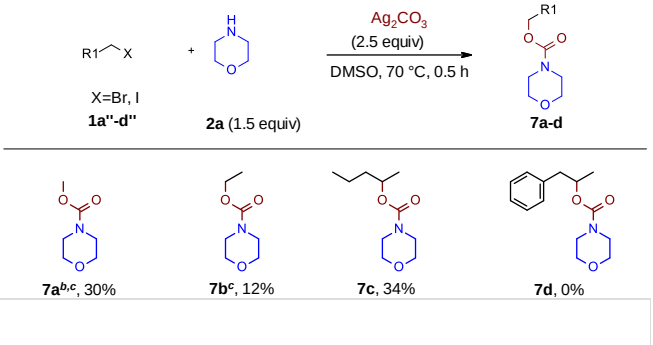


[a] Reaction condition: *α*-bromoalkylphenone **1"a**–**1"f** (1.0 mmol), morpholine **2a** (1.5 equiv) and silver carbonate (2.5 equiv) in 3.5 mL DMSO at 70 °C for 0.5 h, isolated yield.

To study the effect of alkyl side chains R^1 and R^2, different *α*-bromoalkylphenones were subjected to optimized reaction condition (Table 4). The alkyl groups like methyl (optimization substrate), ethyl, *n*-propyl gave the desired product **3a**, **6a**, **6b** respectively in 58%, 44%, 37% yield. Whereas bromo acetophenone (**1"c**), 2-Bromoisobutyrophenone (**1"d**), desyl bromide (**1"e**) and 2-bromo-1-tetralone (**1"f**) gave complex mixture, and desired products **6c**, **6d**, **6e**, **6f** respectively were not obtained.

In order to study the importance of the keto group in the substrate (Table 5), 2-bromopropylbenzene (**1d"**) was reacted with morpholine. In this case the desired product **7d** was not obtained, instead, the elimination product (*β*-methylstyrene) was obtained as a sole product. However 2-bromopentane (**1c"**) provided the corresponding carbamate (**7c**) with 34% yield. Likewise, using ethyl bromide provided the desired product **7b** with 12% yield. Employment of methyl iodide resulted in 30% yield of the corresponding carbamate 7**a**. This suggests that the keto group is not necessary for the synthesis of carbamate under the optimized reaction condition.

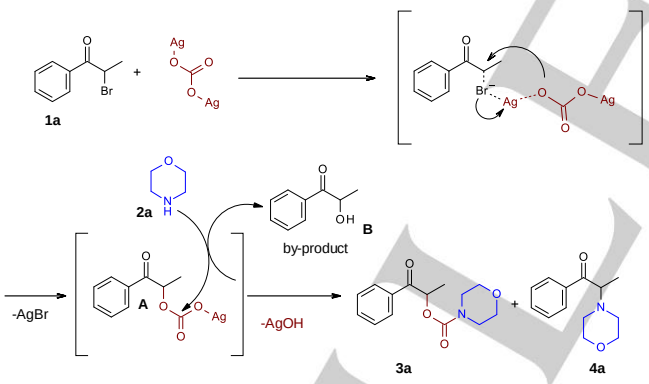
Table 5. Substrate Scope for *α*-haloalkanes[a]



[a] Reaction condition: alkyl halide **1a"**–**1d"** (1.0 mmol), morpholine **2a** (1.5 equiv), and Ag_2CO_3 (2.5 equiv) were used in 3.5 mL of DMSO at 70 °C for 0.5 h. [b] Methyl iodide was used. [c] Reaction carried out at 40 °C used.

Formation of product **3a** under the optimized reaction condition prompted the investigation of the probable pathways. In order to understand the reaction mechanism, a series of ^{1}H NMR and ^{13}C NMR experiments were performed to investigate the

intermediates of the reaction. Initial interaction of the *α*-bromopropiophenone with Ag_2CO_3 in DMSO-d_6 indicated shifts in ppm values of ^{1}H NMR and ^{13}C NMR of the *α*-bromopropiophenone {Ph**CO**C**H**(Br)CH_3} C-H proton and carbonyl carbon (*see supporting information*).^{1}H NMR analysis showed that along with ^{1}H NMR signals of the unreacted bromo compound **1a** and compound **B**, a new ^{1}H NMR signal at *δ* 6.0 ppm was observed. Further, ^{13}C NMR analysis showed **C**-H carbon signal at *δ* 75.07 ppm and carbonyl signals at 196.38 and 153.87 ppm. These signals do not match with that of compound **B** as well as **1a**. These signals were proposed to be of the intermediate **A** (Scheme 2). The signal at *δ* 153.87 ppm in ^{13}C NMR provided additional evidence to the formation of the intermediate **A**. No shift in ppm values was observed when a similar experiment was conducted with morpholine and Ag_2CO_3. In another experiment, *α*-Bromopropiophenone **1a** and Ag_2CO_3 (2.5 equiv) were heated in DMSO at 70 °C, until all the bromo compound was consumed (4 h) and then morpholine **2a** was added. The heating was further continued at 70 °C for another 0.5 h. The ^{1}H NMR of the crude reaction mixture after workup was recorded. This analysis revealed formation compound **B**[16], [17] with no indication of compound of **3a** and **4a**. The above mentioned procedure was repeated in DMF as a solvent. The crude ^{1}H NMR analysis revealed the formation of **3a** (31%), along with the formation of **B** (43%). This indicated that intermediate **A** is more stable in DMF than DMSO. Hence the intermediate **A** is available to react with morpholine **2a**, which is indicated by the formation of product **3a** in DMF. However when the reaction was performed with morpholine initially along with *α*-bromopropiophenone and Ag_2CO_3 in DMSO, the major product obtained was **3a**.



Scheme 2. Proposed Mechanism.

