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Development of the Ireland−Claisen Rearrangement of Alkoxy- and Aryloxy-Substituted Allyl Glycinates

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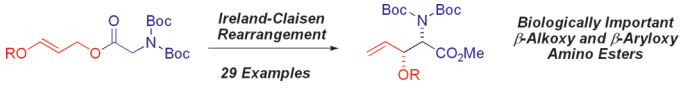

The Ireland−Claisen rearrangement of 3-alkoxy- and 3-aryloxy-substituted allyl glycinates is presented. This [3,3]-sigmatropic rearrangement route offers direct access to *syn* β-alkoxy and β-aryloxy α-amino acid systems. In particular, *N*,*N*-diboc glycine esters rearrange with excellent diastereoselectivities (dr > 25:1). The synthesis of substrates, rearrangement optimization, and a discussion of stereoselection are presented.

Introduction

With serine and threonine constituting 10% of nature's proteinogenic repertoire, β-hydroxy α-amino acids can be viewed as an important set of amino acids. In particular, serine logically contributes to the serine protease family of enzymes, providing the key nucleophilic residue that enables peptide cleavage in many instances. Serine proteases, which include chymotrypsins, trypsins, and elastases, are crucial to the human digestive process.[1]

The importance of β-hydroxy α-amino acid units transcends the incorporation of serine and threonine residues in peptides. This class of amino acid is embedded within a number of important natural products.[2] Kaitocephalin,[3] sphingofungins E and F,[4] altemicidin[5] and the acyl derivatives, lactacystin,[6] salinosporamide,[7] oxazolomycin,[8] and

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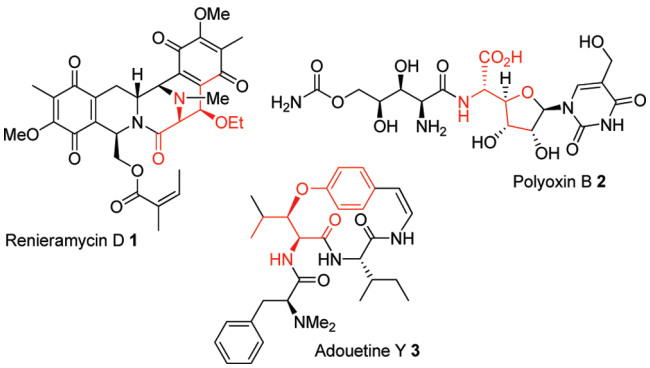

FIGURE 1. Representative natural products containing complex β-alkoxy α-amino acids residues (renieramycin D, **1**, and polyoxin B, **2**) and β-aryloxy α-amino acid (adouetine Y, **3**). Molecular fragment of relevance to this report are highlighted in red.

neooxazolomycin[9] have all resulted in considerable synthetic work in recent years. In contrast, β-alkoxy and β-aryloxy α-amino acid residues do not feature as extensively in natural peptide chemistry. However, there is a significant mapping of such β-alkoxy and β-aryloxy α-amino acid residues into a number of biologically interesting natural products. For example, β-alkoxy α-amino acid residues are observed in renieramycin **1**[10] (Figure 1) brasilicardin A,[11] cyclomarin,[12] papuamide,[13] and callipeltin A.[14] Related to these examples are β-alkoxy α-amino acid incorporates where the ether is cyclic, for example, polyoxin B, **2** (Figure 1).[15] Further examples of this class include amipurimycin[16] and miharamycin B.[17] In addition, β-aryloxy α-amino acid residues are observed in greater frequency within cyclopeptide alkaloids.[18] For example, the cyclopeptide adouetine Y, **3**[19] (Figure 1), features a β-aryl ether unit as a key fragment of the cyclopeptide.

The demonstrable importance of β-hydroxy α-amino acids and their *O*-alkyl and *O*-aryl congeners has led to an impressive wealth of synthetic methodologies for the synthesis of β-hydroxy α-amino acids for proteomic and synthetic examination. These include aldol reactions,[20] enzymatic aldol reactions,[21] enantioselective Mannich reactions,[22] biochemical hydroxylation,[23] reduction of amino β-keto esters,[24] enantioselective dihydroxylations,[25] enantioselective aminohydroxylations,[26] asymmetric *B*-allylation,[27] asymmetric Strecker reactions,[28] nucleophilic epoxide opening,[29] intramo lecular Pd(0)-catalyzed allylic alkylation,[30] photocycloadditions,[31] azomethine ylide cycloadditions,[32] dynamic kinetic resolutions,[33] enantioselective hydrogenations,[34] and oxy-Michael reaction.[35] However, few sigmatropic approaches have been reported, an exception being Sutherland's Pd-catalyzed [3,3]-sigmatropic Overman rearrangement route[36] and the Ireland−Claisen route discussed in this article.[37]

Frequently, *O*-alkylation and *O*-arylation steps are attempted when β-alkoxy and β-aryloxy α-amino acids are required. In some instances such *O*-functionalizations have been reported to be problematic with elimination and retroaldol reactions occurring.[38,39] We envisaged that a novel and synthetically versatile access to functionalized β-alkoxy

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and β-aryloxy amino acids could be achieved through an application of the Ireland−Claisen [3,3]-sigmatropic rearrangement of suitable enol ether substrates. To accomplish this proposal, a combination of Kazmaier's highly diastereoselective Zn-enolate Claisen rearrangement[40] with allylic enol ether ester systems examined by Ireland[41] would be required. On rearrangement, the C_{sp2}−O bond is transposed to a stereogenic C_{sp3}−O bond (Figure 2). If successful, β-alkoxy and β-aryloxy α-amino acids **I** would be formed from enol ether amino esters **II** (Figure 2).

FIGURE 2. Retrosynthetic proposal for a [3,3]-sigmatropic rearrangement entry to β-alkoxy and β-aryloxy α-amino acids.

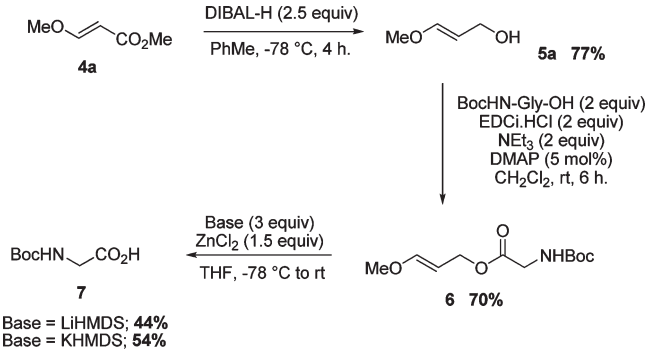
The Ireland−Claisen rearrangement has found widespread application in organic synthesis and target-orientated synthesis.[42] This popularity is due to a key number of advantageous synthetic properties. The Ireland−Claisen rearrangement benefits from ease of substrate synthesis and mild reaction conditions, especially when contrasted with the traditional Claisen [3,3]-sigmatropic rearrangement. It is widely accepted that, for acyclic substrates, the rearrangement of allylic silylketene acetals proceeds through a chair geometry. Subsequently, this rearrangement offers predictable and divergent *syn*/*anti* relative stereochemistry through the judicious choice of either silylketene acetal or allyl alkene geometry. The chair geometry also offers control of absolute stereochemistry through the application of enantiopure substrates derived from chiral secondary alcohols. The chair transition state geometry leads to a highly ordered arrangement that benefits the formation of congested quaternary stereocenters. When considering these properties together, the synthetic utility of the Ireland−Claisen [3,3]-sigmatropic rearrangement reaction is manifest.

Results and Discussion

Preliminary synthetic work concerned the synthesis of a suitable enol ether substrate. We chose to marry the substrate classes studied by Ireland and Kazmaier. Accordingly, we wished to incorporate the enol ether moiety studied by Ireland with the glycinate fragment utilized by Kazmaier in the highly effective chelated Zn-enolate rearrangement chemistry. We believed this would offer a novel set of enol ether amino ester substrates and ultimately on [3,3]-rearrangement a stereocontrolled entry to β-alkoxy α-amino acids (Scheme 1).

Dibal-H reduction of vinylogous carbonate **4** formed the sensitive allylic alcohol **5** in a reproducible yield of 77%. Subsequent carbodiimide coupling with Boc-glycine formed enol ether **6**. This ester was once again observed to be

SCHEME 1. Initial Substrate Synthesis and Rearrangement Attempts



particularly sensitive with facile degradation seen on attempted purification by flash chromatography. However, substrate **6** was obtained cleanly if **5** was submitted to this coupling protocol with sufficient purity. Initial examination of this rearrangement strategy was unpromising, with complex mixtures formed on application of methods developed by Kazmaier. However, it became apparent when using hexamethyldisilazide bases that the parent *N*-Boc glycine was being recovered as the major component of these attempted rearrangements. The incompatible combination of the two previously fruitful Claisen rearrangement structural moieties, i.e., enol ether and glycinate, was confirmed by quickly reproducing a Kazmaier report of the rearrangement of crotyl glycinate in comparable yield and diastereocontrol to that reported.[40] Furthermore, attempts to promote rearrangement reaction using Ireland conditions, similar to those used by Bartlett,[43] were unsuccessful with intractable mixtures seen to form.

