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The Synthesis of α,α-Disubstituted α-Amino Acids via Ichikawa Rearrangement

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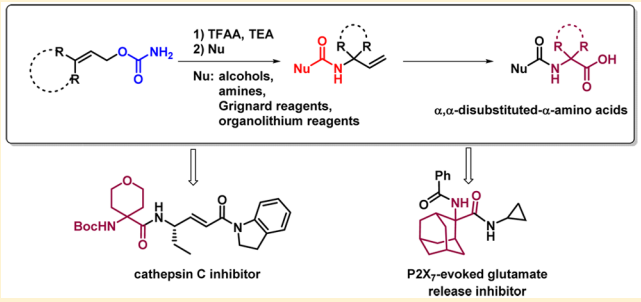
Supporting Information

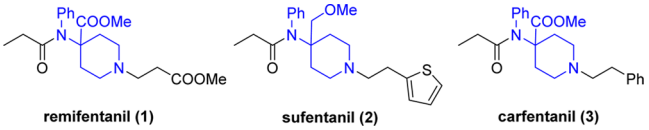
ABSTRACT: An approach to α,α-disubstituted α-amino acids is reported. The key step is allyl cyanate-to-isocyanate rearrangement. As demonstrated, the resultant allyl isocyanates can be directly trapped with various nucleophiles, for instance, alcohols, amines, and organometallic reagents, to provide a broad range of *N*-functionalized allylamines. The developed method has been successfully applied in the synthesis of two bioactive peptides: 2-aminoadamantane-2-carboxylic acid derived $P2X_7$-evoked glutamate release inhibitor and 4-amino-tetrahydropyranyl-4-carboxylic acid derived dipeptide GSK-2793660, which is currently in clinical trials as cathepsin C inhibitor for the treatment of cystic fibrosis, noncystic fibrosis bronchiectasis, ANCA-associated vasculitis and bronchiectasis.



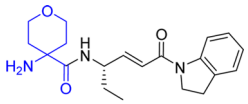
INTRODUCTION

α,α-Disubstituted α-amino acids (α,α-AAs) are an important class of non-natural amino acids.[1,2] Their incorporation into the peptide structure results frequently in conformational distortions and increased rigidity that lead to enhanced resistance toward proteolytic enzymes.[2,3] These conformational restrictions are particularly significant when the α,α-disubstituted α-amino acid moiety is incorporated into a cyclic structure that results in the modulation of conformational preferences[4] and biological activity of such peptides. Therefore, α,α-AAs play an important role in the design of novel peptides and peptidomimetics with enhanced biological properties, and this area of study is of profound interest to leading academic and industrial laboratories.[2,5]

Geminally disubstituted α-amino acids, particularly α,α-cycloalkyl-substituted α-amino acids, have also been found as medicines or potential drug candidates. For example, 4-aminopiperidine-4-carboxylic acid derived remifentanil (**1**) (GlaxoSmithKline: Ultiva)[6] is a short-acting synthetic opioid analgesic drug (an analogue of fentanyl), which is given to patients during surgery to relieve pain and as an adjunct to an anesthetic.[7] It has approximately 100−200 times higher potency than morphine. Even more active are its analogues: sufentanil (**2**) and carfentanil (**3**).[8] The last one exhibits a potency ca. 10 000 times that of morphine and, therefore, is intended for large animal use only since its extreme potency makes it inappropriate for use in humans.[8]



Another interesting example is 4-amino-tetrahydropyranyl-4-carboxylic acid derived dipeptide **4** (GSK-2793660),[9,6] which is currently in phase I of clinical trials as cathepsin C (also known as dipeptidyl peptidase I enzyme) inhibitor for the treatment of cystic fibrosis, noncystic fibrosis bronchiectasis, ANCA-associated[10] vasculitis and bronchiectasis.[11−17]



GSK-2793660 (4)

The typical methodologies to prepare α,α-AAs[1c−f,18,19] involve the use of cyclic compounds as the starting materials, and the most common methods of their preparation include the Bucherer−Bergs[20,21] and the Strecker reactions.[22,23] Other attractive methods are the addition to α-iminoesters,[24] alkylations,[18f,25] cycloadditions,[26] and enolate amination.[27] Among them, the strategies based on rearrangement reactions, for instance, [3,3]-[28−32] or [2,3]-sigmatropic rearrangements,[33,34] are particularly attractive. Because of the concerted mechanism of such rearrangements, which proceeds through a well-defined cyclic transition state, they show a high degree of stereospecificity and/or stereoselectivity. Thanks to their nature, such rearrangements are highly atom-economic processes, which is consistent with the current trends for efficient modern synthetic methods.

Very recently, we demonstrated that the Ichikawa rearrangement[29b,c,35,30,36] is a useful tool for the preparation of functionalized β- and γ-hydroxy-α-amino acids[36b] as well as β-aryl alanines.[36c] It was also used as a key step in the total

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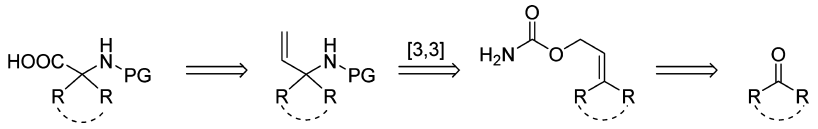
Scheme 1

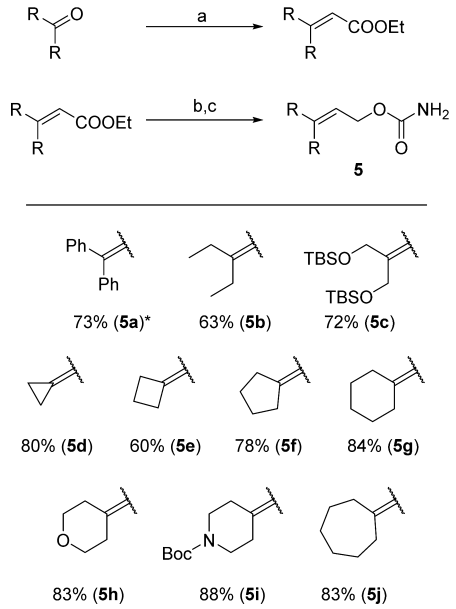


synthesis of lacosamide, a serine-derived anticonvulsant drug for epilepsy treatment.[36a] Herein, we present our extended studies on the synthesis of unnatural amino acids via sigmatropic rearrangement. In particular, we focused our attention on the synthesis of α,α-AAs as outlined in Scheme 1.

RESULTS AND DISCUSSION

We began our investigation with the preparation of a series of allyl carbamates of type **5**. These compounds can be easily synthesized starting from simple acyclic and cyclic ketones via an olefination, reduction, and carbamate formation sequence (Scheme 2).

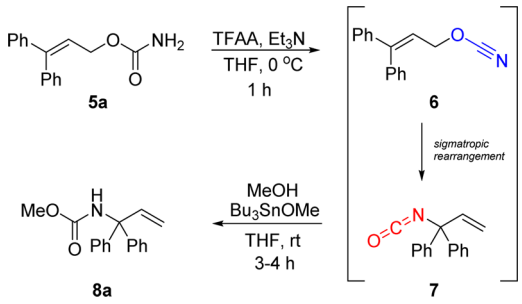
Scheme 2[a]



[a]Reagents and conditions: (a) NaH, ethyl 2-(diethoxyphosphoryl)-acetate, THF, rt; (b) DIBAL-H, CH_2Cl_2, −70 °C; (c) i. TCA-NCO, CH_2Cl_2, rt; ii. aq. K_2CO_3, MeOH. *overall yield of steps *b* and *c*.

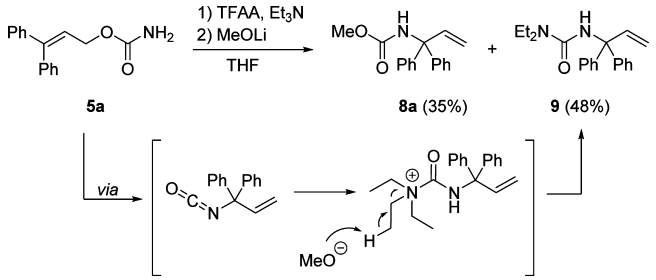
With a library of type **5** carbamates in hand, we began the studies on their transformation into the corresponding allylamines. The treatment of carbamate **5a** with 2 equiv of TFAA in the presence of Et_3N (6 equiv) resulted in its dehydration to allyl cyanate (**6**), which subsequently rearranged to the corresponding allyl isocyanate (**7**) (Scheme 3). Intermediate **7** can be easily trapped by direct reaction with an excess of MeOH in the presence of 10 mol % of Bu_3SnOMe to afford α,α-*gem*-substituted allylamine **8a** in 79% overall yield (after 3 steps). Since the double bond in compound **6** is more substituted, its rearrangement is slower with respect to less substituted allyl carbamates investigated previously;[36] therefore, the reaction time had to be extended from 20 to 30 min (previous studies[36]) to 1−1.5 h in this case. Isocyanate **7** can be also trapped with MeOLi. However, in this case, the formation of byproduct **9** was noticed, which plausibly originated from

Scheme 3



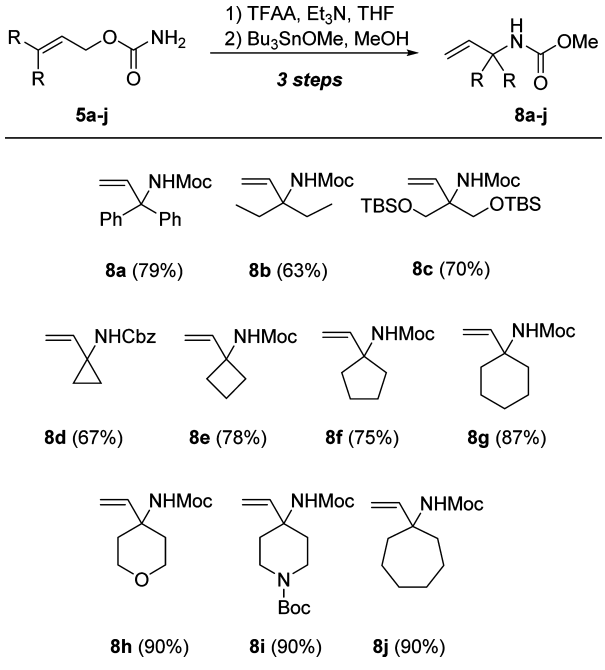
Et_3N addition to **7**, followed by elimination, as depicted in Scheme 4.

Scheme 4



Next, the substrate scope of different carbamates **5a−j** was investigated. As shown in Scheme 5, the above method enables

Scheme 5



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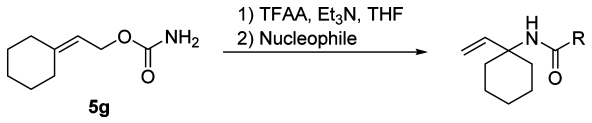
the synthesis of both acyclic (**8a**–**c**) and cyclic allylamines (**8d**–**j**) with high overall yield. The key advantages of the protocol presented in Scheme 5 are mild reaction conditions and no need for any metal catalysts or high temperatures to induce the rearrangement process.

At this stage of studies, the low yield of the desired product was observed only in the case of the cyclopropanone-derived allyl carbamate (15–20%). However, it was a result of problems with product isolation. Fortunately, the change of MeOH to BnOLi as the nucleophile let us obtain the corresponding *N*-Cbz derivative **8d** in 67% overall yield.

Another advantage of the presented rearrangement is the possibility of using various nucleophilic reagents, which allows preparing a broad range of differently *N*-protected geminally substituted allylamines (Table 1). For example, the replacement of MeOH with other alcohols, for instance, *t*-BuOH or BnOH, led to the formation of the corresponding *N*-protected allylamines, namely, *N*-Boc or *N*-Cbz derivatives (**8k** and **8l**). It was done by treatment of the intermediate isocyanate either by lithium alkoxide (e.g., *t*-BuOLi or BnOLi, Table 1, entries 3 and 4) or by ROH in the presence of a catalytic amount of DMAP (Table 1, entry 5). Interestingly, in the case of the carbamate of **5g**, the formation of an analogue of compound **9** was not observed even when MeOLi was applied. The use of $NaBH_4$, as the nucleophile source, furnished formamide **10**. Finally, the use of nitrogen nucleophiles such as ammonia, *n*-dibutylamine, or benzylamine led to the formation of the corresponding ureas **11a**, **11b**, and **11c**, respectively. As summarized in Table 1, all of these products were formed in excellent overall yield after 3 steps.

Table 1. Nucleophile Scope in Rearrangement/Addition Sequence for Carbamate 5g



5g

entry	nucleophile	R	yield [%][a]
1	MeOH/Bu_3SnOMe	OMe (**8g**)	87
2	MeOLi	OMe (**8g**)	82
3	*t*-BuOLi	O*t*-Bu (**8k**)	88
4	BnOLi	OBn (**8l**)	66
5	BnOH[b]	OBn (**8l**)	63
6	$NaBH_4$	H (**10**)	62
7	NH_3	NH_2 (**11a**)	60
8	$BnNH_2$	BnNH (**11b**)	85
9	*n*-Bu_2NH	*n*-Bu_2N (**11c**)	90
10	MeMgBr	Me (**12a**)	64
11	PhMgBr	Ph (**12b**)	65

[a]Isolated yield, overall after 3 steps. [b]In the presence of 10 mol % of DMAP.

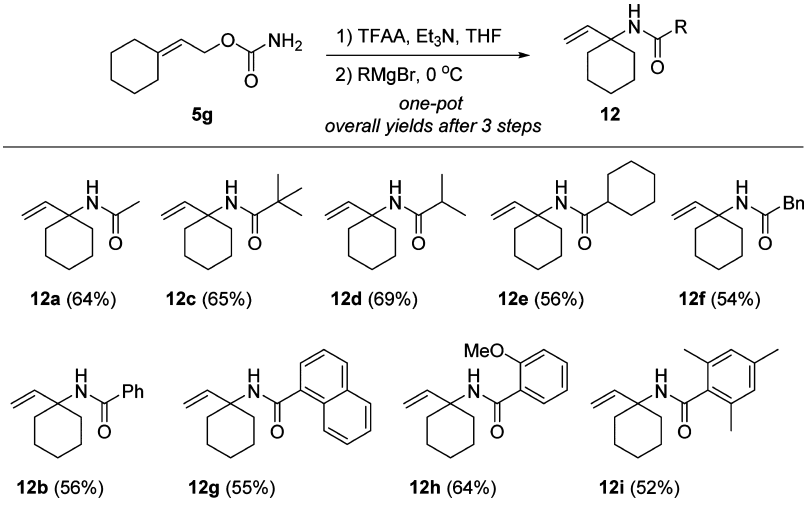
As can be seen from entries 8 and 9, the use of Grignard reagents as the nucleophilic species allowed also the preparation of *N*-acyl disubstituted allylamines **12a** and **12b**. It is worth to stress that oxidative cleavage of the double bond in **12a** and **12b** should provide the corresponding *N*-acyl disubstituted amino acids. Such hindered compounds are not easy to prepare by typical dehydrative coupling of amines and carboxylic acids in the presence of a coupling reagent.[37] The essential problem is the low rate of the reaction of the amine on the activated carboxylic acid. It is even more complicated when sterically hindered carboxylic acids (or their derivatives, e.g., acyl chlorides) are used. Recently, Bode and co-workers demonstrated that isocyanates[38] and *N*-carboxyanhydrides[39] can be an interesting solution for the formation of sterically hindered amides and amino acids.

Encouraged by these reports and our initial work, we decided to examine whether other structurally different Grignard reagents, including bulky ones, can be applied for our dehydration/rearrangement/addition sequence.

As exemplified in Scheme 6, the investigated transformations proceed efficiently not only for simple methyl- or phenylmagnesium bromide but also for more sterically demanding reagents such as isopropyl or *t*-butyl Grignard reagent. Good results were also obtained in the case of 2-methoxyphenylmagnesium bromide or 1-naphthylmagnesium bromide. Quite good yield was also obtained in the case of the addition of the sterically hindered mesitylmagnesium bromide.

The addition of organolithium reagents to the allyl isocyanate generated *in situ* also proceeded smoothly, and the desired products were obtained in moderate yields (Scheme 7). In addition, this approach enabled the synthesis of several

Scheme 6



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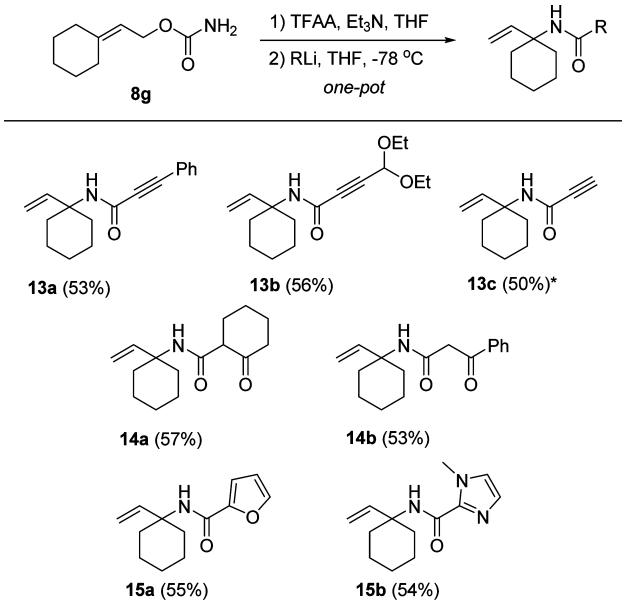
interesting heterocyclic allyl amides (e.g., **15a**, **15b**) in good yield as well (Scheme 7).

