이학석사 학위논문

Synthesis of carbamates from amines and N-tosylhydrazones under atmospheric pressure of carbon dioxide without external base

외부의 염기없이 아민, 엔-토실하이드라존과 대기 압력의 이산화탄소를 이용한 카바메이트 합성법

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홍 지 영

Synthesis of carbamates from amines and N-tosylhydrazones under atmospheric pressure of carbon dioxide without external base

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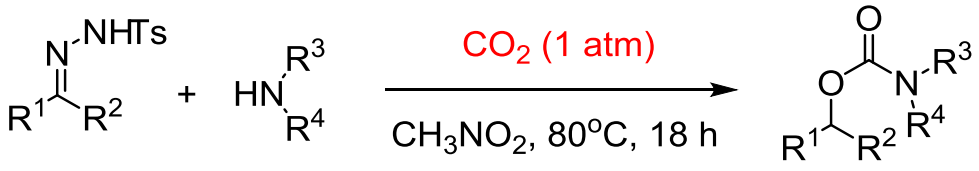
Abstract



Methodology for the synthesis of carbamates via the base−promoted coupling of carbon dioxide, amines, and N−tosylhyderazones using K_2CO_3 as the base and the pressure of 4 MPa of carbon dioxide has published by Jiang et al. (2015). We demonstrated that this method provides the desired carbamates under just 1 atm of carbon dioxide without the addition of the base promoter. Thus, carbamates were successfully synthesized under mild reaction conditions in moderate to high yields.

Keywords: Carbon dioxide; Amines; Tosylhydrazones; Carbamates

Contents

Introduction

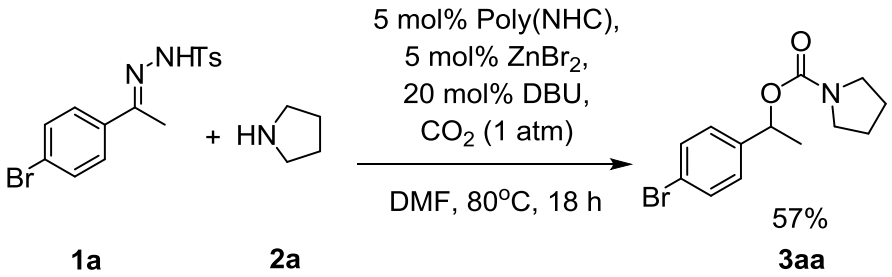
Organic carbamates have shown versatile potentials in medicinal, agricultural chemicals, and coating applications.[1] Conventional methods for the synthesis of carbamates are mainly based on the use of toxic phosgene and isocyanates.[2] Thus, considerable interest has been generated in the development of safe and efficient approaches to the preparation of carbamates. Recently, a variety of phosgene- and isocyanate-free methods have been developed.[3]

Among them, the base-promoted three-component coupling reaction of CO_2, amines, and N-tosylhydrazones to form carbamates under transition-metal-free conditions, described by Jiang et al.[4] is notable. The reaction provides a wide range of organic carbamates from readily available substrates with excellent functional group tolerance, a wide substrate scope, and a facile work-up procedure. However, the reaction is not practical due to the high pressure of carbon dioxide (4 MPa) and the rather harsh conditions (0.5 mmol N-tosylhydrazone, 5 mmol amine, 1.5 mmol K_2CO_3, 4 MPa CO_2, 3 mL MeCN/H_2O (15:1 v/v), 120°C, 24 h). Therefore, the development of a milder method for the synthesis of organic carbamates remains a challenging goal.

Results and Discussion

While studying the use of a polymeric catalyst for organic

reactions,[5] the three-component coupling reaction reported by Jiang et al.[4] attracted our attention. Thus, we explored the reaction in the presence of our polymeric catalyst to identify mild reaction conditions. We speculated that the use of polymeric catalyst, poly(NHC)s, could lead to the formation of carbamates under an atmospheric pressure of CO_2 atmosphere. We were confident that judicious choice of reaction conditions would lead to a favorable outcome. Thus, we studied the reaction in the presence of poly(NHC)s to find mild reaction conditions. During this endeavor, it was discovered that the reaction proceeds without any extra base or catalyst under an atmospheric pressure of carbon dioxide at 80℃ in reasonably high yields comparable to those obtained using the original conditions reported by Jiang et al.[4]



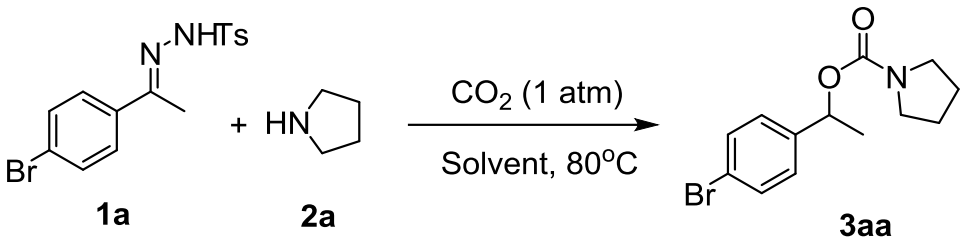
(1)

Scheme 1. Initial observation

The reaction of N-tosylhydrazone **1a** with pyrrolidine (**2a**) in the presence of poly(NHC)/$ZnBr_2$/DBU under 1 atm of carbon dioxide in DMF at 80℃ for 18 h was investigated as a model reaction for the synthesis of carbamates (Scheme 1). To our delight, carbamate

(**3aa**) was isolated in 57% under 1 atm of CO_2 supplied by a balloon, without any specialized gas manipulation. Encouraged by this observation, the reaction parameters were screened to maximize the yield of **3aa**. Selected data related to the screening of reaction solvents are shown in Table **1**.