The inability of Boc-glycinate **6** to perform adequately in this rearrangement reaction led to the consideration that the dianionic nature of the intermediate Li-enolate was of high energy and displayed significant instability. On enolization of the glycinate ester the central C−O σ-bonding orbital and the C−O σ-antibonding orbital is overlapped by two highly electron-rich π-systems (Figure 3).

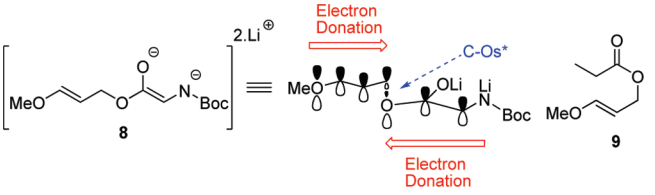


FIGURE 3. Possible explanation for enolate instability.

The possibility exists that this level of donation into this C−O_{σ^*} leads to the decomposition of this enol ether system. Ireland has discussed how the presence of a methoxy group on the allyl group of **9** (Figure 3) leads to a lowering of rearrangement diastereoselectivity. This was explained through a lengthening of the C−O bond, resulting in a transition state possessing higher levels of charge-separated, ionic character. We believe the lack of rearrangement seen with **6** is an electronic extrapolation with strong electron

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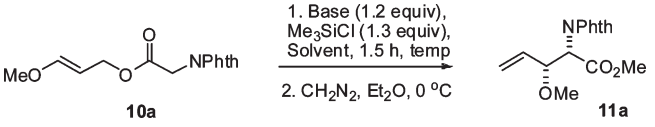
TABLE 1. Optimization of Ireland−Claisen Rearrangement of Phthalimide 7a



entry	base	solvent	temp (°C)	yield (%)	dr[a]
1	LiHMDS	THF	−78	0[b]	
2	NaHMDS	THF	−78	0[b]	
3	KHMDS	THF	−78	0[b]	
4	LiHMDS	THF	−95	74[c]	11:1
5	LiHMDS	Et_2O	−95	65	9:1
6	LiHMDS	PhMe	−95	0[b]	
7	NaHMDS	THF	−95	45	7:1
8	KHMDS	THF	−95	34	6:1
9	LDA	THF	−95	0[b]	
10	LiHMDS	THF	−95	0[c,d]	

[a]Diastereomeric ratio (*syn*/*anti*) determined by ^{1}H NMR analysis of crude reaction mixture. [b]Intractable mixture formed. [c]LiHMDS added *via* syringe pump over 15 min. [d]Me_3SiOTf used as silylation additive.

donation from both π-termini of substrate **6** feeding into this connecting C−O_{σ^*} and ultimately cleavage to form the parent amino acid **7**.[44]

With the unsuccessful attempts to rearrange **6** and the mechanistic postulate discussed, we reconsidered the general structure of our substrates. Accordingly, *N*-phthaloyl substrates were considered for two reasons. First, the presence of two carbonyl groups upon the nitrogen atom would not only remove the *N*-based anion but would also lower the level of *N*-lone pair donation into the enolate and subsequent silylketene acetal. Second, the symmetrical nature of the phthalimide group would lead to simplification in our understanding of the rearrangement with respect to the geometry of substitution around the nitrogen of the amino ester substrate compared to two inequivalent *N*-protecting groups.

Therefore, *N*-phthaloyl ester **10a** was prepared by coupling of allylic alcohol **4** with *N*-phthaloyl glycine in good yield (see Supporting Information for details). This methyl enol ether was subsequently exposed to a traditional Ireland−Claisen protocol using amide bases and silyl chlorides. This process of optimization is detailed in Table 1.

It became apparent that this attempted rearrangement was particularly sensitive to the conditions adopted. After considerable investigation, ester **10a** was observed to rearrange efficiently when LiHMDS is added *via* syringe pump over 15 min to a solution of **10a** and Me_3SiCl at −95 °C before warming to 0 °C and stirring for 90 min (entry 4). The rearranged acid was derivatized as the methyl ester to aid isolation and purification. When the reaction is initiated at higher temperatures (−78 °C, entries 1−3) or when nonethereal solvents (PhMe, entry 6) are used, the reaction provides an intractable reaction product mixture with ^{1}H NMR analysis of crude reaction mixtures suggesting the formation of small amounts of desired rearranged product along with elimination, silylation products together with unconverted starting material. The choice of amide base + counterion is also crucial: Na or KHMDS at −95 °C leads to a significant drop in reaction quality, both in terms of yield and diastereoselectivity compared to LiHMDS (entries 4, 7, and 8). Other Li-amide bases such as LDA (entry 9) are not suitable for this Ireland−Claisen protocol, nor are silyl triflate additives (entry 10).

With an optimized protocol developed, a range of substrates were examined for competency in this Ireland−Claisen rearrangement reaction. We sought to examine a range of *O*-alkyl and *O*-aryl systems including substituents that would offer later synthetic flexibility (Table 2).

It can be seen that *O*-alkyl substrates rearrange smoothly with a similar level of reaction efficiency and diastereoselection (entries 1−8). This set includes functional handles (entries 5, 7) and oxygen protecting groups (entries 5, 6, and 8). Interestingly, aryl-substituted enol ethers are unpredictable substrates. Rearrangement is observed with the phenoxy- and *o*-iodophenoxy enol ethers (entries 9, 13); however, no β-aryloxy α-amino ester is isolated with substrates **10k−l**. Aryl systems bearing electron-withdrawing groups (entries 11−12) fail to react with complete recovery of starting material. In contrast, electron-rich substitution (entry 10) leads to a complex reaction profile. Analysis of crude reaction mixtures by ^{1}H NMR but is consistent with the presence of products derived from anticipated [3,3]-rearrangement and subsequent elimination of *p*-methoxyphenol, forming diene products (entry 10).

While proof of principle had been achieved with *N*-phthaloyl substrates, a number of key issues required subsequent examination. The key issue faced was developing a set of substrates that offered a synthetically practical and versatile *N*-protecting group other than phthaloyl. Second, it may be envisaged that incorporation of suitable functionality upon the nitrogen may allow for subsequent synthetic elaboration. In addition, the diastereoselectivity observed with the phthaloyl substrates, while good in some instances, generally offered significant scope for improvement.

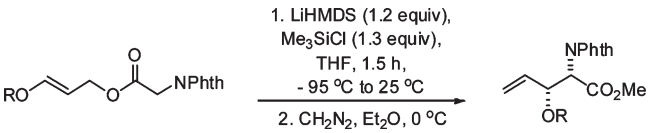
Therefore, a study was initiated to examine the influence of nitrogen substitution upon rearrangement efficiency and diastereoselectivity (Table 3). Initial rearrangement substrates in this study were accessed from the union of (*E*)-3-methoxyprop-2-en-1-ol and suitably protected sarcosines (entries 1−5). These substrates allowed for a probing of electronic and steric influences, and in all instances a successful rearrangement was observed on applying the conditions developed from the previous phthaloyl optimization study (Table 3).

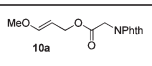
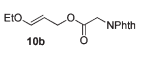
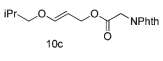
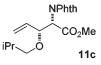
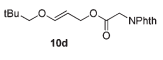
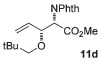
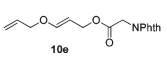
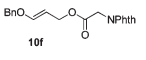
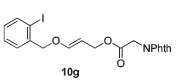
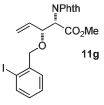
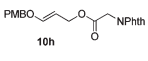
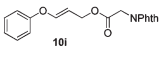
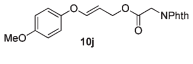
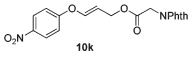
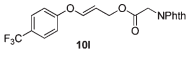
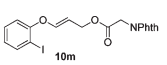
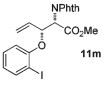
In each instance, negligible diastereoselectivity was observed in the isolated β-methoxy sarcosine methyl esters (*syn*/*anti* 1:1 → 2:1; entries 1−5) with the *N*-Boc and *N*-Ts protection strategies offering the best levels of rearrangement efficiency. Subsequent substrate alterations examined the substitution of an *N*-methyl group for *N*-benzyl and *N*-allyl groups (entries 6, 7). Disappointingly, poor diastereocontrol was once again observed in the isolated methyl esters. However, the introduction of a second *N*-Boc protecting group leads to an impressive level of diastereoselection with only the *syn*-diastereomer observable and isolated in good yield (entry 8).