Scheme 7



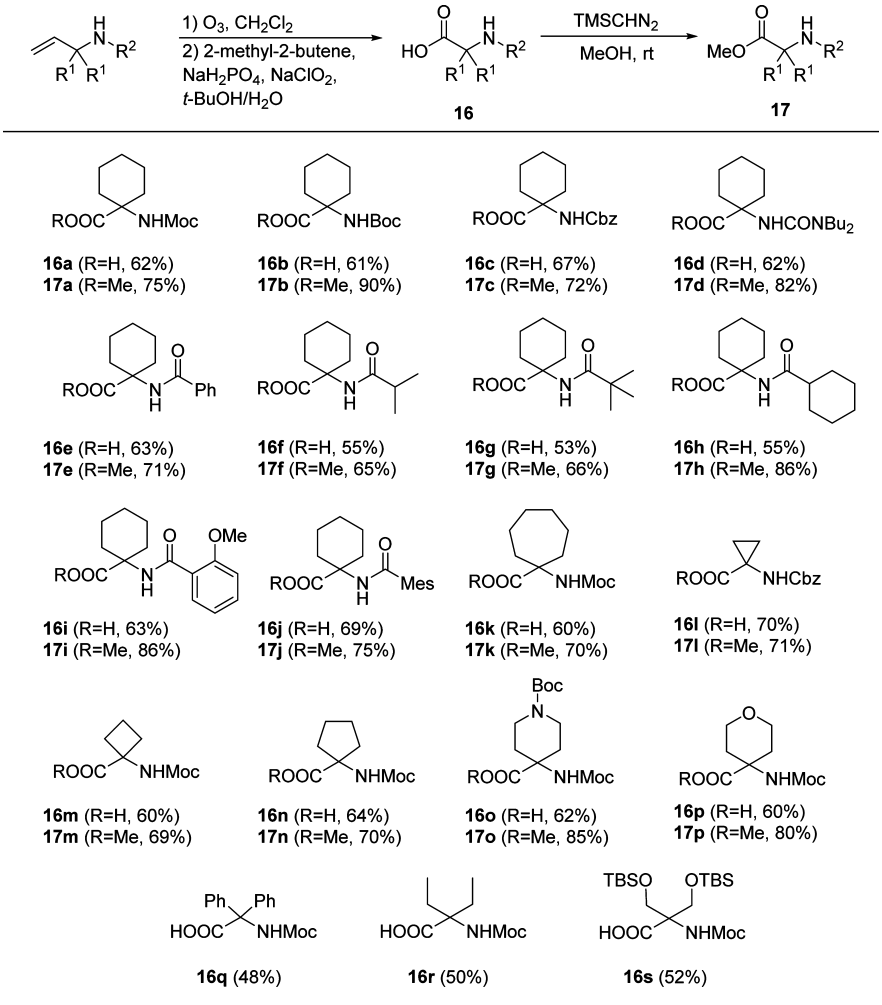
Finally, selected disubstituted allylamine derivatives were converted into the corresponding amino esters. Initially, we planned to perform this transformation by the ozonolysis of the double bond in the presence of 2 M NaOH in MeOH (Marshall protocol[40]), which approach we used successfully in our previous works.[36] Surprisingly, this approach proceeded poorly in the case of investigated α,α-geminally substituted allylamines (yields ca. 30−50%), probably due to a side decarboxylation process and some problems with an isolation of polar amino acids. Thus, the target amino acids or aminoesters were obtained by sequential ozonolysis/Pinnick−Lindgren oxidation,[41] eventually followed by the esterification of the resulting amino acid, as presented in Scheme 8.

Having explored the scope of the one-pot dehydration/rearrangement/addition process, in the next step, the synthetic utility of α,α-disubstituted allylamines for the preparation of biologically active compounds was investigated.

We decided to apply the above approach in the formal synthesis of GSK-2793660 (**4**), a dipeptide which, as already mentioned, is currently in phase I of clinical trials as cathepsin C inhibitor for the treatment of cystic fibrosis, noncystic fibrosis bronchiectasis, ANCA-associated vasculitis and bronchiectasis.[6,11−17] This molecule was planned to be synthesized according to the retrosynthetic scheme outlined in Scheme 9.

Part A of **4** was prepared from carbamate **5h** obtained from tetrahydro-4*H*-pyran-4-one. As presented in Scheme 10, upon

Scheme 8



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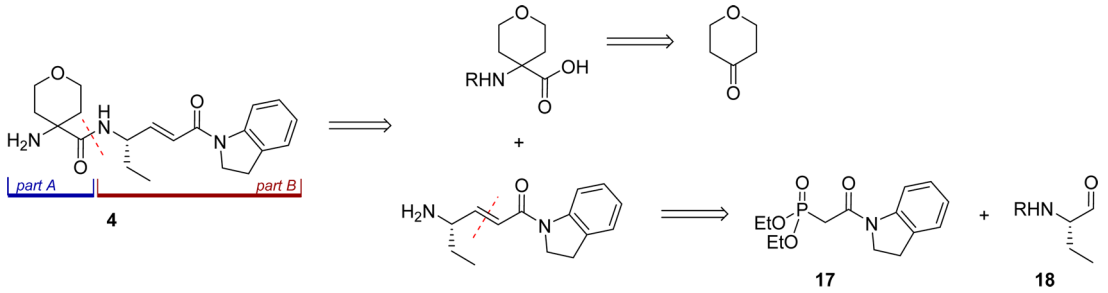
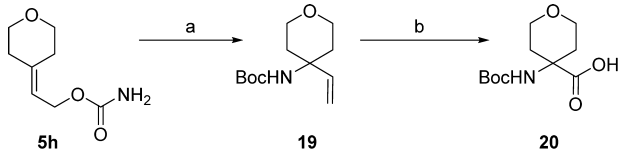
Scheme 9. Retrosynthesis of Compound 4



Scheme 10[a]

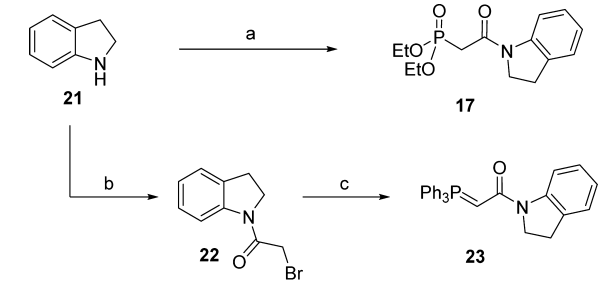


[a]Reagents and conditions: (a) i. TFAA, Et_3N, THF, −10 °C then rt, 1 h; ii. *t*-BuOH, LiHMDS, THF, rt, 5 h, 80% (3 steps); (b) i. O_3, CH_2Cl_2, −78 °C, ii. $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, *t*-BuOH/H_2O, 62% (2 steps).

treatment with TFAA/Et_3N, carbamate **5h** underwent dehydration/rearrangement to provide an isocyanate intermediate which was trapped directly with *t*-BuOLi to provide product **19** in 80% yield after 3 steps. The oxidation of the double bond using ozonolysis/Pinnick−Lindgren oxidation gave *N*-Boc protected amino acid **20** in 62%.

Fragment B of compound **4** was planned to be prepared via HWE olefination of aldehyde **18** with phosphonate **17** (Scheme 9). Phosphonate **17** was obtained from diethylphosphonoacetic acid by its activation with $(COCl)_2$ and treatment with indoline (**21**) according to the procedure reported by Webber et al.[42] (Scheme 11).

Scheme 11[a]



[a]Reagents and conditions: (a) $(COCl)_2$, diethylphosphonoacetic acid, 76%; (b) 2-bromoacetyl bromide, Et_3N, CH_2Cl_2, −10 °C then rt, 65%; (c) i. Ph_3P, PhMe, reflux, 24 h, ii. Et_3N, $CHCl_3$, 4 h, 67% (2 steps).

Chiral aldehyde **26** was prepared starting with L-2-aminobutyric acid (Scheme 12). After *N*-protection with Boc_2O (**24**), this compound was converted into Weinreb amide **25** according to Neipp et al.[9b] Upon treatment with $LiAlH_4$, amide **25** was selectively reduced to aldehyde **26**. Compound **26**, after aqueous workup, was directly subjected to the olefination reaction by its addition to a solution of **17** pretreated with LiHMDS. Unfortunately, the desired product **27** was obtained in moderate 64% yield. Close results were obtained when the olefination was performed under Masamune−Roush conditions[43] by treatment with phosphonate **17** in the presence of LiCl/DBU in MeCN (68%). The highest yield was obtained when **27** was prepared via Wittig reaction with ylide **23** (75%). Compound **23**[44] was prepared as presented in Scheme 11.

Deprotection of **27** with TFA, according to a procedure described by Neipp et al.,[9b] provided the corresponding amine **28** in low yield and with poor purity. Much more effective was deprotection of **27** by the treatment with 4 M HCl in dioxane at rt. After the removal of the solvent, the resulting amine hydrochloride **28** was directly subjected to the coupling reaction with amino acid **20**.

Initially, coupling of **20** with **28** was performed in the presence of T3P[10] in AcOEt according to a procedure reported by Neipp et al.[9b] However, only traces of the desired product **29** were obtained. Poor results were also obtained when other coupling agents were applied (e.g., HATU, DCC, EDCl, HOBt, ClCOO*i*-Bu).[10] LC-MS analysis showed the presence of the desired molecular peak predominantly (458 $[M + H]^+$); however, NMR spectra indicated the presence of a complicated reaction mixture. Deeper analysis of the NMR spectra indicated that the desired compound **29** was formed along with byproducts. The key observation from the analysis of NMR spectra was that these additional products plausibly do not contain a double bond, which suggested that amine **29** undergoes partially unwanted cyclization to isomeric aziridines via intramolecular Michael reaction (at the coupling or the deprotection stage). None of these compounds were isolated in pure form due to their similar polarity. The attempts to separate them by either column chromatography or preparative TLC failed.

Because of the failure of our initial synthetic strategy, an alternative pathway of the formal synthesis of **4** was designed (Scheme 13). Now, amino acid **20** was coupled with methyl (*S*)-2-aminobutanoate[45] in the presence of HATU and *N*-methylmorpholine (NMM). The resulting peptide **30** was reduced to the amino alcohol, which was directly oxidized to the aldehyde with Dess-Martin periodinane (DMP). After aqueous workup, this aldehyde was directly treated with ylide **23** to afford the desired product **29** in 95% yield after 3 steps. The final deprotection has been already described by Neipp et al.[9b]

The adamantyl moiety is an important structural element of numerous biologically active compounds,[46] including several currently used drugs (e.g., amantadine (antiviral, Parkinson's disease),[46a,47] menantadine (Alzeimer's disease),[46] tromantadine (antiviral),[46,48] and antidiabetics vidagliptin[46,49] and saxagliptin.[46,49,50] An interesting example is unnatural amino acid **31** (2-aminoadamantane-2-carboxylic acid), which has been reported to possess interesting biological activity as a

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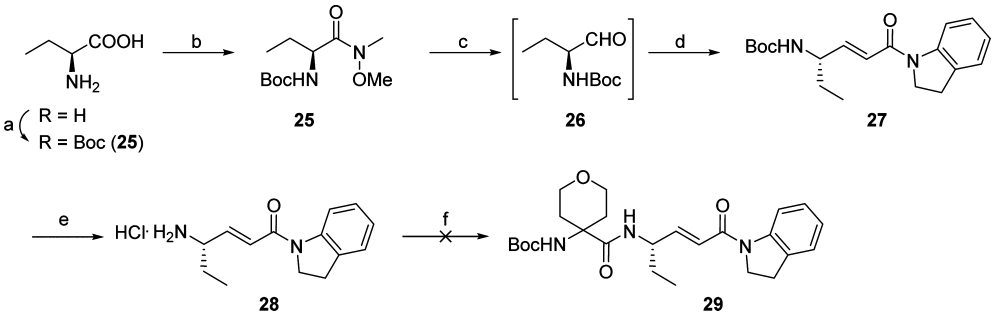
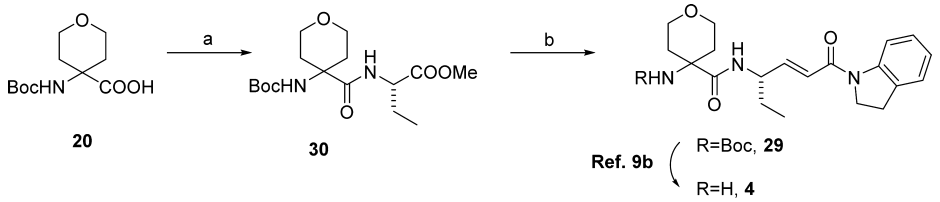
Scheme 12[a]



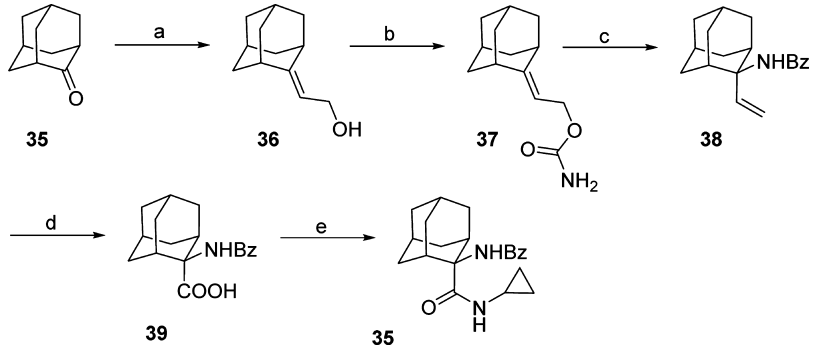
[a]Reagents and conditions: (a) Boc_2O, aq. NaOH, 93%; (b) i. CDI, THF; iii. MeNHOMe·HCl, *i*-Pr_2NEt, CH_2Cl_2, rt, 93%; (c) $LiAlH_4$, THF, −20 °C then rt; (d) ylide **23**, PhMe, 40 °C, 75%; (e) 4 M HCl, dioxane; (f) amino acid **20**, coupling agent.

Scheme 13[a]



[a]Reactants and conditions: (a) methyl (*S*)-2-aminobutanoate hydrochloride, HATU, NMM, THF, rt, 75%; (b) i. $LiAlH_4$, Et_2O; ii. DMP, CH_2Cl_2; iii. ylide **23**, CH_2Cl_2, 40 °C, 95% (3 steps).

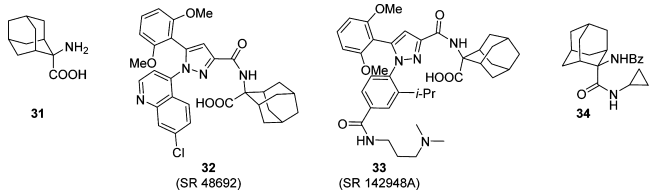
Scheme 14Synthesis of 34[a]



[a]Reagents and conditions: (a) i. $(EtO)_2P(O)CH_2COOEt$, NaH, THF, rt, overnight, yield 79%; ii. DIBAL-H, CH_2Cl_2, −70 °C, 2 h, yield 75%; (b) i. TCA-NCO, CH_2Cl_2, 0 °C then rt, 1 h; ii. aq. K_2CO_3, MeOH, rt, 2 h, yield 63% (2 steps); (c) i. TFAA, Et_3N, THF, −10 °C then rt, 1 h; ii. PhMgBr, THF, −30 °C then rt, overnight, yield 74% (overall after 3 steps); (d) $RuCl_3 \cdot xH_2O$, $NaIO_4$, acetone/H_2O 9:1, rt, 60%; (e) cyclopropylamine, HATU, NMM, THF, rt, 62%.

transport mediator.[51,52] 2-Aminoadamantanecarboxylic residue has been also recognized as a key structural element of SR 48692 (**32**, Meclinertant)[53] and SR 142948A (**33**),[54] responsible for key interactions allowing the selective recognition of neurotensins,[55] seven-transmembrane G protein-coupled receptors acting as neurotransmitters and neuromodulators demonstrating a range of biological activity.[56,57]

Recently, Ley and co-workers[58] reported the synthesis of **31** and its derivative **34**, which demonstrated excellent *in vivo* analgesic properties in the mouse abdominal constriction test.[58b] Further experiments indicated that **34** inhibits also the $P2X_7$-evoked glutamate release.[58b] $P2X_7$ receptors have been associated with chronic pain and arthritis, which makes them potential targets for future drug discovery, especially in the case of neurodegenerative diseases such as multiple sclerosis, Alzheimer's and Huntington's diseases, or amyotrophic lateral sclerosis.[59]



Inspired by the report of Ley and co-workers,[58] we decided to apply our method for the preparation of adamantyl-derived diamide **34**, as outlined in Scheme 14. The reaction sequence began with HWE olefination of 2-adamantanone (**35**), followed by ester reduction and carbamate formation by the treatment of allyl alcohol **36** with trichloroacetyl isocyanate and basic hydrolysis. The obtained carbamate **37** was subjected to a dehydration/rearrangement cascade reaction to provide the isocyanate, which was directly treated with PhMgBr and resulted in the formation of benzamide **38** in 74% yield after 3

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steps. Interestingly, an oxidation of the double bond with $RuCl_3/NaIO_4$ provided carboxylic acid **39** in 60% yield. The comparible results were obtained when ozonolysis/Pinnick–Lindgren oxidation was applied (62%).

Finally, carboxylic acid **39** was subjected to a coupling reaction with cyclopropylamine to provide the target diamide **34**. Initially, acid **39** was activated with $(COCl)_2$ and the resulting acid chloride was reacted with $CyNH_2$. However, the desired product **34** was obtained in poor yield (20%) and with low purity. The same low efficiency was achieved in the case of the mixed anhydride strategy (i.e., with either methyl chloroformate or *s*-butyl chloroformate). The best results were obtained again when HATU was used as the acid activator. The final product **34** was obtained in 62% yield after chromatographic purification.

CONCLUSIONS

In summary, a novel approach to α,α-disubstituted α-amino acids has been developed. The key step of the reported method is cyanate-to-isocyanate rearrangement. Important advantages of this reaction over other [3,3]-sigmatropic rearrangements, for instance, Overman reaction, are mild reaction conditions (~0 °C to rt, short reaction time ca. 1 h) and no need to use any metal catalyst. In addition, generated allyl isocyanates can be directly trapped by various nucleophilic species, for example, alcohols, amines, and organometallic reagents. As a result, this approach enables the synthesis of a broad range of *N*-functionalized allylamines.

The developed method has been successfully applied in the synthesis of two bioactive peptides: 2-aminoadamantane-2-carboxylic acid derived $P2X_7$-evoked glutamate release inhibitor and 4-amino-tetrahydropyranyl-4-carboxylic acid derived dipeptide GSK-2793660, which is currently in phase I of clinical trials as cathepsin C inhibitor for the treatment of cystic fibrosis, noncystic fibrosis bronchiectasis, ANCA-associated vasculitis and bronchiectasis.

EXPERIMENTAL SECTION

Synthesis of Unsaturated Esters. General Procedure. Neat triethyl phosphonoacetate (10 mmol) was added to a suspension of NaH (10 mmol) in dry THF (50 mL). After 30 min, a solution of ketone (8 mmol) in dry THF (10 mL) was added, and the resulting mixture was stirred overnight. The progress of the reaction was followed by TLC. The reaction was quenched by the addition of water (50 mL). The organic layer was separated, and the aqueous one was extracted with ether (3 × 50 mL). The combined organic solutions were dried over anhydr. Na_2SO_4, and then the solvents were removed under diminished pressure and the residue was purified by column chromatography.

Ethyl 3,3-Diphenyl Acrylate. Colorless oil; yield 3.78 g (91%) staring from 3 g (16.46 mmol) of benzophenone; Spectral data in agreement with literature data.[60] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40–7.26 (m, 8H), 7.24–7.15 (m, 2H), 6.34 (s, 1H), 4.02 (q, *J* 7.1 Hz, 2H), 1.10 (t, *J* 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CDCl3) δ: 166.1, 156.4, 140.8, 139.0, 129.5, 129.1, 128.3, 128.1, 128.0, 127.7, 117.3, 60.3, 14.1; Anal. Calcd for $C_{17}H_{16}O_2$: C 80.93, H 6.39; Found C 81.04, H 6.32.