DSC and TGA studies showed no production of CO_2 from Ag_2CO_3under the reaction temperature (70 °C),[18] which is a probable reagent for carbamate formation. This gives a clear indication that in the carbamate formation reaction, there was no involvement of carbon dioxide. Hence we propose, the desired carbamate **3a** was formed by the attack of secondary amine **2a** on the intermediate-alkyl silver carbonate (**A**), which was formed by the interaction of *α*-bromopropiophenones **3a** and Ag_2CO_3 (Scheme 2). In the case of primary amine, the desired carbamate was not formed probably due to the direct attack of primary amine to the oxygen-*α*-carbon bond of intermediate **A**, which generates N-alkylated product. Hydroxy ketone (**B**) is always observed as a by-product due to the hydrolysis of intermediate **A**. Nucleophilicity or steric factor may be responsible for the specificity of this method for secondary amines.

Conclusions

In summary, we have demonstrated a novel methodology for the synthesis of alkyl carbamates using silver carbonate as a carbonate source under mild condition. A wide range of *α*-halopropiophenones with electron-donating groups as well as electron-withdrawing groups were reacted with various secondary amines to furnish the corresponding carbamate derivatives in moderate to good yield. A variety of functional groups like hydroxyl, methoxy, halides, nitrile, nitro, *N*-allyl and ester were well tolerated under the optimized reaction condition. This portrays the broad substrate scope for the various *α*-halopropiophenones using Ag_2CO_3 as a carbonate source. Further, this methodology was successfully employed to convert methyl ester of ciprofloxacin **2o** into its carbamate derivative **3o** with a good yield of 44%. Moreover carbamate of *N,O*-dimethylhydroxylamine **3n** was also prepared with 33% yield with this methodology. Mechanistic investigation suggests the absence of CO_2 generation from silver carbonate, which in turn proves that carbon dioxide is not involved in carbamate formation. Thus the developed method showcases various merits including employment of low temperature (70 °C) condition with short reaction time (0.5 h). It also eliminates the need for the use of gases like CO_2, CO and phosgene derivatives.

Experimental Section

General Information: Unless otherwise noted, reactions were performed with the exclusion of air and moisture, under an inert atmosphere of nitrogen in oven-dried glassware with magnetic stirring. All reagents were obtained from commercial sources and used without further purification. Anhydrous dimethyl sulfoxide (DMSO), dichloroethane (DCE), *N*-methylpyrrolidone (NMP), ethanol and acetone were used as received. Tetrahydrofuran (THF), *N,N*-dimethylformamide (DMF), acetonitrile and toluene were obtained from a dry solvent dispenser. Thin-layer chromatography (TLC) was performed on aluminum plates precoated with silica gel F_{254}. They were visualized with UV-light (254 nm), or by charring with basic $KMnO_4$ solution ($KMnO_4$, Na_2CO_3, H_2O). Flash column chromatography was carried out using 35−70 µm, 230−400 mesh silica gel. ^{1}H NMR and ^{13}C NMR spectra were recorded without any internal standard. ^{1}H NMR spectra and ^{13}C NMR spectra were recorded on 400 MHz and 101 MHz (Bruker) respectively on AVANCE II/AVANCE III instruments. Chemical shifts are reported in ppm and calibrated for $CDCl_3$ (*δ* = 7.26 ppm), DMSO-d_6 (*δ* = 2.50 ppm) for ^{1}H NMR, and $CDCl_3$ (*δ* = 77.16 ppm), DMSO-d_6 (*δ*=40.00 ppm) for ^{13}C NMR spectroscopy. The coupling constants *J*, are reported in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet. High-Resolution Mass Spectrometry (HRMS) data of the products were acquired using Agilent 6520 Q-TOF instrument. Column chromatographic purifications were performed on a CombiFlash Rf (Teledyne Isco) with pre-packed SiO_2 columns (unless otherwise stated) using cyclohexane and ethyl acetate as the mobile phase. FTIR spectra were recorded on Shimadzu DRS Prestige 21. Melting points were determined in open capillary tubes with a SRS-OptiMelt digital melting point apparatus and are uncorrected.

General Procedure for the synthesis of carbamates: To a 0.28 M solution of *α*-bromoketone derivative (1.0 mmol, 1.0 equiv) in DMSO was added silver carbonate (2.5 mmol, 2.5 equiv) followed by secondary amine derivative (1.5 mmol, 1.5 equiv). The resultant mass was heated to 70 °C for 0.5 h. After completion (monitored by TLC) the reaction mass was cooled to room temperature, filtered through a pad of Celite® and the Celite® pad was washed with ethyl acetate. The filtrate was washed with water followed by brine solution. Ethyl acetate layer dried over anhydrous sodium sulphate and concentrated to get crude material. Purification was carried out in combi flash using and cyclohexane and ethyl acetate as eluent.

(1-Methyl-2-oxo-2-phenyl-ethyl) morpholine-4-carboxylate (3a):[12a] Obtained as light yellow solid; 152 mg (58%), mp 92–94 °C. Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.94 (d, *J* = 7.66 Hz, 2 H), 7.52–7.63 (m, 1 H), 7.42–7.52 (m, 2 H), 5.95 (q, *J* = 7.05 Hz, 1 H), 3.59–3.70 (m, 4 H), 3.34–3.63 (m, 4 H), 1.52 (d, *J* = 6.97 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 197.84, 154.72, 134.68, 133.62, 128.88, 128.60, 72.26, 66.71, 44.64, 44.13, 17.40. IR (KBr): 2990, 2878, 2858, 1703, 1691, 1595, 1450, 1421, 1387, 1280, 1246, 1109, 968, 856, 708 cm^{-1}.HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{14}H_{18}NO_4$, 264.1230; found 264.1230.

(1-Methyl-2-oxo-2-phenyl-ethyl) morpholine-4-carboxylate (3a*b*) 1.36 g (52%) from 10 mmol batch.