During the *N*-phthaloyl study, it had become apparent that the nature of the oxygen substituent was crucial to accessing these enol ether substrates. For example, we were unable to prepare enol ethers substrates prepared from simple secondary

(44) In contrast to oxygen substitution at C-3 of ester **6** in the allyl unit, silicon substitution at C-3 and rearrangement is a fruitful method for forming allyl silane amino acids; see: Mohamed, M.; Brook, M. A. *Tetrahedron Lett.* **2001**, *42*, 191–193.

TABLE 2. Scope of Enol Ether Moiety[a]

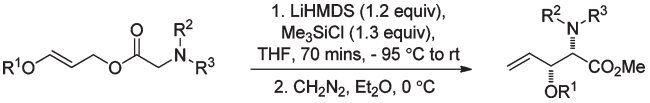


entry	substrate	product	yield (%)	dr[b]
1	 **10a**	 **11a**	74	11:1
2	 **10b**	 **11b**	79	9:1
3	 **10c**	 **11c**	64	18:1
4	 **10d**	 **11d**	78	13:1
5	 **10e**	 **11e**	70	10:1
6	 **10f**	 **11f**	70	10:1
7	 **10g**	 **11g**	50	14:1
8	 **10h**	 **11h**	63	8:1
9	 **10i**	 **11i**	81	14:1
10	 **10j**	-	0	-
11	 **10k**	-	0[c]	-
12	 **10l**	-	0[c]	-
13	 **10m**	 **11m**	50	>25:1

[a]LiHMDS added *via* syringe pump over 15 min. [b]Diastereomeric ratio (*syn*/*anti*) determined by ^{1}H NMR analysis of crude reaction mixture. [c]Starting material recovered (> 95%).

alcohols such as isopropyl alcohol. In contrast, the use of di-*N*-Boc glycine now allowed for the formation of such isopropyl enol ether substrates. Pleasngly, **16b** rearranged under standard conditions to afford the desired β-isopropoxy α-amino ester **17b**, after methylation, in 50% yield and with the excellent level of diastereoselectivity previously observed with methyl enol ether substrate **16a** (entry 9).

TABLE 3. Influence of *N*-Substitution on Rearrangement Diastereoselectivity[a]



entry	R^1	R^2	R^3	yield (%)	dr[b]
1 (**12a**)	Me	Me	Boc	73 (**13a**)	2:1
2 (**12b**)	Me	Me	Cbz	41 (**13b**)	2:1
3 (**12c**)	Me	Me	CO_2Me	42 (**13c**)	1:1
4 (**12d**)	Me	Me	Ts	70 (**13d**)	1:1
5 (**12e**)	Me	Me	Ac	61 (**13e**)	2:1
6 (**14a**)	Me	Bn	Boc	57 (**15a**)	3:1
7 (**14b**)	Me	Allyl	Boc	62 (**15b**)	2:1
8 (**16a**)	Me	Boc	Boc	74 (**17a**)	> 25:1
9 (**16b**)	^{i}Pr	Boc	Boc	50 (**17b**)	> 25:1

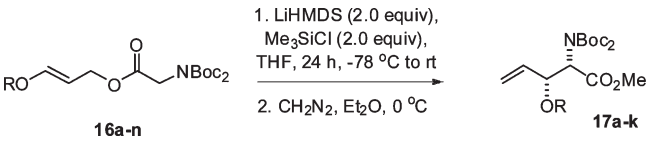
[a]LiHMDS added *via* syringe pump over 15 min. [b]Diastereomeric ratio (*syn*/*anti*) determined by ^{1}H NMR analysis of crude reaction mixture.

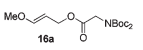
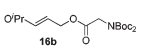
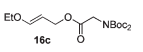
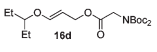
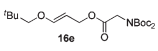
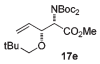
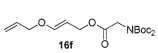
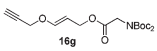
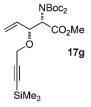
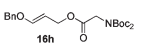
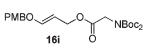
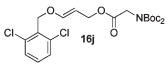
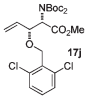
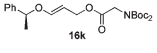
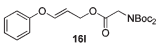
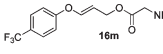
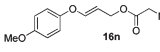
With the rearrangement of di-*N*-Boc protected glycine esters **16a** and **16b** furnishing optimal diastereoselectivity thus far, we felt this *N*-protection system necessitated subsequent evaluation of substrate scope. Therefore, a series of di-*N*-Boc protected substrates were prepared and assessed (Table 4).

Again, excellent levels of diastereoselectivity are encountered throughout this study and confirm the utility of the di-*N*-Boc unit within this Ireland−Claisen rearrangement context. *O*-Alkyl enol ethers rearrange, generally in good yield (entries 1−12), in contrast to *O*-aryl substrates. Of particular note is the rearrangement of neopentyl enol ether **16e** (entry 5) where the product methyl ester is isolated in 80% yield and as a single diastereomer. It is conceivable that synthesizing this β-alkoxy α-amino ester *via* *O*-alkylation of the corresponding β-hydroxy α-amino ester would be synthetically very difficult. Enol ether substrates derived from secondary alcohols rearrange successfully (entries 2, 4). In these instances, a significant quantity of methyl di-*N*-Boc glycinate is isolated. The rearrangement of enol ethers possessing synthetic handles is also possible. Accordingly, *O*-allyl and *O*-propargyl ethers rearrange smoothly (entries 6, 7), although an extra equivalent of base and silyl chloride is required for **16g** as a consequence of product *C*-silylation. Aryl-substituted enol ethers are once again observed to be unproductive substrates, and therefore this reaction, we feel, does not represent a feasible entry to β-aryloxy α-amino ester systems. Generally speaking, the rearrangement of the di-*N*-Boc substrates is slower than the analogous phthalimide systems, requiring 24 h at ambient temperatures and initiation at higher temperatures relative to the *N*-phthalimide substrates.

A chiral benzyl enol ether **16k** was prepared during this study with a view to controlling absolute stereochemistry. Rearrangement was observed to proceed under standard conditions (entry 12) and provided a 70:30 mixture of diastereomers with respect to the 2-phenethyl fragment relative to the *syn*-β-alkoxy α-amino ester fragment. This sense of diastereoselectivity was confirmed after hydrogenation of the terminal alkene and hydrogenolysis of the phenylethyl moiety (Scheme 2).

TABLE 4. Scope of Enol Ether in Ireland−Claisen Rearrangement Reaction



	substrate	product	yield (%)	dr[a]
1	 16a	 17a	72	>25:1
2	 16b	 17b	50[b]	>25:1
3	 16c	 17c	56	>25:1
4	 16d	 17d	45[c]	>25:1
5	 16e	 17e	80	>25:1
6	 16f	 17f	65	>25:1
7[d]	 16g	 17g	71[e]	>25:1
9	 16h	 17h	55	>25:1
10	 16i	 17i	40[f]	>25:1
11	 16j	 17j	78	>25:1
12	 16k	 17k	42	70:30[g]
13	 16l	-	0	
14	 16m	-	0	
15	 16n	-	0	

[a]Determined by ^{1}H NMR analysis of crude reaction mixture. [b]20% methyl di-*N*-Boc glycinate isolated. [c]10% methyl di-*N*-Boc glycinate isolated. [d]3.0 equiv of both LiHMDS and Me_3SiCl used. [e]Isolated as trimethylsilyl alkyne. [f]40% methyl di-*N*-Boc glycinate isolated. [g]2:1 mixture of diastereomers with respect to phenethyl and allyl ether moieties observed; structure of major isomer shown.

The absolute configuration was confirmed by converting to the known β-hydroxy *N*-Boc α-amino ester, *syn*-**19**, with

SCHEME 2. Removal of Stereocontrol Element

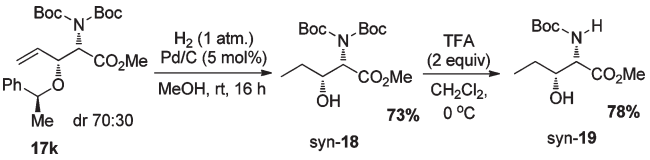
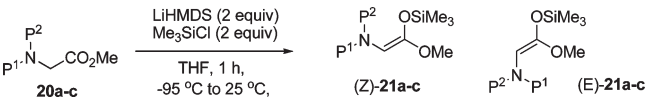


TABLE 5. Silylketene Acetal Formation Using Model Amino Esters



entry	**20**	P^1	P^2	% mass return	**21**/**20**	Z/E[a]
1	**20a**	Me	Boc	100	4:1	2:1
2	**20b**	Phth	Phth	99	7:1	11:1
3	**20c**	Boc	Boc	72	1:3.5	>25:1
4[b]	**20c**	Boc	Boc	89	1.4:1	>25:1

[a]Measured by ^{1}H NMR spectroscopy. [b]Silylketene acetal formation initiated at −78 °C.

the mixture of diastereomers displaying a positive optical rotation (see Supporting Information for details), consistent with the formation of the enantiomer displayed, as the major enantiomer.[45] The magnitude of π-facial selectivity is comparable to that reported by Greene for a [2 + 2]-cycloaddition of a chiral phenethyl enol ether and dichloroketenes.[46] Facial selectivity was rationalized by considering the conformational model used by Greene to understand selectivity of phenethyl enol ethers. Therefore, we believe the selectivity is predicted by the transition state geometry in Figure 4.

