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# Efficient $Cs_2CO_3$-promoted solution and solid phase synthesis of carbonates and carbamates in the presence of TBAI

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**Abstract**—Novel solution and solid-phase methods for the synthesis of carbonates and carbamates were developed using cesium bases and TBAI via a three-component coupling. Cesium carbonate not only promoted successful carbonylations of alcohols and carbamations of amines, but also suppressed common side reactions traditionally seen using existing protocols. Various alcohols and amines were examined, using a wide array of alkyl halides, and the results demonstrated this methodology was highly chemoselective. In particular, use of either sterically demanding substrates or amino acid derivatives afforded the corresponding products exclusively, offering a wide variety of applications such as novel protecting groups and peptidomimetic syntheses. © 2002 Elsevier Science Ltd. All rights reserved.

## 1. Introduction

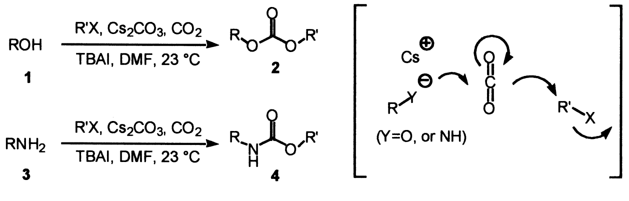
Carbon dioxide has been recognized as an attractive and versatile reagent in organic synthesis primarily due to its environmentally benign and economically inexpensive nature.[1] Specifically, organic carbonates and carbamates are important precursors containing the $CO_2$ moiety which hold unique applications in industry,[2] biological/medicinal fields,[3] and as useful synthetic intermediates.[4] However, common preparations leading to these target compounds are limited since they employ the use of toxic starting materials such as phosgene,[5] its derivatives,[6] or unstable isocyanates.[7] As an alternative approach, carbon dioxide alkylation[8] has also been explored, although harsh reaction conditions are typically required, prompting us to develop more efficient and safer procedures. In our initial studies, we developed a cesium base promoted *O*-alkylation method for the preparation of alkyl carbonates where cesium carbonate behaved as both a base and a carbon dioxide source.[9] Expanding on these results, we recently disclosed an improved protocol using $CO_2$ gas to offer a valuable synthetic method for unsymmetrical carbonates[10] as well as carbamates,[11] where $Cs_2CO_3$ functioned solely as a base. Due to the prospects of mildness and versatility embedded in these techniques, these procedures have gained much attention recently,[12] which led to a successful solid phase synthesis of the title compounds.[13] In this paper, we report our concise efforts described to date regarding both the solution and solid phase synthesis of carbonates and carbamates in further details.

Employing $Cs_2CO_3$, in the presence of tetrabutylammonium iodide (TBAI), using *N*,*N*-dimethylformamide as the solvent of choice, three-components comprising alcohols (or amines), halides, and $CO_2$ were efficiently united as mechanistically demonstrated in Scheme 1. When the reaction suspension was saturated with carbon dioxide gas, which was continuously bubbled throughout the reaction, carbonylation of alcohol **1** or carbamation of amine **3** was complete at ambient temperature, rendering exclusively the desired mixed alkyl carbonate **2** or carbamate **4**, respectively.

## 2. Results and discussion

### 2.1. Synthesis of carbonates and carbamates

As a preliminary study for feasibility, we set out to access the scope and limitations of the reaction conditions beginning with the carbonylation of 4-phenyl-1-butanol (**5**) as a model substrate utilizing various bases. As shown in



**Scheme 1.**

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*Keywords*: carbonates; carbamates; cesium carbonate.

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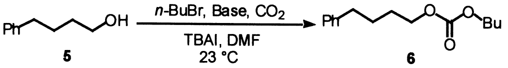
**Table 1.** Carbonate formation of **5** utilizing various bases



**5** **6**

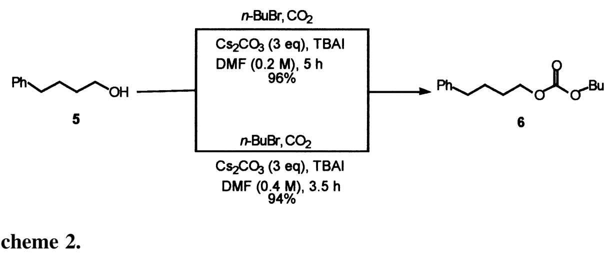
| Entry | Base | Time (h) | Yield of **6** (%) |
|---|---|---|---|
| 1 | $Li_2CO_3$ | 8 | No reaction |
| 2 | $Na_2CO_3$ | 8 | 2 |
| 3 | $K_2CO_3$ | 8 | 2 |
| 4 | $Rb_2CO_3$ | 8 | 10 |
| 5 | $Cs_2CO_3$ | 6 | 85 |
| 6 | $Cs_2CO_3$ (0.5 equiv./$K_2CO_3$) (2.5 equiv.) | 8 | <10 |
| 7 | $Et_3N$ | 8 | 2 |

Table 1, different bases, including various alkali metal carbonates and organic bases were screened in stoichiometric amounts. Of the bases examined, lithium carbonate failed to deliver the desired product (entry 1). Additionally, other alkali metal bases generated only trace amounts of **6** (entries 2–4) giving starting material **5** back. In contrast, cesium carbonate provided the best results in terms of highest yield (85%) and shortest reaction time (entry 5). This dramatic increase in yield is attributed to the 'cesium effect' in which unlike other alkali equivalents, alkoxides generated in situ are weakly conjugated with the cesium ion constituting 'naked anions' to exhibit enhanced nucleophilities.[14] In addition, using a catalytic amount of cesium carbonate in the presence of 2.5 equiv. of $K_2CO_3$ offered the desired product in low conversion yield (entry 6), although yields were higher than those reported in entries 1–3. Employment of amine bases such as TEA also failed, offering similar results to the starting entries (entry 7).

Next, we focused our attention towards the effect of solvent medium for efficient cesium carbonate mediated carbonylation to generate mixed alkyl carbonates (Table 2). Five solvents were screened, and it became evident that carbonate formation proceeded best using anhydrous DMF (entry 1). Reactions in other dry solvents including acetonitrile ($CH_3CN$) and methylene chloride ($CH_2Cl_2$), were less suitable, offering sluggish reaction conditions and offering extremely low yields (entries 2 and 3). Whereas, no reaction took place using dimethylsulfoxide (DMSO) or nitromethane ($CH_3NO_2$) and the starting alcohol **5** was fully recovered (entries 4 and 5).

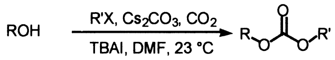
**Table 2.** Carbonylation of **5** utilizing various solvents

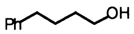
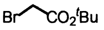
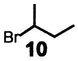
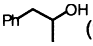
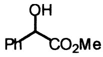
| Entry | Solvent | Time (h) | Yield of **6** (%) |
|---|---|---|---|
| 1 | DMF | 6 | 85 |
| 2 | $CH_3CN$ | 8 | 21 |
| 3 | $CH_2Cl_2$ | 8 | 15 |
| 4 | DMSO | 8 | No reaction |
| 5 | $CH_3NO_2$ | 8 | No reaction |



**Scheme 2.**

**Table 3.** Carbonate formation using alcohols, alkyl halides, and $CO_2$ in the presence of $Cs_2CO_3$

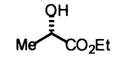
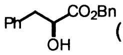
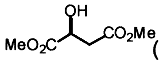
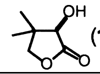


| Entry | Alcohol (ROH) | Halide (R′X) | Time (h) | Yield (%) |
|---|---|---|---|---|
| 1 |  **(5)** |  **(7)** | 4 | 91 |
| 2 | **5** | BnCl (**8**) | 2.5 | 94 |
| 3 | **5** |  **(9)** | 5 | 95 |
| 4 | **5** |  **10** | 23 | 98 |
| 5 |  **(11)** | n-BuBr (**12**) | 4.5 | 92 |
| 6 | **11** | **8** | 3 | 98 |
| 7 | **11** | **9** | 5 | 96 |
| 8 | L-(−)menthol (**13**) | **12** | 5 | 96 |
| 9 |  **(14)** | MPMCl (**15**) | 3 | 92 |

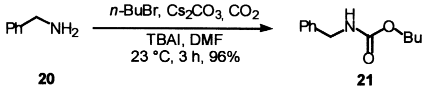
With the correct choice of base and solvent in hand, we then investigated in varying the equivalents of cesium carbonate and solvent concentration in pursuit for the optimum reaction conditions. When three equivalents of $Cs_2CO_3$ were used, it was found that reaction rates accelerated and the yield of the carbonate adduct **6** dramatically increased. At this point, effect of solvent concentration was evaluated. At varying concentrations (0.2 and 0.4 M), similar yields were noted (Scheme 2). However, a higher concentration was found to be suitable, offering shorter reaction times, presumably due to higher alkoxide ion concentrations.

Based on these successful results, we decided to introduce the carbonate functionality into a wide spectrum of alcohols using the developed technology in order to explore versatility. As demonstrated in Table 3, the improved techniques were compatible with various substrates. Primary alcohol **5** reacted expeditiously with numerous active halides (entries 1–3). In addition, a sterically hindered bromide (e.g. 2-bromobutane) was also converted exclusively to the corresponding carbonate **2** in nearly quantitative yield, however, longer reaction time was required (entry 4). In contrast, carbonylation of secondary alcohols with primary halides also demonstrated to be efficient. As an example, 2-methyl-1-phenyl-2-propanol (**11**) reacted quickly using three different halides to generate the desired products in excellent yields (entries 5–7). Subsequently, a secondary alcohol, containing a small degree of sterics, such as L-(−)-menthol (**13**), also proved facile by reacting with 1-bromobutane (**12**) with complete conversion to the desired product after 5 h (entry 8). Since carbonates have been ubiquitously utilized as novel protecting groups, our next synthetic objective was to install a hydroxyl-protecting group using our reported approach. As shown in entry 9, methyl mandelate (**14**) underwent a three-component coupling with carbon dioxide and 3-methoxybenzyl chloride (MPMCl), giving rise to the desired MPM carbonate in high yield (entry 9). Side products stemming from elimination and hydrolysis were not observed, offering important protecting group applications.

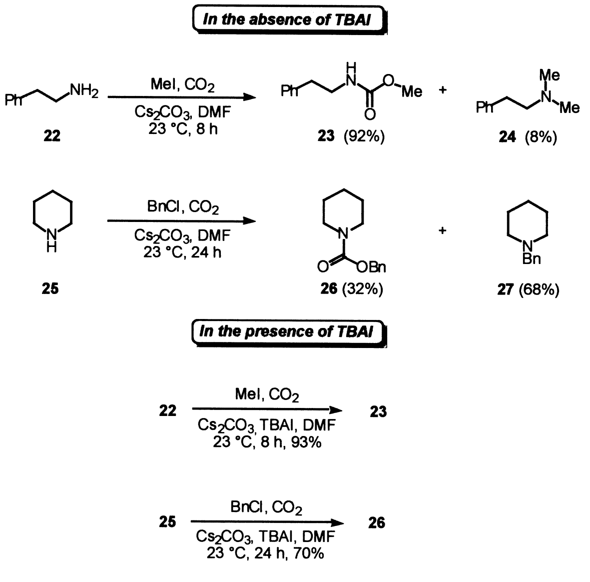
**Table 4.** Carbonate formation using chiral alcohols

| Entry | Alcohol (ROH) | Halide (R′X) | Time (h) | Yield (%) | % ee |
|---|---|---|---|---|---|
| 1 |  **(16)** | **8** | 3 | 90 | 96 |
| 2 | | **15** | 3 | 94 | |
| 3 |  **(17)** | **8** | 3 | 85 | 97 |
| 4 |  **(18)** | **8** | 3 | 65 | 95 |
| 5 |  **(19)** | **8** | 3 | 90 | 97 |
| 6 | | **15** | 3 | 94 | 97 |

To fully exploit the scope of these reaction conditions, we were then prompted to apply our *O*-alkylation method utilizing chiral alcohols which are particularly prone to racemization under basic conditions.[15] As depicted in Table 4, α-hydroxy esters such as lactate **16** and phenyl lactate **17** underwent carbonylations, resulting in the exclusive formation of their corresponding carbonates without any loss of optical activity within detection limits (>95% ee values) (entries 1–3).[16] In addition, dimethyl malate (**18**) was also efficient providing the functionally rich, optically active carbonate in moderate yield (entry 4). Pantolactone (**19**), which is resistant to protection,[17] underwent $CO_2$ incorporation with benzylic halides to deliver the subsequent pantolactone carbonates in high yields (entries 5 and 6). Above all, carbonate formation was exclusive using these chiral templates, and if any optical activity was sacrificed, it was to a negligible extent.[16] As a further advantage, this strategy was found to be mild enough to circumvent common side reactions such as eliminations or hydrolysis which are commonly seen using similar methods.



Scheme 3.

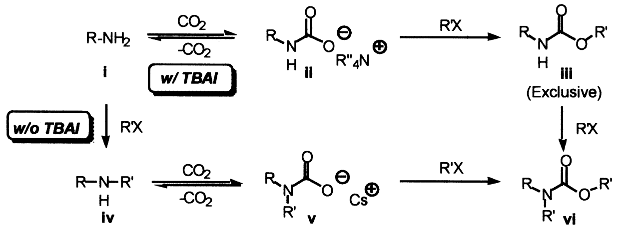


Scheme 4.

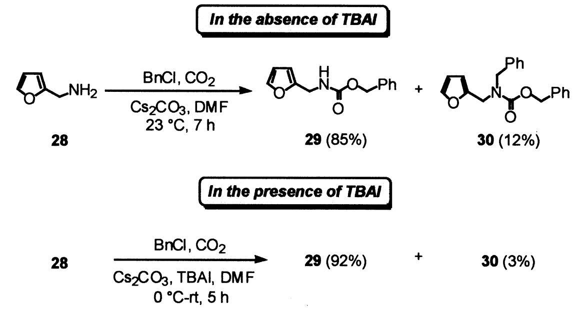
Since the generality for carbonate formation under the disclosed conditions seemed noteworthy, we next decided thus to explore the applicability of the newly developed techniques using various amines for efficient and chemoselective carbamate formation.[11] Although the direct incorporation of carbon dioxide into amines using alkyl halides is known, this method requires high temperature and pressure.[8,18] As a further drawback, these reaction conditions often give rise to nitrogen derived products (trialkylamines), stemming from direct *N*-alkylation.[19] This result may be a reflection of the poor nucleophilicity of the oxygen of the carbamate over the reactivity of the nitrogen center, or as a result of an unfavorable equilibrium concentration of the carbamate anion in solution.[19] In any event, poor yields of the desired carbamate products usually occur, prompting us to apply our protocol, envisioning higher chemoselectivities.

For instance, benzylamine (**20**) smoothly incorporated into $CO_2$ to generate the incipient carbamate anion, which underwent rapid alkylation with 1-bromobutane to generate the corresponding desired product (Scheme 3). Interestingly, tetrabutylammonium iodide (TBAI) was found to be a crucial additive in averting direct *N*-alkylations and overalkylation of the produced carbamate.[20] Thus, this procedure is highly chemoselective, convenient, and efficient, which overcomes the common problems encountered utilizing similar methods (vide supra).