Table 1. Optimization of the reaction conditions[a]



1a **2a** **3aa**

Entry	Additive	Base	Solvent	Temp. (°C)	Time (h)	Yield[b]
1	Poly(NHC), $ZnBr_2$	DBU	DMF	80	18	57
2	$ZnBr_2$	–	DMF	80	18	59
3	–	–	DMF	80	18	57
4	–	–	1,4-dioxane	80	18	60
5	–	–	Toluene	80	18	61
6	–	–	THF	80	18	60
7	–	–	DCE	80	18	26
8	–	–	–	80	18	62
9	–	–	–	50	18	19
10	–	–	–	r.t.	18	N.R.
11	–	–	–	80	6	62
12	–	–	–	80	3	60

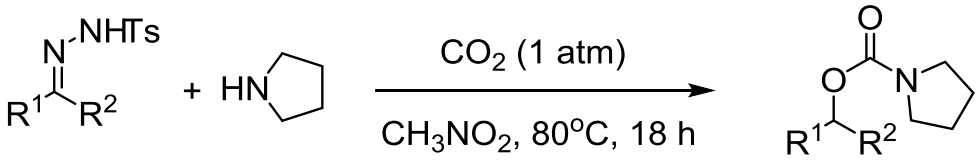
13	–	–	–	80	2	61
14	–	–	–	80	1	51
15	–	–	–	90	2	60
16	–	–	–	100	2	55
17	–	–	CH_3NO_2	80	18	75
18	–	–	CH_3NO_2	80	6	71
19	–	–	CH_3NO_2	80	3	70
20	–	–	CH_3NO_2	80	2	67
21	–	–	CH_3NO_2	100	2	64
22[c]	–	–	MeCN/H_2O	80	18	63

[a] Reaction conditions: 1 mmol **1c**, 10 mmol **2a**, 1.5 mL solvent, 5 mol% additive, 20 mol% base, 1.5 ml solvent, under 1 atm CO_2. [b] Isolated yield. [c] MeCN/H_2O (v/v, 3.0 mL: 0.2 mL).

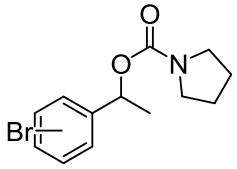
Interestingly, the reaction proceeded in the presence of $ZnBr_2$ only and without any additives. However, the yield was highly sensitive to the reaction solvent. In 1,4-dioxane, toluene, or THF, the yield was ca. 60% but just 26% in dichloroethane. In addition, when the reaction was performed neat without any solvent, the yield remained high (62%). When the reaction was conducted in a mixture solvent of acetonitrile and water (3 mL: 0.2 mL) as Jiang et al. used,[4] the yield was 63%. The best result was observed when the reaction was performed in nitromethane (75%). Shortening the reaction time to 6 h, 3 h, and 2 h provided yields of 71%, 70%, and 67%, respectively. On the contrary, the yield was dependent upon the order of addition of the reactants, with a higher yield obtained when the reactants

were added in the order: amine, CO_2, and N−tosylhydrazone. Finally, when the reaction temperature was raised or lowered, no improvement in the yield was observed. The optimum reaction conditions were established as follows: 1 mmol **1a**, 10 mmol **2a**, 1.5 mL CH_3NO_2, 1 atm CO_2, 80℃, and a reaction time of 18 h.

Table 2. Coupling reactions of N−tosylhydrazones with pyrrolidine **2a**[a]



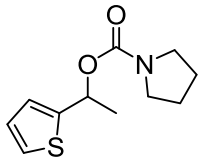
1a-1w **2a** **3aa-3wa**



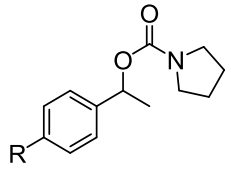
4'−Br, **3aa**, 75 (83) %

3'−Br, **3ba**, 70 (77) %

2'−Br, **3ca**, 60 (57) %



3qa, 65 (61) %



R=F, **3da**, 68 %

R=Cl, **3ea**, 68 (70) %

R=I, **3fa**, 70 (71) %

R=NO2, **3ga**, 38[b](76)%

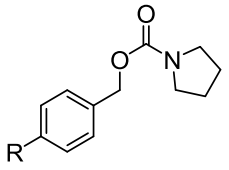
R=CN, **3ha**, 44[b] (84) %

R=CF3, **3ia**, 58 (80) %

R=H, **3ja**, 64 (67) %

R=Me, **3ka**, 62 (64) %

R=OMe, **3la**, 70 %

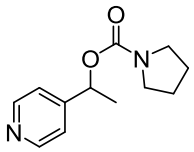
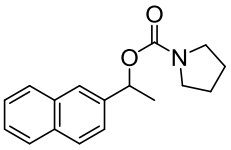
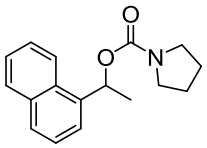
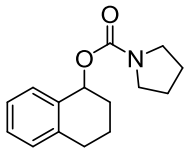
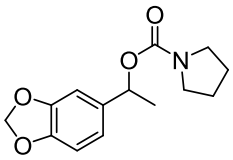
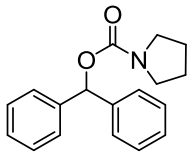


R=Br, **3ma**, 67 (85) %

R=I, **3na**, 66 %

R=H, **3oa**, 67 %

R=Me, **3pa**, 71 (73) %

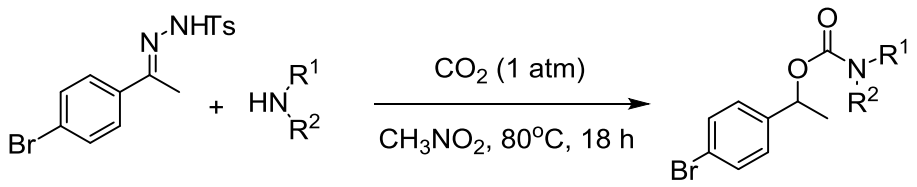
		
3ra, 52[b] (56) %	**3sa**, 75 %	**3ta**, 76 (71) %
		
3ua, 72 (87) %	**3va**, 69 %	**3wa**, 73 (66) %

[a]Reaction conditions: 1 mmol N-tosylhydrazone, 10 mmol **2a**, 1.5 mL CH_3NO_2, 18 h, 80°C, 1 atm of CO_2. Yields of isolated products are given. Data from *Angew. Chem., Int. Ed.*2015, *54*, 3084 are given in parentheses. [b]Reaction time: 3 h.