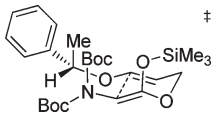


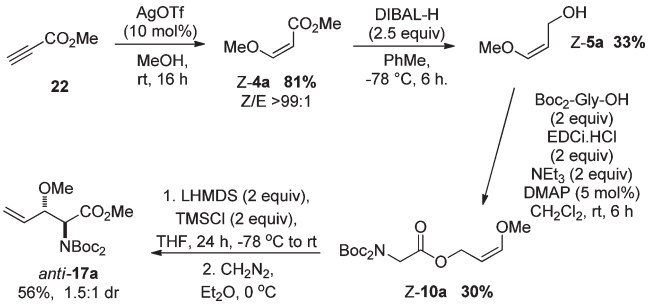
FIGURE 4. Proposed model for understanding the stereoselectivity of chiral enol ether rearrangement.

With the di-*N*-Boc protection strategy superseding the *N*-phthaloyl protection as a result of the superior levels of diastereoselection, the question was asked as to why this improved stereoselection was arising. Indeed, both of these protecting systems feature two carbonyl groups sited upon the nitrogen and point to an electronic influence relative to the sarcosine substrates **12a**−**12e**. To probe the reasoning behind the sensitivity of diastereoselection to structure, a number of model silylketene acetals were prepared to examine *E*/*Z* selectivity on formation. Accordingly, methyl esters **20a**−**20c** were exposed to our rearrangement conditions, and the isolated silylketene acetals were analyzed by ^{1}H NMR (Table 5).

This study was particularly informative with *E*/*Z* ratios observed in the isolated silylketene acetals closely mirroring the magnitude of rearrangement diastereoselection. Furthermore, the major geometrical isomer (*Z*) seen in the model systems is consistent with the same geometrical isomer forming in the rearrangement with subsequent [3,3]-sigmatropic rearrangement

(45) Delle Monache, G.; Di Giovanni, M. C.; Misiti, D.; Zappia, G. *Tetrahedron: Asymmetry* **1997**, *8*, 231–243.
(46) Nebois, P.; Greene, A. E. *J. Org. Chem.* **1996**, *61*, 5210–5211.

SCHEME 3. Preparation and Rearrangement of *Z*-Enol Ether Substrate, *Z*-10a



through a chair geometry. The di-*N*-Boc substrates are seen to convert to *β*-alkoxy α-amino acids considerably more slowly than either the *N*-phthaloyl or *N*-allyl Boc systems, requiring 24 h at room temperature. Therefore, it would appear reasonable to assume that an equilibrium geometry of silylketene acetals is rearranging in the di-*N*-Boc-glycinate systems.

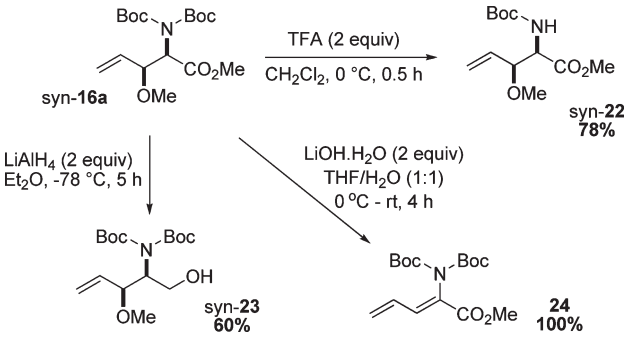
Having assessed the scope and influence of both *O*- and *N*-substitution, a number of key structural influences were explored. The adoption of a cyclic transition state possessing a chair geometry offers the ability to control diastereoselection through controlling the *E*/*Z* geometry of either the vinyl or allyl fragment. As the ability to access the *E*-enolate is out of reach because of the decomposition in HMPA, only utilization of a *Z*-enol ether will offer access to the *anti*-diastereomer and therefore expand the synthetic utility of this chemistry. To examine this idea, *Z*-**6a** was prepared according to Scheme 3. A *Z*-selective silver-catalyzed addition of methyl propiolate was utilized to form *Z*-**4** in good yield.[47] Subsequent reduction and coupling afforded the requisite enol ether *Z*-**10a**

A disappointingly low level of *anti*-diastereoselectivity was observed on rearrangement of enol ether *Z*-**10a** (Scheme 3). Examination of chair transition state geometries for *E*- and *Z*-**10a** is informative (Figure 5) and clearly predicts a substantial steric clash between the methoxy and silyloxy moieties in a 1,3-transannular manner (**II**, Figure 5). Therefore, the possibility exists that a boat geometry (**III**) is energetically competitive with **II**. Alternatively, enol ether geometry may undergo interconversion from *Z* to *E* and subsequent rearrangement *via* **I** or a nonconcerted C−C bond formation event may occur. These possibilities are currently being examined through computational methods.

FIGURE 5. Possible transition state geometries (**I**−**III**) for enol ether substrate geometries.

With a highly stereoselective sigmatropic route to*syn*-*β*-alkoxy-α-amino esters developed, we have sought to demonstrate some synthetic value through a short demonstration of chemoselective deprotection. Accordingly, mono-Boc deprotection[48] is possible as is the full reduction of the ester to primary alcohol (Scheme 4). However, we have been unable to perform a hydrolytic cleavage of the methyl ester, which highlights the sensitivity of these products, by virtue of being allylic ethers, to methanol elimination.

SCHEME 4. Deprotection Strategies



Conclusions

In conclusion, a novel route to *syn*-*β*-alkoxy-α-amino acids that utilizes an Ireland−Claisen [3,3]-sigmatropic rearrangement of enol ethereal amino esters has been developed. When $NBoc_2$-glycinate substrates are used in this rearrangement, excellent diastereoselectivity is observed with a single *syn*-isomer isolable in good yields. Control of absolute stereochemistry, through the application of a chiral enol, is present for the first time in an Ireland−Claisen [3,3]-sigmatropic rearrangement.

Experimental Section

General Procedure for the Synthesis of Vinylogous Esters. To a stirred solution of 1,4-diazabicyclo[2.2.2]octane (0.1 equiv) and alcohol (1.1 equiv) in THF (150 mL) at room temperature was added methyl propiolate (1 equiv) *via* syringe pump over 10 min, with stirring at room temperature for a further 30 min. Sodium hydroxide (10% solution, 200 mL) was added, and the aqueous phase was extracted with CH_2Cl_2 (4 × 100 mL), combined, washed with brine (3 × 150 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Product ester was isolated after subsequent purification on silica gel by flash chromatography.

General Procedure for the Synthesis of Allylic Alcohols. To a stirred solution of the ester (1 equiv) in toluene (100 mL) at −78 °C was added diisobutylaluminium hydride solution (1 M in toluene, 2.5 equiv) at a rate of 1 mL min^{-1}. After addition the reaction was stirred at −78 °C for 6 h, before being poured onto Rochelle salt solution (satd, 100 mL) followed by the addition of EtOAc (100 mL). The biphasic mixture was vigorously stirred for 2 h before separation and extraction with EtOAc (3 × 100 mL). The organics were combined, dried over Na_2SO_4, filtered, and concentrated *in vacuo* to afford the primary allylic alcohol product without further purification, unless stated otherwise.

General Procedure for the Synthesis of Allylic Amino Ester Substrates. To a stirred solution of EDCi·HCl (2 equiv) in CH_2Cl_2 (50 mL) were added triethylamine (2 equiv), amino acid (2 equiv), catalytic DMAP (5 mol %), and allylic alcohol (1 equiv). The reaction was stirred at room temperature for 4 h or until consumption of allylic alcohol was complete by TLC. The mixture was diluted with CH_2Cl_2 to 100 mL, followed by washing with saturated sodium bicarbonate solution (3 × 100 mL), citric acid (10% solution, 3 × 100 mL), and brine (3 × 100 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo* to afford amino esters without any further purification, unless stated otherwise.