Ethyl 3-Ethylpent-2-enoate. Colorless oil, yield 5.66 g (52%) starting from 6 g (69.55 mmol) of 3-pentanone; bp 64–68 °C/5 Torr; Spectral data in agreement with literature data.[61] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.46 (s, 1H), 4.01 (q, *J* 7.1 Hz, 2H), 2.40 (q, *J* 6.8 Hz, 2H), 2.07 (q, *J* 6.7 Hz, 2H), 1.09 (t, *J* 7.1, 3H), 0.90 (2 × t, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.1, 165.3, 113.5, 61.2, 30.9, 25.7, 13.2, 12.5; IR (film) ν: 1734, 1638 cm^{-1}; Anal. Calcd for $C_9H_{16}O_2$: C 69.19, H 10.32; Found: C 69.26, H 10.25.

Ethyl 4-((*t*-Butyldimethylsilyl)oxy)-3-(((*t*-butyldimethylsilyl)-oxy)methyl)but-2-enoate.[62] Pale yellow oil; yield 2.02 g (83%) starting from 2 g (6.28 mmol) of *O*,*O*-TBS-dihydroxyacetone; purification by chromatography on silica gel (3% AcOEt in hexanes); Spectral data in agreement with literature data.[62] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.90 (t, *J* 1.9 Hz, 1H), 4.87–4.85 (m, 2H), 4.45–4.41 (m, 2H), 4.10 (q, *J* 7.1 Hz, 2H), 1.21 (t, *J* 7.1 Hz, 3H), 0.95 (s, 18H), 0.09 (s, 6H), 0.06 (s, 6H); IR (film) ν: 1730, 1633 cm^{-1}; Anal. Calcd for $C_{19}H_{40}O_4Si_2$: C 58.71, H 10.37; Found: C 58.79, H 10.29.

Ethyl 2-Cyclopropylideneacetate. Prepared following the procedure reported by Arai et al.;[63] colorless oil; yield 1.72 g (70%) starting from 3.4 g (19.51 mmol) of (1-ethoxycyclopropoxy)-trimethylsilane; Spectral data in agreement with literature data.[63] ^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.24–6.21 (m, 1H), 4.21 (q, *J* 7.1 Hz, 2H), 1.48–1.42 (m, 2H), 1.30 (t, *J* 7.1 Hz, 3H), 1.25–1.19 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 166.2, 144.8, 111.0, 60.1, 14.3, 4.5, 2.0; IR (film) ν: 1720, 1266, 1181 cm^{-1}; MS (ESI-TOF) *m*/*z* 149 [M + Na$^+$]; Anal. Calcd for $C_7H_{10}O_2$: C 66.65, H 7.99; Found: C 66.72, H 7.85.

Ethyl 2-Cyclobutylideneacetate. Yield 1.54 g (86%) starting from 0.93 g (12.74 mmol) of cyclobutanone; purification by column chromatography on silica gel (5% then 10% AcOEt in hexanes); colorless oil. Spectral data in agreement with literature data.[64] ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.57 (p, *J* 2.3 Hz, 1H), 4.14 (q, *J* 7.1 Hz, 2H), 3.16–3.07 (m, 2H), 2.83 (t, *J* 7.9 Hz, 2H), 2.14–2.01 (m, 2H), 1.26 (t, *J* 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 167.5, 166.6, 112.4, 59.5, 33.7, 32.3, 17.7, 14.3; IR (film) ν: 1718, 1676, 1335, 1189 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_8H_{12}O_2Na$ [M + Na$^+$] 163.0735; Found 163.0732.

Ethyl 2-Cyclopentylideneacetate. Yield 6.01 g (82%) staring from 4 g (47.55 mmol) of cyclopentanone; purification by column chromatography on silica gel (5% then 10% AcOEt in hexanes); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.81 (s, 1H), 4.13 (q, *J* 7.1 Hz, 2H), 2.77 (t, *J* 7.2 Hz, 2H), 2.45 (t, 6.9 Hz, 2H), 1.78–1.64 (m, 4H), 1.25 (t, *J* 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 169.4, 167.4, 111.8, 59.61, 36.1, 32.8, 26.7, 25.6, 14.5; IR (film) ν: 1721, 1271, 1200, 1031 cm^{-1}; MS (ESI-TOF) *m*/*z* 177 [M + Na$^+$]; Anal. Calcd for $C_9H_{14}O_2$: C 70.10, H 9.15; Found: C 70.21, H 9.08.

Ethyl 2-Cyclohexylideneacetate. Yield 22.63 g (88%) starting from 15 g (152.84 mmol) of cyclohexanone; purification by column chromatography on silica gel (5% then 10% AcOEt in hexanes); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.63 (s, 1H), 4.12 (q, *J* 7.1 Hz, 2H), 2.85–2.82 (m, 2H), 2.23–2.18 (m, 2H), 1.74–1.56 (m, 6H), 1.26 (t, *J* 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.8, 163.4, 112.9, 59.4, 37.9, 29.7, 28.6, 27.7, 26.2, 14.3; IR (film) ν: 1724, 1270, 1205, 1032 cm^{-1}; MS (ESI-TOF) *m*/*z* 191 [M + Na$^+$]; Anal. Calcd for $C_{10}H_{16}O_2$: C 71.39, H 9.59; Found: C 71.28, H 9.51.

Ethyl 2-(Tetrahydro-4*H*-pyran-4-ylidene)acetate. Yield 3.03 g (90%) starting from 2 g (19.8 mmol) of tetrahydro-4*H*-pyran-4-one, purification by column chromatography on silica gel (15% then 20% AcOEt in hexanes); yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.67 (s, 1H), 4.15 (q, *J* 7.1 Hz, 2H), 3.76 (t, *J* 5.5 Hz, 2H), 3.73 (t, *J* 5.6 Hz, 2H), 3.00 (t, *J* 5.6 Hz, 2H), 2.32 (t, *J* 5.5 Hz, 2H), 1.27 (t, *J* 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 166.4, 157.1, 114.5, 69.0, 68.5, 59.7, 37.5, 31.0, 14.3; IR (film) ν: 2977, 2909, 2847, 1712, 1651, 1386, 1251, 1201, 1177, 1147, 1097, 1039, 1009, 864, 850, 683 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_9H_{14}O_3$ [M] 170.0943; Found 170.0938.

***N*-Boc 4-(2-Ethoxy-2-oxoethylidene)piperidine.** Yield 2.67 g (79%) starting from 2.5 g (12.55 mmol) of *N*-*t*-butoxycarbonyl-piperidin-4-one; purification by column chromatography on silica gel (10% AcOEt in hexanes); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.62 (s, 1H), 4.06 (q, *J* 7.0 Hz, 2H), 3.52–3.32 (m, 4H), 2.98–2.76 (m, 2H), 2.19 (s, 2H), 1.38 (s, 9H), 1.18 (t, *J* 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.1, 157.7, 154.4, 115.2, 79.7, 59.6, 36.3, 29.4, 28.3, 14.2; IR (film) ν: 1698, 1421, 1254, 1167 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{14}H_{23}NO_4Na$ 292.1525; Found 292.1523.

Ethyl 2-Cycloheptylideneacetate. Yield 5 g (62%) starting from 5 g (44.58 mmol) of cycloheptanone; purification by flash column chromatography on silica gel (3% AcOEt in hexanes); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.67 (t, *J* 1.5 Hz, 1H), 4.16 (q, *J* 7.5 Hz,

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2H), 2.88 (dt, *J* 6.5, 1.5 Hz, 2H), 2.37 (dt, *J* 6.5, 1.5 Hz, 2H), 1.72–1.62 (m, 4H), 1.58–1.50 (m, 4H), 1.28 (t, *J* 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.6, 115.6, 59.0, 38.9, 32.0, 29.8, 29.0, 28.0, 26.6, 14.3; IR (film) *v*: 2990, 2926, 1714, 1635, 1445, 1147, 1038 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_{11}H_{18}O_2$ [M] 182.1307; Found 182.1314.

Synthesis of Allyl Carbamates 5. General Procedure. To a cooled (−70 °C) solution of the unsaturated ester (8 mmol) in CH_2Cl_2 (50 mL) was added a 1 M soln. of DIBAL-H in hexanes (20 mL, 20 mmol). The progress of the reduction was followed by TLC. When the reduction was complete, the reaction was quenched by the addition of sat. aq. Na_2SO_4 (4.4 mL). When a precipitate appeared, the mixture was diluted with Et_2O and stirred for 1 h. Solids were filtered off and washed with Et_2O. After drying over anhydr. Na_2SO_4, the solvent was removed under diminished pressure and the crude alcohol was used in the next step.

To a solution of allyl alcohol (8 mmol) in CH_2Cl_2 (50 mL) cooled to −10 °C was added TCA-NCO (10.4 mmol). After 1 h, the solvent was removed under diminished pressure. The residue was dissolved in a mixture of MeOH/H_2O (50 mL, 4:1 v/v), and K_2CO_3 (4 g) was added in one portion. After 1.5 h, MeOH was removed and the aqueous residue was extracted with CH_2Cl_2 (4 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and filtered through a silica gel pad, and the solvent was removed under diminished pressure. The residue was chromatographed on silica gel to afford the corresponding allyl carbamate **5**.

3,3-Diphenylallyl Carbamate (5a). Yield 0.57 g (73%) starting from 0.65 g (3.09 mmol) of ethyl 3,3-diphenyl acrylate; purification by column chromatography on silica gel (5% AcOEt in hexanes); colorless crystals; mp 111.0–111.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.41–7.16 (m, 10H), 6.19 (t, *J* 7.0 Hz, 1H), 4.65 (d, *J* 7.0 Hz, 2H), 4.59 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 146.2, 141.5, 138.7, 129.7, 128.3, 128.2, 127.8, 127.7, 127.6, 122.7, 63.2; FTIR (film) *v*: 3439, 3328, 3262, 3224, 1688 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{16}H_{15}NO_2Na$ [M + Na$^+$] 276.1000. Found 276.1003.

3-Ethylpent-2-en-1-yl Carbamate (5b). Yield 1.3 g (63%) starting from 1.5 g (13.14 mmol) of ethyl 3-ethylpent-2-enoate; purification by column chromatography on silica gel (15% AcOEt in hexanes); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.29 (t, *J* 7.1 Hz, 1H), 4.71 (s, 2H), 4.60 (d, *J* 7.1 Hz, 2H), 2.15–2.01 (m, 4H), 1.04–0.97 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 149.8, 137.1, 116.6, 61.7, 29.1, 23.7, 13.5, 12.3; FTIR (film) *v*: 3464, 3348, 1710, 1602, 1405, 1330, 1073, 1045 cm^{-1}; MS (ESI-TOF) *m*/*z* 180 [M + Na$^+$], Anal. Calcd for $C_8H_{15}NO_2$: C 61.12, H 9.62, N 8.91; Found C 61.08, H 9.68, N 8.75.

4-(*t*-Butyldimethylsilyloxy)-3-(*t*-butyldimethylsilyloxymethyl)but-2-en-1-yl Carbamate (5c). Yield 1.43 g (72%, 3 steps); purification by column chromatography on silica gel (2% to 5% AcOEt in hexanes); white solid; mp 41–42 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.67 (t, *J* 7.0 Hz, 1H), 4.69 (d, *J* 7.0 Hz, 2H), 4.63 (br s, 2H), 4.24 (s, 2H), 4.20 (s, 2H), 0.91 (s, 9H), 0.89 (s, 9H), 0.07 (s, 6H), 0.06 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 156.7, 142.9, 119.4, 64.1, 61.1, 59.1, 25.9, 25.8, 18.4, 18.2, −5.4; FTIR (film) *v*: 3510, 3356, 3279, 3200, 2954, 2929, 2857, 1726, 1254, 1107, 1052, 837, 777 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{18}H_{39}NO_4Si_2Na$ [M + Na$^+$] 412.2315; Found 412.2317.

2-Cyclopropylideneethyl Carbamate (5d). Yield 396 mg (80%) starting from 490 mg (3.88 mmol) of ethyl 2-cyclopropylideneacetate; white solid; mp 42–42.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.98–5.92 (m, 1H), 4.73 (s, 2H), 4.70 (ddt, *J* 6.6, 2.4, 1.1 Hz, 2H), 1.12 (dt, *J* 2.0, 1.2 Hz, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 149.4, 130.0, 112.8, 65.3, 27.9, 19.0; FTIR (film) *v*: 3475, 3348, 1709, 1602, 1403, 1341, 1051 cm^{-1}; MS (ESI-TOF) *m*/*z* 150 [M + Na$^+$]; Anal. Calcd for $C_6H_9NO_2$: C 56.68, H 7.14, N 11.02; Found C 56.59, H 7.20, N 10.58.

2-Cyclobutylideneethyl Carbamate (5e). Yield 0.96 g (60%) starting from 1.6 g (11.4 mmol) of ethyl 2-cyclobutylideneacetate; purification by flash chromatography on silica gel (from 10% to 20% AcOEt in hexanes); colorless crystals; mp 47–48 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.31–5.23 (m, 1H), 4.73 (br s, 2H), 4.43 (dp, *J* 7.2, 1.1 Hz, 2H), 2.79–2.64 (m, 4H), 2.05–1.92 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 156.9, 148.2, 114.5, 61.9, 31.1, 29.4, 17.0; FTIR (film) *v*: 3433, 3330, 3266, 3211, 1684, 1612, 1414, 1347, 1041 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_7H_{11}NO_2Na$ [M + Na$^+$] 164.0687; Found 164.0689.

2-Cyclopentylideneethyl Carbamate (5f). Yield 2.36 g (78%) starting from 3 g (19.45 mmol) of ethyl 2-cyclopentylideneacetate; purification by flash chromatography on silica gel (from 10% to 20% AcOEt in hexanes); colorless crystals; mp 62–64 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.49–5.38 (m, 1H), 4.78 (s, 2H), 4.54 (d, *J* 7.1 Hz, 2H), 2.36–2.23 (m, 4H), 1.68 (p, *J* 6.8 Hz, 2H), 1.61 (p, *J* 6.7 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 157.1, 150.5, 114.2, 63.4, 33.8, 28.7, 26.2, 26.0; FTIR (film) *v*: 3451, 3333, 3268, 3199, 2952, 1705, 1607, 1356, 1330, 1046, 783 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_8H_{13}NO_2Na$ [M + Na$^+$] 178.0844; Found 178.0845.

2-Cyclohexylideneethyl Carbamate (5g). Yield 4.23 g (84%) starting from 5 g (29.72 mmol) of ethyl 2-cyclohexylideneacetate; purification by column chromatography on silica gel (20% AcOEt in hexanes); white solid, mp 84.0–84.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.30 (t, *J* 7.1 Hz, 1H), 4.62 (s, 2H), 4.58 (d, *J* 7.2 Hz, 2H), 2.23–2.18 (m, 2H), 2.16–2.10 (m, 2H), 1.60–1.51 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.9, 146.9, 115.4, 61.2, 37.0, 29.0, 28.3, 27.7, 26.6; FTIR (film) *v*: 3497, 3447, 3335, 3266, 3798, 1712, 1605, 1331, 1044, 739 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_9H_{15}NO_2Na$ [M + Na$^+$] 192.1002. Found 192.1000.

2-(Tetrahydro-4*H*-pyran-4-ylidene)ethyl Carbamate (5h). Yield 3.34 g (83%) starting from 4 g (23.50 mmol) of ethyl 2-(tetrahydro-4*H*-pyran-4-ylidene)acetate. The crude carbamate was dissolved in a small amount of AcOEt, and hexane was added to precipitate compound **5h** as colorless crystals; mp 84.5–85.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.40 (t, *J* 7.3 Hz, 1H), 4.68 (s, 2H, NH_2), 4.58 (d, *J* 7.3 Hz, 2H), 3.74–3.65 (m, 4H), 2.35 (t, *J* 5.2 Hz, 2H), 2.25 (t, *J* 5.5 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 156.9, 141.4, 117.5, 69.4, 68.7, 60.8, 36.9, 30.1; FTIR (film) *v*: 3424, 3322, 3260, 3208, 1680, 1055 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_8H_{13}NO_3Na$ [M + Na$^+$] 194.0793. Found 194.0790.

***t*-Butyl 4-(2-(Carbamoyloxy)ethylidene)piperidine-1-carboxylate (5i).** Yield 0.873 g (88%) starting from 0.873 g (3.68 mmol) of *N*-Boc 4-(2-ethoxy-2-oxoethylidene)piperidine; purification by column chromatography on silica gel (hexanes/AcOEt 2:1); colorless crystals; mp 150.5–151.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.43 (t, *J* 7.1 Hz, 1H), 4.66–4.61 (br s, 2H, NH), 4.59 (d, *J* 7.1 Hz, 2H), 3.52–3.34 (m, 4H), 2.33–2.25 (m, 2H), 2.23–2.13 (m, 2H), 1.46 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 156.7, 154.7, 141.9, 118.1, 97.3, 79.6, 60.7, 35.7, 28.4; FTIR (film) *v*: 3406, 3260, 3196, 1722, 1685 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{13}H_{22}N_2O_4Na$ [M + Na$^+$] 293.1477. Found 293.1480.

2-Cycloheptylideneethyl Carbamate (5j). Yield 1.96 g (83%) starting from 1.8 g (12.84 mmol) of ethyl 2-cycloheptylideneacetate; purification by column chromatography on silica gel (hexanes/AcOEt 4:1); white solid; mp 49–50 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.30 (t, *J* 7.0 Hz, 1H), 5.00 (s, 2H), 4.52 (d, *J* 7.0 Hz, 2H), 2.34–2.17 (m, 4H), 1.61–1.38 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 157.4, 148.0, 118.9, 61.7, 37.7, 30.0, 29.7, 28.9, 28.6, 27.2; FTIR (film) v: 3450, 3333, 3266, 3202, 2920, 2849, 1702, 1606, 1335, 1058 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{10}H_{17}NO_2Na$ [M + Na$^+$] 206.1157; Found 206.1157.

Rearrangement of Carbamates 5 to Carbamates 8. General Procedure. To a solution of allyl carbamate **5** (0.74 mmol) and Et_3N (450 mg, 620 μL, 4.44 mmol) in dry THF (10 mL) cooled to 0 °C was added TFAA (311 mg, 200 μL, 1.48 mmol), and the resulting mixture was warmed to room temperature slowly. After 1 h, dry MeOH (5 mL) and Bu_3SnOMe (0.1 mmol, 32 mg, 30 μL) were added, and the reaction mixture was stirred overnight. After the removal of the solvents, the crude product was supported on silica gel and chromatographed on silica gel to afford the methoxy carbamate **8**.

Methyl (1,1-Diphenylallyl)carbamate (8a). Yield 127 mg (79%) starting from 150 mg (0.59 mmol) of carbamate **5a**; waxy solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.38–7.21 (m, 10H), 6.88–6.72 (m, 1H), 5.63 (br s, 1H), 5.38 (d, *J* 10.7 Hz, 1H), 4.86 (d, *J* 17.4 Hz, 1H), 3.61 (br s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 143.5, 140.8, 128.2,

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127.7, 127.3, 116.2, 67.1, 51.9; FTIR (film) ν: 3412, 3342, 1737, 1493, 1447, 1246, 1190, 1037, 766, 701 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{17}H_{17}NO_2Na$ [M + Na^+] 290.1157; Found 290.1147.