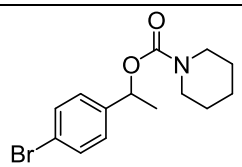
Using the optimized reaction conditions, the substrate scope of the N-tosylhydrazones was then examined by varying the hydrazone moiety (Table **2**). For most of the substrates, the reaction was 18 h; the substrates derived from 1-(4-nitrophenyl)ethan-1-one (**1g**), 4-acetylbenzonitrile (**1h**), and 1-(pyridin-4-yl)ethan-1-one (**1r**), the reaction time was shortened to 3 h because these compounds decomposed under the reaction conditions. As expected, various functional groups on the aryl ring of the N-tosylhydrazone were tolerated. When the functional group at the 4-position on the aryl group of N-tosylhydrazones derived from acetophenone was screened, all the substrates except a nitro- or nitrile substituent

were found to be good substrates, giving high yields (**3aa, 3da – 3la**: 58 – 75%). N–tosylhydrazones derived from benzaldehyde were also found good substrates (**3ma – 3pa**: 66 – 71%) and the best yield was observed with a methyl substituent (**3pa**, 71%). A steric effect was observed for substrates derived from acetophenone bearing 2–bromo and 3–bromoaryl substituents (**3ca** vs **3ba**: 60% vs 70%). However no steric effect was observed for similar substrates bearing 1–naphthyl and 2–naphthyl groups (**3ta** vs **3sa**: 76% vs 75%). N–tosylhydrazones derived from 3,4–dihydronaphthalen–1(2H)–one (**1u**), 1–(benzo[1,3]dioxol–5–yl)ethan–1–one (**1v**), and benzophenone (**1w**) were good substrates, giving an approximate 69–73% yield of the desired products (**3ua** – **3wa**). Substrates containing heteroarene groups, such as thiophene (**1q**) and pyridine (**1r**), gave carbamates in reasonable yields (**3qa**, 65%; **3ra**, 52%). Importantly, the results obtained under the new reaction conditions were comparable to those obtained using Jiang's reaction conditions in most cases. However, substrates derived from 1–(4–nitrophenyl)ethan–1–one (**1g**), 4–acetylbenzonitrile (**1h**), and 1–(4–(trifluoromethyl)phenyl)ethan–1–onewere (**1i**) were poor substrates and afforded lower yields (**3ga**, 38% vs 76%; **3ha**, 44% vs 84%; **3ia**, 58% vs 80%). According to the Jiang's report,[4] N–tosylhydrazones derived from aliphatic ketones or aldehydes failed to yield even a trace of the desired products. Under our reaction conditions, no reaction was observed with an aliphatic N–tosylhydrazone derived from 2–butanone.

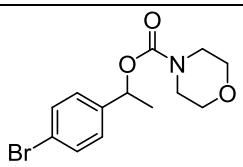
Table 3. Coupling reactions of N−tosylhydrazones **1a** with amines[a]



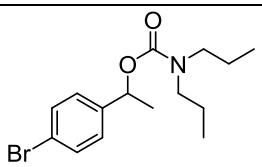
1a **2b-2j** **3ab-3aj**



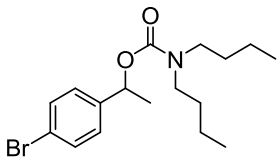
3ab, 67[b] %



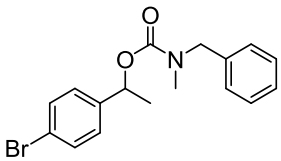
3ac, 43 (40) %



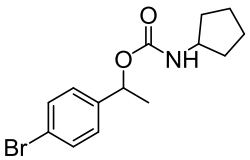
3ad, 29 (55) %



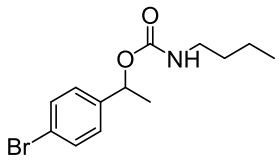
3ae, 28[b] (53) %



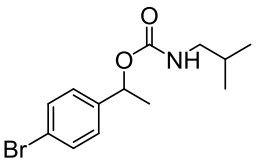
3af, 56 (39) %



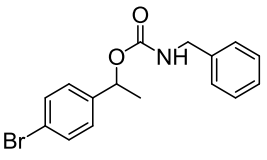
3ag, 55[b] %



3ah, 67 (48) %



3ai, 54 %



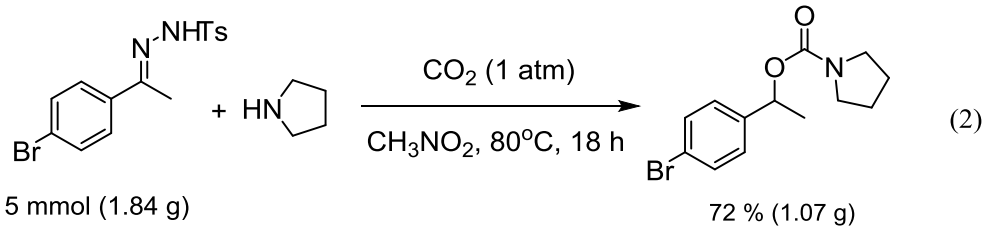
3aj, 44 %

[a]Reaction conditions: 1 mmol **1a**, 10 mmol amine, 1.5 mL CH_3NO_2, 18 h, 80°C, 1 atm of CO_2. Yields of isolated products are given. Data from *Angew. Chem., Int. Ed.*2015, *54*, 3084 are given in parentheses.