General Procedure for the Synthesis of *β*-Alkoxy α-Amino Acids *via* Ireland−Claisen Rearrangement. To a stirred solution of the allylic amino ester (1 equiv) in THF (1 mL) at −78 °C was

(47) Kataoka, Y.; Matsumoto, O.; Tani, K. *Chem. Lett.* **1996**, *25*, 727–728.

(48) Cisar, J. S.; Ferreras, J. A.; Soni, R. K.; Quadri, L. E. N.; Tan, D. S. *J. Am. Chem. Soc.* **2007**, *129*, 7752–7753.

added TMSCl (2 equiv), and the mixture was stirred for 10 min. LiHMDS (1 M in THF, 2 equiv) was added *via* syringe pump at a rate of 3 mL h^{-1}, and the mixture was stirred at −78 °C for a further 10 min before being warmed to room temperature and stirred for 24 h. The reaction was quenched by the addition of methanol (10 mL). Treatment of the crude acid with diazomethane in ether afforded the methyl ester. Purification was achieved by flash chromatography to afford the title compound as a single diastereomer.

(*E*)-Methyl 3-Isopropoxyacrylate (4b). DABCO (0.26 g, 2.38 mmol) in THF (40 mL), 2-propanol (1.43 g, 2.62 mmol), and methyl propiolate (2.00 g, 23.8 mmol) were combined according to general procedure. Purification was achieved by flash chromatography (10:1 pet./EtOAc) to afford the title compound as a colorless oil (2.4 g, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.22 (d, 6H, J = 6.4 Hz), 3.63 (s, 3H), 4.17 (sept, 1H, J = 6.4 Hz), 5.17 (d, 1H, J = 12.9 Hz), 7.47 (d, 1H, J = 12.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.9, 50.9, 75.6, 96.8, 161.6, 168.4. All analytical data are in accordance with reported literature values.[49]

(*E*)-Methyl 3-(Pentan-3-yloxy)acrylate (4c). DABCO (0.26 g, 2.38 mmol) in THF (40 mL), 3-pentanol (2.09 g, 2.62 mmol), and methyl propiolate (2.00 g, 23.8 mmol) were combined according to general procedure. Purification was achieved by flash chromatography (12:1 pet./EtOAc) to afford the title compound as a colorless oil (3.05 g, 75%). FTIR (film/cm^{-1}) υ_{max} 2971.6, 2944.9, 2881.6 2846.7, 1713.4, 1641.7; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.90 (t, 6H, J = 7.6 Hz), 1.61 (quin, 4H, J = 7.6 Hz), 3.68 (s, 3H), 3.75 (quin, 1H, J = 7.6 Hz), 5.23 (d, 1H, J = 12.8 Hz), 7.53 (d, 1H, J = 12.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.5, 26.7, 50.9, 86.9, 96.4, 163.1, 168.7; HRMS (ESI, +ve) m/z calcd for $C_9H_{16}O_3Na$ 195.0992, found 195.0997 $(M + Na)^+$.

(*E*)-Methyl 3-(Prop-2-ynyloxy)acrylate (4d). DABCO (0.40 g, 3.57 mmol) in THF (300 mL), propagyl alcohol (2.3 mL, 3.93 mmol), and methyl propiolate (3.2 mL, 35.7 mmol) were combined according to general procedure. Purification was achieved by flash chromatography (10:1 pet./EtOAc) to afford the title compound as a colorless oil (5.10 g, 98%). FTIR (film/cm^{-1}) υ_{max} 3293.2, 3096.0, 2998.8, 2953.6, 2124.5, 1704.9, 1646.0, 1624.3; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.60 (t, 1H, J = 2.6 Hz), 3.71 (s, 3H), 4.53 (d, 2H, J = 2.6 Hz), 5.35 (d, 1H, J = 12.7 Hz), 7.58 (d, 1H, J = 12.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 51.2, 58.1, 76.6, 77.0, 98.3, 160.6, 167.6; HRMS (ESI, +ve) m/z calcd for $C_7H_8O_3Na$ 163.0371, found 163.0364 $(M + Na)^+$.

(*E*)-Methyl 3-(2,6-Dichlorobenzyloxy)acrylate (4e). DABCO (0.27 g, 23.8 mmol) in THF (300 mL), 2,6-dichlorobenzyl alcohol (4.63 g, 26.2 mmol), and methyl propiolate (2.00 g, 23.8 mmol) were combined according to general procedure. Purification was achieved by flash chromatography (10:1 pet./EtOAc) to afford title compound as a colorless oil (3.82 g, 62%). FTIR (film/cm^{-1}) υ_{max} 3090.0, 2951.1, 2892.8, 1706.6, 1644.1, 1620.7, 1583.0, 1565.4; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.73 (s, 3H), 5.16 (s, 2H), 5.39 (d, 1H, J = 12.6 Hz), 7.25−7.28 (m, 1H) 7.35 (s, 1H), 7.37 (s, 1H), 7.71 (d, 1H, J = 12.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 51.2, 67.5, 128.5, 130.7, 131.0, 137.0, 162.1, 167.9; HRMS (ESI, +ve) m/z calcd for $C_{11}H_{10}Cl_2O_3Na$ 282.9905, found 282.9887 $(M + Na)^+$.

(*S,E*)-Methyl 3-(1-Phenylethoxy)acrylate (4f). DABCO (0.26 g, 2.38 mmol) in THF (200 mL), (*S*)-1-phenylethanol (2.90 g, 26.2 mmol), and methyl propiolate (2.00 g, 23.8 mmol) were combined according to general procedure. Purification was achieved by flash chromatography (30:1 pet./EtOAc) to afford the title compound as a white solid (4.0 g, 81%). $[\alpha]^{20}_D$ = −113 (*c* 1, CH_2Cl_2); mp 38−39 °C; FTIR (film/cm^{-1}) υ_{max} 2993.6, 2950.2, 1713.4, 1643.4; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.60 (d, 3H, J = 7.2 Hz), 3.65 (s, 3H), 5.04 (q, 1H, J = 6.7 Hz), 5.25 (d, 1H, J = 12.5 Hz), 7.39−7.29 (m, 5H), 7.52 (d, 2H, J = 12.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.4, 51.0, 80.5, 98.1, 125.7, 128.2, 128.8, 141.2, 161.5, 168.2; HRMS (ESI, +ve) m/z calcd for $C_{12}H_{14}O_3Na$ 229.0841, found 229.0832. $(M + Na)^+$.

(*E*)-3-(Isopropyloxy)prop-2-enol (5b). (*E*)-Methyl 3-(isopropoxy)acrylate (2.00 g, 13.8 mmol) was reduced according to general procedure to afford the title compound as a yellow oil (1.19 g, 74%). FTIR (film/cm^{-1}) υ_{max} 3371.8, 2976.5, 2931.2, 2874.6, 1670.6, 1650.9; ^{1}H NMR (500 MHz, d_6-acetone) δ 1.15 (d, 6H, J = 6.2 Hz), 3.81 (app. t, 2H, J = 6.5 Hz), 4.00 (quin, 1H, J = 6.2 Hz), 4.36 (t, 1H, J = 6.5 Hz), 4.88 (dt, 1H, J = 12.5, 6.5 Hz), 6.33 (d, 1H, J = 12.5 Hz); ^{13}C NMR (125 MHz, d_6-acetone) δ 22.4, 59.0, 72.3, 105.7, 147.6.

(*E*)-3-(Pentan-3-yloxy)prop-2-enol (5c). (*E*)-Methyl 3-(pentan-3-yloxy)acrylate **4b** (1.32 g, 10.4 mmol) was reduced according to general procedure to afford the title compound as a colorless oil (1.05 g, 68%). FTIR (film/cm^{-1}) υ_{max} 3347.2, 2966.1, 2937.3, 2878.9, 1699.1, 1650.3; ^{1}H NMR (500 MHz, d_6-acetone) δ 0.89 (t, 6H, J=7.4 Hz), 1.55 (m, 4H), 3.31 (t, 1H, J=5.8 Hz), 3.54 (quin, 1H, J=5.9 Hz), 4.00 (dd, 2H, J=7.6, 1.0 Hz), 5.08 (dt, 1H, J=12.3, 7.6 Hz), 6.37 (d, 1H, J=12.3 Hz); ^{13}C NMR (125 MHz, d_6-acetone) δ 8.9, 26.2, 59.4, 82.8, 104.7, 148.8.

(*E*)-3-(Prop-2-ynyloxy)prop-2-en-1-ol (5d). (*E*)-Methyl 3-(prop-2-ynyloxy)acrylate **4c** (1.03 g, 7.35 mmol) was reduced according to general procedure to afford the title compound as a colorless oil (0.63 g, 75%). FTIR (film/cm^{-1}) υ_{max} 3380.5, 3289.2, 2926.0, 2869.7, 2120.7, 1671.8, 1653.0; ^{1}H NMR (500 MHz, d_6-acetone) δ 2.60 (dt, 1H, J = 2.4, 0.8 Hz), 4.06 (d, 2H, J = 7.2 Hz), 4.43 (d, 2H, J = 2.4 Hz), 5.17 (dt, 1H, J = 12.7, 7.2 Hz), 6.52 (d, 1H, J = 12.7 Hz); ^{13}C NMR (125 MHz, d_6-acetone) δ 57.0, 60.1, 75.3, 78.5, 105.4, 148.1.