Methyl (3-Ethylpent-1-en-3-yl)carbamate (8b). Yield 95 mg (63%) starting from 150 mg (0.76 mmol) of carbamate **5b**; colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ: 5.69 (dd, J 17.6, 11.0 Hz, 1H), 5.16 (d, J 11.0 Hz, 1H), 5.02 (d, J 17.6 Hz, 1H), 4.61 (s, 1H), 3.62 (s, 3H), 1.73−1.53 (m, 4H), 0.79 (t, J 7.4 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 155.2, 142.0, 113.0, 59.8, 51.5, 27.7, 15.6; FTIR (film) ν: 3451, 2968, 2937, 1719, 1246, 1102 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_9H_{17}NO_2Na$ [M + Na^+] 194.1157; Found 194.1153.

Methyl (2,2,3,3,9,9,10,10-Octamethyl-6-vinyl-4,8-dioxa-3,9-disilaundecan-6-yl)carbamate (8c). Yield 114 mg (73%) starting from 150 mg (0.386 mmol) of carbamate **5c**; column chromatography on silica gel (2% AcOEt in hexanes); colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ: 6.00 (dd, J 17.6, 11.0 Hz, 1H), 5.25−5.18 (m, 2H), 3.61 (s, 4H), 0.89 (s, 18H), 0.06 (s, 6H), 0.05 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 165.1, 136.8, 115.2, 63.9, 60.5, 52.3, 51.6, 25.8, 18.2, −5.5; FTIR (film) ν: 3434, 3354, 1739, 1498, 1254, 1084, 838, 777 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{19}H_{41}NO_4Si_2Na$ [M + Na^+] 426.2472. Found 426.2476.

Benzyl (1-Vinylcyclopropyl)carbamate (8d). Yield 114 mg (67%) starting from 100 mg (0.786 mmol) of carbamate **5d**; purification by column chromatography on silica gel (10% AcOEt in hexanes); colorless crystals; mp 85−86 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.30 (m, 5H), 5.46 (dd, J 17.0, 10.5 Hz, 1H), 5.26 (s, 1H), 5.10 (s, 2H), 5.06 (d, J 17.0 Hz, 1H), 5.00 (d, J 10.5 Hz, 1H), 1.16−1.05 (m, 2H), 0.98−0.90 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.9, 140.4, 136.5, 128.5, 128.2, 128.1, 110.9, 66.61, 34.8, 16.5; FTIR (film) ν: 3442, 3329, 3088, 3013, 2551, 2924, 2898, 1693, 1661, 1637, 1520, 1258, 1090, 897, 747, 699 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{15}NO_2Na$ [M + Na^+] 240.1000; Found 240.1004

Methyl (1-Vinylcyclobutyl)carbamate (8e). Yield 171 mg (78%) starting from 200 mg (1.42 mmol) of carbamate **5e**; column chromatography on silica gel (15% AcOEt in hexanes); colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ: 6.09 (dd, J 17.2, 10.5 Hz, 1H), 5.16 (d, J 17.2 Hz, 1H), 5.08 (d, J 10.5 Hz, 1H), 4.93 (s, 1H), 3.63 (s, 3H), 2.35−2.16 (m, 4H), 1.97−1.88 (m, 2H), 1.86−1.76 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 155.2, 141.3, 111.6, 57.3, 51.7, 33.0, 14.7; FTIR (film) ν: 3327, 2216, 1705, 1522, 1257, 1085, 915 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_8H_{13}NO_2Na$ [M + Na^+] 178.0844. Found 178.0846.

Methyl (1-Vinylcyclopentyl)carbamate (8f). Yield 75%; colorless oil; column chromatography on silica gel (15% AcOEt in hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ: 5.94 (dd, J 17.3, 10.6 Hz, 1H), 5.09 (dd, J 17.3, 0.8 Hz, 1H), 5.03 (d, J 10.6 Hz, 1H), 4.74 (s, 1H), 3.61 (s, 3H), 2.02−1.88 (m, 2H), 1.82−1.64 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.5, 154.6, 141.9, 111.8, 64.5, 51.6, 38.1, 23.1; FTIR (film) ν: 3340, 2933, 1721, 1525, 1250, 1100 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_9H_{15}NO_2Na$ [M + Na^+] 192.1000. Found 192.1006.

Methyl 1-Vinylcyclohexylcarbamate (8g). Yield 282 mg (87%) starting from 300 mg (1.77 mmol) of carbamate **5g**; yellowish oil; column chromatography on silica gel (20% AcOEt in hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ: 5.92 (dd, J 17.5, 10.7 Hz, 1H), 5.12 (d, J 17.5 Hz, 1H), 5.07 (d, J 10.7 Hz, 1H), 4.60 (s, 1H), 3.62 (s, 3H), 2.00 (m, 2H), 1.70−1.19 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 155.2, 143.6, 112.3, 55.6, 51.5, 35.1, 25.5, 21.6; FTIR (film) ν: 3343, 2933, 1719, 1526, 1251, 1105 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{10}H_{17}NO_2Na$ [M + Na^+] 206.1157; Found 206.1160.

Methyl (4-Vinyltetrahydro-2*H*-pyran-4-yl)carbamate (8h). Yield 292 mg (90%) starting from 300 mg (1.75 mmol) of carbamate **5h**; colorless crystals; mp 56.5−57.5 °C; ^1H NMR (500 MHz, $CDCl_3$) δ: 5.93 (dd, J 17.4, 10.7 Hz, 1H), 5.21−5.08 (m, 2H), 4.67 (s, 1H), 3.79−3.65 (m, 4H), 3.63 (s, 3H), 1.99 (br d, J 14.0 Hz, 2H), 1.85 (ddd, J 14.0, 9.8, 4.4 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 142.1, 113.4, 63.4, 53.4, 51.7, 35.3; FTIR (film) ν: 3519, 3325, 1712, 1532, 1262, 1104 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_9H_{15}NO_3Na$ [M + Na^+] 208.0950. Found 208.0944.

***t*-Butyl 4-((Methoxycarbonyl)amino)-4-vinylpiperidine-1-carboxylate (8i).** Yield 191 mg (90%) starting from 200 mg (0.74 mmol) of carbamate **5i**; colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ: 5.90 (dd, J 17.4, 10.7 Hz, 1H), 5.19−5.11 (m, 2H), 4.64 (s, 1H), 3.80−3.66 (m, 2H), 3.62 (s, 3H), 3.20−3.09 (m, 2H), 2.10−1.93 (m, 2H), 1.77−1.63 (m, 2H), 1.45 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 154.7, 141.9, 113.5, 79.6, 54.3, 51.7, 39.5, 34.5, 28.4, 26.9; FTIR (film) v: 3330, 1732, 1697, 1674, 1250, 1162 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{14}H_{24}N_2O_4Na$ [M + Na^+] 307.1634. Found 307.1633.

Methyl (1-Vinylcycloheptyl)carbamate (8j). Yield 155 mg (90%) starting from 200 mg (0.87 mmol) of carbamate **5j**; yellowish oil; ^1H NMR (400 MHz, $CDCl_3$) δ: 5.90 (dd, J 17.4, 10.7 Hz, 1H), 5.03 (d, J 17.4 Hz, 1H), 4.97 (d, J 10.7 Hz, 1H), 4.75 (s, 1H), 3.56 (s, 3H), 1.92−1.36 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.2, 144.1, 111.2, 59.3, 51.4, 38.4, 29.1, 22.1; FTIR (film) ν: 3342, 2925, 1713, 1525, 1242 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{11}H_{19}NO_2Na$ [M + Na^+] 220.1313; Found 220.1313.

***t*-Butyl (1-Vinylcyclohexyl)carbamate (8k).** To a solution of allyl carbamate **5g** (150 mg, 0.89 mmol) and Et_3N (538 mg, 740 μL, 5.32 mmol) in dry THF (10 mL) cooled to 0 °C was added TFAA (373 mg, 246 μL, 1.77 mmol), and the resulting mixture was warmed to room temperature slowly. In a separate flask, a 1 M soln. of LiHMDS (5.3 mL, 5.32 mmol) was added to a solution of *t*-BuOH (1 mL) in dry THF (10 mL). After 1 h, the solution of *t*-BuOLi was added to the generated allyl isocyanate, and the reaction mixture was stirred for 2 h. Then, the volatiles were removed under diminished pressure. The residue was purified by flash chromatography on silica gel (7% AcOEt in hexanes) to afford 172 mg of compound **8k** (88%) as a waxy solid; ^1H NMR (400 MHz, $CDCl_3$) δ: 5.87 (dd, J 17.4, 10.7 Hz, 1H), 5.05 (dd, J 17.5, 1.0 Hz, 1H), 5.00 (dd, J 10.7, 0.9 Hz, 1H), 4.44 (s, 1H), 1.55−1.42 (m, 10H), 1.38 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 144.0, 128.3, 128.2, 111.8, 55.5, 35.2, 28.40, 28.39, 25.5, 21.6; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{23}NO_2Na$ [M + Na^+] 248.1629 Found 248.1636; FTIR (film) ν: 3449, 3358, 3277, 2977, 2931, 2858, 1725, 1694, 1494, 1451, 1389, 1365, 1247, 1170, 1088, 967, 906, 778 cm^{-1}.

Benzyl (1-Vinylcyclohexyl)carbamate (8l). To a solution of allyl carbamate **5g** (150 mg, 0.89 mmol) and Et_3N (538 mg, 740 μL, 5.32 mmol) in dry THF (10 mL) cooled to 0 °C was added TFAA (373 mg, 246 μL, 1.77 mmol), and the resulting mixture was warmed to room temperature slowly. In a separate flask, a 1 M soln. of LiHMDS (5.43 mL, 5.3 mmol) was added to a solution of BnOH (550 μL, 5.3 mmol) in dry THF (10 mL). After 1 h, the solution of BnOLi was added to the generated allyl isocyanate, and the reaction mixture was stirred for 2 h. Then, the volatiles were removed under diminished pressure. The residue was purified by flash chromatography on silica gel (5% AcOEt in hexanes) to afford 151 mg of **8l** (66%) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.37−7.28 (m, 5H), 5.95 (dd, J 17.5, 10.7 Hz, 1H), 5.13 (d, J 17.5 Hz, 1H), 5.10−5.06 (m, 3H), 4.75 (s, 1H, *NH*), 2.00 (m, 2H), 1.64−1.44 (m, 7H), 1.36−1.21 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 143.6, 136.8, 128.5, 128.06, 128.01, 112.4, 66.2, 55.8, 35.1, 25.5, 21.7; HRMS (ESI-TOF) m/z calcd for $C_{16}H_{21}NO_2Na$ [M + Na^+] 282.1470 Found 282.1476; FTIR (film) ν: 3343, 2932, 2857, 1710, 1499, 1452, 1245, 1211, 1092, 963, 915, 739, 697 cm^{-1}.

***N*-(1-Vinylcyclohexyl)formamide (10).** To a solution of allyl carbamate **5g** (150 mg, 0.89 mmol) and Et_3N (538 mg, 740 μL, 5.32 mmol) in dry THF (10 mL) cooled to 0 °C was added TFAA (373 mg, 246 μL, 1.77 mmol), and the resulting mixture was warmed to room temperature slowly. After 1 h, $NaBH_4$ (5.32 mmol, 205 mg) was added, and the reaction mixture was stirred at room temperature for an additional 2 h. After the removal of the solvent, the residue was chromatographed on silica gel (35% AcOEt in hexanes) to afford 87 mg (64%) of compound **10** as a colorless oil; ^1H NMR (400 MHz, $CDCl_3$, mixture of rotamers in 1:1 ratio) δ: 8.11 (s, 1H), 8.08 (s, 1H), 6.52 (s, 1H), 5.93 (dd, J 17.5, 10.7 Hz, 1H), 5.84 (dd, J 17.4, 10.7 Hz, 1H), 5.64 (s, 1H), 5.20−5.00 (m, 4H), 2.12−1.21 (m, 20H); ^{13}C NMR (101 MHz, $CDCl_3$, mixture of rotamers in 1:1 ratio) δ: 164.8, 160.5, 144.2, 142.8, 114.0, 112.5, 57.1, 55.7, 36.8, 35.1, 25.4, 25.2, 21.7, 21.3; FTIR (film) ν: 3280, 2933, 2857, 1686, 1535 cm^{-1}; HRMS

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(EST-TOF) m/z calcd for $C_9H_{15}NONa$ [M + Na^+] 176.1051; Found 176.1054.

1-(1-Vinylcyclohexyl)urea (11a). To a solution of allyl carbamate **5g** (150 mg, 0.89 mmol) and Et_3N (538 mg, 740 μL, 5.32 mmol) in dry THF (10 mL) cooled to 0 °C was added TFAA (373 mg, 246 μL, 1.77 mmol), and the resulting mixture was warmed to room temperature slowly. After 1 h, a 7 N soln. of NH_3 in MeOH (2 mL) was added, and the resulting mixture was stirred overnight. Next, the volatiles were removed and the residue was chromatographed on silica gel (AcOEt/hexanes 3:1) to afford 89 mg (60%) of **11a** as an off-white solid; mp 99−100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.90 (dd, *J* 17.5, 10.7 Hz, 1H), 5.33 (s, 1H), 5.13 (d, *J* 17.5 Hz, 1H), 5.05 (d, *J* 10.7 Hz, 1H), 4.92 (s, 2H), 1.96−1.80 (m, 2H), 1.61−1.38 (m, 7H), 1.29−1.16 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 158.9, 144.9, 112.7, 55.5, 35.5, 25.6, 21.6; FTIR (film) ν: 3352, 3348, 3206, 3084, 2932, 2855, 1656, 1601, 1552, 1449, 1355 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_9H_{16}N_2ONa$ [M + Na^+] 191.1160; Found 191.1158.

1-Benzyl-3-(1-vinylcyclohexyl)urea (11b). To a solution of allyl carbamate **5g** (150 mg, 0.89 mmol) and Et_3N (538 mg, 740 μL, 5.32 mmol) in dry THF (10 mL) cooled to 0 °C was added TFAA (373 mg, 246 μL, 1.77 mmol), and the resulting mixture was warmed to room temperature slowly. After stirring for 1.5 h, $BnNH_2$ (290 mg, 290 μL, 2.67 mmol) was added, and the reaction mixture was stirred overnight. Then, the reaction mixture was diluted with AcOEt (50 mL) and washed with 1 M HCl (10 mL), water (15 mL), and brine (15 mL). After drying over anhydr. Na_2SO_4, the solvents were removed and the residue was purified by flash chromatography on silica gel (20% to 50% AcOEt in hexanes) to afford 195 mg of **11b** (85%) as colorless crystals; mp 120−121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41−7.12 (m, 5H), 5.95 (dd, *J* 17.6, 10.7 Hz, 1H), 5.19 (dd, *J* 17.6, 0.9 Hz, 1H), 5.13 (dd, *J* 10.7, 0.8 Hz, 1H), 4.88 (br s, 1H), 4.42 (s, 1H), 4.36 (d, *J* 5.7 Hz, 2H), 1.93−1.82 (m, 2H), 1.66−1.43 (m, 6H), 1.28 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 158.0, 145.1, 140.0, 128.3, 127.1, 126.7, 112.1, 55.4, 43.8, 35.7, 25.6, 21.6; FTIR (film) ν: 3331, 3183, 3114, 1641, 1630, 1567 cm^{-1}; HRMS (EST-TOF) m/z calcd for $C_{16}H_{22}N_2ONa$ [M + Na^+] 281.1630; Found 281.1633.

1,1-Dibutyl-3-(1-vinylcyclohexyl)urea (11c). Prepared following the procedure for the synthesis of **11b**; yield 223 mg (90%) starting from 150 mg (0.89 mmol) of carbamate **5g**; purification by chromatography on silica gel (8% to 50% AcOEt in hexanes); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.95 (dd, *J* 17.5, 10.7 Hz, 1H), 5.00−4.90 (m, 2H), 4.11 (s, 1H), 3.11−3.06 (m, 4H), 2.03−1.95 (m, 2H), 1.56−1.15 (m, 16H), 0.84 (t, *J* 7.4 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 156.2, 145.1, 111.1, 55.7, 47.1, 35.6, 30.8, 25.6, 21.9, 20.1, 13.8; FTIR (film) ν: 3468, 3365, 2930, 1634, 1521 cm^{-1}; HRMS (EST-TOF) m/z calcd for $C_{17}H_{32}N_2ONa$ [M + Na^+] 303.2412; Found 303.2413.

***N*-(1-Vinylcyclohexyl)acetamide (12a).** To a solution of allyl carbamate **5g** (150 mg, 0.89 mmol) and Et_3N (538 mg, 740 μL, 5.32 mmol) in dry THF (10 mL) cooled to 0 °C was added TFAA (373 mg, 256 μL, 1.77 mmol), and the resulting mixture was warmed to room temperature slowly. After 1 h, the reaction mixture was cooled to −50 °C and a 3 M soln. of MeMgBr (1.8 mL, 5.3 mmol) was added dropwise. After stirring at −50 °C for 30 min, the reaction mixture was warmed to room temperature and stirred at that temperature for an additional 2 h. Next, the reaction mixture was poured onto sat. NH_4Cl and extracted with Et_2O. The combined organic layers were dried over anhydr. Na_2SO_4. After the removal of the solvent, the residue was chromatographed on silica gel (20% AcOEt in hexanes) to afford 95 mg of **12a** (64%) as a yellowish solid; mp 70−71 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.95 (dd, *J* 17.5, 10.7 Hz, 1H), 5.43 (s, 1H), 5.11−4.92 (m, 2H), 2.06−1.98 (m, 2H), 1.93 (s, 3H), 1.60−1.34 (m, 7H), 1.34−1.15 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 169.2, 143.2, 112.0, 56.7, 34.9, 25.4, 24.3, 21.7; FTIR (film) ν: 3302, 3081, 2930, 2856, 1655, 1549 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{10}H_{17}NONa$ [M + Na^+] 190.1208; Found 190.1201.

***N*-(1-Vinylcyclohexyl)benzamide (12b).** Prepared following the procedure for **12a**; yield 146 mg (56%) starting from 150 mg (0.89 mmol) of compound **5g**; purification by chromatography on silica gel (20% AcOEt in hexanes); yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.73 (d, *J* 7.3 Hz, 2H), 7.58−7.34 (m, 3H), 6.07 (dd, *J* 17.5, 10.7 Hz, 1H), 5.98 (s, 1H), 5.16 (d, *J* 17.5 Hz, 1H), 5.10 (d, *J* 10.7 Hz, 1H), 2.22 (m, 2H), 1.70−1.23 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.8, 143.1, 135.8, 131.3, 128.6, 126.8, 112.5, 57.1, 35.1, 25.6, 22.0; FTIR (film) ν: 3315, 29932, 2857, 1650, 1530, 1176, 1166, 712 cm^{-1}; HRMS (EST-TOF) m/z calcd for $C_{15}H_{19}NONa$ [M + Na^+] 252.1364; Found 252.1369.