Since TBAI was found to be a necessity in diverting direct *N*-alkylations and their ensuing side reactions, we decided to undertake a more detailed study with regards to its inherent role (Scheme 4). For instance, tertiary amines **24** and **27** were formed in considerable amounts along with the desired carbamates **23** and **26**, respectively, when carbamations were carried out in the absence of TBAI. Furthermore, variations in carbon dioxide bubbling time seemed to have no effect in suppressing tertiary amine formation. On



Scheme 5.



**Scheme 6.**

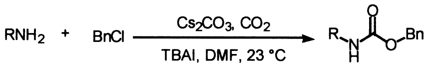
the contrary, the direct *N*-alkylation of the amine was completely avoided by employing the use of TBAI. Under these reaction conditions, carbamates **23** and **26** were exclusively produced in high yields.

As illustrated in Scheme 5, TBAI also helped to minimize or prohibit overalkylation of the produced carbamate presumably by enhancing the rate of $CO_2$ incorporation and/or stabilizing the incipient carbamate anion through the conjugation with the tetrabutylammonium cation.[21]

Whereas, the cesium ion tends to weakly coordinate to conjugate anions, making the anion more nucleophilic. Prior to addition of the halide, the amine and carbon dioxide were reacted to pre-form the incipient carbamate anion, which was believed to prevent the aforementioned *N*-alkylations as well as suppress the overalkylation of the desired carbamate kinetically.

In alkylations of alcohols and amines, TBAI exerted opposite effects on reaction rates and yields.[22] While TBAI facilitated etherifications, *N*-alkylations were significantly retarded to make low conversion. Thus, mechanistically, it was rationalized that the introduction of TBAI would suppress possible *N*-alkylations (**i–iv**), while promoting the desired carbamate formation (**ii–iii**).[21]

**Table 5.** Carbamate formation using aliphatic amines, benzyl chloride, and $CO_2$ in the presence of $Cs_2CO_3$ and TBAI



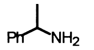
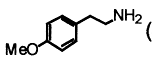
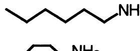
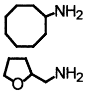
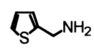
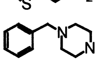
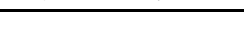
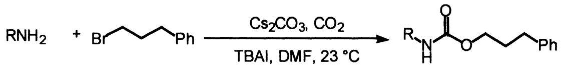
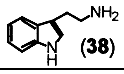
| Entry | Amine ($RNH_2$) | Time (h) | Yield (%) |
|---|---|---|---|
| 1 | **20** | 5 | 96 |
| 2 |  **(31)** | 7 | 97 |
| 3 | **22** | 6 | 88 |
| 4 |  **(32)** | 5 | 85 |
| 5 |  **(33)** | 10 | 93 |
| 6 |  **(34)** | 6 | 78 |
| 7 |  **(35)** | 6 | 93 |
| 8 |  **(36)** | 7 | 90 |
| 9 |  **(37)** | 12 | 85 |

**Table 6.** $Cs_2CO_3$-Promoted carbamate synthesis using an amine, 1-bromo-3-phenylpropane, and $CO_2$



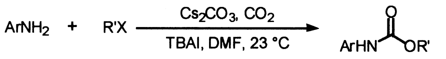
| Entry | Amine ($RNH_2$) | Time (h) | Carbamate yield (%) |
|---|---|---|---|
| 1 | **20** | 7 | 87 |
| 2 | **31** | 7 | 93 |
| 3 | **22** | 7 | 90 |
| 4 | **32** | 6 | 85 |
| 5 | **33** | 10 | 91 |
| 6 | **34** | 12 | 82 |
| 7 | **35** | 7 | 88 |
| 8 | **36** | 7 | 90 |
| 9 | **28** | 6 | 82 |
| 10 |  **(38)** | 8 | 89 |

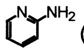
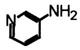
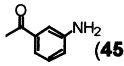
In another comparative study (Scheme 6), treatment of **28** with benzyl chloride in the absence of TBAI gave benzyl carbamate **29** along with a significant amount of overalkylated product **30**, stemming from the *N*-alkylation of carbamate **29**.[20] On the other hand, when the reaction was allowed to proceed in the presence of TBAI at 0°C with gentle warming to room temperature, dialkyl carbamate **30** was suppressed to a negligible extent, and the ratio of the desired carbamate over the overalkylated product was generally greater than 30/1, offering a standard protocol for efficient synthetic conditions.

With the ideal conditions in hand, numerous amines were screened and found to be suitable under this developed protocol using benzyl chloride as the halide of choice (Table 5). Benzylamines reacted efficiently to install the Cbz functionality in high yields (entries 1 and 2). Likewise, phenethylamines **22** and **32** followed similar suite to furnish nearly the same yields within 6 h (entries 3 and 4). As depicted in entry 5, a lipophilic amine such as *n*-hexylamine (**33**) underwent coupling to afford the desired mixed alkyl carbamate in 93% yield. Cycloalkylamines encompassing cyclooctylamine (**34**) were also successful, furnishing the desired product (entry 6). In addition, various heterocyclic amines proved fruitful using the reported conditions (entries 7 and 8), while secondary amine 4-benzylpiperazine (**37**) required a longer reaction time (entry 9).

As shown in Table 6, aliphatic amines were then screened using less reactive alkyl bromides in order to demonstrate compatibility with a wide array of functionality using the enclosed conditions. Benzyl carbamates of **20** and **31** were easily fashioned using 1-bromo-3-phenylpropane (entries 1 and 2). Phenethylamine showcases also proved to be facile, generating the carbamate scaffolding rapidly within 7 h (entries 3 and 4). However, lipophilic amine **33** required slightly longer reaction time to complete the desired process (entry 5). In addition, the sterically more bulky cyclooctyl carbamate was completely generated in high yield after a 12 h time period (entry 6). Heterocyclic amines were also converted to the corresponding carbamates (entries 7–9). Interestingly, tryptamine (**38**) was found to carbonylate at the primary amine selectively, leaving the secondary amine intact (entry 10).

**Table 7.** Carbamate formation using aromatic amines



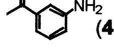
| Entry | Amine (ArNH$_2$) | Halide (R′X) | Time (h) | Carbamate yield (%) |
|---|---|---|---|---|
| 1 | Aniline (**39**) | **8** | 5 | 98 |
| 2 | |  **(40)** | 6 | 94 |
| 3 | *p*-Toluidine (**41**) | **8** | 12 | 83 |
| 4 | | **40** | 4 | 96 |
| 5 | *N*-Ethylaniline (**42**) | **8** | 22 | 78 |
| 6 | | **40** | 22 | 75 |
| 7 |  **(43)** | **8** | 12 | 83 |
| 8 | | **40** | 7 | 80 |
| 9 |  **(44)** | **8** | 12 | 88 |
| 10 | | **40** | 4 | 83 |
| 11 |  **(45)** | **8** | 14 | 47 |
| 12 | *p*-Nitroaniline (**46**) | **40** | 19 | 50 |
| 13 | *m*-Nitroaniline (**47**) | **40** | 12 | 73 |

Following similar suite, we decided to investigate carbamate formation using aromatic amines. As delineated in Table 7, aniline (**39**) and *p*-toluidine (**41**) underwent facile carbamations in high yields using two different electrophiles (entries 1–4). As expected, the secondary aromatic amine, *N*-ethylaniline (**42**), was sluggish to afford the corresponding carbamates after 22 h in similar isolated yields (entries 5 and 6). Subsequently, pyridine examples including 2- and 3-aminopyridines showed high reactivity with both an active (entries 7 and 9) and unreactive bromide (entries 8 and 10). Although, much to our disappointment, aromatic amines containing an electron withdrawing substituent were sluggish to proceed to completion and unreacted amine was accompanied along with the desired carbamate (entries 11–13).[23]

After numerous attempts to improve the yields for carbamate formation using aromatic amines possessing electron withdrawing functionality at ambient temperatures, we discovered that elevated reaction temperatures failed to complete conversions (Table 8).

At higher temperatures (70°C), similar results were noted to Table 7 (entries 11–13), and thus, allowing the reaction to proceed for 24 h improved yields slightly, however a mixture of side products resulted along with the carbamate (entries 2, 4, and 6).[23] Surprisingly, simply allowing the reaction to proceed at room temperature for longer duration (5 d), the starting amine was found to be consumed. Thus, these optimized conditions gave rise to the exclusive carbamate formation in excellent yields (entries 1, 3, and 5) without any concomitant formation of side products.

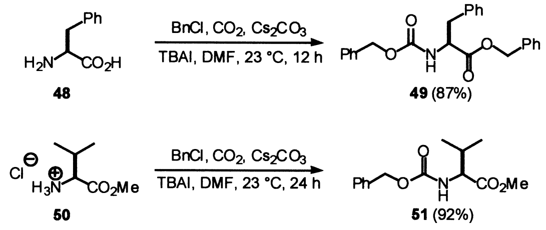
**Table 8.** Carbamate formation using aromatic amines containing electron withdrawing groups with BnCl

| Entry | Amine (ArNH$_2$) | Temperature (°C) | Time | Yield (%) |
|---|---|---|---|---|
| 1 |  **(45)** | 23 | 5 d | 81 |
| 2 | | 70 | 24 h | 70 |
| 3 | *p*-Nitroaniline (**46**) | 23 | 5 d | 87 |
| 4 | | 70 | 24 h | 60 |
| 5 | *m*-Nitroaniline (**47**) | 23 | 5 d | 96 |
| 6 | | 70 | 24 h | 65 |

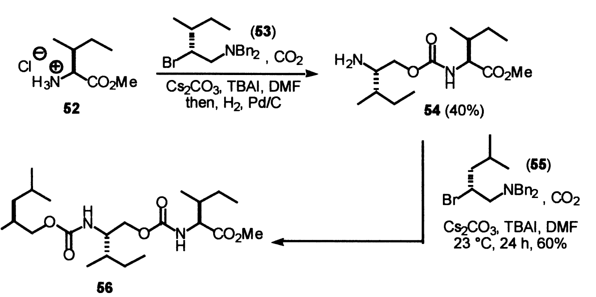
Since peptidomimetic synthesis of artificial biomolecules containing the carbamate scaffolding is a main focus of our research,[24] our efforts were next directed towards successful carbamations using amino acids and derivatives thereof. As depicted in Scheme 7, amino acids and esters were smoothly converted to the corresponding carbamates in excellent yields. For example, when phenylalanine (**48**) was subjected to the standard conditions, carbamation was accompanied along with the anticipated esterification. In addition, valine methyl ester (**50**) underwent conversion to **51** in high yield without any degree of hydrolysis.

Encouraged by the results, we next set out to synthesize a higher order peptidomimetic compound consisting of three amino acids linked via carbamate bridges. Trimer **56** was easily prepared following the carbamation techniques outlined in Scheme 7. After amino bromide **53** was prepared using our previous reported bromination protocol,[25] it was coupled with the methyl ester of isoleucine (**52**), followed by debenzylation, gave rise to the peptidomimetic dimer **54**. The secondary bromide rearranged to the primary form by way of the corresponding aziridinium salt during the alkylation.[25] Dimer **54** was subsequently conjugated with bromide **55**, synthesizing trimer **56** in a remarkably clean fashion (Scheme 8). Using the developed protocol, racemizations were not detected during any alkylations of these chiral substrates, and complications stemming from hydrolysis were also not observed.[26]

As a further application to the carbamation protocol, the methodology was then extended to the development of a new carbamate protecting group for primary and secondary

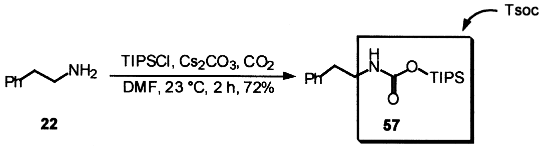


**Scheme 7.**

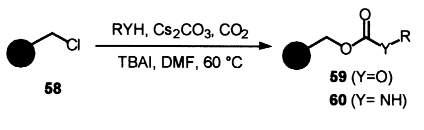


**Scheme 8.**

amines. A plethora of masking groups for nitrogen are available and hold critical importance in amine chemistry.[27] Since they are not free from practical problems during installation and removal, interesting and clever new choices appear on quite a regular basis in challenge to the more popular Boc, Cbz, and Fmoc moieties. Unlike the protection of alcohols, which is heavily weighted on use of silyl groups, relatively few amine derivatives are available due to their hydrolytic lability, which prompted the synthesis of a heartier carbamate, namely *N*-triisopropylsilyloxycarbonyl (‘Tsoc’).[28] As delineated in Scheme 9, N-Tsoc derivative of phenethylamine was easily fashioned by initial treatment of the primary amine dissolved in DMF containing cesium carbonate. After bubbling carbon dioxide into the reaction suspension for 1 h, the carbamic acid salt of phenethylamine (**22**) was consequently *N*-alkylated using TIPSCl. After 2 h, the anticipated carbamate was purified by column chromatography to offer the Tsoc carbamate **57** in 72% isolated yield.



**Scheme 9.**



**Scheme 10.**

## 2.2. Synthesis of carbonates and carbamates on solid supports

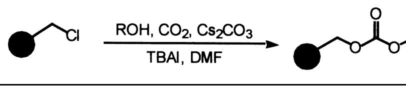
Upon re-examining our solution-phase results obtained for the synthesis of carbonates and carbamates via a three-component coupling using cesium carbonate and TBAI, it then became strikingly evident to us to continue in our endeavors by extending this methodology to an efficient and practical solid-phase synthesis of carbonates and carbamates.[13]

Carbonate and carbamate linkers have been prepared on polymer support utilizing haloformates or carbonate exchange.[29] However, these methods are often costly and the use of hazardous reagents leave these methods far from general use. Using cesium carbonate and TBAI, various alcohols and amines were ligated to Merrifield resin (**58**) via a $CO_2$ bridge to exclusively produce carbonates **59** and carbamates **60**, respectively (Scheme 10). Carbon dioxide was supplied by bubbling into the reaction suspension, using DMF as the solvent.