[b]Reaction time: 3 h.

The substrate scope of amines was also investigated (Table 3). The reactions proceeded smoothly with secondary and primary amines. For example, reactions using piperidine (2b) and cyclopentylamine (2g) were completed within 3 h, affording the desired products in moderate to good yields under the present reaction conditions; the longer reaction times had no influence on the yields. In contrast, dipropylamine (2d) and dibutylamine (2e) afforded rather poor yields of the desired carbamates (3ad, 29%; 3ae, 28%); these isolated yields were lower than those obtained under Jiang's reaction conditions (3ad, 29% vs 55%; 3ae, 28% vs 53%). However, N-benzylmethylamine (2f) and n-butylamine (2h) gave higher yields (3af, 56% vs 39%; 3ah, 67% vs 48%) than those obtained using Jiang's reaction conditions. Piperidine (2b), which has a structure similar to that of pyrrolidine (2a), was a good substrate, yielding 67% of the expected product (3ab). When the yield was not high, a considerable amount of adduct from the reaction of hydrazone with amine was obtained as a byproduct.

Although little mechanistic information has been obtained right now, the above results suggest that the formation of carbocation via the aid of carbonic acid from the reaction of water and carbon dioxide may not occur under our reaction conditions.[4,6]



Scheme 2. Gram-scale test

Finally, it is worth noting that the reaction may be scaled up (Scheme 2). When 1.84 g of **1a** (5 mmol) was reacted with **2a** (50 mmol), 1.07 g (72% yield) of **3aa** was isolated. Therefore, scale-up of the procedure did not result in a reduction in the yield.

Conclusion

In conclusion, we have demonstrated a method for the synthesis of carbamates from readily available N-tosylhydrazones, amines, and carbon dioxide in moderate to high yields under mild reaction conditions. Compared to the original reaction conditions reported by Jiang et al.[4] (3 equiv. K_2CO_3, 4 MPa CO_2, 120℃, and 24 h), the much milder reaction conditions of the present modified method (1 atm CO_2, 80℃, and 18 h) provide the desired carbamates without any considerable loss in yield for most substrates. This reaction is applicable to a gram-scale reaction.

Experimental Section

1. General information

All solvents were obtained by passing through activated alumina columns of solvent purification systems from Glass Contour. n-Hexane and ethyl acetate were used without further purification. Reagents were purchased from Sigma-Aldrich, Alfa Aesar, Acros, and TCI and were used as received. CO_2 (purity >99.999) was used. Reactions were carried out in a flame-dried glassware equipped with a stirring bar and capped with a rubber septum under CO_2, unless otherwise indicated. Elevated temperatures were maintained in thermostat-controlled oil baths. The TLC plate was carried out on 0.25 mm E. Merck silica gel plates (60F-254) visualized by UV-light (254 nm) and treatment with acidic p-anisaldehyde and $KMnO_4$ stain followed by gentle heating. Workup procedures were done in air. Flash chromatography was carried out on Merck 60 silica gel (230 – 400 mesh). ^{1}H and ^{13}C NMR spectra were recorded with Varian spectrometer (400 MHz) spectrometer. ^{1}H NMR spectra were referenced to residual TMS (0 ppm) and reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, qd = quartet of doublets, brs = broad singlet, m = multiplet). Chemical shifts of the ^{13}C NMR spectra were measured relative to $CDCl_3$ (77.16 ppm). Mass spectral data were obtained from the Korea Basic Science Institute (Daegu) on a Jeol JMS 700 high resolution

mass spectrometer.

2. General procedure for the preparation of organic carbamates

Reactions were performed in a tube schlenk equipped with a stirring bar and capped with a rubber septum and the followings were placed in the tube in order: 10 mmol of amine was added and tube was charged with CO_2 by balloon for 30 seconds. Then, 1 mmol of N-Tosylhydrazone and 1.5mL of CH_3NO_2 (Nitromethane) were put into the schlenk. The mixture was stirred at 80 °C for 18 h and CO_2 was provided by balloon (1 atm). After the completion of the reaction, the solvent was removed under reduced pressure. The crude residue was separated by column chromatography on silica gel with n-hexane and ethyl acetate to afford carbamates. The carbamate products were characterized by ^{1}H NMR, ^{13}C NMR, and HRMS.

3. Gram-scale experiment

Reactions were performed in 50-mL flame-dried, two-necked schlenk flask equipped with a stirring bar and capped with a rubber septum and the followings were placed in the schlenk in order: 50 mmol of Pyrrolidine (**2a**, 4.1mL) was added and tube was charged with CO_2 by balloon for 30 seconds. Then, 5 mmol of N'-(1-(4-bromophenyl)ethylidene)-4-methylbenzenesulfonohydrazide (**1a**,

1.84g) and 7.5mL of CH_3NO_2 (Nitromethane) were put into the schlenk. The mixture was stirred at 80°C for 18 h and CO_2 was provided by balloon (1 atm). After the completion of the reaction, the solvent was removed under reduced pressure. The crude residue was separated by column chromatography on silica gel with n-hexane and ethyl acetate (1.074g, 72% isolated yield).