(*E*)-3-(2,6-Dichlorobenzyloxy)prop-2-en-1-ol (5e). (*E*)-Methyl 3-(2,6-dichlorobenzyloxy)acrylate **4d** (1.25 g, 4.79 mmol) was reduced according to the general procedure to afford the title compound as a white solid (0.74 g, 67%). Mp 80−83 °C; FTIR (film/cm^{-1}) υ_{max} 3300.2, 3078.3, 2945.4, 2863.0, 1672.2, 1583.1, 1563.1; ^{1}H NMR (500 MHz, d_6-acetone) δ 3.46 (t, 1H, J = 5.6 Hz), 4.02 (m, 2H), 5.03 (s, 2H), 5.18 (dt, 1H, J = 12.6, 7.2 Hz), 6.63 (d, 1H, J = 12.6 Hz), 7.41−7.45 (m, 1H), 7.49−7.51 (m, 2H); ^{13}C NMR (125 MHz, d_6-acetone) δ 59.2, 65.5, 104.8, 128.6, 131.0, 132.4, 136.5, 148.2.

(*S,E*)-3-(1-phenylethoxy)prop-2-enol (5f). (*S,E*)-Methyl 3-(1-phenylethoxy)acrylate **4e** (2.65 g, 12.9 mmol) was reduced according to general procedure to afford the title compound as a colorless oil (1.72 g, 75%). $[\alpha]^{20}_D$ −68 (*c* 1, CH_2Cl_2); FTIR (film/cm^{-1}) υ_{max} 3347.2, 3086.6, 3062.8, 3031.0, 2977.6, 2930.0, 2872.4, 1670.1, 1671.2, 1651.2; ^{1}H NMR (500 MHz, d_6-DMSO) δ 1.42 (d, 3H, J = 6.5 Hz), 3.75 (app. t, 2H, J = 6.6 Hz), 4.38 (t, 1H, J = 5.4 Hz), 4.88−4.95 (m, 2H), 6.33 (d, 1H, J = 12.4 Hz), 7.30−7.38 (m, 5H); ^{13}C NMR (125 MHz, d_6-DMSO) δ 23.8, 58.8, 77.7, 106.6, 125.7, 126.3, 127.9, 128.4, 128.9, 143.4, 147.4.

(*E*)-3-Methoxyallyl 2-((*tert*-Butoxycarbonyl)amino)acetate (6). EDCi·HCl (2.50 g, 17.0 mmol), triethylamine (1.6 mL, 17.0 mmol), *N*-Boc-Gly-OH (2.24 g, 17.0 mmol), and (*E*)-3-(methoxy)prop-2-enol (0.75 g, 8.51 mmol) were combined according to general procedure to afford the title compound as a colorless oil (1.45 g mass recovery; because of product instability, this ester was used without further purification; see Supporting Information for NMR spectra relating to purity). FTIR (film/cm^{-1}) υ_{max} 2880.3, 1736.1, 1717.6, 1673.9; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.51 (s, 3H), 3.83 (app. q, 2H, J = 5.6 Hz), 4.51 (d, 2H, J = 7.8 Hz), 4.89 (dt, 1H, J = 12.7, 7.8 Hz), 4.99 (br, 1H), 6.59 (d, 1H, J = 12.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.4, 42.7, 55.1, 66.3, 80.2, 125.9, 136.7, 156.0, 171.4; HRMS (ESI, +ve) m/z calcd for $C_{11}H_{19}NO_5Na$ 268.1161, found 268.1175 $(M + Na)^+$.

(*E*)-3-Methoxyallyl 2-(Bis(*tert*-butoxycarbonyl)amino)acetate (16a). EDCi·HCl (1.01 g, 5.27 mmol), triethylamine (0.74 mL, 5.27 mmol), 2-(bis(*tert*-butoxycarbonyl)amido)acetic acid (1.15 g, 5.27 mmol), and (*E*)-3-methoxyprop-2-enol (0.31 g, 2.63 mmol)

(49) Winterfeldt, E.; Preuss, H. *Chem. Ber.* **1966**, *99*, 450.

were combined according to general procedure to afford the title compound as a yellow oil (0.85 g mass recovery; because of product instability, this ester was used without further purification; see Supporting Information for NMR spectra relating to purity). FTIR (film/cm^{-1}) υ_{max} 2980.8, 2936.5, 1732.0, 1697.3; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.49 (s, 18H), 3.55 (s, 3H), 4.30 (s, 2H), 4.56 (d, 2H, J = 7.9 Hz), 4.91 (dt, 1H, J = 12.7, 7.9 Hz), 6.63 (d, 1H, J = 12.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.0, 47.4, 56.1, 63.3, 83.0, 96.6, 151.9, 153.6, 169.2; HRMS (ESI, +ve) m/z calcd for $C_{16}H_{27}NO_7Na$ 368.1685, found 368.1673 $(M + Na)^+$.

(*E*)-3-Isopropyloxyallyl 2-(Bis(*tert*-butoxycarbonyl)amino)-acetate (16b). EDCi·HCl (0.79 g, 4.12 mmol), triethylamine (0.60 mL, 4.12 mmol), 2-(bis(*tert*-butoxycarbonyl)amido)acetic acid (1.13 g, 4.12 mmol), and (*E*)-3-(isopropoxy)prop-2-enol (0.24 g, 2.06 mmol) were combined according to general procedure, omitting the citric acid wash, to afford the title compound as a brown oil (0.72 g mass recovery; because of product instability, this ester was used without further purification; see Supporting Information for NMR spectra relating to purity). FTIR (film/cm^{-1}) υ_{max} 2978.5, 2936.4, 1757.1, 1736.3, 1697.0, 1671.0; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 1.21 (d, 6H, J = 6.3 Hz), 1.49 (s, 18H), 4.12 (sept, 1H, J = 6.3 Hz), 4.27 (s, 2H), 4.55 (d, 2H, J = 7.8 Hz), 4.97 (dt, 1H, J = 12.8, 7.8 Hz), 6.62 (d, 1H, J = 12.8 Hz); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 21.4, 27.3, 47.1, 63.1, 72.9, 82.1, 98.6, 152.0, 168.8; HRMS (ESI, +ve) m/z calcd for $C_{18}H_{31}NO_7Na$ 396.1998, found 396.2005 $(M + Na)^+$.

(*E*)-3-Ethyloxyallyl 2-(Bis(*tert*-butoxycarbonyl)amino)acetate (16c). EDCi·HCl (0.75 g, 3.91 mmol), triethylamine (0.54 mL, 3.91 mmol), 2-(bis(*tert*-butoxycarbonyl)amido)acetic acid (1.07 g, 3.91 mmol), and (*E*)-3-ethoxyprop-2-enol (0.20 g, 1.96 mmol) were combined according to general procedure to afford the title compound as a yellow oil (0.64 g mass recovery; because of product instability, this ester was used without further purification; see Supporting Information for NMR spectra relating to purity). FTIR (film/cm^{-1}) υ_{max} 2980.6, 2935.6, 1755.7, 1743.7, 1697.4, 1652.9; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.20 (t, 3H, J = 6.8 Hz), 1.43 (s, 18H), 3.69 (q, 2H, J = 6.8 Hz), 4.23 (s, 2H), 4.48 (d, 2H, J = 7.9 Hz), 4.85 (dt, 1H, J = 12.7, 7.9 Hz), 6.51 (d, 1H, J = 12.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5, 27.9, 47.3, 63.4, 64.9, 82.8, 97.2, 151.7, 152.7, 169.1; HRMS (ESI, +ve) m/z calcd for $C_{17}H_{29}NO_7Na$ 382.1842, found 382.1853 $(M + Na)^+$.