As demonstrated in our solution phase carbonylations and carbamations, the desired conversions were achieved at ambient temperatures although our solid phase strategies required slightly elevated temperatures. As shown in Table 9, 1-decanol (entry 1), benzyl alcohol (entry 3), and *p*-nitrobenzyl alcohol (entry 5) smoothly conjugated with $CO_2$ at room temperature to give the intermediate carbonate anion in DMF. Upon addition of polystyrene resin **58**, carbonate bound resin **59** was obtained in moderate yields over a 24 h time period. On the other hand, after screening several reaction temperatures including reflux temperature, a 60°C reaction temperature was found to be ideal, which offered shortened reaction times and increased yields significantly (entries 2, 4, and 6, respectively).[30]

Under these conditions, we next shifted our focus to solid phase carbonate synthesis using secondary alcohols and chiral templates (Table 10).[15] Secondary alcohols such as cyclohexanol (**67**) and 3,3-dimethyl-2-butanol (**68**) exhibited similar trends, delivering the resin bound carbonates in excellent yields (entries 1 and 2). Subsequently, using chiral alcohols containing a small degree of sterics such as menthol (**13**), the desired chiral carbonate formed in high yield (entry 3). As depicted in entries 4–6, α-hydroxy esters and lactones encompassing mandelate **69**, phenyl lactate (**17**), and γ-butyrolactone (**70**) underwent

**Table 9.** Conditions for solid phase synthesis of carbonates at various temperatures



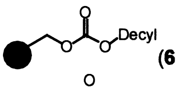
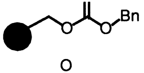
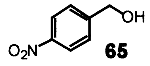
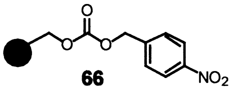
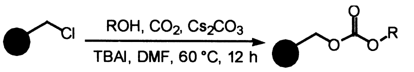
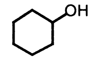
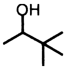
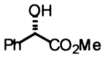
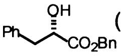
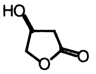
| Entry | Alcohol (ROH) | Conditions | Product | Yield (%) |
|---|---|---|---|---|
| 1 | 1-Decanol (**61**) | 23°C, 20 h |  **(62)** | 55 |
| 2 |  | 60°C, 12 h |  | 70 |
| 3 | BnOH (**63**) | 23°C, 17 h |  **(64)** | 63 |
| 4 |  | 60°C, 12 h |  | 97 |
| 5 |  | 23°C, 24 h |  | 35 |
| 6 |  | 60°C, 12 h |  | 81 |

**Table 10.** Solid phase synthesis using secondary alcohols and chiral templates



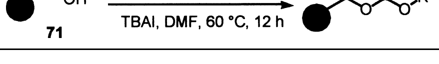
| Entry | Alcohol (ROH) | Carbonate yield (%) |
|---|---|---|
| 1 |  **(67)** | 98 |
| 2 |  **(68)** | 98 |
| 3 | Menthol (**13**) | 83 |
| 4 |  **(69)** | 76 |
| 5 |  **(17)** | 63 |
| 6 |  **(70)** | 58 |

carbonylations to deliver their corresponding carbonates in moderate yields without any loss of stereochemistry.[31]

As summarized in Table 11, carbonylations were also successful upon switching the alcohol component to the solid support. Using Wang resin (**71**) and various bromides, unsymmetrical carbonates formed in high yields, making this method complimentary to the aforementioned reaction.[32]

Reaction of **71** with long chain primary bromides **72** and **73** gave rise to the exclusive synthesis of carbonate resin **59** in excellent yields (entries 1 and 2). Using a reactive bromide such as benzyl bromide (**74**), the desired carbonate was generated in 91% yield (entry 3). In comparison, regardless of electron withdrawing or donating substituents at the 4 position of benzyl bromide, carbonylations were highly efficient (entries 4 and 5).

**Table 11.** Solid phase synthesis using Wang resin with various bromides



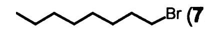
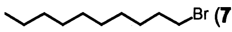
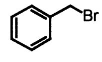
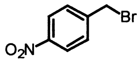
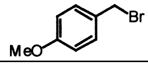
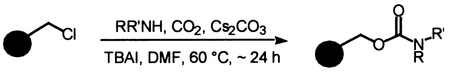
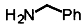
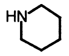
| Entry | Bromide (RBr) | Yield (%) |
|---|---|---|
| 1 |  **(72)** | 97 |
| 2 |  **(73)** | 99 |
| 3 |  **(74)** | 91 |
| 4 |  **(75)** | 83 |
| 5 |  **(76)** | 83 |

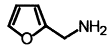
**Table 12.** Solid-phase synthesis of carbamates using Merrifield resin with primary and secondary amines

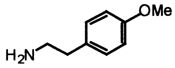


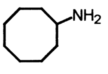

(**20**, 55%)

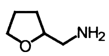

(**22**, 51%)

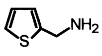

(**25**, 55%)

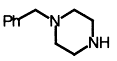

(**28**, 90%)

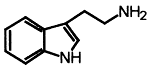

(**32**, 68%)

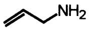

(**34**, 85%)


(**35**, 80%)

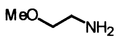

(**36**, 71%)

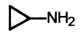

(**37**, 70%)

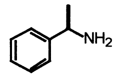

(**38**, 60%)

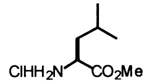

(**77**, 85%)

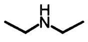
$n$-octyl-$NH_2$
(**78**, 44%)

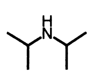

(**79**, 89%)

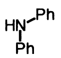

(**80**, 60%)

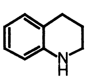

(**81**, 73%)

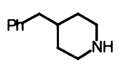

(**82**, 67%)


(**83**, 77%)


(**84**, 50%)


(**85**, 21%)


(**86**, 95%)

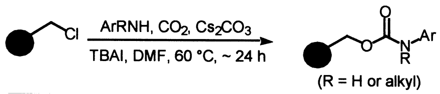

(**87**, 72%)

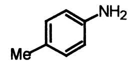
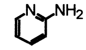
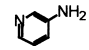
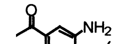
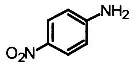
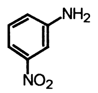
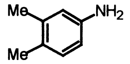
As shown in Table 12, carbamations of amines on solid support were also successful.[33] Activated amines such as **28** and **36** delivered the polymer bound carbamates **60** in moderate to high yields, whereas the carbamate analog of a hydrophobic amine, *n*-octylamine (**78**) formed in lower yield (44%) after the same duration. Furthermore, carbamate scaffoldings containing the phenethylamine moiety (**22** and **32**) gave good results. Whereas, heterocyclic amines (**36**, **38**, and **86**) united under the developed conditions in 60–95% yields. Cycloalkyl amines **34** and **80** were also found to couple with resin **58** efficiently. With chiral auxiliaries in mind, methylbenzylamine (**81**) and amino ester **82** were used as starting amines, and the desired resin bound organic carbamates **60** formed exclusively in good yields. Secondary mixed alkyl carbamates were also advantageous. Treatment of Merrifield's resin (**58**) with either sterically hindered diethylamine (**83**) or diisopropylamine (**84**) both resulted in moderate yields of the carbamate product. In addition, along the same lines, the sterically demanding amine, diphenylamine (**85**), underwent a three-way coupling to afford the desired product, however, in poor yield. Therefore, it was decided that use of such sterically hindered amines as synthons in these protocols should be avoided. Finally, various cyclic secondary amines also proved to be facile and pragmatic (**25**, **37** and **87**).

Since carbamates generated from aromatic amines hold a wide variety of applications, attention was then shifted toward formation of aromatic carbamates on a solid support (Table 13). Using our cesium carbonate promoted carbamate methodology, aniline (**39**) proceeded smoothly under the standard conditions with complete conversion. Comparatively, its electron rich derivatives **41** and **88**, and electron deficient anilines (entries 6–8) were proficient. Complimentary 2- and 3-aminopyridines reacted smoothly offering moderate yields (entries 4 and 5). Likewise, secondary aromatic amine, *N*-ethylaniline (**42**), led to the corresponding carbamate in 86% yield.

In order to address issues concerning selectivity and purity

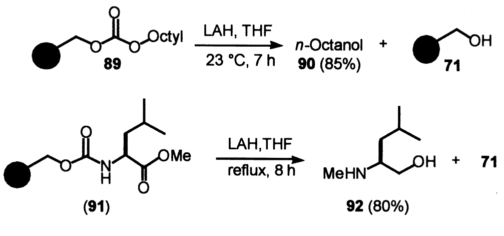
**Table 13.** Solid phase synthesis of carbamates using aromatic amines with Merrifield resin



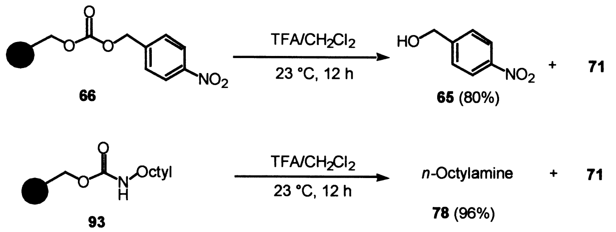
| Entry | Amine (ArRNH) | Yield (%) |
|---|---|---|
| 1 | Aniline (**39**) | 70 |
| 2 |  **(41)** | 81 |
| 3 | *N*-Ethylaniline (**42**) | 86 |
| 4 |  **(43)** | 66 |
| 5 |  **(44)** | 72 |
| 6 |  **(45)** | 62 |
| 7 |  **(46)** | 55 |
| 8 |  **(47)** | 44 |
| 9 |  **(88)** | 97 |

utilizing this solid phase protocol, the resulting carbonates and carbamates were further verified by cleavage from the Merrifield resin using two different conditions.[34] As delineated in Scheme 11, resin bound *n*-octyl carbonate **89** was cleaved by LAH reduction at room temperature to return the starting alcohol (*n*-octanol, **90**) after 7 h. However, leucine carbamate furnished from amine **82** required elevated temperatures such as reflux, which gave rise to the *N*-methylated amino alcohol **92** in 80% yield after 8 h. Numerous examples of cleavages and their yields are reported in Section 4, after the respective preparation of the corresponding carbamate.

As an alternative approach, hydrolytic cleavage of carbonate **66** or the corresponding carbamate **93** with TFA/$CH_2Cl_2$ (75:25, v/v) at room temperature released the starting alcohol **65** or amine **78** in high yields (Scheme 12).[34] In all cases, crude NMR spectra were clean and no other side products were noticed within NMR detection limits. Furthermore, IR spectra of all cleaved resins yielded only the corresponding polymer supported benzyl alcohol **71** exclusively.



**Scheme 11.** LAH cleavage from polymer support.



**Scheme 12.** Hydrolytic cleavage from polymer support.

## 3. Conclusion

In conclusion, a three-component coupling was performed using alcohols (or amines), carbon dioxide, and halides, leading to the efficient solution phase synthesis of carbonates and carbamates, respectively, in the presence of cesium carbonate and TBAI. Various aliphatic and aromatic alcohols and amines containing a diverse range of functionality such as electron donating and electron withdrawing groups were compatible, while reactive, unreactive, and secondary halides demonstrate substrate versatility. Chiral substrates encompassing amino acids and amino acid derivatives were resistant to racemization, and labile functionalities including esters were tolerant under the developed conditions, offering numerous applications such as efficient peptidomimetic synthesis.

In addition to the preceding results, we also established a cesium-promoted one-step three-way coupling uniting Merrifield resin, carbon dioxide, and various alcohols or amines, which led to the exclusive synthesis of mixed alkyl carbonates, or carbamates, respectively, on solid supports. These procedures discussed herein were mild enough to avert common side reactions such as hydrolysis or elimination commonly seen using similar methods, and chiral templates susceptible to racemization survived the conditions. Moreover, generation of large combinatorial libraries for rapid screening in order to determine the pertinent activity of molecules holding new or interesting properties is currently underway and will be reported in due course. Therefore, both our solution and solid-phase strategies are believed to be far more superior to existing methods possessing a wide variety of applications.

## 4. Experimental

### 4.1. General

Proton nuclear magnetic resonance ($^1H$ NMR) spectra were recorded in deuterated $CDCl_3$ on a Bruker AMX-360 (360 MHz). Chemical shifts were reported in parts per million (ppm, $\delta$) relative to either tetramethylsilane ($\delta$ 0.00 ppm) or trace amount of the undeuterated chloroform residue ($CDCl_3$, $\delta$ 7.27 ppm) as internal standard. $^1H$ NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). Coupling constants are presented in Hertz (Hz). Carbon nuclear magnetic resonance ($^{13}C$ NMR) spectra were recorded on a Bruker AMX-360 (90 MHz). Chemical shifts are reported in ppm ($\delta$) relative to the central line of the $CDCl_3$ triplet ($\delta$ 77.0 ppm). Infrared spectra (IR) were recorded on a Nicolet

FT-IR spectrometer 550. Absorption maxima were reported in wavenumbers (cm$^{-1}$). Optical rotations were measured at 25°C using a Perkin–Elmer 241MC polarimeter set on the sodium D line. Elemental analysis was performed by Atlantic Microlab, Inc.

Analytical thin layer chromatography (TLC) was carried out on EM TLC plates precoated with silica gel 60F$_{254}$ (250 mm layer thickness). Compounds were visualized on the TLC plate by either an UV light or *p*-anisaldehyde charring solution (18 mL *p*-anisaldehyde, 7.5 mL glacial acetic acid, 2.5 mL concentrated sulfuric acid in 675 mL absolute ethanol). Fisher chromatographic silica gel (170–400 mesh) was utilized for flash column chromatography (FCC). Eluent systems for FCC as well as TLC were reported in v/v ratios.

All glassware were flame-dried or oven-dried and purged with nitrogen prior to use. Anhydrous *N*,*N*-dimethylformamide (99.8%) was purchased from Aldrich Chemical Co. Tetrahydrofuran (THF) and diethyl ether (Et$_2$O) were purified from sodium and benzophenone. Likewise, acetonitrile and methylene chloride were distilled from calcium hydride. All other commercially available reagents and solvents were used without further purification unless otherwise indicated. Cesium bases were acquired from Acros, Aldrich or Chemetall.

**4.1.1. General procedure for carbonate preparation (solution phase).** To a solution of **5** (100 mg, 0.67 mmol) in anhydrous *N*,*N*-dimethylformamide (1.6 mL, 0.4 M), cesium carbonate (625 mg, 2.10 mmol, 3 equiv.) and tetrabutylammonium iodide (208 mg, 0.67 mmol, 1 equiv.) were added. Carbon dioxide gas (flow rate ~25–30 mL/min) was bubbled through the solution for 1 h before 1-bromobutane (274 mg, 0.22 mL, 2.0 mmol) was added to the solution. The reaction proceeded at room temperature with CO$_2$ gas bubbling for 3.5 h after which all the starting material (4-phenyl-1-butanol) was consumed. The reaction mixture was then poured into water (30 mL) and extracted by 3:1 hexanes–EtOAc (60 mL) thoroughly. The organic layer was washed with water (2×30 mL), brine (30 mL), and dried over sodium sulfate. Evaporation of solvent and subjection to flash column chromatography (9:1, hexanes–EtOAc) afforded **6** as a clear liquid (157 mg, 94%). $R_f$ 0.49 (9:1, hexanes–EtOAc); IR (thin film) 3082, 3061, 3028, 2958, 2896, 1742, 1602, 1498, 1457, 1399, 1259, 1057, 1016, 932, 793, 746, 699 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 0.95–1.00 (t, $J$=7.4 Hz, 2H), 1.40–1.50 (m, $J$=7.4 Hz, 2H), 1.64–1.72 (m, 2H), 1.72–1.77 (m, 4H), 2.64–2.70 (m, 2H), 4.13–4.20 (m, 4H), 7.19–7.33 (m, 5H); $^{13}$C NMR (CDCl$_3$) δ 13.9, 19.2, 27.8, 28.6, 31.0, 35.7, 68.0, 126.2, 128.6, 128.7, 142.2, 155.7. Anal. calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.02; H, 8.78.

**4.1.2. Alkyl carbonate 2 (Table 3, entry 1).** Yield 91%; clear oil; $R_f$ 0.32 (15:1, hexanes–EtOAc); IR (thin film) 3086, 3064, 3033, 2947, 2861, 1743, 1654, 1604, 1496, 1453, 1394, 1256, 796, 748, 703 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 1.60–1.74 (m, 4H), 2.65–2.67 (m, 2H), 4.18–4.20 (m, 2H), 4.62–4.64 (d, $J$=5.8 Hz, 2H), 5.26–5.30 (d $J$=10.4 Hz, 1H), 5.35–5.40 (d, $J$=17.2 Hz, 1H), 5.90–6.01 (ddt, $J$=16.2, 11.4, 6.6 Hz, 1H), 7.18–7.32 (m, 5H); $^{13}$C NMR (CDCl$_3$) δ 27.19, 27.96, 35.10, 67.66, 68.03, 118.55, 125.56, 128.05, 128.10, 131.36, 141.60, 154.79. Anal. calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.81; H, 7.76.