***N*-(1-Vinylcyclohexyl)pivalamide (12c).** Prepared following the procedure for **12a**; yield 120 mg (65%) starting from 150 mg of carbamate **5g**; purification by chromatography on silica gel (hexanes/AcOEt 6:1); yellowish solid; mp 74−76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.91 (dd, *J* 17.5, 10.7 Hz, 1H), 5.38 (br s, 1H), 5.03−4.96 (m, 2H), 2.10−2.02 (m, 2H), 1.59−1.19 (m, 8H), 1.16 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 177.2, 143.5, 111.7, 55.9, 39.2, 34.8, 27.7, 25.4, 21.8; FTIR (film) ν: 3363, 2929, 1650, 1524 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{23}NONa$ [M + Na^+] 232.1677; Found 232.1671.

***N*-(1-Vinylcyclohexyl)isobutyramide (12d).** Prepared following the procedure for **12a**; yield 120 mg (69%) starting from 150 mg of carbamate **5g**; purification by chromatography on silica gel (hexanes/AcOEt 6:1); yellowish solid; mp 102−103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.93 (dd, *J* 17.5, 10.7 Hz, 1H), 5.28 (br s, 1H), 5.09−4.90 (m, 2H), 2.31 (hept, *J* 6.9 Hz, 1H), 2.13−1.98 (m, 2H), 1.62−1.19 (m, 8H), 1.12 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 176.0, 143.4, 111.8, 56.2, 36.3, 34.9, 25.5, 21.8, 19.8; FTIR (film) ν: 3434, 3312, 1652, 1543, 1243 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{12}H_{21}NONa$ [M + Na^+] 218.1521; Found 218.1522.

***N*-(1-Vinylcyclohexyl)cyclohexanecarboxamide (12e).** Prepared following the procedure for **12a**; yield 117 mg (56%) starting from 150 mg (0.89 mmol) of carbamate **5e**; purification by chromatography on silica gel (hexanes/AcOEt 8:1 v/v); off-white solid; mp 142−143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.93 (dd, *J* 17.5, 10.7 Hz, 1H), 5.25 (s, 1H), 5.06−4.95 (m, 2H), 2.12−1.07 (m, 21H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 175.2, 143.6, 111.8, 56.3, 46.3, 35.0, 30.0, 25.8, 25.5, 21.9; FTIR (film) ν: 3280, 3081, 3006, 2926, 2852, 1651, 1555, 1448, 1260, 1222, 902 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{15}H_{25}NONa$ [M + Na^+] 258.1834; Found 258.1830.

2-Phenyl-*N*-(1-vinylcyclohexyl)acetamide (12f). Prepared following the procedure for **12a**; yield 150 mg (70%) starting from 150 mg (0.89 mmol) of carbamate **5g**; purification by chromatography on silica gel (hexanes/AcOEt 8:1 v/v); yellowish solid; mp 96−97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40−7.31 (m, 2H), 7.31−7.22 (m, 3H), 5.94 (dd, *J* 17.7, 10.5 Hz, 1H), 5.23 (s, 1H), 5.03−4.98 (m, 2H), 3.53 (s, 2H), 2.01−1.92 (m, 2H), 1.53−1.12 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 170.0, 143.2, 135.6, 129.4, 129.1, 127.4, 112.1, 56.7, 45.0, 34.8, 25.4, 21.7; FTIR (film) ν: 3310, 3084, 3063, 3030, 2931, 2854, 1652, 1546, 1451, 899, 724, 699 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{16}H_{21}NONa$ [M + Na^+] 266.1521; Found 266.1523.

***N*-(1-Vinylcyclohexyl)-1-naphthamide (12g).** Yield 136 mg (55%) starting from 150 mg (0.89 mmol) of carbamate **5g**; yellowish solid; mp 132−133 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.32 (d, *J* 8.2 Hz, 1H), 7.89 (d, *J* 8.2 Hz, 1H), 7.86 (d, *J* 7.5 Hz, 1H), 7.61 (d, *J* 7.0 Hz, 1H), 7.58−7.49 (m, 2H), 7.48−7.41 (m, 1H), 6.20 (dd, *J* 17.5, 10.7 Hz, 1H), 5.79 (br s, 1H), 5.30 (d, *J* 17.5 Hz, 1H), 5.21 (d, *J* 10.7 Hz, 1H), 2.32−2.23 (m, 2H), 1.75−1.51 (m, 7H), 1.42−1.33 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 168.8, 143.1, 135.7, 133.7, 130.2, 130.1, 128.2, 127.0, 126.3, 125.4, 124.7, 124.4, 112.5, 57.5, 35.1, 25.5, 22.0; FTIR (film) ν: 3281, 3047, 2930, 2855, 1646, 1533, 1513, 1257, 780 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{19}H_{21}NONa$ [M + Na^+] 302.1521; Found 302.1515.

2-Methoxy-*N*-(1-vinylcyclohexyl)benzamide (12h). Prepared following the procedure for **12a**; yield 147 mg (64%) starting from 150 mg (0.89 mmol) of carbamate **5g**; purification by chromatography on silica gel (hexanes/AcOEt 8:1 v/v); yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.14 (dd, *J* 7.8, 1.8 Hz, 1H), 7.86 (s, 1H), 7.42−7.33 (m, 1H), 7.07−6.97 (m, 1H), 6.95−6.90 (m, 1H), 6.08 (dd, *J* 17.5, 10.7 Hz, 1H), 5.12 (dd, *J* 17.5, 1.0 Hz, 1H), 5.04 (dd, *J* 10.7, 1.0 Hz, 1H), 3.92 (s, 3H), 2.32−2.15 (m, 2H), 1.70−1.41 (m, 7H), 1.34−1.19 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 163.8, 157.2, 143.9, 132.4,

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132.0, 122.6, 121.2, 111.7, 111.3, 56.7, 55.9, 35.1, 25.5, 21.7; IR (film) ν: 3392, 3077, 2932, 2856, 1661, 1600, 1535, 143, 1300, 1236, 1020, 757 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{16}H_{21}NO_2Na$ [M + Na^+] 282.1470; Found 282.1465.

2,4,6-Trimethyl-*N*-(1-vinylcyclohexyl)benzamide (12i). Prepared following the procedure for **12a**; yield 125 mg (52%) starting from 150 mg (0.89 mmol) of carbamate **5g**. The Grignard reagent was generated in a separate flask from 2-bromomesitylene and magnesium in dry THF; purification by chromatography on silica gel (hexanes/AcOEt 8:1 v/v); mp 141−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.82 (s, 2H), 6.23 (dd, J 17.6, 10.8 Hz, 1H), 5.48 (s, 1H), 5.24 (dd, J 17.6, 0.7 Hz, 1H), 5.17 (dd, J 10.8, 0.7 Hz, 1H), 2.33 (s, 6H), 2.27 (s, 3H), 2.23−2.13 (m, 2H), 1.77−1.31 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 169.6, 143.4, 138.1, 135.8, 134.1, 128.2, 112.9, 56.9, 35.0, 25.6, 22.0, 21.0, 19.3; IR (film) ν: 3261, 2999, 2933, 2850, 1637, 1533, 1449, 848 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{18}H_{25}NONa$ [M + Na^+] 294.1834; Found 294.1827.

3-Phenyl-*N*-(1-vinylcyclohexyl)propiolamide (13a). To a solution of allyl carbamate **5g** (150 mg, 0.89 mmol) and Et_3N (538 mg, 740 μL, 5.32 mmol) in dry THF (10 mL) cooled to 0 °C was added TFAA (373 mg, 246 μL, 1.77 mmol), and the resulting mixture was warmed to room temperature slowly. In a separate flask, a solution of phenylacetylene (580 μL, 541 mg, 5.32 mmol) in dry THF (10 mL) was cooled to −78 °C and 2.5 M n-BuLi (2.1 mL) was added dropwise. After 1 h, the solution of generated allyl isocyanate was added to the solution of the organolithium reagent, and the reaction mixture was stirred at −78 °C for 2 h. The reaction was quenched with the addition of water (10 mL), and the postreaction mixture was extracted with Et_2O. The combined organic layers were dried over anhydr. Na_2SO_4. After the removal of volatiles, the residue was purified by flash chromatography on silica gel (5% AcOEt in hexanes) to afford 120 mg of **13a** (53%) as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.56−7.46 (m, 2H), 7.42−7.24 (m, 3H), 5.99 (dd, J 17.5, 10.7 Hz, 1H), 5.80 (s, 1H), 5.17 (d, J 17.5 Hz, 1H), 5.10 (d, J 10.7 Hz, 1H), 2.17−2.04 (m, 2H), 1.69−1.44 (m, 7H), 1.35−1.24 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.4, 142.2, 132.5, 132.1, 129.9, 129.4, 128.4, 128.3, 120.4, 112.9, 58.0, 34.9, 25.3, 21.7; FTIR (film) ν: 3253, 3038, 3056, 2932, 2857, 2218, 1631, 1537, 1444, 1302, 1198, 757, 689 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{17}H_{19}NONa$ [M + Na^+] 276.1364; Found 276.1360.

4,4-Diethoxy-*N*-(1-vinylcyclohexyl)but-2-ynamide (13b). Yield 215 mg (57%) starting from 150 mg (0.89 mmol) of compound **5g**; yellowish oil; ^{1}H NMR (500 MHz, C_6D_6) δ: 5.88 (dd, J 17.5, 10.7 Hz, 1H), 5.33−5.28 (m, 1H), 5.22 (s, 1H), 5.04 (dd, J 17.5, 0.9 Hz, 1H), 4.97 (dd, J 10.7, 0.8 Hz, 1H), 3.66−3.57 (m, 2H), 3.44−3.37 (m, 2H), 1.92−1.79 (m, 2H), 1.29−1.10 (m, 8H), 1.04 (t, J 7.1 Hz, 6H); ^{13}C NMR (126 MHz, C_6D_6) δ: 150.9, 142.7, 112.8, 91.7, 80.3, 78.4, 61.5, 57.9, 34.7, 25.5, 21.8, 15.1; FTIR (film) ν: 3277, 2978, 2932, 2860, 1642, 1534, 1449, 1325, 1286, 1269, 1119, 1054, 1015, 918, 658 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{16}H_{25}NO_3Na$ [M + Na^+] 302.1732; Found 302.1722.

***N*-(1-Vinylcyclohexyl)propiolamide (13c).** Prepared in the same manner as compound **13a**; yield 82 mg (54%) starting from 150 mg (0.89 mmol) of carbamate **5g** and trimethylsilylacetylene (522 mg, 750 μL, 5.32 mmol); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.94 (dd, J 17.5, 10.7 Hz, 1H), 5.13 (d, J 17.5 Hz, 1H), 5.09 (d, J 10.8 Hz, 1H), 2.70 (s, 1H), 2.10−1.99 (m, 2H), 1.67−1.39 (m, 7H), 1.35−1.21 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 151.1, 142.0, 113.1, 78.2, 71.6, 58.1, 34.9, 25.4, 21.8; FTIR (film) ν: 3287, 3085, 3045, 2933, 2857, 2106, 1640, 1533, 1450, 1284, 1267, 921, 670 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{11}H_{15}NONa$ [M + Na^+] 200.1051; Found 200.1043.

2-Oxo-*N*-(1-vinylcyclohexyl)cyclohexane-1-carboxamide (14a). Waxy solid; yield 127 mg (57%) starting from 150 mg (0.89 mmol) of carbamate **5g**; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.87 (s, 1H), 5.94 (dd, J 17.5, 10.7 Hz, 1H), 5.06 (d, J 17.5 Hz, 1H), 5.02 (d, J 10.8 Hz, 1H), 3.19−3.06 (m, 1H), 2.48−2.29 (m, 4H), 2.00−1.21 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 207.2, 168.5, 145.2, 113.5, 61.3, 56.4, 40.1, 33.4 (×2), 26.5, 25.4, 24.5, 24.3, 21.8 (×2); FTIR (film) ν: 3276, 3083, 2927, 2859, 1711, 1650, 1637, 1557 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{15}H_{23}NO_2Na$ [M + Na^+] 272.1626; Found 272.1623.

3-Oxo-3-phenyl-*N*-(1-vinylcyclohexyl)propanamide (14b). Yield 129 mg (53%) starting from 150 mg (0.888 mmol) of carbamate **5g**; waxy solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.01−7.97 (m, 2H), 7.62−7.56 (m, 1H), 7.51−7.44 (m, 2H), 6.97 (s, 1H), 5.97 (dd, J 17.5, 10.7 Hz, 1H), 5.07 (dd, J 17.5, 0.8 Hz, 1H), 5.03 (dd, J 10.7, 0.8 Hz, 1H), 3.91 (s, 2H), 2.15−2.05 (m, 2H), 1.61−1.39 (m, 7H), 1.31−1.25 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 196.7, 164.3, 143.1, 136.3, 134.0, 128.8, 128.6, 112.1, 57.0, 46.5, 34.9, 25.4, 21.7; FTIR (film) ν: 3315, 3082, 3063, 2932, 2856, 1688, 1650, 1544, 1448, 1334, 1277, 1210, 756, 689 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{17}H_{21}NO_2Na$ [M + Na^+] 294.1470; Found 294.1464.

***N*-(1-Vinylcyclohexyl)furan-2-carboxamide (15a).** To a solution of allyl carbamate **5g** (150 mg, 0.89 mmol) and Et_3N (538 mg, 740 μL, 5.32 mmol) in dry THF (10 mL) cooled to 0 °C was added TFAA (373 mg, 246 μL, 1.77 mmol), and the resulting mixture was warmed to room temperature slowly. In a separate flask, a solution of furan (450 μL, 6.22 mmol) in dry THF (10 mL) was cooled to −78 °C and 2.5 M n-BuLi (2.1 mL) was added dropwise. After 1 h, a solution of the generated allyl isocyanate was added to the solution of organolithium reagent, and the reaction mixture was stirred at −78 °C for 2 h. The reaction was quenched with the addition of water (10 mL), and the postreaction mixture was extracted with Et_2O. The combined organic layers were dried over anhydr. Na_2SO_4. After the removal of the volatiles, the residue was purified by flash chromatography on silica gel (5% AcOEt in hexanes) to afford 107 mg of **15a** (55%) as a waxy solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41−7.37 (m, 1H), 7.04−6.99 (m, 1H), 6.45 (dd, J 3.4, 1.8 Hz, 1H), 6.16 (s, 1H), 6.02 (dd, J 17.5, 10.7 Hz, 1H), 5.13 (d, J 17.5 Hz, 1H), 5.07 (d, J 10.7 Hz, 1H), 2.18 (m, 2H), 1.66−1.42 (m, 7H), 1.36−1.23 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 157.4, 148.6, 143.4, 142.9, 113.7, 112.5, 112.1, 56.8, 35.1, 25.4, 21.8; FTIR (film) ν: 3428, 3321, 3117, 1662, 1591, 1518, 1475, 1181, 759 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{17}NO_2Na$ [M + Na^+] 242.1157; Found 242.1152.

1-Methyl-*N*-(1-vinylcyclohexyl)-1*H*-imidazole-2-carboxamide (15b). Prepared following the procedure for **15a**; yield 112 mg (54%) starting from 150 mg (0.89 mmol) of carbamate **5g**; waxy solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.30 (s, 1H), 6.93 (s, 1H), 6.89 (s, 1H), 5.99 (dd, J 17.5, 10.7 Hz, 1H), 5.14 (d, J 17.5 Hz, 1H), 5.06 (d, J 10.7 Hz, 1H), 3.98 (s, 3H), 2.23−2.09 (m, 2H), 1.72−1.41 (m, 7H), 1.33−1.19 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 158.4, 143.2, 139.5, 127.2, 125.4, 112.4, 56.7, 35.6, 35.1, 25.4, 21.8; FTIR (film) ν: 3383, 3231, 3102, 2931, 2857, 1677, 1537, 1501, 1473 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{19}N_3ONa$ [M + Na^+] 256.1426; Found 256.1416.

Oxidation of Allylamines to Amino Acids 16. General Procedure. Ozone was passed through a solution of carbamate **8g** (166 mg, 0.91 mmol) in dry CH_2Cl_2 (20 mL) cooled to −78 °C until the solution turned blue. Then, the excess of ozone was removed by the bubbling of oxygen. After the addition of Me_2S (4 mL), the resulting mixture was warmed to room temperature and stirred for 1 h. After that, the solvent was removed under diminished pressure. The residue was dissolved in t-BuOH/H_2O (4:1 v/v, 15 mL), followed by the addition of $NaH_2PO_4{\cdot}H_2O$ (364 mg, 2.64 mmol), 2-methyl-2-butene (230 μL), and $NaClO_2$ (pur. 80%, 304 mg, 2.69 mmol). The resulting mixture was stirred overnight. After the removal of the solvents, the residue was purified by flash chromatography on silica gel (30% AcOEt in hexanes) to afford 113 mg (62%, 2 steps) of amino acid **16a** as an off-white solid.

1-((Methoxycarbonyl)amino)cyclohexane-1-carboxylic Acid (16a). mp 177−178 °C; ^{1}H NMR (400 MHz, MeOH-d_4) δ: 3.60 (s, 3H), 2.02 (d, J 11.5 Hz, 2H), 1.80 (td, J 13.7, 12.7, 4.0 Hz, 2H), 1.66−1.44 (m, 5H), 1.37−1.27 (m, 1H); ^{13}C NMR (101 MHz, MeOH-d_4) δ: 177.1, 157.1, 58.7, 50.8, 32.1, 25.1, 21.0; IR (film) ν: 3338, 3127, 2931, 2847, 1717, 1672, 1531, 1457, 1389, 1211, 1122, 1059, 782 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_9H_{15}NO_4Na$ [M + Na^+] 224.0899; Found 224.0895.

1-((*t*-Butoxycarbonyl)amino)cyclohexane-1-carboxylic Acid (16b). Yield 109 mg (61%) starting from 160 mg (0.74 mmol) of

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compound **8k**; purification by flash column chromatography on silica gel (40% AcOEt in hexanes); colorless crystals, mp 168−170 °C decomp.; ^{1}H NMR (400 MHz, MeOH-d_4) δ: 2.03−1.90 (m, 2H), 1.84−1.73 (m, 2H), 1.63−1.47 (m, 5H), 1.42 (s, 9H), 1.36−1.24 (m, 1H); ^{13}C NMR (101 MHz, MeOH-d_4) δ: 177.4, 155.9, 63.1, 58.5, 32.3, 27.4, 27.3, 25.1, 21.1; IR (film) ν: 3315, 2977, 2937, 2860, 1714, 1651, 1399, 1250, 1166 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{12}H_{21}NO_4Na$ [M + Na$^+$] 266.1368; Found 266.1366.

1-(((Benzyloxy)carbonyl)amino)cyclohexane-1-carboxylic Acid (16c). Yield 144 mg (67%) starting from 200 mg (0.77 mmol) of compound **8l**; purification by flash column chromatography on silica gel (40% AcOEt in hexanes); colorless crystals; mp 145−146 °C; ^{1}H NMR (400 MHz, MeOH-d_4) δ: 7.37−7.22 (m, 5H), 5.04 (s, 2H), 2.10−1.99 (m, 2H), 1.90−1.74 (m, 2H), 1.70−1.41 (m, 5H), 1.39−1.24 (m, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ: 177.1, 156.4, 136.9, 128.0, 127.5, 127.3, 65.8, 58.8, 32.1, 25.1, 21.0; IR (film) ν: 3331, 2938, 2860, 1712, 1513, 1453, 1415, 1348, 1249, 739, 697 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{15}H_{19}NO_4Na$ [M + Na$^+$] 300.1212; Found 300.1200.