(1-Methyl-2-oxo-2-phenyl-ethyl) 4-methylpiperidine-1-carboxylate (3b): Obtained as light brown solid; 116 mg (42.13%), mp 57–59 °C. Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.95 (d, *J* = 7.65 Hz, 2 H), 7.51–7.63 (m, 1 H), 7.40–7.51 (m, 2 H), 5.91 (q, *J* = 6.97 Hz, 1 H), 4.12 (br s, 2 H), 2.65–2.91 (m, 2 H), 1.70 (br s, 1 H), 1.53–1.64 (m, 2 H), 1.50 (d, *J* = 6.97 Hz, 3 H), 1.03–1.18 (m, 2 H), 0.93 (d, *J* = 6.48 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 198.28, 154.73, 134.94, 133.41, 128.78, 128.62, 71.94, 44.53, 34.04, 30.97, 21.94, 17.34. IR (KBr): 2924, 2357, 2328, 1693, 1470, 1447, 1435, 1236, 1153, 1099, 968, 700 cm^{-1}. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{16}H_{22}NO_3$, 276.1594; found 276.1597.

(1-Methyl-2-oxo-2-phenyl-ethyl) 4-cyanopiperidine-1-carboxylate (3c): Obtained as off white solid; 140 mg (48.9%), mp 97–99 °C. Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* ppm 7.89–7.96 (m, 2 H), 7.41–7.60 (m, 3 H), 5.93 (q, *J* = 7.09 Hz, 1 H), 3.28–3.93 (m, 4 H), 2.85 (br s, 1 H), 1.75–2.00 (m, 4 H), 1.51 (d, *J* = 7.09 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* ppm 197.80, 154.46, 134.59, 133.62, 128.85, 128.50, 120.95, 72.34, 42.21, 28.38, 26.24, 17.32. IR (KBr): 2955, 2905, 2235, 1707, 1692, 1449, 1429, 1306, 1279, 1234, 1138, 1036, 970, 939, 766, 700 cm^{-1}. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{16}H_{19}N_2O_3$ 287.1390; found 287.1391.

(1-Methyl-2-oxo-2-phenyl-ethyl) 4-methylpiperazine-1-carboxylate (3d):[12a] Obtained as light yellow oil; 99.5 mg (36%). Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* ppm 7.89–7.97 (m, 2 H), 7.56 (t, *J* = 7.40 Hz, 1 H), 7.45 (t, *J* = 7.64 Hz, 2 H), 5.92 (q, *J* = 7.01 Hz, 1 H), 3.36–3.73 (m, 4 H), 2.41 (br s, 4 H), 2.31 (s, 3 H), 1.50 (d, *J* = 6.97 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* ppm 197.94, 154.59, 134.72, 133.51, 128.81, 128.57, 72.14, 54.65, 46.11, 43.96, 43.67, 17.34. IR (NaCl): 2936, 2849, 2795, 1701, 1693, 1597, 1460, 1448, 1433, 1292, 1261, 1240, 1151, 1151, 1111, 1103, 968, 893, 762, 702 cm^{-1}. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{15}H_{21}N_2O_3$, 277.1547; found 277.1533.

(1-Methyl-2-oxo-2-phenyl-ethyl) 4-hydroxypiperidine-1-carboxylate (3e): Obtained as yellow gummy mass; 97 mg (34.98%). Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* ppm 7.94 (d, *J* = 7.21 Hz, 2 H), 7.57 (t, *J* = 7.34 Hz, 1 H), 7.46 (t, *J* = 7.58 Hz, 2 H), 5.92 (q, *J* = 6.97 Hz, 1 H), 3.75–4.01 (m, 3 H), 3.03–3.31 (m, 2 H), 1.85 (m, 3 H), 1.51 (d, *J* = 6.97 Hz, 5 H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* ppm 198.15, 154.74, 134.80, 133.54, 128.85, 128.61, 72.14, 67.47, 41.62, 34.11, 17.37. IR (KBr): 2922, 2851, 1688, 1647, 1470, 1437, 1375, 1271, 1225, 1136, 1094, 1072, 1028, 968, 760, 702 cm^{-1}. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{15}H_{20}NO_4$, 278.1387; found 278.1398.

(1-Methyl-2-oxo-2-phenyl-ethyl) piperidine-1-carboxylate (3f):[12a] Obtained as light yellow oil; 128.9 mg (49.33%). Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* ppm 7.95 (d, *J* = 7.68 Hz, 2 H), 7.51–7.62 (m, 1 H), 7.46 (t, *J* = 7.55 Hz, 2 H), 5.92 (q, *J* = 7.01 Hz, 1 H), 3.31–3.56 (m, 4 H), 1.46–1.61 (m, 9 H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* ppm 198.30, 154.76, 134.93, 133.42, 128.79, 128.64, 71.93, 45.17, 25.76, 24.46, 17.36. IR (NaCl): 2936, 2855, 1693, 1433, 1263, 1234, 1150, 1097, 966, 702 cm^{-1}. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{15}H_{20}NO_3$, 262.1438; found 262.1444.

(1-Methyl-2-oxo-2-phenyl-ethyl) 3-phenylpyrrolidine-1-carboxylate (3g): Obtained as light brown gummy mass; 163 mg (50.40%). Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): (Mixture of two rotational isomers in the ration 1:1) *δ* ppm: 7.98 (br d, *J* = 7.95 Hz, 2 H), 7.52–7.62 (m, 1 H), 7.42–7.52 (m, 2 H), 7.26–7.37 (m, 2 H), 7.20–7.24 (m, 3 H), 5.94–6.02 (m, 1 H), 3.83–4.07 (m, 1 H), 3.63–3.80 (m, 1 H), 3.32–3.60 (m, 3 H), 2.17–2.36 (m, 1 H), 1.88–2.15 (m, 1 H), 1.45–1.60 (m, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* ppm 198.14, 198.11, 154.13, 141.21, 141.12, 141.05, 134.81, 133.42, 128.75, 128.69, 128.59, 127.11, 127.08, 126.92, 126.90, 71.81, 71.76, 52.44, 52.37, 52.36, 52.23, 46.23, 46.19, 45.95, 45.89, 44.28, 44.15, 43.44, 43.24, 33.40, 33.24, 32.57, 32.30, 17.43, 17.39. IR (KBr): 2926, 2359, 2342, 1697, 1450, 1425, 1231, 1138, 1119, 968, 758, 700cm^{-1}. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{22}NO_3$, 324.1594; found 324.1583.