4. Characterization data for isolated products

1-(4-bromophenyl)ethyl pyrrolidine-1-carboxylate(3aa):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.5 Hz, 2 H), 7.23 (d, *J* = 8.2 Hz, 2 H), 5.77 (q, *J* = 6.6 Hz, 1 H), 3.39 (dd, *J* = 13.6, 6.8 Hz, 4 H), 1.86 (dd, *J* = 11.0, 4.9 Hz, 4 H), 1.51 (d, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 141.5, 131.2, 127.4, 121.0, 71.5, 45.8, 45.5, 25.4, 24.6, 22.5 ppm. HRMS (EI^+) calc. for [$C_{13}H_{16}BrNO_2$]: 297.0364, found: 297.0361; pale yellow oil.

1-(3-bromophenyl)ethyl pyrrolidine-1-carboxylate (3ba):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (s, 1 H), 7.29 (d, *J* = 7.9 Hz, 1 H), 7.18 (d, *J* = 7.7 Hz, 1 H), 7.10 (t, *J* = 7.8 Hz, 1 H), 5.69 (q, *J* = 6.6 Hz, 1 H), 3.37 – 3.24 (m, 4 H), 1.76 (dt, *J* = 11.9, 6.2 Hz, 4 H), 1.42 (d, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 145.0, 130.4, 129.9, 128.8, 124.5, 122.4, 71.6, 46.1, 45.7, 25.6, 24.8, 22.9 ppm. HRMS (EI^+) calc. for [$C_{13}H_{16}BrNO_2$]: 297.0364, found: 297.0362; pale yellow oil.

1-(2-bromophenyl)ethyl pyrrolidine-1-carboxylate (3ca):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 8.0 Hz, 1 H), 7.36 (d, J = 7.7 Hz, 1 H), 7.22 (t, J = 7.6 Hz, 1 H), 7.01 (t, J = 7.6 Hz, 1 H), 6.02 (q, J = 6.5 Hz, 1 H), 3.41 – 3.26 (m, 4 H), 1.84 – 1.71 (m, 4 H), 1.43 (d, J = 6.5 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$)154.0, 142.2, 132.7, 128.7, 127.6, 126.7, 121.5, 71.8, 46.1, 45.7, 25.7, 24.9, 21.8 ppm. HRMS (FAB^+) calc. for [$C_{13}H_{16}BrNO_2$]: 298.0443, found: 298.0439; pale yellow oil.

1-(4-fluorophenyl)ethyl pyrrolidine-1-carboxylate(3da):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.20 (m, 2 H), 6.91 (t, J = 7.9 Hz, 2 H), 5.72 (q, J = 6.2 Hz, 1 H), 3.36 – 3.22 (m, 4 H), 1.75 (brs, 4 H), 1.43 (d, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0 (d, J = 245.4 Hz), 154.2, 138.5 (d, J = 3.1 Hz), 127.5 (d, J = 8.1 Hz), 115.0 (d, J = 21.4 Hz), 71.7, 46.0, 45.6, 25.5, 24.8, 22.8 ppm. HRMS (EI^+) calc. for [$C_{13}H_{16}FNO_2$]: 237.1165, found:237.1166; yellow oil.

1-(4-chlorophenyl)ethyl pyrrolidine-1-carboxylate(3ea):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (brs, 4 H), 5.69 (q, J = 6.5 Hz, 1 H), 3.34 – 3.22 (m, 4 H), 1.74 (d, J = 4.8 Hz, 4 H), 1.41 (d, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 141.2, 133.0, 128.4, 127.2, 71.7, 46.0, 45.6, 25.6, 24.8, 22.7 ppm. HRMS (EI^+) calc. for [$C_{13}H_{16}ClNO_2$]: 253.0870, found: 253.0871; pale yellow oil.

1-(4-iodophenyl)ethyl pyrrolidine-1-carboxylate(3fa):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.3 Hz, 2 H), 7.02 (d, *J* = 8.2 Hz, 2 H), 5.67 (q, *J* = 6.5 Hz, 1 H), 3.30 (d, *J* = 16.9 Hz, 4 H), 1.76 (d, *J* = 3.0 Hz, 4 H), 1.42 (d, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 142.4, 137.3, 127.8, 92.9, 71.8, 46.0, 45.7, 25.6, 24.8, 22.7 ppm. HRMS (EI^+) calc. for [$C_{13}H_{16}INO_2$]: 345.0226, found: 345.0226; pale yellow oil.

1-(4-nitrophenyl)ethyl pyrrolidine-1-carboxylate(3ga):

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.5 Hz, 2 H), 7.44 (d, *J* = 8.5 Hz, 2 H), 5.81 (q, *J* = 6.5 Hz, 1 H), 3.42 – 3.26 (m, 4 H), 1.81 (dd, *J* = 15.3, 5.9 Hz, 4 H), 1.48 (d, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 150.3, 147.4, 126.6, 123.8, 71.6, 46.3, 45.9, 25.8, 25.0, 22.9 ppm. HRMS (EI^+) calc. for [$C_{13}H_{16}N_2O_4$]: 264.1110, found:264.1113; yellow oil.

1-(4-cyanophenyl)ethyl pyrrolidine-1-carboxylate(3ha):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.2 Hz, 2 H), 7.38 (d, *J* = 8.2 Hz, 2 H), 5.75 (q, *J* = 6.6 Hz, 1 H), 3.40 – 3.25 (m, 4 H), 1.86 – 1.74 (m, 4 H), 1.45 (d, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 148.1, 132.2, 126.4, 118.7, 111.1, 71.6, 46.1, 45.7, 25.6, 24.8, 22.7 ppm. HRMS (EI^+) calc. for [$C_{14}H_{16}N_2O_2$]: 244.1212, found: 244.1211; pale yellow oil.