**4.1.3. Alkyl carbonate 2 (Table 3, entry 2).** Yield 94%; clear oil; $R_f$ 0.42 (9:1, hexanes–EtOAc); IR (thin film) 3098, 3067, 3035, 2948, 1748, 1610, 1492, 1459, 1376, 1263, 796, 758, 701 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 1.72–1.80 (m, 4H), 2.66–2.71 (m, 2H), 4.18–4.27 (m, 2H), 5.20–5.23 (s, 2H); 7.22–7.45 (m, 10H); $^{13}$C NMR (CDCl$_3$) δ 27.60, 28.35, 35.50, 68.11, 69.57, 125.96, 128.45, 128.51, 128.60, 128.69, 135.46, 141.99, 155.34. Anal. calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.11; H, 7.07.

**4.1.4. Alkyl carbonate 2 (Table 3, entry 3).** Yield; 95%; colorless oil; $R_f$ 0.43 (9:1, hexanes–EtOAc); IR (thin film) 3065, 3033, 2980, 2940, 2861, 1756, 1607, 1501, 1453, 1290, 1223, 1163, 1035, 793, 753, 699 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 1.50 (s, 9H), 1.71–1.76 (m, 4H), 2.63–2.67 (t, $J$=7.1 Hz, 2H), 4.19–4.23 (t, $J$=7.2 Hz, 2H), 4.51 (s, 2H), 7.17–7.29 (m 5H); $^{13}$C NMR (CDCl$_3$) δ 27.12, 27.67, 27.89, 35.05, 63.32, 68.04, 82.15, 125.55, 128.03, 128.10, 141.55, 154.62, 166.25. Anal. calcd for $C_{17}H_{24}O_5$: C, 66.21; H 7.84. Found: C, 66.29; H, 7.80.

**4.1.5. Alkyl carbonate 2 (Table 3, entry 4).** Yield 98%; $R_f$ 0.46 (9:1, hexanes–EtOAc); IR (thin film) 3086, 3067, 3029, 2978, 2940, 2884, 1742, 1610, 1502, 1458, 1269, 1099, 796, 752, 704 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 0.94–0.98 (t, $J$=7.4 Hz, 3H), 1.28–1.31 (d, $J$=6.2 Hz, 3H), 1.57–1.63 (m, 2H), 1.63–1.74 (m, 4H), 2.66–2.68 (m, 2H), 4.15–4.17 (m, 2H), 4.70–4.76 (m, 1H), 7.19–7.32 (m, 5H); $^{13}$C NMR (CDCl$_3$) δ 9.67, 19.44, 27.62, 28.35, 28.82, 35.49, 67.56, 76.40, 125.89, 128.38, 128.45, 141.99, 155.08. Anal. calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.85; H, 8.70.

**4.1.6. Alkyl carbonate 2 (Table 3, entry 5).** Yield 92%; clear oil; $R_f$ 0.47 (9:1, hexanes–EtOAc); IR (thin film) 3092, 3065, 3032, 2967, 2941, 2875, 1743, 1460, 1395, 1262, 1137, 1062, 933, 795, 752, 703 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 0.93–0.98 (t, $J$=7.3 Hz, 3H), 1.28–1.31 (d, $J$=6.3 Hz, 3H), 1.35–1.46 (m, 2H), 1.60–1.69 (m, 2H), 2.80 (*A*BX, $J_{AB}$=13.5 Hz, $J_{AX}$=6.9 Hz, 1H), 3.04 (A*B*X, $J_{AB}$=13.5 Hz, $J_{AB}$=6.5 Hz, 1H), 4.09–4.14 (t, $J$=6.6 Hz, 2H), 4.97–5.03 (m, 1H), 7.22–7.34 (m, 5H); $^{13}$C NMR (CDCl$_3$) δ 13.78, 19.04, 19.51, 30.81, 42.42, 67.70, 75.57, 126.68, 128.52, 128.57, 137.39, 154.92. Anal. calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 72.20; H, 8.57.

**4.1.7. Alkyl carbonate 2 (Table 3, entry 6).** Yield 98%; colorless oil; $R_f$ 0.27 (15:1, hexanes–EtOAc); IR (thin film) 3086, 3067, 3035, 2985, 2940, 1748, 1603, 1502, 1458, 1383, 1263, 1137, 1048, 916, 790, 752, 701 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 1.28–1.31 (d, $J$=6.3 Hz, 3H), 2.80 (A*B*X, $J_{AB}$=13.6 Hz, $J_{AX}$=6.8 Hz, 1H), 3.03 (*A*BX, $J_{AB}$=13.6 Hz, $J_{BX}$=6.5 Hz, 1H), 4.98–5.05 (m, 1H), 5.13 (s, 2H), 7.20–7.39 (m, 5H); $^{13}$C NMR (CDCl$_3$) δ 19.51, 42.36, 69.39, 75.98, 126.72, 128.32, 128.53, 128.55, 128.68, 129.58, 135.58, 137.29, 154.76.

**4.1.8. Alkyl carbonate 2 (Table 3, entry 7).** Yield 96%; colorless liquid; $R_f$ 0.40 (9:1, hexanes–EtOAc); IR (neat)

3061, 3037, 2987, 2837, 2885, 1750, 1458, 1371, 1290, 1234, 1159, 1060, 786, 755, 699 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 1.29–1.30 (d, *J*=4.2 Hz, 3H), 1.48 (s, 9H), 2.78–2.82 (*A*BX, $J_{AB}$=13.5 Hz, $J_{AX}$=7.0 Hz, 1H), 3.03–3.09 (A*B*X, $J_{AB}$=13.5 Hz, $J_{BX}$=7.62 Hz, 1H), 4.44–4.54 (AB, $J_{AB}$=13.4 Hz, 1H), 4.96–5.05 (m, 1H), 7.21–7.31 (m, 5H); $^{13}$C NMR ($CDCl_3$), δ 19.47, 28.28, 42.35, 63.91, 76.70, 82.79, 126.92, 128.74, 128.78, 137.30, 154.59, 166.86. Anal. calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.33; H, 7.56.

**4.1.9. Alkyl carbonate 2 (Table 3, entry 8).** Yield 96%; $R_f$ 0.51 (9:1, hexanes–EtOAc); IR (thin film) 2962, 2931, 2875, 1749, 1460, 1394, 1262, 1183, 992, 953, 922, 793 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 0.69–0.72 (d, *J*=4.9 Hz, 3H), 0.80–0.87 (m, 10H), 0.94–0.97 (m, 2H), 1.28–1.35 (m, 4H), 1.54–1.61 (m, 4H), 1.86–1.92 (m, 1H), 1.92–1.99 (m, 1H), 4.03 (td, *J*=6.3, 1.1 Hz, 2H), 4.43 (td, *J*=10.8, 4.3 Hz, 1H); $^{13}$C NMR ($CDCl_3$) δ 13.2, 15.8, 18.5, 20.3, 21.6, 22.9, 25.7, 30.3, 31.2, 33.8, 40.4, 46.6, 67.1, 77.7, 154.6. Anal. calcd for $C_{15}H_{28}O_3$: C, 70.27; H, 11.01. Found: C, 70.32; H, 10.94.

**4.1.10. Alkyl carbonate 2 (Table 3, entry 9).** Yield 92%; colorless oil; IR (thin film) 3036, 2957, 2838, 1748, 1614, 1517, 1456, 1383, 1246, 1175, 1028, 928, 824 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 3.73 (s, 3H), 3.79 (s, 3H), 5.16 (s, 2H), 5.88 (s, 1H), 6.88–7.48 (m, 9H); $^{13}$C NMR ($CDCl_3$) δ 52.57, 55.11, 70.04, 113.81, 127.47, 128.67, 129.30, 130.26, 133.10, 154.27, 159.83, 168.90. Anal. calcd for $C_{18}H_{18}O_6$: C, 65.45; H, 5.49. Found: C, 65.51; H, 5.55.

**4.1.11. Alkyl carbonate 2 (Table 4, entry 1).** Yield 90%; ee=96%; IR (thin film) 2988, 2942, 1748, 1456, 1383, 1266, 1207, 1136, 1075, 1028, 918, 789, 753, 698 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 1.19 (t, *J*=7.13 Hz, 3H), 1.46 (d, *J*=7.06 Hz, 3H), 4.15 (q, *J*=7.08 Hz, 2H), 4.49 (q, *J*=7.08 Hz, 1H), 5.13 (s, 2H), 7.26–7.32 (m, 5H); $^{13}$C NMR ($CDCl_3$) δ 13.82, 16.72, 61.27, 69.69, 71.60, 128.09, 128.14, 128.30, 128.35, 128.40, 134.82, 154.27, 170.15. Anal. calcd for $C_{13}H_{16}O_5$: C, 61.90; H, 6.39. Found: C, 61.87; H, 6.31.

**4.1.12. General procedure for determination of enantiomeric excess using (*R*)-methoxyphenyl acetic acid.** A solution of (*R*)-(+)-methoxyphenyl acetic acid (17 mg, 0.1 mmol), *N*,*N*-dicyclohexylcarbodiimide (DCC, 11 mg, 0.1 mmol), ethyl (*S*)-(−)-lactate (11 μL, 0.1 mmol) which was provided by hydrogenolysis, and a catalytic amount of DMAP in $CH_2Cl_2$ (2 mL) was allowed to stand at 0°C for 30 min until esterification was complete. *N*,*N*-Dicyclohexylurea was filtered and the filtrate was concentrated in vacuo to provide crude oil, which was purified by column chromatography (3:1, hexanes–EtOAc) to afford the desired product (26 mg, 95%, 96% ee): IR (thin film) 2989, 2940, 2830, 1749, 1456, 1272, 1201, 1108, 735 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 1.23 (t, 3H, *J*=7.13 Hz), 1.42 (d, *J*=7.09 Hz, 2H), 3.45 (s, 3H), 4.18 (q, *J*=7.13 Hz, 2H), 4.87 (s, 1H), 5.08 (q, 1H, *J*=7.06 Hz), 7.34–7.48 (m, 5H); $^{13}$C NMR ($CDCl_3$) δ 13.93, 16.65, 57.41, 61.39, 69.18, 82.18, 127.21, 128.51, 128.71, 135.85, 170.08, 170.25. Anal. calcd for $C_{14}H_{18}O_3$: C, 63.15; H, 6.81. Found: C, 63.10; H, 6.87.

**4.1.13. Alkyl carbonate 2 (Table 4, entry 2).** Yield 94%; IR (thin film) 2987, 2839, 1748, 1613, 1516, 1456, 1383, 1248, 1205, 1135, 1074, 1032, 921, 823, 790 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 1.20 (t, *J*=7.13 Hz, 3H), 1.45 (d, *J*=7.09 Hz, 3H), 3.76 (s, 3H), 4.16 (q, *J*=7.13 Hz, 2H), 4.94 (q, *J*=7.06 Hz, 1H), 5.07 (s, 2H), 6.83 (d, *J*=8.50 Hz, 2H), 7.28 (d, *J*=8.43 Hz, 2H); $^{13}$C NMR ($CDCl_3$) δ 13.95, 16.86, 61.41, 69.77, 71.64, 113.84, 127.00, 130.24, 154.40, 159.83, 170.36. Anal. calcd for $C_{14}H_{18}O_6$: C, 59.57; H, 6.43. Found: 59.58; H, 6.41.

**4.1.14. Alkyl carbonate 2 (Table 4, entry 3).** Yield 85%; ee=97%; IR (thin film) 3089, 3032, 2958, 1955, 1878, 1748, 1605, 1479, 1455, 1385, 1252, 1026, 908, 750, 697 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 3.17 (*A*BX, 1H, $J_{AB}$=14.3 Hz, $J_{AX}$=8.6 Hz), 3.18 (A*B*X, 1H, $J_{AB}$=14.3 Hz, $J_{BX}$=4.6 Hz), 5.14–5.19 (m, 4H), 5.21 (m, 1H), 7.19–7.34 (m, 15H); $^{13}$C NMR ($CDCl_3$) δ 37.30, 67.17, 69.97, 76.09, 127.05, 128.20, 128.26, 128.31, 128.48, 128.52, 129.34, 134.79, 135.30, 154.45, 169.11.

**4.1.15. Alkyl carbonate 2 (Table 4, entry 4).** Yield 65%: ee=95%; IR (thin film) 3034, 2957, 1746, 1439, 1383, 1216, 1042, 909, 756, 699 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 2.93 (d, *J*=6.26 Hz, 2H), 3.71 (s, 3H), 3.78 (s, 3H), 5.22 (s, 2H), 5.43 (t, *J*=6.08 Hz, 1H), 7.34–7.38 (m, 5H); $^{13}$C NMR ($CDCl_3$) δ 35.60, 51.97, 52.55, 70.00, 71.13, 128.17, 128.43, 153.94, 168.80, 169.10.

**4.1.16. Alkyl carbonate 2 (Table 4, entry 5).** Yield 90%; ee=97% IR (thin film) 2965, 2932, 1790, 1455, 1121, 1007, 740, 699, 558 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 1.08 (s, 3H), 1.18 (s, 3H), 3.97–3.99 (AB, *J*=9.07 Hz), 5.14 (s, 1H), 5.19 (s, 1H), 7.32–7.35 (m, 5H); $^{13}$C NMR ($CDCl_3$) δ 19.58, 22.76, 39.98, 70.54, 75.95, 78.43, 128.58, 128.63, 128.69, 134.43, 154.30, 171.64. Anal. calcd for $C_{14}H_{16}O_5$: C, 63.63; H, 6.10. Found: C, 63.31; H, 6.20.

**4.1.17. Alkyl carbonate 2 (Table 4, entry 6).** Yield 94%; ee=97%; IR (thin film) 2967, 1798, 1753, 1613, 1516, 1465, 1381, 1246, 1175, 1131, 1022, 824 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 1.06 (s, 3H), 1.20 (s, 3H), 3.75 (s, 3H), 3.95–3.98 (AB, *J*=9.04 Hz), 5.12 (s, 1H), 6.8 5 (d, 2H, *J*=8.6 Hz, 2H), 7.29 (d, 2H, *J*=8.6 Hz); $^{13}$C NMR ($CDCl_3$) δ 19.57, 22.77, 39.97, 55.19, 70.48, 75.96, 78.34, 113.93, 126.53, 130.37, 154.31, 159.96, 171.68. Anal. calcd for $C_{15}H_{18}O_6$: C, 61.22; H, 6.16. Found: C, 61.47; H, 6.17.