(1-Methyl-2-oxo-2-phenyl-ethyl) 3,4-dihydro-1H-isoquinoline-2-carboxylate (3h): Obtained as light yellow oil; 158.4 mg (51.2%). Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* ppm 7.96 (d, *J* = 7.19 Hz, 2 H), 7.51–7.61 (m, 1 H), 7.38–7.51 (m, 2 H), 7.08–7.22 (m, 4 H), 5.99 (br d, *J* = 7.09 Hz, 1 H), 4.73 (br s, 1 H), 4.61 (br s., 1 H), 3.53–3.84 (m, 2 H), 2.77–2.95 (m, 2 H), 1.54–1.56 (d, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* ppm 198.03, 154.95, 134.84, 134.63, 133.52, 132.10, 128.84, 128.64, 126.66, 126.47, 126.39, 72.24, 72.17, 45.92, 41.98, 41.59, 29.12, 28.85, 17.47. IR (NaCl): 3068, 3020, 2929, 2401, 1695, 1436, 1215, 767, 754, 699 cm^{-1}. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{19}H_{20}NO_3$, 310.1438; found 310.1440.

(1-Methyl-2-oxo-2-phenyl-ethyl) 1,3,4,5-tetrahydro-2-benzazepine-2-carboxylate(3i): Obtained as off white solid; 200 mg (62%), mp 113–115 °C. Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, DMSO-d_6): Mixture of two rotational isomers (ratio ~0.75 : 1) *δ* ppm 7.90 (br d, *J* = 7.78 Hz, 2 H), 7.63 (q, *J* = 7.19 Hz, 1 H), 7.40–7.55 (m, 2 H), 7.05–7.27 (m, 4 H), 5.84 (q, *J* = 6.78 Hz, 0.43 H), 5.73 (q, *J* = 6.86 Hz, 0.57 H), 4.31–4.62 (m, 2 H), 3.82 (br d, *J* = 14.31 Hz, 1 H), 3.35–3.73 (m, 1 H), 2.83–3.05 (m, 2 H), 1.43–1.79 (m, 2 H), 1.40 (d, *J* = 6.8Hz, 1.66 H), 1.34 (d, *J* = 6.8Hz, 1.34 H). ^{13}C NMR (101 MHz, DMSO-d_6): *δ* ppm 198.02, 197.84, 154.46, 154.28, 142.42, 142.24, 138.90, 138.65, 134.52, 134.43, 134.03, 133.95, 129.86, 129.79, 129.58, 129.29, 129.24, 128.68, 127.89, 127.79, 126.28, 126.17, 72.55, 71.99, 52.17, 51.75, 50.47, 34.81, 34.74, 28.71, 28.27, 17.55, 17.44. IR (KBr): 3017, 2982, 2928, 2841, 1693, 1685, 1466, 1449, 1423, 1285, 1225, 1105, 968, 764, 700 cm^{-1}. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{22}NO_3$, 324.1594; found 324.1589.

(1-Methyl-2-oxo-2-phenyl-ethyl) N,N-diethylcarbamate (3j):[12a] Obtained as light yellow oil; 122.9 mg (49.3%). Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz,

$CDCl_3$): δ ppm 7.95 (d, *J* = 7.46 Hz, 2 H), 7.50–7.61 (m, 1 H), 7.40–7.50 (m, 2 H), 5.95 (q, *J* = 6.97 Hz, 1 H), 3.31 (br s, 4 H), 1.50 (d, *J* = 6.97 Hz, 3 H), 1.12 (br s, 6 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm 198.30, 155.20, 135.04, 133.35, 128.76, 128.60, 71.71, 42.09, 41.61, 17.33, 14.06, 13.54. IR (NaCl): 3563, 3019, 2928, 1693, 1477, 1431, 1381, 1275, 1215, 1175, 1097, 962, 758 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{20}NO_3$, 250.1438; found 250.1450.

(1-Methyl-2-oxo-2-phenyl-ethyl) N,N-dibenzylcarbamate (3k):[12a] Obtained as light brown gummy mass; 180.15 mg (48.25%). Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.00 (d, *J* = 7.63 Hz, 2 H), 7.54–7.65 (m, 1 H), 7.49 (t, *J* = 7.56 Hz, 2 H), 7.25–7.38 (m, 8 H), 7.19–7.21 (d, *J* = 8 Hz, 2H), 6.06 (q, *J* = 6.97 Hz, 1 H), 4.36–4.54 (m, 4 H), 1.56 (d, *J* = 6.97 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm 197.95, 156.10, 137.23, 137.17, 134.93, 133.47, 128.86, 128.73, 128.66, 128.11, 128.00, 127.56, 72.75, 49.43, 49.27, 17.35. IR (KBr): 3063, 3028, 2926, 1693, 1597, 1495, 1464, 1452, 1425, 1229, 1134, 1115, 972, 756, 700 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{24}H_{24}NO_3$, 374.1751; found 374.1762.

(1-Methyl-2-oxo-2-phenyl-ethyl) N-benzyl-N-methyl-carbamate (3l):[12a] Obtained as light yellow gummy mass; 150 mg (50.4%). Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): Mixture of rotational isomers in the ratio 1:1, δ ppm 7.98 (d, *J* = 7.70 Hz, 2 H), 7.58 (tt, *J* = 7.38, 1.24 Hz, 1 H), 7.47 (t, *J* = 7.58 Hz, 2 H), 7.18–7.37 (m, 5 H), 5.99 (dq, *J* = 14.56, 7.05 Hz, 1 H), 4.43–4.60 (m, 2 H), 2.86–2.92 (d, 3 H, -NCH3), 1.54 (br dd, *J* = 13.88, 7.03 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm 198.12, 197.98, 156.20, 155.67, 137.27, 134.87, 133.46, 128.82, 128.71, 128.63, 127.76, 127.73, 127.51, 72.49, 72.28, 52.67, 52.61, 34.31, 33.80, 17.39. IR (KBr): 2930, 1697, 1479, 1450, 1402, 1229, 1144, 970, 700 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{20}NO_3$, 298.1438; found 298.1432.