1-(3,3-Dibutylureido)cyclohexane-1-carboxylic Acid (16d). Yield 131 mg (62%) starting from 200 mg (0.71 mmol) of compound **11c**; purification by flash column chromatography on silica gel (45% AcOEt in hexanes); colorless crystals; mp 47−48 °C; ^{1}H NMR (400 MHz, MeOH-d_4) δ: 4.89 (s, 1H), 3.28−3.21 (m, 4H), 2.13−2.02 (m, 2H), 1.87−1.76 (m, 2H), 1.67−1.46 (m, 10H), 1.40−1.26 (m, 4H), 0.94 (t, J 7.4 Hz, 6H); ^{13}C NMR (101 MHz, MeOH-d_4) δ: 178.0, 157.8, 58.7, 46.5, 32.6, 30.3, 25.3, 21.4, 19.7, 13.0; IR (film) ν: 3364, 2656, 2932, 2862, 1714, 1637, 1582, 1520, 1454, 1290, 1233 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{16}H_{30}N_2O_3Na$ [M + Na$^+$] 321.2154; Found 321.2149.

1-Benzamidocyclohexane-1-carboxylic Acid (16e). Yield 85 mg (63%) starting from 125 mg (0.55 mmol) of compound **12b**; off-white solid; mp 179−180 °C; ^{1}H NMR (400 MHz, CD_3OD) δ: 8.11 (s, 1H), 7.89−7.75 (m, 2H), 7.57−7.49 (m, 1H), 7.49−7.39 (m, 1H), 2.27−2.16 (m, 2H), 1.97−1.88 (m, 2H), 1.74−1.54 (m, 5H), 1.46−1.35 (m, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ: 176.5, 169.1, 134.7, 131.1, 128.0, 127.1, 59.3, 32.0, 25.2, 21.4; IR (film) ν: 3395, 3060, 3032, 2932, 2858, 1712, 1636, 1451, 1417, 1264, 1248, 1227, 1186, 1158, 712 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{14}H_{17}NO_3Na$ [M + Na$^+$] 270.1106; Found 270.1105.

1-Isobutyramidocyclohexane-1-carboxylic Acid (16f). Yield 54 mg (55%) starting from 90 mg of compound **12d**; colorless crystals; mp 199−201 °C; ^{1}H NMR (400 MHz, $CDCl_3$ + 20% CD_3OD) δ: 6.46 (s, 1H), 2.37−2.25 (m, 1H), 1.94−1.85 (m, 2H), 1.74−1.62 (m, 2H), 1.57−1.40 (m, 3H), 1.36−1.11 (m, 3H), 0.99 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$ + 20% CD_3OD) δ: 178.0, 176.4, 58.5, 34.9, 31.9, 27.0, 25.0, 21.2, 19.0; IR (film) v: 3313, 2970, 2934, 2861, 1708, 1646, 1539, 1287, 1242 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{11}H_{19}NO_3Na$ [M + Na$^+$] 236.1263; Found 236.1261.

1-Pivalamidocyclohexane-1-carboxylic Acid (16g). Yield 60 mg (55%) starting from 100 mg of compound **12c**; colorless crystals; mp 168−169 °C; ^{1}H NMR (400 MHz, $CDCl_3$ + 15% CD_3OD) δ: 5.85 (s, 1H), 2.07−1.91 (m, 2H), 1.85−1.69 (m, 2H), 1.66−1.51 (m, 3H), 1.36−1.21 (m, 3H), 1.16−1.09 (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$ + 5% CD_3OD) δ: 179.0, 178.1, 51.9, 38.7, 31.9, 27.2, 25.1, 21.5; IR (film) ν: 3357, 2969, 2950, 2924, 2856, 1707, 1637, 1517, 1410, 1286, 934, 686, 557 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{12}H_{21}NO_3Na$ [M + Na$^+$] 250.1419; Found 250.1420.

1-(Cyclohexanecarboxamido)cyclohexane-1-carboxylic Acid (16h). Yield 128 mg (55%) starting from 215 mg (0.91 mmol) of compound **12e**; off-white solid; mp 176−178 °C; ^{1}H NMR (400 MHz, CD_3OD) δ: 7.65 (s, 1H), 2.34−2.23 (m, 1H), 2.08−1.99 (m, 2H), 1.84−1.72 (m, 6H), 1.71−1.15 (m, 12H); ^{13}C NMR (101 MHz, CD_3OD) δ: 177.5, 176.8, 58.3, 44.4, 31.9, 29.2, 25.6, 25.4, 25.1, 21.2; IR (film) ν: 3355, 2931, 2850, 1721, 1615, 1450, 1228, 1201, 657, 544 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{14}H_{23}NO_3Na$ [M + Na$^+$] 276.1576; Found 276.1579.

1-(2-Methoxybenzamido)cyclohexane-1-carboxylic Acid (16i). Yield 148 mg (63%) starting from 219 mg (0.84 mmol) of compound **12h**; purification by flash column chromatography on silica gel (100% AcOEt); white solid; mp 189−190 °C; ^{1}H NMR (400 MHz, CD_3OD) δ: 8.46 (s, 1H), 7.91 (dd, J 7.8, 1.7 Hz, 1H), 7.53−7.44 (m, 1H), 7.14 (d, J 8.3 Hz, 1H), 7.09−7.01 (m, 1H), 4.00 (s, 3H), 2.23−2.13 (m, 2H), 1.91−1.80 (m, 2H), 1.77−1.62 (m, 3H), 1.59−1.44 (m, 2H), 1.41−1.27 (m, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ: 176.3, 165.5, 157.8, 133.0, 130.8, 121.3, 120.8, 111.7, 58.8, 55.5, 32.0, 25.0, 21.3; IR (film) ν: 3369, 2940, 2858, 2513, 1735, 1715, 1639, 1601, 1539, 1469, 1443, 1418, 1278, 1160, 1020, 757 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{15}H_{19}NO_4Na$ [M + Na$^+$] 300.1212; Found 300.1214.

1-(2,4,6-Trimethylbenzamido)cyclohexane-1-carboxylic Acid (16j). Yield 90 mg (69%) starting from 122 mg (0.45 mmol) of compound **12i**; white solid; mp 184−186 °C; ^{1}H NMR (400 MHz, CD_3OD) δ: 4.31 (br s, 1H), 2.32 (s, 6H), 2.25 (s, 3H), 2.18−2.08 (m, 2H), 1.98−1.89 (m, 2H), 1.71−1.54 (m, 5H), 1.43−1.32 (m, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ: 176.3, 172.0, 138.1, 134.5, 134.4, 127.6, 59.0, 32.1, 25.1, 21.5, 19.8, 18.0; IR (film) ν: 3330, 2934, 2859, 1712, 1632, 1612, 1452, 1408, 1283, 1249, 1194, 1163, 849, 736 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{17}H_{23}NO_3Na$ [M + Na$^+$] 312.1576; Found 312.1568.

1-((Methoxycarbonyl)amino)cycloheptane-1-carboxylic Acid (16k). Yield 56 mg (60%) starting from 85 mg (0.43 mmol) of compound **8j**; purification by flash chromatography on silica gel (AcOEt/hexanes 1:1); colorless crystals; mp 145−146 °C; ^{1}H NMR (400 MHz, MeOH-d_4) δ: 3.60 (s, 3H), 2.17−2.05 (m, 2H), 2.03−1.91 (m, 2H), 1.68−1.49 (m, 8H); ^{13}C NMR (101 MHz, MeOH-d_4) δ: 177.4, 157.0, 62.2, 50.9, 41.1, 35.7, 29.4, 22.3; IR (film) ν: 3327, 3075, 2935, 2857, 1714, 1672, 1534, 1460, 1391, 1281, 1235, 1193, 1119, 1047, 816, 784 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{10}H_{17}NO_4Na$ [M + Na$^+$] 238.1055; Found 238.1050.

1-(((Benzyloxy)carbonyl)amino)cyclopropane-1-carboxylic Acid (16l). Yield 51 mg (70%) starting from 67 mg (0.31 mmol) of compound **8d**; white solid; mp 153−154 °C; ^{1}H NMR (400 MHz, CD_3OD) δ: 7.42−7.11 (m, 5H), 5.08 (s, 2H), 1.52−1.42 (m, 2H), 1.19−1.01 (m, 2H); ^{13}C NMR (101 MHz, CD_3OD) δ: 175.2, 157.9, 136.8, 128.0, 127.5, 127.3, 66.1, 16.6; IR (film) ν: 3339, 3028, 2953, 2916, 2849, 1686, 1525, 1436, 1323, 1257, 1212, 1114, 1076, 926, 724, 693 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{12}H_{13}NO_4Na$ [M + Na$^+$] 258.0742; Found 258.0744.

1-((Methoxycarbonyl)amino)cyclobutane-1-carboxylic Acid (16m). Yield 87 mg (60%) starting from 130 mg (0.84 mmol) of compound **8e**; purification by flash column chromatography on silica gel (20% AcOEt in hexanes); white solid, mp 159−160 °C; ^{1}H NMR (400 MHz, $CDCl_3$-CD_3OD) δ: 4.53 (s, 1H), 3.55 (s, 3H), 2.61−2.41 (m, 2H), 2.33−2.16 (m, 2H), 2.02−1.83 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$-CD_3OD) δ: 176.2, 156.4, 58.0, 51.8, 31.0, 14.9; FTIR (film) v: 3310, 3061, 2988, 3950, 1718, 1656, 1550, 1314, 1281, 1226, 792 cm^{-1}; HRMS (EI) m/z calcd for $C_7H_{11}NO_4$ [M] 173.0688; Found 173.0685.

1-((Methoxycarbonyl)amino)cyclopentane-1-carboxylic Acid (16n). Yield 119 mg (64%) starting from 160 mg (0.95 mmol) of compound **8f**; white solid, mp 136−137 °C; ^{1}H NMR (400 MHz, CD_3OD) δ: 3.60 (s, 3H), 2.21−2.10 (m, 2H), 2.02−1.88 (m, 2H), 1.82−1.69 (m, 4H); ^{13}C NMR (101 MHz, CD_3OD) δ: 176.9, 157.3, 65.8, 50.9, 36.8, 24.0; IR (film) v: 3332, 3113, 2958, 2878, 1718, 1535, 1286 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_8H_{12}NO_4$ [M − H$^-$] 186.0766; Found 186.0756.

1-(*t*-Butoxycarbonyl)-4-((methoxycarbonyl)amino)piperidine-4-carboxylic Acid (16o). Yield 110 mg (62%) starting from 167 mg (0.59 mmol) of compound **8i**; purification by flash column chromatography on silica gel (60% AcOEt in hexanes); waxy solid; ^{1}H NMR (400 MHz, CD_3OD) δ 3.79 (dt, J 13.1, 4.1 Hz, 2H), 3.61 (s, 3H), 3.19−3.04 (m, 2H), 2.06−1.86 (m, 4H), 1.45 (s, 9H); ^{13}C NMR (101 MHz, CD_3OD) δ: 175.7, 157.2, 155.0, 79.9, 73.8, 57.1, 51.0, 41.1, 27.3; IR (film) ν: 3332, 2976, 2933, 1711, 1528, 1432, 1368, 1281, 1250, 1162, 1056, 774 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{22}N_2O_6Na$ [M + Na$^+$] 325.1376; Found 325.1370.

4-((Methoxycarbonyl)amino)tetrahydro-2*H*-pyran-4-carboxylic Acid (16p). Yield 98 mg (60%) starting from 150 mg (0.81

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mmol) of compound **8h**; purification by flash column chromatography on silica gel (60% AcOEt in hexanes to 100 AcOEt); colorless crystals; mp 127−128 °C; ^{1}H NMR (500 MHz, CD_3OD) δ: 5.49 (s, 1H), 3.77 (dt, J 11.7, 4.0 Hz, 2H), 3.69−3.60 (m, 5H), 2.11 (ddd, J 14.9, 10.7, 4.6 Hz, 2H), 2.00−1.93 (m, 2H); ^{13}C NMR (126 MHz, CD_3OD) δ: 175.9, 157.1, 63.0, 50.9, 41.1, 32.2; IR (film) ν: 3347, 3016, 2931, 2854, 1712, 1292, 1138, 936, 763, 500 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_8H_{13}NO_5Na$ [M + Na$^+$] 226.0691; Found 226.0686.

2-((Methoxycarbonyl)amino)-2,2-diphenylacetic Acid (16q). Yield 36 mg (48%) starting from 70 mg (0.26 mmol) of compound **8a**; off-white solid; mp 58−60 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.35 (d, J 7.3 Hz, 4H), 7.28 (t, J 7.5 Hz, 4H), 7.24−7.17 (m, 2H), 5.76 (s, 1H), 4.81 (s, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ: 176.2, 173.3, 144.5, 127.8, 126.8, 126.3, 75.6; IR (film) ν: 3383, 3086, 3061, 3029, 2917, 1726, 1595, 1494, 1453, 1186, 1017, 762, 739, 699 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{16}H_{15}NO_4Na$ [M + Na$^+$] 308.0899; Found 308.0896.

2-Ethyl-2-((methoxycarbonyl)amino)butanoic Acid (16r). Yield 36 mg (50%) starting from 65 mg (0.38 mmol) of compound **8b**; white solid; mp 106−107 °C; ^{1}H NMR (400 MHz, CD_3OD) δ: 3.60 (s, 3H), 2.19−2.04 (m, 2H), 1.89−1.75 (m, 2H), 0.79 (t, J = 7.5 Hz, 6H); ^{13}C NMR (101 MHz, CD_3OD) δ: 175.1, 155.6, 64.0, 50.8, 27.1, 7.0; IR (film) ν: 3358, 3085, 2960, 2937, 2878, 1728, 1675, 1525, 1472, 1461, 1395, 1334, 1263, 1234, 1116, 1103 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_8H_{15}NO_4Na$ 212.0899; Found 212.0901.

3-((*t*-Butyldimethylsilyl)oxy)-2-(((*t*-butyldimethylsilyl)oxy)-methyl)-2-((methoxycarbonyl)amino)propanoic Acid (16s). Yield 60 g (52%) starting from 110 mg (0.27 mmol) of compound **8c**; colorless oil; ^{1}H NMR (400 MHz, CD_3OD) δ: 4.00−3.91 (m, 4H), 3.60 (s, 3H), 0.88 (s, 18H), 0.04 (s, 12H); ^{13}C NMR (101 MHz, MeOD) δ 177.0, 170.8, 71.1, 61.0, 50.9, 24.9, 17.7, −6.8; IR (film) ν: 3418, 2954, 2930, 2888, 2857, 1723, 1511, 1469, 1255, 1112, 1082, 837, 778 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{18}H_{39}NO_6Si_2Na$ [M + Na$^+$] 444.2214; Found 444.2209.

Synthesis of Amino Esters 17. General Procedure. (Trimethylsilyl)diazomethane (3 equiv, 2 M soln. in Et_2O) was added slowly to a solution of the amino acid (1 equiv) in MeOH. The progress of the reaction was followed by MS. When the reaction was completed, the solvent was removed and the crude product was purified by flash column chromatography.

Methyl 1-((Methoxycarbonyl)amino)cyclohexane-1-carboxylate (17a). Yield 28 mg (75%) starting from 35 mg (0.174 mmol) of amino acid **16a**; off-white solid; mp 58−59 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.88 (s, 1H), 3.71 (s, 3H), 3.65 (s, 3H), 2.03−1.94 (m, 2H), 1.89−1.80 (m, 2H), 1.65−1.57 (m, 3H), 1.51−1.38 (m, 2H), 1.37−1.23 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 175.0, 156.0, 59.2, 52.5, 52.2, 32.8, 25.3, 21.4; IR (film) ν: 3354, 2946, 2859, 1733, 1526, 1453, 1282, 1260, 1235, 1167, 1106, 1069, 991, 781 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{10}H_{17}NO_4Na$ [M + Na$^+$] 238.1055; Found 238.1058.

Methyl 1-((*t*-Butoxycarbonyl)amino)cyclohexane-1-carboxylate (17b). Purification by flash column chromatography on silica gel (14% AcOEt in hexanes). Yield 110 mg (90%) starting from 107 mg (0.48 mmol) of compound **16b**; waxy solid; R_f 0.33 (1:4 AcOEt/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.73 (s, 1H), 3.67 (s, 3H), 1.93 (d, J 13.3 Hz, 2H), 1.84−1.74 (m, 2H), 1.63−1.53 (m, 3H), 1.51−1.42 (m, 2H), 1.39 (s, 9H), 1.32−1.20 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 175.2, 154.8, 58.8, 52.0, 32.8, 28.2, 25.2, 21.2; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{23}NO_4Na$ [M + Na$^+$] 280.1525; Found 280.1535; IR (film) ν: 3373, 2936, 2859, 1741, 1706, 1510, 1454, 1366, 1281, 1238, 1164, 1092, 1068, 984, 784 cm^{-1}.

Methyl 1-(((Benzyloxy)carbonyl)amino)cyclohexane-1-carboxylate (17c). Purification by flash column chromatography on silica gel (14% AcOEt in hexanes). Yield 110 mg (72%) starting from 145 mg (0.56 mmol) of compound **16c**; waxy solid; TLC: R_f 0.35 (1:4 AcOEt/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35−7.31 (m, 5H), 5.08 (s, 2H), 3.65 (s, 3H), 2.07−1.24 (m, 10H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 201.5, 174.9, 155.34, 155.26, 128.6, 128.5, 128.09, 128.04, 66.7, 59.1, 52.3, 32.6, 25.1, 25.0, 21.2, 20.9; HRMS (ESI-TOF) m/z calcd for $C_{16}H_{21}NO_4Na$ [M + Na$^+$] 314.1368 Found 314.1375; IR (film) ν: 3349, 2941, 2859, 1719, 1523, 1454, 1281, 1256, 1235, 1167, 1096, 1068, 986, 778, 740, 698 cm^{-1}.

Methyl 1-(3,3-Dibutylureido)cyclohexane-1-carboxylate (17d). Yield 86 mg (82%) starting from 100 mg (0.34 mmol) of compound **16d**; purification by flash column chromatography on silica gel (20% AcOEt in hexanes); white solid; mp 78−79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.39 (s, 1H), 3.65 (s, 3H), 3.22−3.08 (m, 4H), 2.03−1.94 (m, 2H), 1.86−1.74 (m, 2H), 1.65−1.20 (m, 14H), 0.90 (t, J 7.4 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 175.9, 156.7, 58.6, 52.0, 47.0, 33.1, 30.7, 25.4, 21.6, 20.1, 13.9; IR (film) ν: 3397, 3335, 2951, 2867, 1737, 1629, 1518, 1452, 1291, 1239 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{17}H_{32}N_2O_3Na$ [M + Na$^+$] 335.2311. Found 335.2309.