(*E*)-3-(Pentan-3-yloxy)allyl 2-(Bis(*tert*-butoxycarbonyl)amino)-acetate (16d). EDCi·HCl (0.62 g, 3.23 mmol), triethylamine (0.45 mL, 3.23 mmol), 2-(bis(*tert*-butoxycarbonyl)amido)acetic acid (0.89 g, 3.23 mmol), and (*E*)-3-(pentan-3-yloxy)prop-2-enol (0.24 g, 1.62 mmol) were combined according to general procedure, omitting the citric acid wash, to afford the title compound as a brown oil (0.49 g mass recovery; because of product instability, this ester was used without further purification; see Supporting Information for NMR spectra relating to purity). FTIR (film/cm^{-1}) υ_{max} 2978.7, 2937.9, 2881.5, 1798.9, 1755.9, 1736.3, 1697.7, 1669.7; ^{1}H NMR (500 MHz, d_6-acetone) δ 0.90 (t, 6H, J = 7.5 Hz), 1.49 (s, 22H), 3.70 (quin, 1H, J = 5.8 Hz), 4.28 (s, 2H), 4.55 (d, 2H, J = 7.9 Hz), 4.99 (dt, 1H, J = 12.2, 7.9 Hz), 6.66 (d, 1H, J = 12.2 Hz); ^{13}C NMR (125 MHz, d_6-acetone) δ 8.9, 26.3, 27.3, 47.1, 63.2, 82.1, 3.6, 98.2, 151.8, 153.2, 168.9; HRMS (ESI, +ve) m/z calcd for $C_{20}H_{35}NO_7Na$ 424.2311, found 424.2349 $(M + Na)^+$.

(*E*)-3-(Neopentyloxy)allyl 2-(Bis(*tert*-butoxycarbonyl)amino)-acetate (16e). EDCi·HCl (0.45 g, 2.33 mmol), triethylamine (0.32 mL, 2.33 mmol), 2-(bis(*tert*-butoxycarbonyl)amido)acetic acid (0.64 g, 2.33 mmol), and (*E*)-3-(neopentyloxy)prop-2-en-1-ol (0.17 g, 1.16 mmol) were combined according to general procedure to afford the title compound as a yellow oil (0.33 g mass recovery; because of product instability, this ester was used without further purification; see Supporting Information for NMR spectra relating to purity). FTIR (film/cm^{-1}) υ_{max} 2979.9, 2868.7, 1796.5, 1756.3, 1736.1, 1698.4, 1651.9; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.92 (s, 9H), 1.48 (s, 18H), 3.32 (s, 2H), 4.28 (s, 2H), 4.55 (d, 2H, J = 7.8 Hz), 4.89 (dt, 1H, J = 12.6, 7.8 Hz), 6.61 (d, 1H, J = 12.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.4, 28.0, 43.0, 47.4, 63.6, 79.3, 82.9, 96.6, 151.8, 153.6, 169.2; HRMS (ESI, +ve) m/z calcd for $C_{20}H_{35}NO_7Na$ 424.2311, found 424.2299 $(M + Na)^+$.

(*E*)-3-(Allyloxy)allyl 2-(Bis(*tert*-butoxycarbonyl)amino)acetate (16f). EDCi·HCl (0.53 g, 2.76 mmol), triethylamine (0.40 mL, 2.76 mmol), 2-(bis(*tert*-butoxycarbonyl)amido)acetic acid (0.76 g, 2.76 mmol), and (*E*)-3-(allyloxy)prop-2-enol (0.16 g, 1.38 mmol) were combined according to general procedure to afford the title compound as a yellow oil (0.40 g mass recovery; because of product instability, this ester was used without further purification; see Supporting Information for NMR spectra relating to purity). FTIR (film/cm^{-1}) υ_{max} 2981.3, 2936.0, 1755.8, 1735.8, 1698.0, 1673.1, 1654.7; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (s, 18H), 4.26 (dt, 2H, J = 5.6, 1.5 Hz) 4.32 (s, 2H), 4.58 (d, 2H, J = 7.8 Hz), 4.99 (dt, 1H, J = 12.7, 7.8 Hz), 5.26 (dq, 1H, J = 10.5, 1.5 Hz), 5.34 (dq, 1H, J = 17.2, 1.5 Hz), 5.90−5.98 (m, 1H), 6.60 (d, 1H, J = 12.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.0, 47.4, 63.4, 70.3, 83.0, 98.1, 118.0, 132.7, 151.9, 152.3, 169.2; HRMS (ESI, +ve) m/z calcd for $C_{18}H_{29}NO_7Na$ 394.1842, found 394.1831 $(M + Na)^+$.

(*E*)-3-(prop-2-yn-1-yloxy)allyl 2-(Bis(*tert*-butoxycarbonyl)amino)-acetate (16g). EDCi·HCl (1.09 g, 5.69 mmol), triethylamine (0.80 mL, 5.69 mmol), 2-(bis(*tert*-butoxycarbonyl)amido)acetic acid (1.57 g, 5.69 mmol), and (*E*)-3-(prop-2-yn-1-yloxy)prop-2-en-1-ol (0.32 g, 2.84 mmol) were combined according to general procedure to afford the title compound as a yellow oil (0.90 g mass recovery; because of product instability, this ester was used without further purification; see Supporting Information for NMR spectra relating to purity). FTIR (film/cm^{-1}) υ_{max} 2980.4, 2940.0, 2146.1, 1796.1, 1753.6, 1734.5, 1696.5, 1654.5; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.47 (s, 18H), 2.52 (t, 1H, J = 2.5 Hz), 4.28 (s, 2H), 4.36 (d, 2H, J = 2.5 Hz), 4.55 (dd, 2H, J = 7.9, 0.6 Hz), 5.05 (dt, 1H, J = 12.7, 7.9 Hz), 6.55 (d, 1H, J = 12.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.9, 47.3, 57.0, 62.9, 75.9, 77.7, 83.0, 99.5, 150.9, 151.8, 169.1; HRMS (ESI, +ve) m/z calcd for $C_{18}H_{27}NO_7Na$ 392.1685, found 392.1705 $(M + Na)^+$.

(*E*)-3-(Benzyloxy)allyl 2-(Bis(*tert*-butoxycarbonyl)amino)-acetate (16h). EDCi·HCl (0.94 g, 4.90 mmol), triethylamine (0.70 mL, 4.90 mmol), 2-(bis(*tert*-butoxycarbonyl)amido)acetic acid (1.35 g, 4.90 mmol), and (*E*)-3-bezyloxyprop-2-enol (0.20 g, 2.45 mmol) were combined according to general procedure. Purifcation was achieved by flash chromatography (Al_2O, 10:1 petrol/EtOAc) to afford the title compound as a colorless oil (0.32 g mass recovery; because of product instability, this ester was used without further purification; see Supporting Information for NMR spectra relating to purity). FTIR (film/cm^{-1}) υ_{max} 2980.4, 2938.6, 1757.7, 1736.4, 1698.3; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (s, 18H), 4.33 (s, 2H), 4.60 (d, 2H, J = 7.8 Hz), 4.78 (s, 2H), 5.08 (dt, 1H, J = 12.4, 7.8 Hz), 6.71 (d, 1H, J = 12.4 Hz), 7.33−7.41 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.0, 47.4, 63.4, 71.4, 83.1, 98.2, 127.7, 128.2, 128.6, 136.2, 151.9, 152.5, 169.2; HRMS (ESI, +ve) m/z calcd for $C_{22}H_{31}NO_7Na$ 444.1998, found 444.1996 $(M + Na)^+$.

(*E*)-3-(4-Methoxybenzyloxy)allyl 2-(Bis(*tert*-butoxycarbonyl)-amino)acetate (16i). EDCi·HCl (0.44 g 2.31 mmol), triethylamine (0.32 mL, 2.31 mmol), 2-(bis(*tert*-butoxycarbonyl)amido)acetic acid (0.64 g, 2.31 mmol), and (*E*)-3-((4-methoxybenzyl)oxy)-prop-2-en-1-ol (0.22 g, 1.15 mmol) were combined according to general procedure to afford the title compound as a yellow oil (0.73 g mass recovery; because of product instability, this ester was used without further purification; see Supporting Information for NMR spectra relating to purity). FTIR (film/cm^{-1}) υ_{max} 3054.2, 3026.5, 2998.7, 2968.1, 1759.6, 1731.9, 1698.3; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.49 (s, 18H), 3.80 (s, 3H), 4.31 (s, 2H), 4.57 (d, 2H, J = 7.6 Hz), 4.68 (s, 2H), 5.04 (dt, 1H, J = 12.6, 7.6 Hz), 6.66 (d, 1H, J = 12.6 Hz), 6.86−6.90 (m, 2H), 7.24−7.29 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.0, 47.4, 55.3, 63.4, 71.2, 83.0, 98.1, 114.0,

128.3, 129.4, 151.9, 152.5, 159.6, 169.2; HRMS (ESI, +ve) m/z calcd for $C_{23}H_{33}NO_8Na$ 474.2104, found 474.2123 $(M + Na)^+$.