(1-Methyl-2-oxo-2-phenyl-ethyl) N-allyl-N-cyclopentyl-carbamate (3m): Obtained as light yellow oil; 174.64 mg (58%). Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.93–7.99 (m, 2 H), 7.57 (tt, *J* = 7.46 Hz, 1 H), 7.43–7.50 (m, 2 H), 5.96 (d, *J* = 6.36 Hz, 1 H), 5.84 (br. s., 1 H), 5.07–5.17 (m, 2 H), 4.31 (br. s., 1 H), 3.83 (br. s., 2 H), 1.84 (br. s., 2 H), 1.58–1.72 (m, 3 H), 1.51 (d, *J* = 6.97 Hz, 6 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm 198.21, 155.57, 135.50, 134.99, 133.39, 128.78, 128.65, 115.70, 72.01, 58.25, 46.34, 29.68, 23.95, 17.32. IR (KBr): 2955, 2870, 1697, 1653, 1449, 1420, 1373, 1256, 1229, 1136, 1101, 970, 772, 700 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{24}NO_3$, 302.1751; found 302.1752.

(1-Methyl-2-oxo-2-phenyl-ethyl) N-methoxy-N-methyl-carbamate (3n): Obtained as light yellow oil; 78.80 mg (33.21%). Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, CDCl3): δ ppm 7.94 (d, *J* = 7.01 Hz, 2 H), 7.52–7.62 (m, 1 H), 7.46 (t, *J* = 7.64 Hz, 2 H), 5.96 (q, *J* = 7.01 Hz, 1 H), 3.72 (s, 3 H), 3.18 (s, 3 H), 1.55 (d, *J* = 7.09 Hz, 3 H). ^{13}C NMR (101 MHz, CDCl3): δ ppm 197.31, 156.15, 134.60, 133.62, 128.85, 128.59, 72.75, 61.68, 35.52, 17.42. IR (KBr): 2988, 2974, 2936, 2909, 1719, 1701, 1456, 1420, 1377, 1231, 1165, 1092, 1045, 974, 756, 704 cm^{-1}. HRMS (ESI): m/z $[M + Na]^+$ calcd for C12H15NNaO4, 260.0893; found 260.0884.

Methyl 1-cyclopropyl-6-fluoro-7-[4-(1-methyl-2-oxo-2-phenyl-ethoxy)carbonylpiperazin-1-yl]-4-oxo-quinoline-3-carboxylate (3o): Obtained as off white solid; 230 mg (44.10%), mp 75–77 °C. Purification by reverse phase flash column chromatography on C-18 column [30% acetonitrile (0.1% formic acid)/water (0.1% formic acid)]. ^{1}H NMR (400 MHz, CDCl3): δ ppm 8.54 (s, 1 H), 8.04 (d, *J* = 13.08 Hz, 1 H), 7.96 (d, *J* = 7.71 Hz, 2 H), 7.56–7.62 (m, 1 H), 7.48 (t, *J* = 7.58 Hz, 2 H), 7.24–7.29 (m, 1 H), 5.99 (q, *J* = 6.97 Hz, 1 H), 3.94 (br s., 1 H), 3.91 (s, 3H), 3.76–3.85(m, 1H), 3.64–3.75(m, 1H), 3.54–3.63(m, 1H), 3.35–3.48(m, 1H), 3.13–3.34 (m, 4 H), 1.55 (d, *J* = 7.09 Hz, 3 H), 1.27–1.37 (m, 2 H), 1.10–1.20 (m, 2 H). ^{19}F NMR (377 MHz, $CDCl_3$): δ ppm -123.84 (s, 1 F). ^{13}C NMR (101 MHz, CDCl3): δ ppm 197.84, 173.08, 173.06, 166.35, 154.59, 153.46 (d, $^1J_{C-F}$ = 246.40 Hz), 148.52, 144.42 (d, $^2J_{C-F}$ = 10.30 Hz), 138.05, 134.59, 133.68, 128.89, 128.55, 123.47 (d, $^3J_{C-F}$ = 7.37 Hz), 113.42 (d, $^2J_{C-F}$ =23.63 Hz), 110.14, 105.32 (d, $^3J_{C-F}$ =2.12 Hz), 72.36, 52.12, 49.97, 44.24, 43.74, 34.66, 17.42, 8.25. IR (KBr): 3061, 2988, 2949, 2847, 1719, 1713, 1701, 1697, 1624, 1585, 1493, 1452, 1433, 1342, 1246, 1223, 1138, 1121, 1092, 1026, 995, 968, 924, 893, 837, 802, 704 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{28}H_{29}FN_3O_6$, 522.2035; found 522.2055.

[2-(4-Chlorophenyl)-1-methyl-2-oxo-ethyl] morpholine-4-carboxylate (5a): Obtained as off white solid; 172 mg (57.77%), mp 60–62 °C. Purification by flash column chromatography on silica (10% EtOAc/cyclohexane) ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.87–7.92 (m, 2 H), 7.34–7.55 (m, 2 H), 5.88 (q, *J* = 6.97 Hz, 1 H), 3.58–3.73 (m, 4 H), 3.36–3.56 (m, 4 H), 1.50 (d, *J* = 6.97 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm 196.72, 154.66, 140.13, 133.03, 130.02, 129.25, 72.12, 66.70, 44.64, 44.13, 17.28. IR (KBr): 2967, 2864, 1707, 1693, 1587, 1449, 1425, 1279, 1244, 1111, 972, 850, 764 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{17}ClNO_4$: 298.0841; found 298.0834.

[2-(4-Bromophenyl)-1-methyl-2-oxo-ethyl] morpholine-4-carboxylate (5b): Obtained as light brown solid; 165 mg (48.21%), mp 101–103 °C. Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.78–7.83 (m, 2 H), 7.56–7.65 (m, 2 H), 5.86 (q, *J* = 6.97 Hz, 1 H), 3.58–3.70 (m, 5 H), 3.49 (br d, *J* = 12.84 Hz, 3 H), 1.49 (d, *J* = 7.09 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm 196.89, 154.60, 133.41, 132.20, 130.07, 128.80, 72.07, 66.66, 44.62, 44.15, 17.23. IR (KBr): 2990, 2957, 2920, 2866, 1697, 1580, 1420, 1277, 1238, 1136, 1113, 1074, 968, 849 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{17}BrNO_4$, 342.0335; found 342.0331.