1-(4-(trifluoromethyl)phenyl)ethyl pyrrolidine-1-carboxylate (3ia):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.9 Hz, 2 H), 7.45 (d, *J* =

8.0 Hz, 2 H), 5.84 (q, J = 6.6 Hz, 1 H), 3.46 – 3.31 (m, 4 H), 1.88 – 1.80 (m, 4 H), 1.52 (d, J = 6.6 Hz, 3 H) ppm.^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 146.9, 129.6 (q, J = 32.3 Hz), 126.1, 125.4 (q, J = 3.8 Hz), 122.8, 71.9, 46.1, 45.8, 25.7, 24.9, 22.9ppm. HRMS (EI^+) calc. for [$C_{14}H_{16}F_3NO_2$]: 287.1133, found: 287.1135; pale yellow oil.

1-phenylethyl pyrrolidine-1-carboxylate(3ja):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.21 (m, 4 H), 7.13 – 7.17 (m, 1 H), 5.74 (q, J = 6.6 Hz, 1 H), 3.35 – 3.22 (m, 4 H), 1.79 – 1.67 (m, 4 H), 1.44 (d, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 142.6, 128.3, 127.4, 125.7, 72.4, 46.0, 45.6, 25.6, 24.8, 22.9 ppm. HRMS (EI^+) calc. for [$C_{13}H_{17}NO_2$]: 219.1259, found: 219.1260; pale yellow oil.

1-(p-tolyl)ethyl pyrrolidine-1-carboxylate(3ka):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, J = 7.9 Hz, 2 H), 7.06 (d, J = 7.8 Hz, 2 H), 5.72 (q, J = 6.5 Hz, 1 H), 3.36 – 3.24 (m, 4 H), 2.25 (s, 3 H), 1.76 (brs, 4 H), 1.44 (d, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 139.8, 137.1, 129.1, 125.9, 72.4, 46.1, 45.7, 25.7, 25.0, 22.9, 21.1 ppm. HRMS (EI^+) calc. for [$C_{14}H_{19}NO_2$]: 233.1416, found: 233.1419; pale yellow oil.

1-(4-methoxyphenyl)ethyl pyrrolidine-1-carboxylate (3la):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, J = 8.7 Hz, 2 H), 6.78 (d, J = 8.7 Hz, 2 H), 5.71 (q, J = 6.6 Hz, 1 H), 3.69 (s, 3 H), 3.35 – 3.21 (m, 4 H), 1.82 – 1.67 (m, 4 H), 1.44 (d, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR

(100 MHz, $CDCl_3$) δ 158.9, 154.5, 134.8, 127.3, 113.7, 72.2, 55.2, 46.0, 45.7, 25.7, 24.9, 22.7 ppm. HRMS (EI^+) calc. for [$C_{14}H_{19}NO_3$]: 249.1365, found: 249.1367; yellow oil.

4-bromobenzyl pyrrolidine-1-carboxylate (3ma):

^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 8.4 Hz, 2 H), 7.15 (d, J = 8.2 Hz, 2 H), 4.98 (s, 2 H), 3.35 – 3.23 (m, 4 H), 1.73 – 1.79 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 136.1, 131.4, 129.4, 121.7, 65.6, 46.2, 45.7, 25.6, 24.8 ppm. HRMS (EI^+) calc. for [$C_{12}H_{14}BrNO_2$]: 283.0208, found: 283.0212; pale yellow oil.

4-iodobenzyl pyrrolidine-1-carboxylate (3na):

^1H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.2 Hz, 2 H), 7.02 (d, J = 8.1 Hz, 2 H), 4.97 (s, 2 H), 3.33 – 3.24 (m, 4 H), 1.76 (brs, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 137.3, 136.7, 129.6, 93.3, 65.7, 46.1, 45.7, 25.6, 24.8 ppm. HRMS (EI^+) calc. for [$C_{12}H_{14}INO_2$]: 331.0069, found: 331.0070; yellow oil.

benzyl pyrrolidine-1-carboxylate (3oa):

^1H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.15 (m, 5 H), 5.05 (s, 2 H), 3.35 – 3.26 (m, 4 H), 1.80 – 1.72 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 137.1, 128.4, 127.8, 127.8, 66.5, 46.2, 45.8, 25.7, 24.9 ppm. HRMS (EI^+) calc. for [$C_{12}H_{15}NO_2$]: 205.1103, found: 205.1103; pale yellow oil.

4-methylbenzyl pyrrolidine-1-carboxylate (3pa):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 7.6 Hz, 2 H), 7.02 (d, *J* = 7.6 Hz, 2 H), 4.97 (s, 2 H), 3.22 – 3.27 (m, 4 H), 2.21 (s, 3 H), 1.70 – 1.68 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 137.2, 133.9, 128.8, 127.7, 66.2, 45.9, 45.5, 25.4, 24.7, 20.9 ppm. HRMS (EI^+) calc. for [$C_{13}H_{17}NO_2$]: 219.1259, found: 219.1257; pale yellow oil.

1-(thiophen-2-yl)ethyl pyrrolidine-1-carboxylate (3qa):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (d, *J* = 5.0 Hz, 1 H), 6.95 (d, *J* = 3.4 Hz, 1 H), 6.86 (dd, *J* = 5.0, 3.5 Hz, 1 H), 6.01 (q, *J* = 6.5 Hz, 1 H), 3.33 – 3.24 (m, 4 H), 1.79 – 1.71 (m, 4 H), 1.56 (d, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 145.8, 126.5, 124.7, 124.5, 68.1, 46.1, 45.7, 25.6, 24.9, 22.7 ppm. HRMS (EI^+) calc. for [$C_{11}H_{15}NO_2S$]: 225.0823, found: 225.0824; yellow oil.