Methyl 1-Benzamidocyclohexane-1-carboxylate (17e). Purification by flash column chromatography on silica gel (20% AcOEt/hexanes); yield 30 mg (71%) starting from 40 mg (0.162 mmol) of amino acid **16e**; colorless crystals, mp 146−147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.72−7.64 (m, 2H), 7.41 (t, J 7.3 Hz, 1H), 7.34 (t, J 7.4 Hz, 2H), 6.14 (s, 1H), 3.64 (s, 3H), 2.08 (br d, J 14.0 Hz, 2H), 1.86 (td, J 14.0, 13.0, 3.8 Hz, 2H), 1.68−1.50 (m, 3H), 1.47−1.35 (m, 2H), 1.33−1.22 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 174.6, 167.0, 134.6, 131.8, 128.7, 127.1, 59.2, 52.5, 32.7, 25.4, 21.8; IR (film) ν: 3347, 3060, 3028, 2929, 2855, 1739, 1642, 1527, 1487, 1292, 1278, 1238, 1071, 715 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{15}H_{19}NO_3Na$ [M + Na$^+$] 284.1263; Found 284.1262.

Methyl 1-Isobutyramidocyclohexane-1-carboxylate (17f). Yield 28 mg (65%) starting from 40 mg (0.19 mmol) of compound **16f**; white solid, mp 96−97 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.58 (s, 1H), 3.67 (s, 3H), 2.37 (hept, J 6.9 Hz, 1H), 2.07−1.97 (m, 2H), 1.88−1.75 (m, 2H), 1.70−1.54 (m, 3H), 1.46−1.26 (m, 3H), 1.15 (s, 3H), 1.13 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 176.3, 174.6, 58.4, 52.1, 35.4, 32.4, 27.4, 25.2, 21.5, 19.4; FTIR (film) ν: 3302, 3060, 2970, 2929, 2865, 1741, 1729, 1639, 1540, 1277, 1253, 1236, 1071 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{12}H_{21}NO_3Na$ [M + Na$^+$] 250.1419; Found 250.1402.

Methyl 1-Pivalamidocyclohexane-1-carboxylate (17g). Yield 45 mg (66%) starting from 65 mg (0.29 mmol) of compound **16g**; white solid, mp 94−95 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.71 (s, 1H), 3.69−3.65 (m, 3H), 2.09−1.98 (m, 2H), 1.90−1.76 (m, 2H), 1.70−1.54 (m, 3H), 1.41−1.26 (m, 3H), 1.20 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 177.6, 174.6, 58.2, 52.1, 38.7, 32.3, 27.4, 25.2, 21.6; FTIR (film) ν: 3367, 2967, 2935, 2858, 1739, 1657, 1520, 1454, 1276, 1237, 1073, 903, 699 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{23}NO_3Na$ [M + Na$^+$] 264.1576; Found 264.1572.

Methyl 1-(Cyclohexanecarboxamido)cyclohexane-1-carboxylate (17h). Yield 95 mg (86%) starting from 105 mg of amino acid **16h**; colorless crystals; mp 140−141 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.64 (s, 1H), 3.63 (s, 3H), 2.07 (tt, J 11.6, 3.5 Hz, 1H), 2.02−1.94 (m, 2H), 1.85−1.69 (m, 6H), 1.64−1.52 (m, 4H), 1.44−1.12 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 175.4, 174.6, 58.3, 52.1, 45.1, 32.3, 29.5, 25.7, 25.6, 25.2, 21.5; FTIR (film) ν: 3314, 3213, 3070, 2988, 2930, 2854, 1730, 1667, 1646, 1549, 1449, 1297, 1276, 1242, 1223, 1070 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{15}H_{25}NO_3Na$ [M + Na$^+$] 290.1732; Found 290.1729.

Methyl 1-(2-Methoxybenzamido)cyclohexane-1-carboxylate (17i). Yield 91 mg (86%) starting from 100 mg (0.361 mmol) of amino acid **16i**; colorless crystals, mp 124−125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.27 (s, 1H), 8.14 (dd, J 7.8, 1.8 Hz, 1H), 7.45−7.39 (m, 1H), 7.07−7.01 (m, 1H), 6.97 (d, J 8.3 Hz, 1H), 3.97 (s, 3H), 3.70 (s, 3H), 2.16 (d, J 13.5 Hz, 2H), 1.87−1.83 (m, 2H), 1.73−1.60 (m, 3H), 1.52−1.39 (m, 2H), 1.38−1.24 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 174.8, 164.1, 157.6, 133.0, 132.3, 121.4, 121.4, 111.5, 58.7, 56.2, 52.3, 32.5, 25.4, 21.7; FTIR (film) ν: 3346, 2941, 2858, 1739, 1656, 1529, 1483, 1289, 1235, 1162, 1071, 1018, 758 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{16}H_{21}NO_4Na$ [M + Na$^+$] 314.1368; Found 314.1372.

Methyl 1-(2,4,6-Trimethylbenzamido)cyclohexane-1-carboxylate (17j). Purification by flash column chromatography on silica gel (20% AcOEt/hexanes); yield 40 mg (75%) starting from 50 mg (0.173 mmol) of amino acid **16j**; colorless crystals, mp 119−120

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°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.74 (s, 2H), 5.73 (s, 1H), 3.66 (s, 3H), 2.25 (s, 6H), 2.18 (s, 3H), 2.06−1.97 (m, 2H), 1.90−1.80 (m, 2H), 1.65−1.48 (m, 3H), 1.43−1.31 (m, 2H), 1.30−1.21 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 174.3, 169.8, 138.5, 134.7, 134.4, 128.2, 58.9, 52.0, 32.5, 25.2, 21.6, 21.0, 19.1; FTIR (film) ν: 3261, 2939, 2857, 1742, 1635, 1529, 1453, 1237, 1069, 849 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{18}H_{25}NO_3Na$ [M + Na$^+$] 326.1732; Found 326.1734.

Methyl 1-((Methoxycarbonyl)amino)cycloheptane-1-carboxylate (17k). Yield 38 mg (70%) starting from 50 mg (0.23 mmol) of amino acid **16k**; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.93 (s, 1H), 3.70 (s, 3H), 3.63 (s, 3H), 2.11 (dd, J 14.4, 9.3 Hz, 2H), 1.93 (dd, J 14.5, 7.4 Hz, 2H), 1.65−1.43 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 175.3, 155.9, 62.6, 52.4, 52.0, 36.5, 29.3, 22.5; FTIR (film) ν: 3355, 2927, 2858, 1731, 1525, 1463, 1261, 1196, 1045, 783 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{11}H_{19}NO_4Na$ [M + Na$^+$] 252.1212; Found 252.1211.

Methyl 1-(((Benzyloxy)carbonyl)amino)cyclopropane-1-carboxylate (17l). Yield 19 mg (71%) starting from 25 mg (0.106 mmol) of compound **16l**; colorless crystals, mp 99−100 °C (Lit.[65] 99−99.5 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40−7.29 (m, 5H), 5.13 (s, 2H), 3.68 (s, 3H), 1.60−1.49 (m, 2H), 1.25−1.16 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 173.3, 156.7, 145.8, 136.5, 128.6, 128.3, 67.1, 52.6, 34.6, 18.0; IR (film) ν: 3338, 3090, 3063, 3032, 2953, 2925, 2852, 1731, 1520, 1345, 1246, 1200, 1166, 1073, 753, 698 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{15}NO_4Na$ [M + Na$^+$] 272.0899; Found 272.0899.

Methyl 1-((Methoxycarbonyl)amino)cyclobutane-1-carboxylate (17m). Yield 173 mg (69%) starting from 206 mg of compound **16m**; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.59 (s, 1H), 3.71 (s, 3H), 3.60 (s, 3H), 2.60−2.46 (m, 2H), 2.37−2.16 (m, 2H), 2.06−1.88 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 174.2, 155.9, 58.4, 52.5, 31.3, 15.0; IR (film) ν: 3341, 3001, 2955, 2846, 1727, 1523, 1440, 1321, 1268, 1225, 1120, 1079, 985, 783 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_8H_{13}NO_4Na$ [M + Na$^+$] 210.0742; Found 210.0743.

Methyl 1-((Methoxycarbonyl)amino)cyclopentane-1-carboxylate (17n). Yield 65 mg (70%) starting from 85 mg (0.49 mmol) of amino acid **16n**; purification by flash column chromatography on silica gel (25% AcOEt/cyclohexane); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.12 (s, 1H), 3.71 (s, 3H), 3.63 (s, 3H), 2.26−2.10 (m, 2H), 2.01−1.87 (m, 2H), 1.81−1.72 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 175.0, 156.1, 66.2, 52.5, 52.0, 37.6, 24.5; IR (film) ν: 3345, 2955, 2876, 1725, 1526, 1450, 1270, 1194 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_9H_{15}NO_4Na$ [M + Na$^+$] 224.0899; Found 224.0896.

1-(*t*-Butyl) 4-Methyl 4-((Methoxycarbonyl)amino)piperidine-1,4-dicarboxylate (17o). Yield 133 mg (85%) starting from 150 mg (0.5 mmol) of compound **16o**; off-white solid; mp 130−131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.18 (s, 1H), 3.88−3.74 (m, 2H), 3.70 (s, 3H), 3.62 (s, 3H), 3.16−3.02 (m, 2H), 2.07−1.87 (m, 4H), 1.41 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 173.9, 156.0, 154.6, 79.8, 57.6, 52.6, 52.2, 32.2, 28.4; IR (film) ν: 3328, 2976, 2954, 1742, 1696, 1530, 1429, 1281, 1240, 1281, 1162, 1064, 736 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{14}H_{24}N_2O_6Na$ [M + Na$^+$] 339.1532; Found 339.1529.

Methyl 4-((Methoxycarbonyl)amino)tetrahydro-2*H*-pyran-4-carboxylate (17p). Yield 98 mg (80%) starting from 115 mg (0.57 mmol) of compound **16p**; off-white solid, mp 73−73.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.20 (s, 1H), 3.77 (dt, J 11.7, 4.0 Hz, 2H), 3.72 (s, 3H), 3.68−3.60 (m, 5H), 2.17 (ddd, J 14.3, 10.3, 4.3 Hz, 2H), 1.94−1.85 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 173.8, 156.0, 63.2, 56.7, 52.6, 52.2, 32.9; IR (film) v: 3334, 2956, 2862, 1728, 1529, 1276, 1256, 1240, 1107, 1067 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_9H_{15}NO_5Na$ [M + Na$^+$] 240.0848; found 240.0856.

***t*-Butyl (4-Vinyltetrahydro-2*H*-pyran-4-yl)carbamate (19).** To a solution of carbamate **5h** (250 mg, 1.46 mmol) and Et_3N (886 mg, 1.2 mL, 8.76 mmol) in dry THF (20 mL) cooled to 0 °C was added TFAA (614 mg, 406 μL, 2.92 mmol), and the resulting mixture was slowly warmed to room temperature. The progress of the reaction was followed by TLC (50% AcOEt in hexanes). In a separate flask, a 1 M soln. of LiHMDS in THF (8.8 mL, 8.76 mmol) was added to anhydr. *t*-BuOH (2 mL) in 10 mL of THF. When the rearrangement was completed (ca. 1 h), the solution of *t*-BuOLi was cannulated, and the reaction mixture was stirred overnight at room temperature. Progress of the reaction was followed by TLC (20% AcOEt in hexanes). After the removal of the solvents, the crude product was supported on silica gel and chromatographed (20% AcOEt in hexanes) to give 266 mg of carbamate **19** (80%) as an off-white solid; mp 74−74.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.89 (dd, J 17.4, 10.7 Hz, 1H), 5.16−5.08 (m, 2H), 4.55 (s, 1H), 3.89−3.55 (m, 4H), 2.09−1.69 (m, 4H), 1.41 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 163.6, 142.5, 112.9, 63.4, 53.4, 35.4, 28.4; IR (film) ν: 3342, 1697, 1521, 1365, 1239, 1170, 1107 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{12}H_{21}NO_3Na$ [M + Na$^+$] 250.1419; Found 250.1414.

4-((*t*-Butoxycarbonyl)amino)tetrahydro-2*H*-pyran-4-carboxylic Acid (20). Prepared in the same manner as compound **16a**; purification by flash column chromatography on silica gel (50% AcOEt in hexanes); yield 1.02 g (62%) starting from 1.54 g (6.78 mmol) of compound **19**; white solid, mp 142−143 °C; ^{1}H NMR (400 MHz, CD_3OD) δ: 3.75 (dt, J 11.8, 4.2 Hz, 2H), 3.70−3.62 (m, 2H), 2.08 (ddd, J 14.6, 10.4, 4.6 Hz, 2H), 1.96−1.88 (m, 2H), 1.42 (s, 9H); ^{13}C NMR (101 MHz, CD_3OD) δ: 176.0, 156.0, 73.8, 63.0, 56.0, 32.4, 27.4; FTIR (film) ν: 3336, 2977, 1714, 1518, 1368, 1297, 1167, 1143 cm-1; HRMS (ESI-TOF) m/z calcd for $C_{11}H_{19}NO_5Na$ [M + Na$^+$] 268.1161; Found 1151.

(S)-2-*t*-Butoxycarbonylaminobutyric Acid (24).[66] To a solution of (*S*)-2-aminobutyric acid (3.1 g, 30.0 mmol) in 15 mL of 2 M NaOH and 20 mL of MeOH was added $(Boc)_2O$ (7.86 g, 36.0 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 12 h. After most of the methanol was evaporated, the solution was acidified to pH 2 with 1 M HCl and extracted with EtOAc (3 × 100 mL). The organic extracts were combined, washed with brine (2 × 10 mL), and dried over anhydr. Na_2SO_4. The evaporation of the solvent gave the title compound (5.7 g, 93%) as a colorless oil. R_f 0.43 (*n*-hexanes/EtOAc/HOAc 10:10:1); $[\alpha]_D^{22}$ −16.7 (*c* 2.6, MeOH) (Lit.:[66] $[\alpha]_D^{29}$ −15.2 (*c* 1.0, MeOH)); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 12.35 (s, 1H), 6.97 (d, J 7.8 Hz, 1H), 3.78 (q, J 8.2 Hz, 1H), 1.73−1.61 (m, 1H), 1.60−1.50 (m, 1H), 1.37 (s, 9H), 0.86 (t, J 7.3 Hz, 3H).^{13}C NMR (126 MHz, DMSO-d_6) δ: 174.0, 155.6, 77.9, 54.9, 28.2, 24.1, 10.5; IR (film) ν: 3324, 3104, 1714, 1514, 1395, 1368, 1253, 1165 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_9H_{17}NO_4Na$ [M + Na$^+$] 226.1055; Found 226.1061.

***t*-Butyl (*S*)-(1-(Methoxy(methyl)amino)-1-oxobutan-2-yl)-carbamate (25).**[9b] To a solution of (S)-2-*t*-butoxycarbonylaminobutyric acid (**24**) (1.50 g, 7.39 mmol) in THF (30.0 mL) was added carbonyldiimidazole (1.43 g, 8.86 mmol) portionwise over about 10 min. After stirring for 30 min at room temperature, a solution of MeNHOMe·HCl (0.8 g, 8.2 mmol) and *i*-Pr_2NEt (1.4 mL, 8.2 mmol) in DMF (10 mL) was added. The reaction mixture was stirred overnight at room temperature, followed by concentration *in vacuo*. The residue was diluted with EtOAc (50 mL) and washed with 1 M aq. HCl (2 × 20 mL), sat. aq. $NaHCO_3$ (2 × 20 mL), and brine (20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo* to afford the compound **25** (1.69 g, 93%) as a clear, yellowish oil. $[\alpha]_D^{23}$ +3.8 (*c* 0.72, $CHCl_3$); ^{1}H NMR (500 MHz, C_6D_6) δ: 5.37 (br s, 1H), 4.89−4.76 (m, 1H), 3.14 (s, 3H), 2.75 (s, 3H), 1.83−1.74 (m, 1H), 1.57−1.45 (m, 1H), 1.42 (s, 9H), 0.87 (t, J 7.4 Hz, 3H); ^{13}C NMR (126 MHz, C_6D_6) δ: 155.9, 78.9, 62.3, 60.8, 52.0, 31.7, 28.4, 26.2, 9.9; IR (film) ν: 3332, 2974, 2934, 1713, 1663, 1500, 1390, 1366, 1171 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{11}H_{22}N_2O_4Na$ [M + Na$^+$] 269.1477; Found 269.1480.

Diethyl (2-(Indolin-1-yl)-2-oxoethyl)phosphonate (17). Prepared following the procedure reported by Dragovich et al.[67] Oxalyl chloride (5.96 mL, 68.3 mmol, 1.05 equiv) was slowly added to a solution of diethylphosphonoacetic acid (12.8 g, 65.0 mmol, 1 equiv) and DMF (0.03 mL, 0.39 mmol, 0.006 equiv) in benzene (150 mL) at rt. The reaction mixture was stirred at rt for 1 h and then concentrated under reduced pressure. The resulting oil was dissolved in THF (30 mL) and added by cannula to a solution of indoline (7.38 g, 61.9 mmol, 0.95 equiv) and triethylamine (10.9 mL, 78.0 mmol, 1.2 equiv) in THF (200 mL) at 0 °C. The reaction mixture was stirred at −10 °C

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for 1 h and partitioned between 0.5 M HCl (150 mL) and EtOAc (2 × 150 mL). The combined organic layers were dried over Na_2SO_4 and concentrated to afford a tan solid. Recrystallization from Et_2O provided the phosphonate derivative (7.3 g, 76%) as a yellowish solid: mp: 97−99 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.20 (d, J 8.0 Hz, 1H), 7.22−7.13 (m, 2H), 7.02 (t, J 7.4 Hz, 1H), 4.25 (t, J 8.4 Hz, 2H), 4.22−4.13 (m, 4H), 3.18 (t, J 8.5 Hz, 2H), 3.12 (d, $J_{P\text{-}H}$ 22.2 Hz, 2H), 1.33 (t, J 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 162.6, 142.7, 131.6, 127.4, 124.5, 124.1, 117.3, 62.8 (d, $J_{C\text{-}P}$ 6.5 Hz), 49.0, 36.9, 35.6, 27.9, 16.4, 16.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 20.6; IR (film) ν: 3505, 3476, 1659, 1482, 1394, 1255, 1052, 1026, 970, 758 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{14}H_{20}NO_4PNa$ [M + Na$^+$] 320.1028; Found 320.1030.

2-Bromo-1-(indolin-1-yl)ethan-1-one (22).[44] Bromoacetyl bromide (7.62 g, 3.3 mL, 37.76 mmol) was added to a cooled (−10 °C) solution of indoline (3 g, 2.8 mL, 25.18 mmol) and Et_3N (3.84, 5.3 mL, 37.76 mmol) in dry CH_2Cl_2 (100 mL). The bath was removed, and the reaction mixture was stirred at room temperature overnight. Next, the reaction mixture was washed with water (50 mL), 1 M HCl (20 mL), and sat. Na_2CO_3 (25 mL). The organic layer was dried over anhydr. $MgSO_4$. After the removal of the solvent, the residue was dissolved in AcOEt and hexane was added. The precipitate was collected and washed with AcOEt and hexanes to afford 3.1 g (65%) of the amide, which was used directly in the next step. White solid; mp 124−126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.21 (d, J 8.0 Hz, 1H), 7.28−7.15 (m, 2H), 7.06 (t, J 7.1 Hz, 1H), 4.18 (t, J 8.4 Hz, 2H), 3.94 (s, 2H), 3.24 (t, J 8.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.2, 142.5, 131.3, 127.7, 124.6, 124.5, 117.4, 48.3, 28.4, 28.2; IR (film) ν: 1665, 1598, 1482, 762 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{10}H_{10}NOBrNa$ [M + Na$^+$] 261.9843; Found 261.9847.