[2-(2-Bromophenyl)-1-methyl-2-oxo-ethyl] morpholine-4-carboxylate (5c): Obtained as light yellow gummy mass; 202 mg (59.03%). Purification by flash column chromatography on silica (10% EtOAc/cyclohexane) ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.58 (br dd, *J* = 10.70, 1.41 Hz, 1 H), 7.52–7.63 (m, 1 H), 7.37 (td, *J* = 7.49, 1.16 Hz, 1 H), 7.27–7.33 (m, 1 H), 5.70 (q, *J* = 7.09 Hz, 1 H), 3.54–3.77 (m, 4 H), 3.32–3.52 (m, 4 H), 1.47 (d, *J* = 7.09 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm 201.38, 154.54, 139.44, 133.65, 131.96, 129.04, 127.39, 119.38, 74.76, 66.65, 44.57, 44.19, 16.27. IR (KBr):2965, 2920, 2897, 2856, 1701, 1697, 1585, 1460, 1429, 1277, 1242, 1219, 1140, 1115, 1038, 968, 854, 762, 742 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{17}BrNO_4$, 342.0335; found 342.0326.

[2-(2-Iodophenyl)-1-methyl-2-oxo-ethyl] morpholine-4-carboxylate (5d): Obtained as light yellow oil; 225.7 mg (57.99%). Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.92 (dd, *J* = 8.03, 0.75 Hz, 1 H), 7.59 (dd, *J* = 7.53, 1.51 Hz, 1 H), 7.41 (td, *J* = 7.53, 1.00 Hz, 1 H), 7.08–7.20 (td, *J* = 7.53, 1.00 Hz, 1 H), 5.71 (q, *J* = 7.03 Hz, 1 H), 3.39–3.67 (m, 8 H), 1.48 (d, *J* = 7.03 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm 201.88, 154.56, 142.45, 140.59, 132.13, 128.67, 128.02, 92.11, 74.17, 66.67, 44.60, 44.16, 16.24. IR (KBr): 2963, 2920, 2897, 2855, 1711, 1693, 1579, 1460, 1427, 1277, 1242, 1219, 1142, 1115, 966, 893, 854, 762, 738, 683 cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{14}H_{16}INNaO_4$, 412.0016; found 412.0023.

[2-(2,4-Dichlorophenyl)-1-methyl-2-oxo-ethyl] morpholine-4-carboxylate (5e): Obtained as off white solid; 167 mg (50.27%), mp 80–82 °C. Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.58 (d, *J* = 8.31 Hz, 1 H), 7.45 (d, *J* = 1.96 Hz, 1 H), 7.32 (dd, *J* = 8.31, 1.96 Hz, 1 H), 5.69 (q, *J* = 7.09 Hz, 1 H), 3.59–3.70 (m, 4 H), 3.47 (br s, 4 H), 1.47 (d, *J* = 7.09 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm 199.62, 154.53, 137.74, 135.50, 132.47, 130.45, 130.42, 127.36, 74.80, 66.65, 44.60, 44.18, 16.19. IR (KBr): 2966, 2930, 2868, 2858, 1711, 1697, 1682, 1580, 1553, 1429,

1377, 1277, 1246, 1221, 1119, 1103, 964, 887, 825, 775, 752 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{16}Cl_2NO_4$, 332.0451; found 332.0454.

[2-(3,4-Dichlorophenyl)-1-methyl-2-oxo-ethyl] morpholine-4-carboxylate (5f): Obtained as light yellow solid; 140 mg (42.14%), mp 69–71 °C. Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* ppm 8.01 (d, *J* = 1.96 Hz, 1 H), 7.76 (dd, *J* = 8.38, 2.02 Hz, 1 H), 7.54 (d, *J* = 8.44 Hz, 1 H), 5.78 (q, *J* = 6.97 Hz, 1 H), 3.54–3.74 (m, 5 H), 3.48 (br d, *J* = 12.84 Hz, 2 H), 3.30–3.44 (m, 1 H), 1.49 (d, *J* = 6.97 Hz, 3 H). ^{13}C NMR (101 MHz, CDCl3): *δ* ppm 195.85, 154.51, 138.17, 134.23, 133.58, 130.99, 130.53, 127.55, 72.16, 66.60, 44.62, 44.12, 17.12. IR (KBr): 3402, 3063, 2966, 2868, 1712, 1693, 1680, 1580, 1553, 1443, 1433, 1221, 1117, 964, 887, 862, 825, 775, 752 cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{14}H_{15}Cl_2NNaO_4$, 354.0270; found: 354.0276.

[2-(4-Methoxycarbonylphenyl)-1-methyl-2-oxo-ethyl] morpholine-4-carboxylate (5g): Obtained as light yellow oil; 116.6 mg (36.28%). Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* ppm 8.08–8.15 (m, 2 H), 7.95–8.01 (m, 2 H), 5.90 (q, *J* = 7.01 Hz, 1 H), 3.94 (s, 3 H), 3.62–3.69 (m, 4 H), 3.32–3.60 (m, 4 H), 1.51 (d, *J* = 7.09 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* ppm 197.57, 166.19, 154.60, 138.10, 134.29, 130.02, 128.48, 72.44, 66.66, 52.61, 44.62, 44.15, 17.14. IR (KBr): 1724, 1697, 1460, 1435, 1408, 1281, 1246, 1227, 1138, 1109, 995, 970, 854, 758, 719 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{16}H_{20}NO_6$, 322.1285; found 322.1291.