1-(pyridin-4-yl)ethyl pyrrolidine-1-carboxylate (3ra):

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (dd, *J* = 4.6, 1.4 Hz, 2 H), 7.18 (dd, *J* = 4.6, 1.1 Hz, 2 H), 5.72 (q, *J* = 6.7 Hz, 1 H), 3.41 – 3.27 (m, 4 H), 1.86 – 1.75 (m, 4 H), 1.45 (d, *J* = 6.7 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 151.5, 149.8, 120.5, 70.9, 46.1, 45.7, 25.6, 24.8, 22.5 ppm. HRMS (EI^+) calc. for [$C_{12}H_{16}N_2O_2$]: 220.1212, found: 220.1213; yellow oil.

1-(naphthalen-2-yl)ethyl pyrrolidine-1-carboxylate (3sa):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.74 (m, 4 H), 7.45 – 7.30 (m, 3 H), 5.92 (q, *J* = 6.6 Hz, 1 H), 3.39 – 3.24 (m, 4 H), 1.80 – 1.69 (m,

4 H), 1.54 (d, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 140.0, 133.1, 132.8, 128.1, 127.9, 127.5, 126.0, 125.8, 124.6, 124.1, 72.6, 46.0, 45.7, 25.6, 24.8, 22.8 ppm. HRMS (EI^+) calc. for [$C_{17}H_{19}NO_2$]: 269.1416, found: 269.1415; pale yellow oil.

1-(naphthalen-1-yl)ethyl pyrrolidine-1-carboxylate (3ta):

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.5 Hz, 1 H), 7.73 (d, J = 7.8 Hz, 1 H), 7.65 (d, J = 8.2 Hz, 1 H), 7.49 (d, J = 7.0 Hz, 1 H), 7.42 – 7.37 (m, 1 H), 7.37 – 7.28 (m, 2 H), 6.48 (q, J = 6.6 Hz, 1 H), 3.24 – 3.39 (m, 4 H), 1.69 – 1.74 (m, 4 H), 1.60 (d, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 138.4, 133.8, 130.2, 128.7, 128.1, 126.0, 125.5, 125.3, 123.5, 123.1, 70.1, 46.1, 45.8, 25.6, 24.9, 22.5 ppm. HRMS (EI^+) calc. for [$C_{17}H_{19}NO_2$]: 269.1416, found: 269.1418; pale yellow oil.

1,2,3,4-tetrahydronaphthalen-1-yl pyrrolidine-1-carboxylate (3ua):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J = 7.2 Hz, 1 H), 7.10 – 7.03 (m, 2 H), 6.99 (d, J = 6.8 Hz, 1 H), 5.78 – 5.79 (m, 1 H), 3.32 (brs, 2 H), 3.18 (brs, 2 H), 2.76 – 2.72 (m, 1 H), 2.66 – 2.63 (m, 1 H), 1.91 – 1.84 (m, 3 H), 1.72 (brs, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 137.5, 135.5, 129.2, 128.7, 127.5, 125.7, 70.2, 46.0, 45.6, 29.5, 28.9, 25.5, 24.8, 18.9 ppm. HRMS (EI^+) calc. for [$C_{15}H_{19}NO_2$]: 245.1416, found: 245.1413; pale yellow oil.

1-(benzo[d][1,3]dioxol-5-yl)ethyl pyrrolidine-1-carboxylate (3va):

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.75 (m, 2 H), 6.67 (d, *J* = 7.9 Hz, 1 H), 5.84 (s, 2 H), 5.65 (q, *J* = 6.6 Hz, 1 H), 3.35 – 3.23 (m, 4 H), 1.81 – 1.69 (m, 4 H), 1.41 (d, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 147.6, 146.8, 136.7, 119.4, 108.0, 106.5, 100.9, 72.3, 46.0, 45.7, 25.7, 24.9, 22.9 ppm. HRMS (EI^+) calc. for [$C_{14}H_{17}NO_4$]: 263.1158, found: 263.1158; yellow oil.

benzhydryl pyrrolidine-1-carboxylate (3wa):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 7.4 Hz, 4 H), 7.23 (t, *J* = 7.4 Hz, 4 H), 7.16 (t, *J* = 7.1 Hz, 2 H), 6.76 (s, 1 H), 3.42 (t, *J* = 6.6 Hz, 2 H), 3.30 (t, *J* = 6.6 Hz, 2 H), 1.81 – 1.72 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 141.2, 128.4, 127.6, 127.0, 77.2, 46.3, 45.9, 25.7, 24.9 ppm. HRMS (EI^+) calc. for [$C_{18}H_{19}NO_2$]: 281.1416, found: 281.1415; m.p. = 125 °C; white solid.

1-(4-bromophenyl)ethyl piperidine-1-carboxylate (3ab):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.4 Hz, 2 H), 7.21 (d, *J* = 8.2 Hz, 2 H), 5.75 (q, *J* = 6.6 Hz, 1 H), 3.42 (brs, 4 H), 1.58 (d, *J* = 8.4 Hz, 6 H), 1.50 (d, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 141.9, 131.6, 127.6, 121.4, 72.3, 44.9, 25.7, 24.4, 22.7 ppm. HRMS (EI^+) calc. for [$C_{14}H_{18}BrNO_2$]: 311.0521, found: 311.0520; yellow oil.

1-(4-bromophenyl)ethyl morpholine-4-carboxylate (3ac):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.4 Hz, 2 H), 7.20 (d, *J* = 8.3 Hz, 2 H), 5.76 (q, *J* = 6.6 Hz, 1 H), 3.63 (d, *J* = 4.7 Hz, 4 H), 3.47 (brs, 4 H), 1.51 (d, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 141.3, 131.7, 127.7, 121.7, 72.9, 66.6, 44.2, 22.6 ppm. HRMS (EI^+) calc. for [$C_{13}H_{16}BrNO_3$]: 313.0314, found: 313.0310; pale yellow oil.