**4.1.18. General procedure for carbamate preparation (solution phase).** To **20** (200 mg, 1.9 mmol) in anhydrous DMF (10 mL), were added cesium carbonate (1.8 g, 6.0 mmol, 3 equiv.) and tetrabutylammonium iodide (2.1 g, 6.0 mmol, 3 equiv.). Carbon dioxide gas (flow rate ∼30 mL/min) was bubbled into the reaction mixture for 1 h, then 1-bromobutane (770 mg, 0.6 mL, 6.0 mmol, 3 equiv.) was added into the suspension. The reaction proceeded at an ambient temperature with $CO_2$ gas bubbling for 3 h, during which time the starting material (benzylamine) was consumed. The reaction mixture was then poured into water (30 mL), and extracted with EtOAc (3×30 mL). The organic layers were washed with water (2×30 mL), brine (30 mL), and dried over anhydrous sodium sulfate. Evaporation of solvent followed by flash column chromatography (hexanes–EtOAc, 9:1 v/v) afforded carbamate **21** (480 mg, 96%) as an oil. $^{1}$H NMR ($CDCl_3$) $\delta$ 0.85 (t, *J*=7.23 Hz, 3H) 1.32 (m, 2H), 1.52 (m, 2H), 4.02 (t, *J*=6.26 Hz, 2H), 4.28 (d, *J*=4.71 Hz, 2H), 4.93 (bs, N*H*), 7.17–7.27 (m, 5H). $^{13}$C NMR ($CDCl_3$) $\delta$ 13.72, 19.03, 31.04, 44.99, 64.88, 127.40, 127.47, 128.61, 138.59, 156.77. Anal. calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.31; H, 8.21; N, 6.76.

**4.1.19. Synthesis of alkyl carbamate 23 with TBAI.** Into a flame dried flask **22** (206 mg, 1.7 mmol) in anhydrous DMF (8.5 mL), were added cesium carbonate (1.65 g, 5.1 mmol, 3 equiv.) and tetrabutylammonium iodide (1.88 g, 5.1 mmol, 3 equiv.). Carbon dioxide gas (flow rate ∼30 mL/min) was bubbled into the reaction mixture for 45 min, then methyl iodide (724 mg, 5.1 mmol, 3 equiv.) was added to the suspension. The reaction proceeded at an ambient temperature with $CO_2$ gas bubbling for 8 h, during which time phenethylamine was consumed. The reaction mixture was then poured into water (30 mL), and extracted with EtOAc (3×30 mL). The organic layers were washed with water (2×30 mL), brine (30 mL), and dried over anhydrous sodium sulfate. Evaporation of solvent followed by flash column chromatography (hexanes–EtOAc, 9:1 v/v) afforded carbamate **23** (283 mg, 93%) as an oil. $^{1}$H NMR ($CDCl_3$) $\delta$ 2.81 (t, 2H, *J*=7.0 Hz), 3.44 (q, 2H), 3.66 (s, 3H), 4.81 (bs, N*H*), 7.17–7.36 (m, 5H). $^{13}$C NMR ($CDCl_3$) $\delta$ 36.05, 42.19, 47.81, 126.50, 128.10, 129.25, 138.60, 156.21.

**4.1.20. Synthesis of alkyl carbamate 23 without TBAI.** The above reaction was duplicated in the absence of TBAI yielding **23** (280 mg, 92%) and **24** (18 mg, 8%) as products after 8 h.

**4.1.21. Synthesis of alkyl carbamate 26 with TBAI.** Into a flame dried flask **25** (200 mg, 2.34 mmol) in anhydrous DMF (5.4 mL), were added cesium carbonate (2.29 g, 7.05 mmol, 3 equiv. and tetrabutylammonium iodide (2.60 g, 7.05 mmol, 3 equiv.). Carbon dioxide gas (flow rate ∼30 mL/min) was bubbled into the reaction mixture for 45 min, then benzyl chloride (892 mg, 7.05 mmol, 3 equiv.) was added into the suspension. The reaction proceeded at an ambient temperature with $CO_2$ gas bubbling for 24 h, after which the reaction was stopped. The reaction mixture was then poured into water (30 mL), and extracted with EtOAc (3×30 mL). The organic layers were washed with water (2×30 mL), brine (30 mL), and dried over anhydrous sodium sulfate. Evaporation of solvent followed by flash column chromatography (hexanes–EtOAc, 9:1 v/v) afforded carbamate **26** (360 mg, 70%) as an oil along with **25** (60 mg, 30%). $^{1}$H NMR ($CDCl_3$) $\delta$ 1.47 (m, 2H), 1.57–1.66 (m, 4H), 2.41 (m, 4H), 5.17 (s, 2H), 7.27–7.40 (m, 5H). $^{13}$C NMR ($CDCl_3$) $\delta$ 24.25, 26.08, 54.50, 66.51, 126.83, 128.10, 129.24, 138.63, 156.29.

**4.1.22. Synthesis of alkyl carbamate 26 without TBAI.** The above reaction was duplicated in the absence of TBAI yielding **26** (164 mg, 32%) and **27** (280 mg, 68%) as products.

**4.1.23. Alkyl carbamate 29.** Yield 92%; IR (thin film) 3326, 3033, 2951, 1716, 1539, 1248, 1132, 1008, 737 cm$^{-1}$; $^{1}$H NMR ($CDCl_3$) $\delta$ 4.37 (d, 2H, *J*=4.4 Hz), 5.12 (s, 2H), 5.13 (bs, N*H*), 6.23 (s, 1H), 6.30–6.32 (s, 1H), 7.33–7.36 (m, 6H). $^{13}$C NMR ($CDCl_3$) $\delta$ 38.06, 66.89, 107.22, 110.36, 128.12, 128.49, 136.34, 142.18, 151.50, 156.13. Anal. calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.57; N, 6.06. Found: C, 67.33; H, 5.56; N, 5.92.

**4.1.24. Alkyl carbamate 4 (Table 5, entry 1).** Yield 96%; IR (thin film) 3331, 3087, 3032, 2957, 2897, 1690, 1534, 1455, 1266, 1140, 748 cm$^{-1}$; $^{1}$H NMR ($CDCl_3$) $\delta$ 4.21 (d, 2H, *J*=5.1 Hz), 4.97 (s, 2H), 6.96–7.18 (m, 11H). $^{13}$C NMR ($CDCl_3$) $\delta$ 45.12, 66.84, 127.49, 128.11, 128.50, 128.65, 136.45, 138.35, 156.38. Anal. calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.90; H, 7.32; N, 4.88.

**4.1.25. Alkyl carbamate 4 (Table 5, entry 2).** Yield 97%; IR (thin film) 3324, 3087, 3063, 3031, 2974, 2931, 1697, 1531, 1452, 1329, 1242, 1056, 1028 cm$^{-1}$; $^{1}$H NMR ($CDCl_3$) $\delta$ 1.56 (s, 3H), 4.97 (m, 1H), 5.14 (q, *J*=12.0 Hz, 2H), 5.68 (m, 1H), 7.35–7.39 (m, 10H). $^{13}$C NMR ($CDCl_3$) $\delta$ 22.11, 50.37, 66.30, 125.68, 126.90, 127.82, 128.16, 128.27, 143.45, 155.40.

**4.1.26. Alkyl carbamate 4 (Table 5, entry 3).** Yield 88%; pale yellow oil; IR (thin film) 3332, 3058, 2936, 1699, 1520, 1456, 1252, 1136, 1084, 742, 697 cm$^{-1}$; $^{1}$H NMR ($CDCl_3$) $\delta$ 2.83 (t, *J*=6.8 Hz, 2H), 3.48 (q, *J*=6.5 Hz, 2H), 4.82 (bs, N*H*), 5.11 (s, 2H), 7.18–7.36 (m, 10H). $^{13}$C NMR ($CDCl_3$) $\delta$ 36.05, 42.19, 66.61, 126.50, 128.09, 128.50, 128.61, 128.77, 136.56, 138.69, 156.21.

**4.1.27. Alkyl carbamate 4 (Table 5, entry 4).** Yield 85%; oil; IR (thin film) 3330, 3060, 3029, 2962, 2942, 2840, 1682, 1612, 1540, 1464, 1295, 1248, 1184, 1029 cm$^{-1}$; $^{1}$H NMR ($CDCl_3$) $\delta$ 2.76 (t, *J*=6.9 Hz, 2H), 3.41–3.43 (m, 2H), 3.78 (s, 3H), 4.9 (bs, *NH*), 5.10 (s, 2H), 6.85 (2, *J*=8.5 Hz, 2H), 7.00 (d, *J*=8.5 Hz, 2H), 7.43 (m, 5H). $^{13}$C NMR ($CDCl_3$) $\delta$ 35.01, 42.28, 55.10, 66.44, 113.9, 127.96, 128.37, 129.59, 130.58, 136.51, 156.21, 158.12. Anal. calcd for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.91. Found: C, 71.64; H, 6.67; N, 4.91.

**4.1.28. Alkyl carbamate 4 (Table 5, entry 5).** Yield 93%; pale oil; IR (thin film) 3337, 3065, 3033, 2955, 2930, 2858, 1700, 1534, 1455, 1249, 1138 cm$^{-1}$; $^{1}$H NMR ($CDCl_3$) $\delta$ 0.79 (t, 3H, *J*=6.9 Hz), 1.20–1.40 (m, 8H), 3.02–3.12 (m, 2H), 4.78 (bs, N*H*), 5.01 (s, 2H), 7.17–7.30 (m, 5H). $^{13}$C NMR ($CDCl_3$) $\delta$ 13.93, 22.46, 26.30, 29.81, 31.36, 66.43, 127.97, 128.40, 136.59, 156.32.

**4.1.29. Alkyl carbamate 4 (Table 5, entry 6).** Yield 78%; pale yellow oil; IR (thin film) 3330, 3087, 3063, 3031, 2920, 2853, 1697, 1528, 1452, 1311, 1233, 1049 cm$^{-1}$; $^{1}$H NMR ($CDCl_3$) $\delta$ 1.36–1.78 (m, 16H), 4.66 (s, 2H), 7.08–7.17 (m, 5H). $^{13}$C NMR ($CDCl_3$) $\delta$ 23.40, 25.27, 27.10, 32.20, 50.98, 66.28, 127.90, 127.98, 128.36, 136.62, 155.33.

**4.1.30. Alkyl carbamate 4 (Table 5, entry 7).** Yield 93%; oil; IR (thin film) 3345, 3087, 3063, 3030, 2970, 2947, 2871, 1700, 1496, 1465, 1455, 1417, 1364, 1237, 1131, 1100, 1063 cm$^{-1}$; $^{1}$H NMR ($CDCl_3$) $\delta$ 1.31–1.35 (m, 1H), 1.67–1.77 (m, 3H), 2.95–3.68 (m, 4H), 4.37–4.95 (m, 2H), 5.02 (s, 2H), 6.79–7.20 (m, 5H). $^{13}$C NMR ($CDCl_3$) $\delta$ 25.41, 29.01, 50.95, 67.18, 67.86, 78.04, 118.80, 125.87, 128.40, 137.84, 156.50.

**4.1.31. Alkyl carbamate 4 (Table 5, entry 8).** Yield 90%; IR (thin film) 3342, 3034, 2962, 2927, 1684, 1539, 1455, 1254, 1125, 969, 697 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 4.47–4.49 (d, *J*=8.4 Hz, 2H), 5.08 (s, 2H), 5.23 (bs, N*H*), 6.88–7.30 (m, 8H). $^{13}$C NMR ($CDCl_3$) $\delta$ 39.87, 66.88, 125.11, 125.75, 126.83, 128.11, 128.48, 136.30, 141.14, 156.02. Anal. calcd for $C_{13}H_{13}NO_2S$: C, 63.13; H, 5.30; N, 5.66; S, 12.97 Found: C, 63.33; H, 5.87; N, 5.20; S, 12.78.

**4.1.32. Alkyl carbamate 4 (Table 5, entry 9).** Yield 85%; oil; IR (thin film) 3317, 3061, 3025, 2942, 2857, 1701, 1428, 1296, 1227, 1121, 1013, 933, 747, 699 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 2.02 (q, *J*=7.0 Hz, 2H), 2.74 (t, *J*=7.6 Hz, 2H), 2.86 (bs, 2H), 3.69 (bs, 2H), 4.18 (t, *J*=6.5 Hz, 2H), 4.61 (d, 2H, *J*=13.0 Hz), 7.13–7.32 (m, 10H). $^{13}$C NMR ($CDCl_3$) $\delta$ 30.60, 32.32, 45.61, 64.86, 125.92, 126.28, 126.45, 128.78, 141.39, 155.65.

**4.1.33. Alkyl carbamate 4 (Table 6, entry 1).** Yield 87%; IR (thin film) 3330, 3085, 3062, 3027, 2949, 2859, 1699, 1524, 1496, 1453, 1256, 1138 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.96 (m, 2H), 2.70 (t, *J*=7.5 Hz, 2H), 4.14 (t, *J*=6.5 Hz, 2H), 4.38 (d, *J*=5.8 Hz, 2H), 5.04 (bs, N*H*), 7.18–7.39 (m, 10H). $^{13}$C NMR ($CDCl_3$) $\delta$ 30.63, 32.11, 45.01, 64.38, 125.90, 127.43, 128.36, 128.62, 138.54, 141.33, 156.62. Anal. calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.27; H, 7.42; N, 5.05.

**4.1.34. Alkyl carbamate 4 (Table 6, entry 2).** Yield 93%; IR (thin film) 3324, 3061, 3027, 2972, 1698, 1532, 1453, 1328, 1245, 1061, 748, 699 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.50 (d, *J*=6.7 Hz, 3H), 1.93 (m, 2H), 2.68 (m, 2H), 4.06–4.11 (m, 2H), 4.82 (m, 1H), 4.98 (m, 1H), 7.17–7.38 (m, 10H). $^{13}$C NMR ($CDCl_3$) $\delta$ 22.41, 30.61, 32.10, 50.51, 64.23, 125.87, 127.24, 128.34, 128.59, 141.35, 143.58, 155.77. Anal. calcd for $C_{18}H_{11}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 75.56; H, 7.53; N, 4.92.

**4.1.35. Alkyl carbamate 4 (Table 6, entry 3).** Yield 90%; pale yellow oil; IR (thin film) 3335, 3061, 3026, 2943, 2862, 1716, 1539, 1454, 1250, 1139, 1030, 910, 844, 743, 699 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.96 (m, 2H), 2.70 (t, *J*=7.5 Hz, 2H), 4.14 (t, *J*=6.5 Hz, 2H), 4.38 (d, *J*=5.8 Hz, 2H), 5.04 (bs, N*H*), 7.18–7.39 (m, 10H). $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 30.63, 32.11, 36.13, 42.08, 64.17, 125.90, 127.43, 128.36, 128.62, 138.54, 141.33, 156.62. Anal. calcd for $C_{18}H_{11}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 75.53; H, 7.55; N, 4.89.

**4.1.36. Alkyl carbamate 4 (Table 6, entry 4).** Yield 85%; yellow oil; IR (thin film) 3323, 3062, 3029, 2959, 2941, 2866, 2836, 1680, 1611, 1537, 1512, 1468, 1298, 1246, 1032 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.93–1.95 (m, 2H), 2.66 (t, *J*=7.4 Hz, 2H), 2.77 (t, *J*=6.7 Hz, 2H), 3.42 (m, 2H), 3.79 (s, 3H), 4.1 (m, 2H), 4.69 (bs, N*H*), 6.83–7.38 (m, 9H). $^{13}$C NMR ($CDCl_3$) $\delta$ 30.66, 32.14, 35.20, 42.29, 55.24, 64.17, 114.02, 125.92, 128.39, 129.71, 130.79, 141.40, 156.58, 158.25.