[1-Methyl-2-(3-nitrophenyl)-2-oxo-ethyl] morpholine-4-carboxylate (5h): Obtained as off white solid; 152 mg (49.3%), mp 79–81 °C. Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* ppm 8.79 (t, *J* = 1.90 Hz, 1 H), 8.44 (ddd, *J* = 8.19, 2.20, 0.98 Hz, 1 H), 8.29 (dt, *J* = 7.83, 1.28 Hz, 1 H), 7.70 (t, *J* = 8.01 Hz, 1 H), 5.86 (q, *J* = 6.97 Hz, 1 H), 3.63–3.70 (m, 4 H), 3.36–3.60 (m, 4 H), 1.56 (d, *J* = 6.97 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* ppm 196.07, 154.53, 148.57, 136.00, 134.20, 130.22, 127.82, 123.47, 72.46, 66.66, 44.70, 44.15, 17.12. IR (KBr): 3092, 2955, 2864, 1707, 1691, 1611, 1524, 1431, 1354, 1277, 1246, 1229, 1123, 1101, 984, 901, 858, 814, 789, 766, 711, 658 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{17}N_2O_6$, 309.1081; found 309.1086.

[1-Methyl-2-oxo-2-[4-(trifluoromethyl)phenyl]ethyl] morpholine-4-carboxylate (5i): Obtained as light yellow oil; 162.4 mg (49%). Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* ppm 8.05 (d, *J* = 8.07 Hz, 2 H), 7.74 (d, *J* = 8.19 Hz, 2 H), 5.90 (q, *J* = 6.97 Hz, 1 H), 3.55–3.69 (m, 4 H), 3.35–3.55 (m, 4 H), 1.52 (d, *J* = 6.97 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm 197.19, 154.61, 137.63, 134.85 (q, $^2J_{C\text{-}F}$ = 33.33 Hz, 1C), 128.93, 125.94 (q, $^3J_{C\text{-}F}$ = 3.67 Hz), 123.63 (q, $^1J_{C\text{-}F}$ = 273.71 Hz, CF3), 72.33, 66.67, 44.64, 44.17, 17.07. ^{19}F NMR (377 MHz, CDCl3): *δ* ppm -63.22 (s, 3 F). IR (KBr): 2966, 2922, 2902, 2856, 1701, 1697, 1580, 1512, 1460, 1433, 1325, 1277, 1246, 1169, 1128, 1115, 1067, 970, 893, 854, 764 cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{16}F_3NNaO_4$, 354.0924; found: 354.0936.

[2-(3-Methoxyphenyl)-1-methyl-2-oxo-ethyl] morpholine-4-carboxylate (5j): Obtained as light brown solid; 129 mg (43.98%), mp 75–77 °C. Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* ppm 7.53 (d, *J* = 7.70 Hz, 1 H), 7.48 (d, *J* = 2.32 Hz, 1 H), 7.38 (t, *J* = 7.95 Hz, 1 H), 7.12 (dd, *J* = 8.19, 1.96 Hz, 1 H), 5.92 (q, *J* = 7.05 Hz, 1 H), 3.85 (s, 3 H), 3.65–3.71 (m, 4 H), 3.36–3.65 (m, 4 H), 1.52 (d, *J* = 7.09 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* ppm 197.65, 160.05, 154.72, 135.94, 129.86, 121.08, 120.23, 112.87, 72.38, 66.72, 55.58, 44.69, 44.15, 17.48. IR (KBr):2995, 2905, 2866, 1703, 1693, 1582, 1487, 1464, 1433, 1294, 1261, 1246, 1205, 1130, 1101, 1068, 1043, 976, 897, 868, 852, 792 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{20}NO_5$, 294.1336; found 294.1339.

[2-(4-Methoxyphenyl)-1-methyl-2-oxo-ethyl] morpholine-4-carboxylate (5k): Obtained as off white solid; 155.6 mg (53.05%), mp 100–102 °C. Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* ppm 7.91–7.97 (m, 2 H), 6.91–6.97 (m, 2 H), 5.92 (q, *J* = 6.97 Hz, 1 H), 3.86 (s, 3 H), 3.59–3.71 (m, 4 H), 3.36–3.59 (m, 4 H), 1.51 (d, *J* = 6.97 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* ppm 196.13, 163.98, 154.80, 130.96, 127.52, 114.11, 71.97, 66.74, 55.64, 44.67, 44.17, 17.63. IR (KBr): 2993, 2924, 2872, 1701, 1686, 1599, 1572, 1508, 1468, 1458, 1433, 1279, 1246, 1136, 1103, 1070, 1020, 962, 893, 854, 818, 771, 756, 690 cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{19}NNaO_5$, 316.1155; found: 316.1161.

[1-Methyl-2-oxo-2-(6-quinolyl)ethyl] morpholine-4-carboxylate (5l): Obtained as light brown solid; 166.5 mg (52.97%), mp = 115–117 °C. Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* ppm 9.03 (br d, *J* = 2.93 Hz, 1 H), 8.50 (s, 1 H), 8.31 (d, *J* = 8.19, 1H), 8.19–8.26 (m, 2 H), 7.51 (dd, *J* = 8.25, 4.22 Hz, 1 H), 6.08 (q, *J* = 7.05 Hz, 1 H) 3.66–3.72 (m, 4 H), 3.33–3.65 (m, 4 H), 1.58 (d, *J* = 6.97 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* ppm 197.39, 154.72, 152.83, 150.13, 137.88, 132.65, 130.33, 130.07, 128.05, 127.65, 122.23, 72.26, 66.68, 44.68, 44.15, 17.39. IR (KBr): 3051, 2963, 2922, 2870, 1967, 1703, 1691, 1620, 1572, 1460, 1433, 1283, 1244, 1117, 1072, 984, 900, 843, 767, 725 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{19}N_2O_4$, 315.1339; found 315.1352.

[2-(2-Furyl)-1-methyl-2-oxo-ethyl] morpholine-4-carboxylate (5m): Obtained as light brown solid; 109 mg (43.04%), mp 86–88 °C. Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, CDCl3): *δ* ppm 7.61 (s, 1 H), 7.25–7.31 (m, 1 H), 6.56 (dd, *J* = 3.61, 1.65 Hz, 1 H), 5.72 (q, *J* = 7.01 Hz, 1 H), 3.58–3.75 (m, 5 H), 3.37–3.58 (m, 3 H), 1.53 (d, *J* = 6.97 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* ppm 186.44, 154.64, 150.70, 146.95, 118.56, 112.54, 72.38, 66.71, 44.54, 44.02, 17.20. IR (KBr): 3142, 3127, 2988, 2864, 1699, 1674, 1468, 1437, 1400, 1265, 1248, 1115, 1042, 976, 885, 799, 769 cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{12}H_{15}NNaO_5$, 276.0842; found 276.0848.