1-(Indolin-1-yl)-2-(triphenylphosphanylidene)ethan-1-one (23).[44] A solution of bromide **22** (2.5 g, 10.4 mmol) and PPh_3 (3 g, 11.5 mmol) in 100 mL of toluene was refluxed overnight. Next, the solids were filtered off, washed with toluene and hexanes, and dried in vacuo. The phosphonium salt (3.67 g) was dissolved in $CHCl_3$ (50 mL), and Et_3N (1.3 mL) was added. The resulting mixture was stirred at room temperature for 4 h. The reaction mixture was washed with water, and the organic layer was dried over $MgSO_4$. The removal of the solvent provided 2.96 g (67%) of ylide **23**. Yellowish soild, mp 153−155 °C (lit.[44] 155−156 °C]); *Spectral data:*[44] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09−6.69 (m, 19H), 4.06 (t, J 8.7 Hz, 2H), 3.11 (t, J 8.7 Hz, 2H), 3.00−2.90 (m, 1H); Anal. Calcd for $C_{28}H_{24}NOP$: C 79.79, H 5.74, N 3.32; Found: 79.69, H 5.76, N 3.30.

***t*-Butyl (*S*,*E*)-(6-(Indolin-1-yl)-6-oxohex-4-en-3-yl)carbamate (27).** *Method 1 (via HWE Olefination).* To a solution of Weinreb amide **25** (3.25 mmol, 0.8 g) in dry THF (50 mL) cooled to −20 °C was added a 2 M soln. of $LiAlH_4$ in Et_2O (3.57 mmol, 1.7 mL). The progress of the reaction was followed by TLC (hexanes/AcOEt, 1:1). After 1.5 h, the reaction was quenched by the addition of sat. Na_2SO_4 (0.5 mL), diluted with Et_2O (50 mL), and stirred for 1 h. Solids were removed by filtration, and anhydr. Na_2SO_4 was added to the filtrate. After the removal of the drying agent and the solvent, the crude aldehyde was used directly in the olefination step. A 1 M soln. of LiHMDS (3.4 mmol, 3.4 mL) was added to a solution of phosphonate **17** (3.4 mmol, 1.01 g) in dry THF (50 mL). After stirring for 40 min, the reaction mixture was cooled to −10 °C and a solution of the aldehyde in THF was added. After stirring overnight, the reaction mixture was diluted with Et_2O and washed with water. The organic layer was dried over anhydr. Na_2SO_4, and the solvent was removed under diminished pressure. The product was isolated by flash column chromatography on silica gel (AcOEt/hexanes 1:2 to 2:3) to give 682 mg of product **27** (64%) as a yellowish oil.

Method 2 (via Masamune−Roush Modification of HWE Reaction). To a solution of Weinreb amide **25** (3.25 mmol, 0.8 g) in dry THF (50 mL) cooled to −20 °C was added a 2 M soln. of $LiAlH_4$ in Et_2O (3.57 mmol, 1.7 mL). The progress of the reaction was followed by TLC (hexanes/AcOEt, 1:1). After 1.5 h, the reaction was quenched by the addition of sat. Na_2SO_4 (0.5 mL), diluted with Et_2O (50 mL), and stirred for 1 h. The solids were removed by filtration, and anhydr. Na_2SO_4 was added to the filtrate. After the removal of the drying agent and the solvent, the crude aldehyde was used directly in the olefination step. The crude aldehyde was dissolved in dry MeCN (15 mL) and added to a mixture of dry LiCl (62 mg, 1.46 mmol) and DBU (220 uL, 222 mg, 1.46 mmol) and phosphonate **17** (3.4 mmol, 1.01 g) in dry MeCN (10 mL). After stirring at room temperature overnight, the solvent was removed. The product was isolated by flash column chromatography on silica gel (AcOEt/hexames 1:2 to 2:3) to give 274 mg of product **27** (68%) as yellowish oil.

Method 3 (via Wittig Reaction). To a solution of Weinreb amide **25** (3.25 mmol, 0.8 g) in dry THF (50 mL) cooled to −20 °C was added a 2 M soln. of $LiAlH_4$ in Et_2O (3.57 mmol, 1.7 mL). The progress of the reaction was followed by TLC (hexanes/AcOEt, 1:1). After 1.5 h, the reaction was quenched by the addition of sat. Na_2SO_4 (0.5 mL), diluted with Et_2O (50 mL), and stirred for 1 h. The solids were removed by filtration, and anhydr. Na_2SO_4 was added to the filtrate. After the removal of the drying agent and the solvent, the crude aldehyde was used directly in the olefination step. The crude aldehyde was dissolved in PhMe (55 mL), ylide **23** (1.5 g, 3.57 mmol) was added, and the reaction mixture was stirred at room temperature overnight. Next, the solvent was removed and the residue was chromatographed on silica gel (AcOEt/hexames 1:2 to 2:3) to give 805 mg of product **23** (75%) as a yellowish oil. $[\alpha]_D^{23}$ −22.9 (c 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.10 (d, J 6.1 Hz, 1H), 7.21 (d, J 7.3 Hz, 1H), 7.13 (t, J 7.8 Hz, 1H), 7.08 (d, J 8.4 Hz, 1H), 6.98 (td, J 7.4, 1.0 Hz, 1H), 6.70 (dd, J 15.1, 6.3 Hz, 1H), 6.38 (d, J 15.1 Hz, 1H), 4.21−4.10 (m, 2H), 4.09−3.98 (m, 1H), 3.20−3.09 (m, 2H), 1.59−1.42 (m, 2H), 1.38 (s, 9H), 0.85 (t, J 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 163.8, 155.2, 146.1, 142.9, 131.4, 127.5, 124.4, 123.8, 122.0, 117.4, 79.5, 53.3, 48.0, 28.3, 27.9, 27.8, 10.1; IR (film) ν: 3323, 2971, 2932, 2876, 1709, 1663, 1262, 1520, 1482, 1409, 1169, 756 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{19}H_{26}N_2O_3Na$ [M + Na$^+$] 353.1841; Found 353.1837.

Compound 30. *N*-Methylmorpholine (470 uL, 4.27 mmol) was added to a solution of amino acid **20** (260 mg, 1.06 mmol), methyl (*S*)-2-aminobutanoate hydrochloride[45] (164 mg, 1.07 mmol), and HATU (425 mg, 1.10 mmol) in dry THF (20 mL) at room temperature. The progress of the reaction was followed by TLC (AcOEt/hexanes 1:1). After the removal of the solvent, the residue was chromatographed on silica gel (AcOEt in hexanes 10% to 50%) to afford 275 mg (75%) of peptide **30** as a white solid; mp 139−141 °C; $[\alpha]_D^{23}$ +2.0 (c 1.02, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.75 (s, 1H), 4.59−4.46 (m, 1H), 3.87−3.76 (m, 2H), 3.73 (s, 3H), 3.65 (ddt, J 12.6, 9.8, 3.0 Hz, 2H), 2.26 (tdd, J 14.1, 9.9, 4.1 Hz, 2H), 1.97−1.81 (m, 3H), 1.79−1.65 (m, 2H), 1.45 (s, 9H), 0.91 (t, J 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 173.1, 172.7, 154.8, 80.6, 63.2, 56.7, 53.3, 52.1, 33.2, 28.2, 25.4, 9.4; FTIR (film) ν: 3330, 3302, 2968, 2936, 2875, 2844, 1747, 1685, 1652, 1520, 1159 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{16}H_{28}N_2O_6Na$ [M + Na$^+$] 367.1845; Found 367.1846.

Compound 29. $LiAlH_4$ (2 M soln. in THF, 320 uL, 0.64 mmol) was added to a cooled (0 °C) solution of peptide **30** (200 mg, 0.58 mmol). After stirring at room temperature for 2 h, the reaction was quenched by the addition of sat. Na_2SO_4. The precipitate was filtered off, and the remaining liquid was dried over anhydr. Na_2SO_4. After the removal of the solvent, the crude amino alcohol was dissolved in dry CH_2Cl_2 (15 mL) and Dess−Martin periodinane (370 mg, 0.87 mmol) was added. After 2 h, the reaction mixture was diluted with Et_2O (30 mL) and treated with brine (10 mL) and sat. $NaHCO_3$ (5 mL). The organic layer was dried over anhydr. Na_2SO_4. After the removal of the solvent, the crude amino aldehyde was dissolved in benzene (10 mL), ylide **23** (244 mg, 0.58 mmol) was added, and the reaction mixture was kept at 45 °C for 3 h. Next, the solvent was removed and the residue was chromatographed on silica gel (AcOEt/hexanes 3:2 to 100% AcOEt) to afford 254 mg (95%) of product **29**; white solid, mp 128−130 °C; $[\alpha]_D^{23}$ −1.3 (c 1.75, $CHCl_3$); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.01 (s, 1H), 7.27 (d, J 8.0 Hz, 1H), 7.22 (d, J 7.3 Hz, 1H), 7.14 (t, J 7.7 Hz, 1H), 6.98 (t, J 7.0 Hz, 1H), 6.76 (dd, J 15.2, 5.6 Hz, 1H), 6.57 (s, 1H), 6.42 (dd, J 15.2, 1.5 Hz, 1H), 4.44−4.35 (m, 1H), 4.20−4.08 (m, 2H), 3.71−3.62 (m, 2H), 3.61−3.55 (m, 2H), 3.14 (t, J 8.5 Hz, 2H), 2.06−1.95 (m, 2H), 1.91 (d, J 13.6 Hz, 2H), 1.70−1.54 (m, 2H), 1.39 (s, 9H), 0.90 (t, J 7.4 Hz, 3H); ^{13}C NMR

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(126 MHz, $CDCl_3$) δ: 173.4, 163.9, 155.1, 145.7, 132.8, 131.7, 127.4, 124.5, 123.8, 122.3, 117.4, 80.4, 63.2, 57.0, 51.8, 48.1, 33.0, 28.3, 28.0, 27.5, 10.2; FTIR (film) v: 3420, 3302, 3056, 2966, 2930, 2859, 1712, 1662, 1628, 1524, 1482, 1438, 1408, 1272, 1173, 1119, 723, 696, 542 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{25}H_{35}N_3O_5Na$ [M + Na^+] 480.2474; Found 480.2475.

2-(Adamantan-2-ylidene)ethan-1-ol (36). *Step 1*: Neat triethyl phosphonoacetate (4 mL, 3.36 g, 20 mmol) was added to a suspension of NaH (0.8 g of 60% disp. in oil, 20 mmol) in dry THF (150 mL). After 30 min, a solution of 2-adamantanone (2 g, 13.3 mmol) in dry THF (20 mL) was added, and the resulting mixture was stirred for 5 h. The progress of the reaction was followed by TLC (20% AcOEt in hexanes). The reaction was quenched by the addition of water (50 mL). The organic layer was separated, and the aqueous one was extracted with ether (3 × 50 mL). The combined organic solutions were dried over anhydr. Na_2SO_4, and then the solvents were removed under diminished pressure. The residue was chromatographed on silica gel (FCC, 5% to 20% AcOEt in hexanes) to give 2.3 g of ethyl 2-(adamantan-2-ylidene)acetate (79%) as a colorless oil. Spectral data in agreement with literature data:[68] ^1H NMR (500 MHz, $CDCl_3$) δ: 5.58 (s, 1H), 4.14 (q, *J* 7.1 Hz, 2H), 4.06 (s, 1H), 2.43 (s, 1H), 2.00−1.91 (m, 6H), 1.88−1.80 (m, 6H), 1.27 (t, *J* 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 172.1, 167.0, 108.6, 59.3, 41.4, 40.1, 39.2, 36.9, 32.9, 27.9, 14.3; IR (film) v: 2910, 2851, 1713, 1644, 1236, 1156 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{14}H_{20}O_2Na$ [M + Na^+] 243.1361. Found 243.1369. *Step 2*: To a cooled (−70 °C) solution of ester (2.3 g, 10 mmol) in CH_2Cl_2 (150 mL) was added a 1 M soln. of DIBAL-H in hexanes (29 mL, 29 mmol). The progress of the reduction was followed by TLC (20% AcOEt/hexanes). When the reduction was completed, the reaction was quenched by the addition of sat. aq. Na_2SO_4 (1.6 mL). When a precipitate appeared, the mixture was diluted with Et_2O and stirred for 1 h. The solids were filtered off and washed with Et_2O. After drying over anhydr. Na_2SO_4, the solvent was removed under diminished pressure and the residue was chromatographed on silica gel (10% to 20% AcOEt in hexanes, FCC) to give the desired alcohol **36** (1.4 g, 75%) as a yellowish oil. Spectral data in agreement with literature data:[68] ^1H NMR (500 MHz, $CDCl_3$) δ: 5.34 (t, *J* 7.1 Hz, 1H), 4.13 (d, *J* 7.1 Hz, 2H), 2.88 (s, 1H), 2.38 (s, 1H), 2.00−1.68 (m, 12H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 152.8, 115.4, 58.2, 40.4, 39.7, 39.2, 37.1, 32.4, 28.5; HRMS (ESI-TOF) m/z calcd for $C_{12}H_{18}ONa$ [M + Na^+] 201.1255. Found 201.1255.

2-(Adamantan-2-ylidene)ethyl Carbamate (37). To a solution of allyl alcohol **36** (1.35 g, 7.57 mmol) in CH_2Cl_2 (50 mL) cooled to −10 °C was added TCA-NCO (1 mL, 1.54 g, 8.2 mmol). After 1 h, the solvent was removed under diminished pressure (TLC: H/O 4:1). The residue was dissolved in a mixture of MeOH/H_2O (40 mL, 3:1 v/v), and K_2CO_3 (4.4 g) was added in one portion. After 1.5 h, MeOH was removed and the aqueous residue was extracted with CH_2Cl_2 (4 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and filtered through a silica gel pad, and the solvent was removed under diminished pressure. The residue was purified by flash column chromatography on silica gel (10% to 20% AcOEt in hexanes) to give the carbamate **37** as colorless crystals (1.05 g, 63%); mp 90.5−91 °C; ^1H NMR (500 MHz, $CDCl_3$) δ: 5.26 (t, *J* 7.3 Hz, 1H), 4.62 (s, 2H), 4.58 (d, *J* 7.3 Hz, 2H), 2.90 (s, 1H), 2.40 (s, 1H), 1.99−1.68 (m, 12H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 157.0, 155.0, 110.5, 61.0, 40.4, 39.7, 39.0, 37.1, 32.5, 28.4; IR (film) ν: 3448, 3387, 3337, 3304, 3251, 3199, 2905, 2847, 1725, 1705, 1337, 1035 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{19}NO_2Na$ [M + Na^+] 244.1313. Found 244.1316.

***N*-(2-Vinyladamantan-2-yl)benzamide (38).** Prepared in the same manner as compound **12b**; yellowish waxy solid; yield 886 mg (74%) starting from 950 mg of carbamate **37**; purification by column chromatography on silica gel (20% to 35% AcOEt in hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.78−7.73 (m, 2H), 7.51−7.38 (m, 3H), 6.36 (dd, *J* 17.6, 10.8 Hz, 1H), 6.08 (s, 1H), 5.28 (dd, *J* 17.6, 0.9 Hz, 1H), 5.23 (dd, *J* 10.8, 1.0 Hz, 1H), 2.53−2.47 (m, 2H), 2.13−2.04 (m, 4H), 1.91−1.86 (m, 2H), 1.78−1.70 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 165.8, 141.7, 135.9, 131.1, 128.5, 126.7, 113.9, 60.7, 38.0, 34.7, 33.3, 33.2, 27.4, 26.9; IR (film) ν: 3292, 2902, 1645, 1528 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{19}H_{23}NONa$ [M + Na^+] 304.1677. Found 304.1674.

2-Benzamidoadamantane-2-carboxylic Acid (39). $NaIO_4$ (685 mg, 3.2 mmol) was added to a solution of **38** (300 mmol, 1.07 mg) in a mixture of acetone/H_2O (10:1 v/v, 20 mL). $RuCl_3 \cdot xH_2O$ (11 mg) was added to the resulting suspension, and the obtained brown mixture was stirred for 2 h. Then, the reaction mixture was diluted with acetone and filtered through Celite. After the removal of the solvent, the residue was evaporated a few times with toluene to afford **39** (204 mg, 64%) as an off-white solid; mp 234−235.5 °C (Lit.[58a] 234−236 °C); ^1H NMR (500 MHz, $CDCl_3/CD_3OD$) δ: 7.86−7.72 (m, 2H), 7.57−7.49 (m, 1H), 7.48−7.39 (m, 2H), 2.75−2.60 (m, 2H), 2.31−2.13 (m, 4H), 1.91−1.65 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3/CD_3OD$ 1:1) δ: 174.3, 168.2, 134.2, 131.4, 128.2 (×2), 126.8 (×2), 63.8, 37.4, 33.5 (×2), 32.8 (×2), 32.1 (×2), 26.6, 26.4; IR (film) ν: 3389, 1743, 1627, 1575, 1529, 1243, 1210, 716 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{18}H_{21}NO_3Na$ [M + Na^+] 322.1419; Found 322.1420.

2-Benzamido-*N*-cyclopropyladamantane-2-carboxamide (34). *N*-methylmorpholine (37 μL, 34 mg, 0.33 mmol) was added to a solution of carboxylic acid **39** (0.17 mmol, 50 mg), HATU (78 mg, 0.2 mmol), and cyclopropylamine (0.84 mmol, 48 mg, 58 μL) in dry CH_2Cl_2 (5 mL). After stirring at rt overnight, the solvent was removed and the residue was chromatographed on silica gel (30% AcOEt in hexanes) to afford 35 mg (62%) of **34** as a white solid; mp 238−240 °C (Lit.[58a] 238−242 °C); ^1H NMR (400 MHz, $CDCl_3$) δ: 7.73−7.69 (m, 2H), 7.61 (s, 1H), 7.53−7.48 (m, 1H), 7.47−7.39 (m, 2H), 6.01 (s, 1H), 2.82−2.77 (m, 2H), 2.76−2.70 (m, 1H), 2.05−1.91 (m, 4H), 1.88−1.62 (m, 8H), 0.78−0.71 (m, 2H), 0.52−0.46 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 173.7, 167.9, 134.8, 131.8, 128.7 (×2), 126.8 (×2), 64.7, 37.3, 34.0 (×2), 32.7 (×2), 32.1 (×2), 26.6, 26.5, 22.6, 6.5 (×2); IR (film) v: 3350, 3263, 1637, 1523 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{21}H_{26}N_2O_2Na$ [M + Na^+] 361.1892; Found 361.1895.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02628.

Copies of ^1H and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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