**4.1.37. Alkyl carbamate 4 (Table 6, entry 5).** Yield 91%; colorless oil; IR (thin film) 3336, 3062, 3026, 2954, 2929, 2857, 1697, 1535, 1454, 1249, 1142, 1030 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 0.72 (t, *J*=6.87 Hz, 3H), 1.12–1.30 (m, 8H), 1.74 (s, 2H), 2.39 (m, 2H), 2.86 (m, 2H), 3.90 (m, 2H), 5.11 (bs, N*H*), 6.99–7.08 (m, 5H). $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 13.62, 22.18, 26.04, 29.54, 30.36, 31.11, 31.71, 40.05, 63.46, 125.47, 127.94, 140.96, 156.42. Anal. calcd for $C_{16}H_{25}NO_2$: C, 72.96; H, 9.57; N, 5.32. Found: C, 72.89; H, 9.57; N, 5.33.

**4.1.38. Alkyl carbamate 4 (Table 6, entry 6).** Yield 82%; clear yellow oil. IR (thin film) 3326, 3061, 3026, 2920, 2855, 1695, 1529, 1497, 1452, 1312, 1246, 1051 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.26–1.67 (m, 14H), 1.71–1.78 (m, 2H), 2.47 (t, *J*=7.5 Hz, 2H), 2.28 (m, 1H), 3.89 (t, *J*=6.5 Hz, 2H), 7.00–7.13 (m, 6H). $^{13}$C NMR ($CDCl_3$) $\delta$ 23.42, 25.26, 27.09, 30.62, 32.08, 32.20, 50.80, 63.80, 125.77, 128.25, 141.33, 155.60. Anal. calcd for $C_{18}H_{27}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 74.13; H, 9.46; N, 4.90.

**4.1.39. Alkyl carbamate 4 (Table 6, entry 7).** Yield 88%; yellow oil; IR (thin film) 3330, 2949, 2870, 1719, 1538, 1454, 1248, 1149, 1082, 1024, 747, 700 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.34–1.39 (m, 2H), 1.68–1.80 (m, 4H), 2.49 (t, *J*=7.3 Hz, 2H), 2.90–2.98 (m, 1H), 3.22–3.27 (m, 1H), 3.55–3.91 (m, 5H), 5.04 (bs, N*H*), 6.98–7.11 (m, 5H). $^{13}$C NMR ($CDCl_3$) $\delta$ 25.82, 28.40, 30.66, 32.12, 44.75, 64.20, 68.07, 76.79, 125.0, 128.37, 141.39, 156.86. Anal. calcd for $C_{15}H_{21}NO_3$: C, 68.42; H, 8.04; N, 5.32. Found: C, 68.78; H, 8.57; N, 5.32.

**4.1.40. Alkyl carbamate 4 (Table 6, entry 8).** Yield 90%; IR (thin film) 3328, 3105, 3083, 3061, 3025, 2948, 2860, 1700, 1517, 1453, 1327, 1246, 1130 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 2.01 (m, 2H), 2.73 (t, *J*=7.5 Hz, 2H), 4.17 (t, *J*=6.5 Hz, 2H), 4.55 (s, 2H), 5.52 (bs, N*H*), 6.97–7.36 (m, 8H). $^{13}$C NMR ($CDCl_3$) $\delta$ 30.35, 31.80, 39.48, 64.12, 124.69, 125.36, 125.67, 126.23, 128.12, 141.04, 141.39, 156.19.

**4.1.41. Alkyl carbamate 4 (Table 6, entry 9).** Yield 82%; IR (thin film) 3330, 3147, 3318, 3084, 3061, 3026, 2951, 2861, 1705, 1602, 1524, 1453, 1327, 1247 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.96 (m, 2H), 2.68 (t, *J*=7.5 Hz, 2H), 4.12 (t, *J*=6.5 Hz, 2H), 4.35 (d, 2H, *J*=5.3 Hz) 5.06 (bs, N*H*), 6.24 (s, 1H), 6.32–6.33 (s, 1H), 7.17–7.36 (m, 6H). $^{13}$C NMR ($CDCl_3$) $\delta$ 30.36, 31.83, 37.72, 64.19, 106.88, 110.14, 125.69, 128.14, 141.08, 141.83, 151.58, 156.31.

**4.1.42. Alkyl carbamate 4 (Table 6, entry 10).** Yield 89%; IR (thin film) 3413, 3330, 3058, 3025, 2942, 2855, 1697, 1520, 1455, 1338, 1257, 1082 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 2.40 (m, 2H), 2.84 (m, 2H), 3.14 (m, 2H), 3.60 (m, 2H), 4.24 (m, 2H), 4.94 (brs, N*H*), 7.01–8.60 (m, 9H). $^{13}$C NMR ($CDCl_3$) $\delta$ 25.85, 30.72, 32.20, 41.39, 64.31, 111.42, 112.67, 118.75, 119.41, 122.12, 122.30, 126.03, 127.37, 128.50, 136.51, 141.47, 156.93. Anal. calcd for $C_{20}H_{22}N_2O_2$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.44; H, 6.66; N, 8.23.

**4.1.43. Aromatic carbamate 4 (Table 7, entry 1).** Yield 98%; oil; IR (thin film) 3317, 3061, 3035, 2988, 2945, 2892, 1693, 1597, 1532, 1444, 1313, 1227 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 5.04 (s, 2H), 6.75–7.34 (m, 10H). $^{13}$C NMR ($CDCl_3$) $\delta$ 66.88, 118.63, 123.39, 126.89, 127.51, 128.51, 128.94, 135.95, 137.71, 153.37.

**4.1.44. Aromatic carbamate 4 (Table 7, entry 2).** Yield 94%; oil; IR (thin film) 3320, 3137, 3060, 3026, 2954, 2858, 1700, 1600, 1539, 1443, 1213, 1220, 1063 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$) $\delta$ 2.12 (m, 2H), 2.80 (t, $J$=7.5 Hz, 2H), 4.28 (t, $J$=6.5 Hz, 2H), 7.17–7.61 (m, 11H). $^{13}$C NMR (CDCl$_3$) $\delta$ 29.67, 30.44, 64.53, 118.6, 123.29, 125.93, 128.33, 128.94, 137.86, 141.14, 153.6. Anal. calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.76; H, 7.32; N, 4.81.

**4.1.45. Aromatic carbamate 4 (Table 7, entry 3).** Yield 83%; IR (thin film) 3318, 3063, 3032, 2948, 2921, 1700, 1597, 1537, 1408, 1315, 1224, 1062 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$) $\delta$ 2.71 (s, 3H), 5.04 (s, 2H), 6.87–7.24 (m, 10H). $^{13}$C NMR (CDCl$_3$) $\delta$ 20.82, 66.74, 118.77, 126.79, 127.16, 128.44, 130.40, 132.87, 135.14, 136.06, 153.49. Anal. calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.90; H, 7.32; N, 4.88.

**4.1.46. Aromatic carbamate 4 (Table 7, entry 4).** Yield 96%; oil; IR (thin film) 3318, 3061, 3026, 2950, 2922, 2860, 1704, 1599, 1530, 1453, 1408, 1315, 1223, 1065 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$) $\delta$ 2.00 (m, 2H), 2.31 (s, 3H), 2.69 (t, $J$=7.5 Hz, 2H), 4.18 (t, $J$=6.5 Hz, 2H), 7.05–7.33 (m, 11H). $^{13}$C NMR (CDCl$_3$) $\delta$ 20.54, 30.38, 31.94, 64.6, 125.80, 126.97, 128.94, 129.28, 129.42, 132.60, 135.29, 141.06, 155.65. Anal. calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.66; H, 7.32; N, 5.11.

**4.1.47. Aromatic carbamate 4 (Table 7, entry 5).** Yield 78%; oil; IR (thin film) 3085, 3060, 3024, 2966, 2925, 2866, 1732, 1598, 1505, 1452, 1370, 1268 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$) $\delta$ 1.17–1.22 (t, $J$=7.0 Hz, 3H), 3.75–3.80 (q, $J$=7.2 Hz, 2H), 5.19 (s, 2H), 7.24–7.41 (m, 10H). $^{13}$C NMR (CDCl$_3$) $\delta$ 13.58, 45.27, 66.85, 126.52, 127.38, 127.65, 128.25, 128.44, 128.82, 136.65, 141.53, 155.06.

**4.1.48. Aromatic carbamate 4 (Table 7, entry 6).** Yield 75%; oil; IR (thin film) 3085, 3060, 3024, 2966, 2925, 2866, 2851, 1732, 1598, 1505, 1452, 1370, 1268 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$) $\delta$ 0.98 (t, 3H, $J$=7.0 Hz), 1.71–1.83 (m, 2H), 2.52 (t, $J$=6.5 Hz, 2H), 3.10–3.23 (m, 4H), 6.95–7.16 (m, 10H). $^{13}$C NMR (CDCl$_3$) $\delta$ 12.27, 28.94, 33.92, 44.91, 49.84, 111.88, 115.40, 125.84, 126.12, 128.33, 128.46, 129.20, 141.76, 147.84.

**4.1.49. Aromatic carbamate 4 (Table 7, entry 7).** Yield 83%; pale yellow oil; IR (thin film) 3181, 3118, 3037, 2953, 2925, 2895, 2852, 1733, 1592, 1546, 1438, 1307, 1221, 1064 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$) $\delta$ 5.07 (s, 2H), 6.61–7.99 (m, 9H), 10.19 (s, N*H*). $^{13}$C NMR (CDCl$_3$) $\delta$ 67.04, 112.47, 118.32, 128.39, 128.56, 129.35, 135.88, 138.43, 147.62, 152.36, 153.47.

**4.1.50. Aromatic carbamate 4 (Table 7, entry 8).** Yield 80%; yellow oil; IR (thin film) 3280, 3183, 3083, 3059, 3025, 2931, 2857, 1729, 1648, 1586, 1513, 1495, 1439, 1374, 1331, 1306 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$) $\delta$ 1.97–1.99 (m, 2H), 2.6–2.75 (m, 2H), 4.20–4.30 (m, 2H) 6.99–7.30 (m, 6H), 8.1–8.70 (m, 4H). $^{13}$C NMR (CDCl$_3$) $\delta$ 30.87, 33.08, 64.55, 106.79, 112.43, 125.84, 128.30, 128.32, 141.37, 146.77, 158.25. Anal. calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.83; H, 6.82; N, 10.12.

**4.1.51. Aromatic carbamate 4 (Table 7, entry 9).** Yield 88%; pale yellow oil; IR (thin film) 3244, 3186, 3111, 3029, 2960, 2877, 2821, 2778, 1720, 1617, 1590, 1559, 1429, 1291, 1227, 1039 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$) $\delta$ 5.04 (s, 2H), 6.99–8.29 (m, 10H). $^{13}$C NMR (CDCl$_3$) $\delta$ 67.38, 123.73, 125.78, 128.39, 128.53, 128.67, 140.23, 144.51, 153.33.

**4.1.52. Aromatic carbamate 4 (Table 7, entry 10).** Yield 83%; yellow oil; IR (thin film) 3227, 3184, 3121, 3026, 2956, 2925, 2855, 1727, 1608, 1552, 1484, 1300, 1230, 1070 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$) $\delta$ 1.85 (m, 2H), 2.54 (t, $J$=7.5 Hz, 2H), 4.01 (t, $J$=6.5 Hz, 2H), 6.93–7.86 (m, 10H). $^{13}$C NMR (CDCl$_3$) $\delta$ 30.39, 32.06, 64.92, 126.0, 128.32, 128.41, 140.06, 141.02, 143.91, 153.76. Anal. calcd $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.83; H, 6.82; N, 10.12.

**4.1.53. Aromatic carbamate 4 (Table 7, entry 11).** Yield 47%; oil; IR (thin film) 3345, 3084, 3061, 3028, 2917, 2866, 1734, 1682, 1596, 1494, 1450, 1356, 1264 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$) $\delta$ 2.52 (s, 3H), 4.73 (s, 2H), 6.94–7.43 (m, 10H). $^{13}$C NMR (CDCl$_3$) $\delta$ 26.53, 54.19, 111.42, 117.01, 126.54, 127.00, 127.44, 128.19, 128.29, 128.65, 129.29, 138.42, 149.07, 198.20.

**4.1.54. Aromatic carbamate 4 (Table 7, entry 12).** Yield 50%; a pale yellow oil; IR (thin film) 3336, 3085, 3026, 2955, 2856, 1715, 1599, 1549, 1509, 1413, 1332, 1216, 1112 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$) $\delta$ 1.82 (m, 2H), 2.56 (t, $J$=7.1 Hz, 2H), 4.05 (t, $J$=6.5 Hz, 2H), 7.00–8.02 (m, 10H). $^{13}$C NMR (CDCl$_3$) $\delta$ 30.24, 32.01, 65.29, 117.64, 125.14, 126.05, 128.30, 129.42, 140.89, 142.81, 144.01, 152.84. Anal. calcd for $C_{16}H_{16}NO_2$: C, 75.57; H, 6.34; N, 5.51. Found: C, 75.55; H, 6.30; N, 5.45.

**4.1.55. Aromatic carbamate 4 (Table 7, entry 13).** Yield 73%; yellow oil; IR (thin film) 3325, 3086, 3062, 3026, 2955, 2925, 2856, 1710, 1532, 1350, 1283, 1222 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$) $\delta$ 1.89 (m, 2H), 2.54 (t, $J$=7.5 Hz, 2H), 4.05 (t, $J$=6.5 Hz, 2H), 6.76–8.12 (m, 10H). $^{13}$C NMR (CDCl$_3$) $\delta$ 30.35, 32.09, 65.20, 113.26, 117.95, 124.08, 126.06, 128.46, 129.82, 139.19, 140.99, 148.66, 153.25. Anal. calcd for $C_{16}H_{16}NO_2$: C, 75.57; H, 6.34; N, 5.51. Found: C, 75.50; H, 6.32; N, 5.47.

**4.1.56. Carbamate 49.** Yield 87%; colorless oil; IR (thin film) 3338, 3063, 3031, 2953, 1718, 1519, 1345, 1256, 1212, 1055, 742, 697 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$) $\delta$ 3.12 (m, 2H), 4.84 (m, 1H), 5.03–5.18 (m, 4H), 5.21 (bs, N*H*), 7.02–7.34 (m, 15H). $^{13}$C NMR (CDCl$_3$) $\delta$ 38.15, 54.80, 68.96, 67.24, 127.08, 128.08, 128.17, 128.52, 128.56, 129.31, 135.04, 135.51, 136.21, 156.61, 171.36.

**4.1.57. Carbamate 51.** Yield 92%; oil; IR (thin film) 3348, 3063, 2963, 2676, 1714, 1519, 1454, 1372, 1312, 1213, 1162, 1094, 1026, 1016, 739 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$) $\delta$ 0.88 (m, 3H), 0.91 (m, 3H), 2.10 (m, 1H), 3.81 (s, 3H), 4.30 (m, 1H), 5.10 (s, 2H), 5.25 (m, 1H), 7.15–7.35 (m, 5H). $^{13}$C NMR (CDCl$_3$) $\delta$ 17.51, 18.91, 31.27, 52.12, 59.00, 67.01, 128.16, 128.52, 136.23, 156.20, 172.84.