[1-Methyl-2-oxo-2-(2-thienyl)ethyl] morpholine-4-carboxylate (5n): Obtained as light brown solid; 113.4 mg (42.11%), mp 114–116 °C. Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* ppm 7.80 (d, *J* = 3.42 Hz, 1 H), 7.67 (d, *J* = 4.77 Hz, 1 H), 7.14 (t, *J* = 4.22 Hz, 1 H), 5.71 (q, *J* = 6.97 Hz, 1 H), 3.66 (br s, 5 H), 3.35–3.58 (m, 3 H), 1.55 (d, *J* = 6.97 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* ppm 190.47, 154.51, 140.62, 134.39, 132.68, 128.32, 73.14, 66.64, 44.60, 44.09, 17.86. IR (KBr): 2963, 2924, 2857, 1703, 1674, 1518, 1458, 1433, 1416, 1360, 1277, 1244, 1138, 1115, 852, 752, 729 cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{12}H_{15}NNaO_4S$, 292.0614; found 292.0621.

1-Benzoylpropyl morpholine-4-carboxylate (6a): Obtained as light yellow oil; 121 mg (43.63%). Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* ppm 7.94 (d, *J* = 7.68 Hz, 2 H), 7.57 (tt, *J* = 7.40, 1.28 Hz, 1 H), 7.43–7.49 (m, 2 H),), 5.80 (dd, *J* = 8.01, 4.34 Hz, 1 H), 3.67 (br s, 5 H), 3.35–3.60 (m, 3 H), 1.75–2.01 (m, 3 H), 1.01 (t, *J* = 7.40 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* ppm 197.52, 154.95, 135.12, 133.55, 128.85, 128.49, 77.07, 66.69, 44.63, 44.10, 24.99, 10.00. IR (KBr): 2970, 2857, 1693, 1427, 1277, 1240, 1221, 1115, 700 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{20}NO_4$, 278.1387; found 278.1398.

1-Benzoylbutyl morpholine-4-carboxylate (6b): Obtained as light yellow oil; 108 mg (37.07%). Purification by flash column chromatography on silica (10% EtOAc/cyclohexane). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* ppm 7.94 (d, *J* = 7.08 Hz, 2 H), 7.50–7.62 (m, 1 H), 7.46 (t, *J* = 7.70 Hz, 2 H), 5.83–5.89 (m, 1 H), 3.67 (br s, 5 H), 3.52 (br dd, *J* = 8.93, 5.38 Hz, 2 H), 3.42 (br s, 1 H), 1.75–1.88 (m, 2 H), 1.39–1.56 (m, 2 H), 0.93 (t, *J* = 7.40 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm 197.62, 154.91, 135.02, 133.49,

128.81, 128.46, 75.87, 66.63, 44.62, 44.09, 33.57, 18.95, 13.84. IR (KBr): 2961, 2926, 2858, 1697, 1597, 1448, 1431, 1277, 1240, 1113, 1072, 1005, 953, 862, 764, 700 cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{16}H_{21}NNaO_4$, 314.1363; found 314.1367.

Methyl morpholine-4-carboxylate (7a):[19] Obtained as colourless oil; 44 mg (30.3%) with respect to morpholine. Purification by flash column chromatography on silica (25% EtOAc/cyclohexane). The reaction mass was heated upto 40 °C. ^1H NMR (400 MHz, $CDCl_3$): δ ppm 3.65 (s, 3 H), 3.55–3.62 (m, 4 H), 3.36–3.43 (m, 4 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm 155.92, 66.57, 52.66, 44.07.

Ethyl morpholine-4-carboxylate (7b):[20] Obtained as light yellow oil; 39.5 mg (12.4%). Purification by flash column chromatography on silica (30% EtOAc/cyclohexane). ^1H NMR (400 MHz, $CDCl_3$): *δ* ppm 4.08 (q, *J* = 7.05 Hz, 2 H), 3.58 (br s, 4 H), 3.33–3.47 (m, 4 H), 1.20 (br t, *J* = 7.03 Hz, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ ppm 155.54, 66.58, 61.48, 44.00, 14.62.

1-Methylbutyl morpholine-4-carboxylate (7c): Obtained as light yellow oil; 68.8 mg (34.18%). Purification by flash column chromatography on silica (30% EtOAc/CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): *δ* ppm 4.76–4.85 (m, 1 H), 3.57–3.67 (m, 4 H), 3.35–3.51 (m, 4 H), 1.52–1.61 (m, 1 H), 1.25–1.48 (m, 3 H), 1.20 (d, *J* = 6.2 Hz, 3 H), 0.85–0.94 (m, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* ppm 155.47, 72.17, 66.74, 44.10, 38.46, 20.44, 18.75, 14.07. IR (KBr): 2961, 2934, 2860, 1703, 1697, 1454, 1423, 1418, 1277, 1242, 1119, 1074, 856, 677 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{10}H_{20}NO_3$, 202.1438; found 202.1438.

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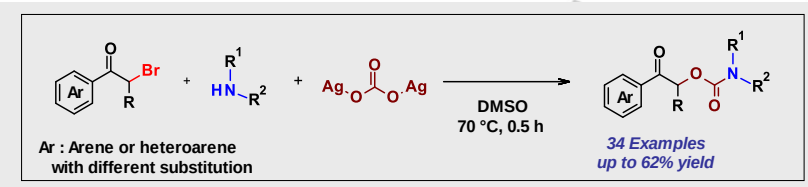

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Carbamate synthesis*

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Title: Synthesis of Carbamates from Alkyl Bromides and Secondary Amines using Silver Carbonate

- Synthesis of carbamate using silver carbonate as carbonate source.
- Both symmetric and unsymmetric secondary amines, and a wide range of *α*-halopropiophenones were converted into their carbamates.