1-(4-bromophenyl)ethyl dipropylcarbamate (3ad):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 6.6 Hz, 2 H), 7.21 (d, *J* = 6.8 Hz, 2 H), 5.74 (q, *J* = 6.5 Hz, 1 H), 3.17 (brs, 4 H), 1.57 – 1.51 (m, 4 H), 1.5 – 1.48 (m, 3 H), 0.86 – 0.88 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 141.9, 131.6, 127.7, 121.4, 72.2, 49.3, 48.7, 22.7, 22.0, 21.4, 11.4 ppm. HRMS (EI^+) calc. for [$C_{15}H_{22}BrNO_2$]: 327.0834, found: 327.0836; pale yellow oil.

1-(4-bromophenyl)ethyl dibutylcarbamate (3ae):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.5 Hz, 2 H), 7.20 (d, *J* = 8.3 Hz, 2 H), 5.74 (q, *J* = 6.6 Hz, 1 H), 3.20 (brs, 4 H), 1.59 – 1.41 (m, 7 H), 1.29 (d, *J* = 6.7 Hz, 4 H), 0.97 – 0.82 (m, 6 H)^{13}C NMR (100 MHz, $CDCl_3$) δ 155.5, 141.8, 131.5, 127.7, 121.3, 72.2, 47.3, 46.6, 30.9, 30.3, 22.7, 20.1, 13.9 ppm. HRMS (EI^+) calc. for [$C_{17}H_{26}BrNO_2$]: 355.1147, found: 355.1147; pale yellow oil.

1-(4-bromophenyl)ethyl benzyl(methyl)carbamate (3af):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (m, 2 H), 7.22 (m, 7 H), 5.82 (q, *J* = 6.5 Hz, 1 H), 4.54 – 4.38 (m, 2 H), 2.88 (s, 3 H), 1.50 – 1.54 (m,

3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 141.5, 137.5, 131.6, 128.6, 127.7, 127.4, 127.2, 121.5, 72.8, 52.5, 52.4, 34.6, 33.6, 22.8 ppm. HRMS (EI^+) calc. for [$C_{17}H_{18}BrNO_2$]: 347.0521, found: 347.0518; pale yellow oil.

1-(4-bromophenyl)ethyl cyclopentylcarbamate (3ag):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.3 Hz, 2 H), 7.20 (d, *J* = 8.3 Hz, 2 H), 5.71 (q, *J* = 6.2 Hz, 1 H), 4.62 (brs, 1 H), 3.99 – 3.86 (m, 1 H), 1.92 (d, *J* = 6.5 Hz, 2 H), 1.68 – 1.60 (m, 2 H), 1.53 – 1.58 (m, 2 H), 1.47 (d, *J* = 6.3 Hz, 3 H), 1.42 – 1.29 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 141.5, 131.6, 127.8, 121.6, 71.8, 52.8, 34.6, 33.3, 24.2, 23.6, 22.5 ppm. HRMS (EI^+) calc. for [$C_{14}H_{18}BrNO_2$]: 311.0521, found: 311.0522; m.p. = 86 °C; white solid

1-(4-bromophenyl)ethyl butylcarbamate (3ah):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.3 Hz, 2 H), 7.20 (d, *J* = 8.3 Hz, 2 H), 5.72 (q, *J* =6.3 Hz, 1 H), 4.86 (brs, 1 H), 3.22 – 3.04 (m, 2 H), 1.53 – 1.39 (m, 5 H), 1.35 – 1.25 (m, 2 H), 0.89 (t, *J* = 7.3 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.8, 141.4, 131.5, 127.7, 121.5, 71.8, 40.7, 32.0, 22.4, 19.9, 13.7 ppm. HRMS (EI^+) calc. for [$C_{13}H_{18}BrNO_2$]: 299.0521, found: 299.0521; pale yellow oil.

1-(4-bromophenyl)ethyl isobutylcarbamate (3ai):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.3 Hz, 2 H), 7.20 (d, *J* = 8.3 Hz, 2 H), 5.72 (q, *J* = 6.5 Hz, 1 H), 4.93 (brs, 1 H), 3.02 – 2.89

(m, 2 H), 1.66 – 1.74 (m, 1 H), 1.47 (d, J = 6.6 Hz, 3 H), 0.87 (d, J = 6.7 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 141.4, 131.5, 127.7, 121.4, 71.8, 48.4, 28.7, 22.3, 19.9 ppm. HRMS (EI^+) calcfor [$C_{13}H_{18}BrNO_2$]: 299.0521, found: 299.0522; yellow oil.

1-(4-bromophenyl)ethyl benzylcarbamate (3aj):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 7.9 Hz, 2 H), 7.20 (m, 7 H), 5.69 (q, J = 6.6 Hz, 1 H), 5.06 (brs, 1 H), 4.31 – 4.20 (m, 2 H), 1.43 (d, J = 6.5 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.8, 141.3, 138.4, 131.6, 128.7, 127.8, 127.5, 121.6, 72.3, 45.1, 22.4 ppm. HRMS (EI^+) calc. for [$C_{16}H_{16}BrNO_2$]: 333.0364, found: 333.0363; m.p. = 103 °C; white soild.

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국문초록

탄산칼륨을 염기로 사용하여 40기압의 이산화탄소, 아민, 엔-토실하이드라존 간의 염기로 촉진되는 카바메이트 합성법이 Jiang 연구진에 의해 개발되었다 (2015). 여기서는 염기 촉진제의 첨가 없이 단 1기압의 이산화탄소를 사용하여 원하는 카바메이트 생성물을 합성하는 방법을 제시한다. 그러므로, 카바메이트를 온화한 조건에서 적절하게 높은 수율로 합성한다.

주요어: 이산화탄소, 아민, 엔-토실하이드라존, 카바메이트

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