**4.1.58. Carbamate dimer 54 (prior to deprotection).** Yield 40%; oil; IR (thin film) 3436, 3347, 3061, 3027, 2963, 2932, 2876, 2802, 1723, 1508, 1453, 1380, 1335, 1258, 1207, 1160 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 0.6–1.08 (m, 12H), 1.11–1.17 (m, 2H), 1.3–1.4 (m, 1H), 1.65–1.67 (m, 2H), 1.78–1.83 (m, 2H), 2.43–2.44 (m, 1H), 3.45 (d, $J_{AB}$=11.0 Hz, 2H), 3.67 (s, 3H), 3.77 (d, $J_{AB}$=13.6 Hz, 2H), 4.23–4.33 (m, 3H), 5.12 (brs, 1H, N*H*), 7.11–7.27 (m, 10H). $^{13}$C NMR (CDCl$_3$) $\delta$ 10.84, 11.55, 15.48, 15.91, 25.00, 26.12, 33.96, 38.01, 52.10, 54.52, 58.3, 60.06, 62.57, 126.74, 128.07, 129.00, 140.19, 156.19, 172.63.

**4.1.59. Carbamate trimer 56.** Yield 60%; oil; $^1$H NMR (CDCl$_3$) $\delta$ 0.59–0.98 (m, 18H), 1.0–1.9 (m, 6H), 2.8–3.1 (m, 3H), 3.62–3.69 (d, $J_{AB}$=11.0 Hz, 2H), 3.72–3.75 (d, $J_{AB}$=11.0 Hz, 2H), 3.72 (s, 3H), 3.90–4.50 (m, 7H), 4.81 (bs, N*H*), 5.25 (bs, N*H*), 7.1–7.7 (m, 10H). $^{13}$C NMR (CDCl$_3$) $\delta$ 11.42, 11.51, 15.38, 22.11, 22.91, 23.21, 24.49, 24.6, 24.87, 34.1, 37.7, 44.20, 52.09, 53.78, 53.96, 58.28, 66.12, 66.28, 72.68, 126.76, 127.89, 128.06, 128.79, 128.93, 140.32, 156.11, 174.26.

**4.1.60. Preparation of silyl carbamate 57.** To a solution of phenethylamine **22** (0.25 g, 1 mmol) in anhydrous DMF (20 mL), cesium carbonate (0.98 g, 1.5 mmol, 1.5 equiv.) was added to the solution with vigorous stirring. Carbon dioxide was bubbled into the solution continuously for 1 h before triisopropylsilyl chloride (0.23 g, 1.2 mmol, 1 equiv.) was added. The reaction was allowed to proceed at room temperature with constant carbon dioxide bubbling and stirring for 2 h at which point the amine was consumed. The reaction mixture was quenched with water and extracted with dichloromethane (3×30 mL), bicarbonate (30 mL), brine (30 mL) and dried over anhydrous sodium sulfate. Evaporation of the solvent and subjection of the crude residue to column chromatography (5:1, hexanes–EtOAc) afforded silyl carbamate **57** (0.38 g, 72%) as a pale yellow oil. IR (thin film) 3360, 3300, 3085, 3063, 3027, 2942, 2891, 2865, 1679, 1497, 1463, 1259 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.01 (m, 21H), 2.71 (t, 2H, *J*=7.1 Hz), 3.30 (q, 2H, *J*=6.9 Hz), 7.08–7.22 (m, 6H). $^{13}$C NMR (CDCl$_3$) $\delta$ 12.05, 17.76, 36.09, 42.32, 126.33, 128.49, 128.79, 157.06.

**4.1.61. Representative general procedure for solid phase synthesis of carbonate 58 using Merrifield's resin (Table 10, entry 5).** Benzyl-(*S*)-2-hydroxy-3-phenylpropionate (1.54 g, 6 mmol, 3 equiv.) **17** was dissolved in anhydrous DMF (20 mL) to make a clear solution. To the solution, were consecutively added cesium carbonate (1.95 g, 6 mmol, 3 equiv.) and tetrabutylammonium iodide (2.22 g, 6 mmol, 3 equiv.). The suspension was stirred at room temperature while passing carbon dioxide gas through for 1 h before Merrifield's peptide resin (1 g, 2 mmol) was added to the solution. Carbon dioxide gas was continuously bubbled through the solution and the reaction was allowed to proceed overnight at 60°C. The mixture was then cooled to room temperature, and diluted with water. The resin was washed successively with MeOH/H$_2$O, H$_2$O, 0.2N HCl, H$_2$O, THF, CH$_2$Cl$_2$, and MeOH. After drying in vacuo for 24 h, 1.33 g of resin bound carbonate of **17** was obtained (63% yield). The loading and yield for the carbonate resin of **17** was determined by gravimetric analysis as follows (for Supporting Information see Ref. 13). IR (KBr pellet) 3071, 3035, 2921, 2846, 1943, 1874, 1611, 1495, 1462, 1394, 1253, 1172, 1036, 765, 700 cm$^{-1}$. The resulting resin bound benzyl 3-phenylpropionate carbonate of **59** was converted back to the starting alcohol **17** (1.5 g; 70%) by hydrolytic cleavage using TFA–CH$_2$Cl$_2$ (75:25 v/v) after stirring at room temperature for 12 h.[34] The product was spectroscopically ($^1$H NMR) compared with the authentic sample and the optical rotation was taken and compared with the starting material, as well as with the reported value. The observed value was −53° (*c* 2, CH$_2$Cl$_2$) whereas the reported value was −55° (*c* 1.8, CH$_2$Cl$_2$), respectively.

**4.1.62. Merrifield resin-bound decyl carbonate (62).** Yield 70%; IR (KBr pellet) 3051, 3017, 2918, 2841, 1942, 1862, 1789, 1740, 1601, 1491, 1361, 763, 700, 544 cm$^{-1}$.

**4.1.63. Merrifield resin bound benzyl carbonate (64).** Yield 97%; IR (KBr pellet) 3061, 3020, 2918, 2851, 1945, 1870, 1816, 1744, 1605, 1499, 1448, 1361, 763, 698, 546 cm$^{-1}$.

**4.1.64. Merrifield resin-bound *p*-nitrobenzyl carbonate (66).** Yield 81%; IR (KBr pellet): 3063, 3021, 2918, 2871, 1954, 1883, 1826, 1736, 1601, 1503, 1463, 1398, 1361, 1235, 961, 738 cm$^{-1}$.

**4.1.65. Cleavage of 66.** A 100 mL round bottomed flask, equipped with a magnetic stir bar and a reflux condenser, was charged with 1 g (1.5 mmol) of carbonate resin and 100 mL of trifluoroacetic acid in methylene chloride (3:1 v/v). The mixture was stirred overnight at room temperature, and the reaction mixture was filtered through a coarse filtration fritted glass to remove the resin and the latter was washed four times with methylene chloride. The combined filtrates and washings were dried over magnesium sulfate and concentrated under reduced pressure. The crude product was further concentrated in vacuo for 12 h to provide *p*-nitrobenzyl alcohol **65** in 80% yield. $^1$H NMR (CDCl$_3$) $\delta$ 1.89 (s, 1H), 4.76 (s, 3H), 7.46 (d, *J*=8.2 Hz, 2H), 8.14 (d, 2H, *J*=8.2 Hz).

**4.1.66. Merrifield resin-bound cyclohexyl carbonate 59 (Table 10, entry 1).** Yield 98%; IR (KBr pellet): 3068, 3025, 2931, 2854, 1950, 1735, 1606, 1498, 1445, 1390, 1252, 1024, 934, 761, 696, 551 cm$^{-1}$.

**4.1.67. Merrifield resin-bound 3,3-dimethyl-2-butyl carbonate 59 (Table 10, entry 2).** Yield 98%; IR (KBr pellet): 3070, 3031, 2928, 1973, 1900, 1741, 1604, 1461, 1383, 1261, 1081, 931, 761, 700, 549 cm$^{-1}$.

**4.1.68. Merrifield resin-bound menthol carbonate 59 (Table 10, entry 3).** Yield 83%; IR (KBr pellet): 3031, 2928, 2871, 1950, 18731, 1739, 1601, 1503, 1450, 1383, 1357, 956, 763, 701, 536 cm$^{-1}$.

**4.1.69. Merrifield resin-bound methyl mandelate carbonate 59 (Table 10, entry 4).** Yield 76%; IR (KBr pellet): 3020, 2918, 2843, 1964, 1740, 1605, 1498, 1445, 1375, 1351, 1031, 771, 701, 551 cm$^{-1}$.

**4.1.70. Merrifield resin-bound pantolactone carbonate 59 (Table 10 entry 6).** Yield 58%; IR (KBr pellet): 3068, 3031, 2963, 2932, 1983, 1900, 1749, 1610, 1501, 1461, 1387, 1251, 1024, 824, 750, 698, 541 cm$^{-1}$.

**4.1.71. General procedure for solid phase preparation of carbonate 59 from Wang resin 71 (Table 11, entry 1).** Wang resin **71** (1.0 g, 1.5 mmol) was added to anhydrous DMF (20 mL) to make a suspension. To the solution, were consecutively added cesium carbonate (1.47 g, 4.5 mmol, 3 equiv.) and tetrabutylammonium iodide (1.66 g, 4.5 mmol, 3 equiv.). The suspension was stirred at room temperature while passing carbon dioxide gas through for 1 h before 1-bromooctane (0.78 mL, 4.5 mmol, 3 equiv.) was added to the solution. Carbon dioxide gas continuously bubbled through the solution and the reaction was allowed to proceed overnight at 60°C. The mixture was then cooled to room temperature, and diluted with water. The resin was washed successively with MeOH/$H_2O$, $H_2O$, 0.2N HCl, $H_2O$, THF, $CH_2Cl_2$, and MeOH. After drying under vacuum, 1.30 g of resin was obtained (97% yield). IR (KBr pellet): 3061, 3034, 2931, 2854, 1953, 1894, 1741, 1606, 1507, 1468, 1249, 1176, 1015, 951, 843, 774, 700, 543 $cm^{-1}$.

**4.1.72. Wang resin-bound decyl carbonate 59 (Table 11, entry 2).** Yield 99%; IR (KBr pellet): 3071, 3042, 2934, 2853, 1971, 1894, 1743, 1603, 1508, 1462, 1249, 1171, 1023, 833, 764, 701, 547 $cm^{-1}$.

**4.1.73. Wang resin-bound benzyl carbonate 59 (Table 11, entry 3).** Yield 91%; IR (KBr pellet): 3080, 3032, 2931, 1951, 1881, 1745, 1614, 1506, 1543, 1400, 1243, 1031, 841, 763, 552 $cm^{-1}$.

**4.1.74. Wang resin-bound *p*-nitrobenzyl carbonate 59 (Table 11, entry 4).** Yield 83%; IR (KBr pellet): 3070, 3031, 2924, 1954, 1877, 1746, 1605, 1461, 1246, 1178, 1034, 837, 771, 701, 541 $cm^{-1}$.

**4.1.75. Cleavage of 4-nitrobenzyl Wang resin 59.** A 50 mL round bottomed flask, equipped with a magnetic stirring bar and a reflux condenser, was charged with 20 mL of methanol and 1 g (1 mmol) of *p*-nitrobenzyl carbonate resin **59** and 10 equiv. of triethylamine. The mixture was heated at reflux for overnight and then cooled to room temperature. The reaction mixture was filtered through a coarse filtration fritted glass to remove the resin, and the latter was washed four times with 10 mL of methanol. The combined filtrates and washings were dried over magnesium sulfate and concentrated under reduce pressure. The crude product was purified using flash chromatography to provide 141 mg (92%) of *p*-nitrobenzyl alcohol **65**. $^1H$ NMR ($CDCl_3$) $\delta$ 1.89 (s, 1H), 4.76 (s, 3H), 7.46 (d, 2H, $J$=8.2 Hz), 8.14 (d, $J$=8.2 Hz, 2H).

**4.1.76. Wang resin bound *p*-methoxybenzyl carbonate 59 (Table 11, entry 5).** Yield 83%; IR (KBr pellet): 3065, 3031, 2931, 1951, 1882, 1740, 1605, 1461, 1398, 1247, 1008, 821, 761, 700, 551 $cm^{-1}$.

**4.1.77. Typical solid phase procedure for the preparation of carbamate resin from amine 86.** 1,2,3,4-Tetrahydroquinoline (0.67 g, 5 mmol, 2.5 equiv.) was dissolved in DMF (40 mL). Cesium carbonate (2.44 g, 7.5 mmol, 3.75 equiv.) and tetrabutylammonium iodide (2.77 g, 7.5 mmol, 3.75 equiv.) were added to the solution under vigorous stirring. The temperature of reaction was then raised to 60°C after which carbon dioxide was allowed to pass into the stirred suspension at the same temperature for 10 h. Merrifield's resin (1 g, 2 mmol, 1 equiv.) was added and the reaction was continually stirred at 60°C for 12 h with constant carbon dioxide bubbling. The reaction mass was then cooled to room temperature and filtered through a coarse fritted filter disc. The resin was subsequently washed with 20 mL aliquots of water, methanol–water (1:1 v/v), water, tetrahydrofuran, dichloromethane, and methanol in the given order and then dried in vacuo for 24 h to yield the desired carbamate bound resin of **86** (1.27 g, 95%) as a solid. IR (KBr pellet) 3440, 3075, 3045, 2920, 2850, 1900, 1875, 1740, 1695, 1590, 1560, 1505, 1450, 1395, 1320, 1250, 1220, 1170, 1115, 1010, 950, 905, 830, 820, 740, 695, 530 $cm^{-1}$.

**4.1.78. Cleavage of carbamate resin of 86.** Carbamate resin of **86** (1.21 g, 1.83 mmol) was placed in a flame dried round-bottom flask containing anhydrous tetrahydrofuran (20 mL) under a nitrogen atmosphere. Lithium aluminum hydride (0.38 g, 10 mmol) was added in portions to the resulting suspension over a period of 20 min. The reaction was then refluxed for 8 h. The reaction was subsequently cooled to 0°C and quenched with dropwise addition of water (0.4 mL), followed by 15% sodium hydroxide solution (0.4 mL) and finally water (1.1 mL). The reaction mixture was then filtered through a coarse filtration frit to remove insoluble aluminum salts, and the residual salts were washed with diethyl ether (4×8 mL). The combined filtrate and washings were dried over sodium sulfate and concentrated in vacuo. The crude product is then purified by flash chromatography (1:1, hexanes–ethyl acetate) to yield the desired N-methylated product (0.154 g, 54%). $^1H$ NMR ($CDCl_3$) $\delta$ 1.99 (m, 2H), 2.78 (t, $J$=6.5 Hz, 2H), 2.88 (s, 3H), 3.22 (t, $J$=5.8 Hz, 2H), 6.58–7.26 (m, 4H).

**4.1.79. Benzyl carbamate resin 60 from 20.** Yield 55%; IR (KBr pellet) 3400, 3350, 3080, 3060, 3020, 3040, 2920, 2840, 1950, 1870, 1780, 1722, 1590, 1520, 1505, 1495, 1465, 1210, 1120, 1020, 750, 695 $cm^{-1}$.

**4.1.80. Phenethyl carbamate resin 60 from 22.** Yield 51%; IR (KBr pellet) 3400, 3080, 3060, 3040, 2920, 2850, 1940, 1729, 1710, 1595, 1525, 1485, 1450, 1210, 1130, 1000, 840, 695 $cm^{-1}$.

**4.1.81. Piperidine carbamate resin 60 from 25.** Yield 55%; IR (KBr pellet) 3400, 3090, 3060, 3030, 2915, 2870, 2785, 2720, 1950, 1850, 1765, 1698, 1585, 1525, 1480, 1440, 1375, 1345, 1300, 1250, 1225, 1175, 1090, 1030, 1000, 995, 800, 735, 695, 530 $cm^{-1}$.

**4.1.82. Furfuryl carbamate resin 60 from 28.** Yield 90%; IR (KBr pellet) 3475, 3360, 3080, 3060, 3030, 2915, 2865, 1701, 1600, 1530, 1450, 1345, 1225, 1120, 1010, 998, 850, 730, 695 $cm^{-1}$.

**4.1.83. *p*-Methoxyphenethyl carbamate resin 60 from 32.** Yield 68%; IR (KBr pellet) 3080, 3060, 3020, 2920, 2860, 1950, 1875, 1825, 1722, 1595, 1510, 1495, 1440, 1210, 1150, 1020, 815, 740, 695 $cm^{-1}$.

**4.1.84. Cyclooctyl carbamate resin 60 from 34.** Yield

85%; IR (KBr pellet) 3450, 3370, 3080, 3060, 3035, 2915, 2820, 1722, 1595, 1500, 1480, 1440, 1205, 1030, 820, 770, 695 530 cm$^{-1}$.

**4.1.85. Tetrahydrofurfuryl carbamate resin 60 from 35.** Yield 80%; IR (KBr pellet) 3475, 3360, 3080, 3065, 3025, 2915, 2865, 1722, 1600, 1510, 1490, 1470, 1375, 1225, 1070, 1020, 815, 775, 695, 530 cm$^{-1}$.

**4.1.86. 2-Thiophenemethyl carbamate resin 60 from 36.** Yield 71%; IR (KBr pellet) 3430, 3325, 3080, 3040, 3020, 2930, 2850, 1705, 1600, 1510, 1465, 1360, 1210, 1150, 1110, 1020, 950, 830, 750, 690, 530 cm$^{-1}$.

**4.1.87. 1-Benzylpiperidine carbamate resin 60 from 37.** Yield 74%; IR (KBr pellet) 3450, 3080, 3060, 3025, 2920, 2805, 2760, 1920, 1850, 1790, 1701, 1595, 1490, 1450, 1350, 1285, 1210, 1130, 1010, 910, 695, 720, 695, 530 cm$^{-1}$.

**4.1.88. Tryptamine carbamate resin 60 from 38.** Yield 60%; IR (KBr pellet) 3450, 3385, 3080, 3065, 3015, 2920, 2835, 1708, 1580, 1495, 1475, 1420, 1380, 1360, 1200, 1105, 1080, 995, 801, 720, 695, 530 cm$^{-1}$.

**4.1.89. Allyl carbamate resin 60 from 77.** Yield 85%; IR (KBr pellet) 3420, 3320, 3080, 3060, 3020, 2935, 2850, 1722, 1712, 1650, 1595, 1525, 1500, 1450, 1215, 750, 695 cm$^{-1}$.

**4.1.90. *n*-Octyl carbamate resin 60 from 78.** Yield 44%; IR (KBr pellet) 3400, 3320, 2980, 2950, 2930, 2915, 2825, 1729, 1710, 1595, 1500, 1480, 1450, 1400, 1230, 1040, 1020, 740, 695 cm$^{-1}$.

**4.1.91. 2-Methoxyethyl carbamate resin 60 from 79.** Yield 89%; IR (KBr pellet) 3420, 3320, 3080, 3060, 3040, 2925, 2840, 1722, 1590, 1525, 1495, 1450, 1220, 1110, 1020, 830, 740, 695 cm$^{-1}$.

**4.1.92. Cyclopropyl carbamate resin 60 from 80.** Yield 60%; IR (KBr pellet) 3380, 3080, 3060, 3040, 3020, 2925, 2830, 1920, 1722, 1600, 1525, 1495, 1450, 1365, 1345, 1220, 1210, 1195, 1020, 810, 750, 695 cm$^{-1}$.

**4.1.93. Methylbenzyl carbamate resin 60 from 81.** Yield 73%; IR (KBr pellet) 3400, 3320, 3080, 3060, 3020, 2980, 2825, 1900, 1850, 1735, 1722, 1595, 1480, 1440, 1330, 1210, 1040, 1015, 720, 695 cm$^{-1}$.

**4.1.94. Cleavage of solid support of methylbenzyl carbamate 60.** Under a nitrogen atmosphere, resin bound methylbenzylamine carbamate **60** (1.06 g, 1.31 mmol) was placed in a flame dried round-bottom flask containing anhydrous tetrahydrofuran (20 mL). Lithium aluminum hydride (0.38 g, 10 mmol) was added in portions to the resulting suspension over a period of 20 min. The reaction was then refluxed under a nitrogen atmosphere for 8 h. The reaction was subsequently cooled to 0°C and quenched with dropwise addition of water (0.4 mL), followed by 15% sodium hydroxide solution (0.4 mL) and finally water (1.1 mL). The reaction mixture was then filtered through a coarse filtration frit to remove aluminum salts, and the residual salts were washed with diethyl ether (4×8 mL). The combined filtrate and washings were dried over sodium sulfate and concentrated in vacuo. The crude product was then purified by flash chromatography (1:1, hexanes–ethyl acetate) to yield the desired *N*-methylated product (0.118 g, 66%). $^1$H NMR (CDCl$_3$) $\delta$ 1.35 (d, 2H), 1.45 (s, N*H*), 2.30 (s, 3H), 3.65 (q, 1H), 7.15–7.40 (m, 5H).

**4.1.95. Leucine methyl ester carbamate resin 60 from 82.** Yield 67%; IR (KBr pellet) 3420, 3360, 3080, 3040, 3020, 2935, 2840, 1950, 1722, 1595, 1515, 1495, 1450, 1240, 1190, 1160, 810, 750, 695 cm$^{-1}$.

**4.1.96. Cleavage from solid support of leucine methyl ester carbamate 60.** Under a nitrogen atmosphere, leucine resin bound carbamate **60** (1.06 g, 0.865 mmol) was placed in a flame dried round-bottom flask containing anhydrous tetrahydrofuran (20 mL). Lithium aluminum hydride (0.38 g, 10 mmol) was then added in portions to the resulting suspension over a period of 20 min, and the reaction was refluxed under a nitrogen atmosphere for 8 h. The reaction was subsequently cooled to 0°C and quenched with dropwise addition of water (0.4 mL), followed by 15% sodium hydroxide solution (0.4 mL) and finally water (1.1 mL). The reaction mixture was then filtered through a coarse filtration frit to remove aluminum salts, and the residual salts were washed with diethyl ether (4×8 mL). The combined filtrate and washings were dried over sodium sulfate and concentrated in vacuo. The crude product is then purified by flash chromatography (1:1, hexanes–ethyl acetate) to yield the desired *N*-methylated product (0.103 g, 80%). $^1$H NMR (CDCl$_3$) $\delta$ 0.90 (d, $J$=7.0 Hz, 6H), 1.25 (t, $J$=4.4 Hz, 2H), 1.7 (m, 1H), 2.4 (s, 3H), 3.5 (m, 3H), 3.8 (s, 2H).

**4.1.97. Diethyl carbamate resin 60 from 83.** Yield 77%; IR (KBr pellet) 3030, 3040, 3020, 2990, 2920, 1709, 1595, 1495, 1480, 1450, 1425, 1375, 1350, 1250, 1175, 1080, 980, 800, 740, 695, 595, 530 cm$^{-1}$.

**4.1.98. Diisopropyl carbamate resin 60 from 84.** Yield 50%; IR (KBr pellet) 3400, 3080, 3050, 3020, 2950, 2925, 2850, 1703, 1580, 1490, 1450, 1360, 1290, 1275, 1030, 770, 695, 530 cm$^{-1}$.

**4.1.99. Diphenyl carbamate resin 60 from 85.** Yield 21%; IR (KBr pellet) 3150, 3090, 3040, 2950, 1716, 1595, 1535, 1530, 1515, 1485, 1465, 1327, 1201, 1111, 1040, 857, 753, 696 cm$^{-1}$.

**4.1.100. 4-Benzylpiperidine carbamate resin 60 from 87.** Yield 72%; IR (KBr pellet) 3400, 3080, 3065, 3010, 3025, 2920, 2805, 2795, 2760, 1930, 1850, 1800, 1699, 1590, 1495, 1470, 1350, 1340, 1245, 1215, 1150, 1085, 1078, 1015, 995, 882, 800, 725, 695, 535 cm$^{-1}$.

**4.1.101. Aniline carbamate resin 60 from 39.** Yield 70%; IR (KBr pellet) 3420, 3300, 3080, 3060, 3040, 2925, 1730, 1600, 1510, 1485, 1445, 1210, 1120, 995, 695 cm$^{-1}$.

**4.1.102. *p*-Toluidine carbamate resin 60 from 41.** Yield 81%; IR (KBr pellet) 3420, 3330, 3080, 3060, 3020, 2915, 2850, 1950, 1900, 1722, 1605, 1525, 1445, 1405, 1315, 1200, 1035, 1010, 815, 740, 695 cm$^{-1}$.

**4.1.103. *N*-Ethylaniline carbamate resin 60 from 42.** Yield 86%; IR (KBr pellet) 3090, 3050, 3020, 2915, 1930, 1795, 1722, 1699, 1600, 1490, 1450, 1395, 1300, 1275, 1140, 1120, 1040, 1010, 810, 780, 695 $\mathrm{cm}^{-1}$.

**4.1.104. 2-Aminopyridine carbamate resin 60 from 43.** Yield 66%; IR (KBr pellet) 3400, 3085, 3065, 3025, 2930, 2850, 1920, 1722, 1570, 1520, 1490, 1415, 1385, 1300, 1210, 1180, 1170, 1080, 1010, 720, 695 $\mathrm{cm}^{-1}$.

**4.1.105. 3-Aminopyridine carbamate resin 60 from 44.** Yield 72%; IR (KBr pellet) 3400, 3080, 3060, 3040, 2915, 2860, 1722, 1595, 1575, 1490, 1480, 1410, 1210, 1050, 1020, 740, 695 $\mathrm{cm}^{-1}$.

**4.1.106. 3-Aminoacetophenone carbamate resin 60 from 45.** Yield 62%; IR (KBr pellet) 3370, 3080, 3060, 3035, 2915, 2835, 1920, 1870, 1830, 1710, 1690, 1595, 1530, 1495, 1450, 1385, 1335, 1270, 1240, 1205, 1050, 775, 695 $\mathrm{cm}^{-1}$.

**4.1.107. *p*-Nitroaniline carbamate resin 60 from 46.** Yield 55%; IR (KBr pellet) 3420, 3080, 3060, 3020, 2910, 2840, 1920, 1707, 1600, 1520, 1495, 1450, 1365, 1330, 1270, 1210, 1105, 1020, 960, 900, 850, 695, 530 $\mathrm{cm}^{-1}$.

**4.1.108. *m*-Nitroaniline carbamate resin 60 from 47.** Yield 44%; IR (KBr pellet) 3085, 3065, 3030, 2925, 2850, 1722, 1570, 1520, 1495, 1450, 1385, 1340, 1220, 1180, 1110, 1020, 695 $\mathrm{cm}^{-1}$.

**4.1.109. Cleavage of solid support of 3-aminoacetophenone carbamate 60.** Under a nitrogen atmosphere, resin bound 3-aminoacetophenone carbamate **60** (1.07 g, 1.15 mmol) was placed in a flame dried round-bottom flask containing anhydrous tetrahydrofuran (20 mL). Lithium aluminum hydride (0.38 g, 10 mmol) was added in portions to the resulting suspension over a period of 20 min. The reaction was refluxed under a nitrogen atmosphere for 8 h. The reaction was subsequently cooled to 0°C and quenched with dropwise addition of water (0.4 mL), followed by 15% sodium hydroxide solution (0.4 mL), and finally water (1.1 mL). The reaction mixture was then filtered through a coarse filtration frit to remove aluminum salts, and the residual salts were washed with diethyl ether (4×8 mL). The combined filtrate and washings were dried over sodium sulfate and concentrated in vacuo. The crude product was then purified by flash chromatography (1:1, hexanes–ethyl acetate) to yield the desired *N*-methylated product (0.109 g, 63%). $^1$H NMR (CDCl$_3$) $\delta$ 1.38 (d, $J$=6.4 Hz, 3H), 2.73 (s, 3H), 3.02 (bs, N*H*, O*H*), 4.69 (q, $J$=6.4 Hz, 1H), 6.42–7.10 (m, 4H).

**4.1.110. Cleavage of solid support of 3-aminopyridine carbamate 60.** Under nitrogen atmosphere, resin bound 3-aminopyridine carbamate **60** (1.13 g, 1.4 mmol) was placed in a flame dried round-bottom flask containing anhydrous tetrahydrofuran (20 mL). Lithium aluminum hydride (0.38 g, 10 mmol) was added in portions to the resulting suspension over a period of 20 min. The reaction was then refluxed under a nitrogen atmosphere for 8 h. The reaction was subsequently cooled to 0°C and quenched with dropwise addition of water (0.4 mL), followed by 15% sodium hydroxide solution (0.4 mL) and finally water (1.1 mL). The reaction mixture was filtered through a coarse filtration frit to remove aluminum salts, and the residual salts were washed with diethyl ether (4×8 mL). The combined filtrate and washings were dried over sodium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography (1:1, hexanes–ethyl acetate) to yield the desired *N*-methylated product (0.082 g, 54%). $^1$H NMR (CDCl$_3$) $\delta$ 2.73 (s, 3H), 4.81 (bs, N*H*), 6.72–8.91 (m, 4H).

**4.1.111. 3,4-Dimethylaniline carbamate resin 60 from 88.** Yield 97%; IR (KBr pellet) 3415, 3335, 3050, 2925, 2805, 1950, 1875, 1729, 1610, 1595, 1530, 1450, 1390, 1300, 1270, 1205, 1140, 1050, 995, 795, 750, 695 $\mathrm{cm}^{-1}$.

**4.1.112. Cleavage of solid support of 3,4-dimethylaniline carbamate 60.** Under a nitrogen atmosphere, resin bound 3,4-dimethylaniline carbamate **60** (1.14 g, 1.38 mmol) was placed in a flame dried round-bottom flask containing anhydrous tetrahydrofuran (20 mL). Lithium aluminum hydride (0.38 g, 10 mmol) was added in portions to the resulting suspension over a period of 20 min. The reaction was then refluxed under a nitrogen atmosphere for 8 h. The reaction was subsequently cooled to 0°C and quenched with dropwise addition of water (0.4 mL), followed by 15% sodium hydroxide solution (0.4 mL) and finally water (1.1 mL). The reaction mixture was filtered through a coarse filtration frit to remove aluminum salts, and the residual salts were washed with diethyl ether (4×8 mL). The combined filtrate and washings were dried over sodium sulfate and concentrated in vacuo. The crude product was then purified by flash chromatography (1:1, hexanes–ethyl acetate), to yield the desired *N*-methylated product (0.198 g, 73%). $^1$H NMR (CDCl$_3$) $\delta$ 2.20 (s, 3H), 2.25 (s, 3H), 2.81 (s, 3H), 6.80–7.25 (m, 3H).

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