(*E*)-3-((2,6-dichlorobenzyl)oxy)allyl 2-(Bis(*tert*-butoxycarbonyl)-amino)acetate (16j). EDCi·HCl (0.55 g, 2.87 mmol), triethylamine (0.40 mL, 2.87 mmol), 2-(bis(*tert*-butoxycarbonyl)amido)acetic acid (0.79 g, 2.87 mmol), and (*E*)-3-(2,6-dichlorobenzyloxy)-prop-2-enol (0.34 g, 1.43 mmol) were combined according to general procedure to afford the title compound as a yellow oil (0.74 g mass recovery; because of product instability, this ester was used without further purification; see Supporting Information for NMR spectra relating to purity). FTIR (film/cm^{-1}) υ_{max} 2980.9, 2939.7, 2887.4, 1754.9, 1735.3, 1696.7, 1651.4; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.52 (s, 18H), 4.34 (s, 2H), 4.62 (d, 2H, J = 8.8 Hz), 5.03 (s, 2H), 5.13 (dt, 1H, J = 12.7, 7.8 Hz), 6.73 (d, 1H, J = 12.7 Hz), 7.23−7.36 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.0, 47.4, 63.2, 66.1, 83.0, 98.4, 128.4, 130.6, 131.7, 136.9, 151.9, 152.3, 169.2; HRMS (ESI, +ve) m/z calcd for $C_{22}H_{29}NO_7Cl_2Na$ 512.1190, found 512.1194 $(M + Na)^+$.

(*S*,*E*)-3-(1-Phenylethoxy)allyl 2-(Bis(*tert*-butoxycarbonyl)-amino)acetate (16k). EDCi·HCl (0.56 g, 2.90 mmol), triethylamine (0.40 mL, 2.90 mmol), 2-(bis(*tert*-butoxycarbonyl)amido)acetic acid (0.80 g, 2.90 mmol), and (*S*,*E*)-3-(1-phenylethoxy)prop-2-enol (0.26 g, 1.45 mmol) were combined according to general procedure to afford the title compound as a yellow oil (0.31 g mass recovery; because of product instability, this ester was used without further purification; see Supporting Information for NMR spectra relating to purity). $[\alpha]^{20}_D$ = −60 (c 1, CH_2Cl_2); FTIR (film/cm^{-1}) υ_{max} 3002.5, 2999.3, 2985.2, 1754.6, 1734.2, 1698.21651.7; ^{1}H NMR (500 MHz, d_6-acetone) δ 1.02−1.13 (m, 3H), 1.37 (s, 18H), 4.14 (s, 2H), 4.38 (d, 2H, J = 7.9 Hz), 4.85−4.97 (m, 2H), 6.53 (d, 1H, J = 12.7 Hz), 7.08−7.34 (m, 5H); ^{13}C NMR (125 MHz, d_6-acetone) δ 23.9, 28.4, 46.4, 58.8, 77.7, 82.6, 106.6, 125.7, 126.3, 127.9, 128.4, 128.9, 143.4, 147.4, 152.7, 169.5; HRMS (ESI, +ve) m/z calcd for $C_{23}H_{33}NO_7Na$ 458.2155, found 458.2140 $(M + Na)^+$.

(*E*)-3-Phenoxyallyl 2-(Bis(*tert*-butoxycarbonyl)amino)acetate (16l). EDCi·HCl (0.58 g, 3.03 mmol), triethylamine (0.42 mL, 3.03 mmol), 2-(bis(*tert*-butoxycarbonyl)amido)acetic acid (0.84 g, 3.03 mmol), and (*E*)-3-phenoxyprop-2-enol (0.23 g, 1.51 mmol) were combined according to general procedure to afford the title compound as a yellow oil (0.62 g mass recovery; because of product instability, this ester was used without further purification; see Supporting Information for NMR spectra relating to purity). FTIR (film/cm^{-1}) υ_{max} 2980.1, 2936.0, 1755.7, 1735.9, 1697.0; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (s, 18H), 4.35 (s, 2H), 4.67 (d, 2H, J = 7.9 Hz), 5.45 (dt, 1H, J = 12.4, 7.9 Hz), 6.82 (d, 1H, J = 12.4 Hz), 7.01 (d, 2H, J = 8.3 Hz), 7.11 (t, 1H, J = 7.7 Hz), 7.34 (t, 2H, J = 8.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.4, 47.6, 62.6, 83.0, 105.1, 117.2, 123.6, 130.0, 148.5, 152.0, 156.8, 169.3; HRMS (ESI, +ve) m/z calcd for $C_{21}H_{29}NO_7Na$ 430.1842, found 430.1827 $(M + Na)^+$.

(*E*)-3-(4-Trifluoromethylphenoxyallyl 2-(Bis(*tert*-butoxycarbonyl)amino)acetate (16m). EDCi·HCl (0.33 g, 1.72 mmol), triethylamine (0.22 mL, 1.72 mmol), 2-(bis(*tert*-butoxycarbonyl)-amido)acetic acid (0.47 g, 1.72 mmol), and (*E*)-3-bezyloxyprop-2-enol (0.19 g, 0.86 mmol) were combined according to general procedure to afford the title compound as a colorless oil (0.40 g mass recovery; because of product instability, this ester was used without further purification; see Supporting Information for NMR spectra relating to purity). FTIR (film/cm^{-1}) υ_{max} 3013.2, 2937.1, 1795.5, 1756.0, 1735.2, 1698.6, 1612.7; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (s, 18H), 4.36 (s, 2H), 4.69 (dd, 2H, J = 7.6, 1.0 Hz), 5.55 (dt, 1H, J = 12.2, 7.6 Hz), 6.82 (dt, 1H, J = 12.2, 1.0 Hz), 7.09 (app. d, 2H, J = 8.6 Hz), 7.60 (app. d, 2H, J = 8.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.0, 47.3, 61.7, 83.2, 107.3, 116.9, 125.4, 125.7, 127.2 (q, J = 3.8 Hz), 146.9, 152.0, 158.9, 169.1; HRMS (ESI, +ve) m/z calcd for $C_{22}H_{28}F_3NO_7Na$ 498.1716, found 498.1719 $(M + Na)^+$.

(*E*)-3-(4-Methoxyphenyloxy)allyl 2-Bis(*tert*-butoxycarbonyl)-amino)acetate (16n). EDCi·HCl (0.41 g, 2.14 mmol), triethylamine (0.30 mL, 2.14 mmol), 2-(bis(*tert*-butoxycarbonyl)amido)acetic acid (0.59 g, 2.14 mmol), and (*E*)-3-(4-methoxyphenyloxy)prop-2-enol (0.20 g, 1.07 mmol) were combined according to general procedure to afford the title compound as a yellow oil (0.41 g mass recovery; because of product instability, this ester was used without further purification; see Supporting Information for NMR spectra relating to purity). FTIR (film/cm^{-1}) υ_{max} 2979.9, 2940.1, 1796.2, 1755.6, 1735.3, 1697.3, 1673.1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.47 (s, 18H), 3.75 (s, 3H), 4.30 (s, 2H), 4.60 (d, 2H, J = 7.7 Hz), 5.29 (dt, 1H, J = 12.2, 7.7 Hz), 6.72 (d, 1H, J = 12.2 Hz), 6.82 (app. dt, 2H, J = 8.9, 2.9 Hz), 6.90 (app. dt, 2H, J = 8.9, 2.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.9, 47.4, 55.6, 62.4, 83.1, 103.7, 114.7, 118.6, 150.0, 150.3, 151.8, 155.9, 169.1; HRMS (ESI, +ve) m/z calcd for $C_{22}H_{31}NO_8Na$ 460.1947, found 460.1916 $(M + Na)^+$.

(±)-(2*R*,3*S*)-Methyl 2-(Bis(*tert*-butoxycarbonyl)amino)-3-methoxypent-4-enoate (17a). (*E*)-3-Methoxyallyl 2-(bis(*tert*-butoxycarbonyl)amino)acetate **16a** (0.10 g, 0.28 mmol), TMSCl (0.07 mL, 0.55 mmol), and LiHMDS (0.55 mL, 0.55 mmol) were combined according to the general procedure. Treatment with diazomethane and purification by flash chromatography (15:1 pet./EtOAc + 1% NEt_3) afforded the title compound as a colorless oil (0.07 g, 72%). FTIR (film/cm^{-1}) υ_{max} 2986.3, 2938.0, 1752.4, 1698.1, 1649.9; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (s, 18H), 3.27 (s, 3H), 3.70 (s, 3H), 4.18 (app. t, 1H, J = 7.8 Hz), 4.87 (d, 1H, J = 8.5 Hz), 5.33 (dq, 1H, J = 10.4, 1.2 Hz), 5.42 (dq, 1H, J = 17.1, 1.2 Hz), 5.88 (ddd, 1H, J = 17.1, 10.4, 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.0, 52.0, 56.8, 61.4, 79.1, 82.9, 118.6, 136.4, 152.2, 169.4; HRMS (ESI, +ve) m/z calcd for $C_{17}H_{29}NO_7Na$ 382.1842, found 382.1830 $(M + Na)^+$.

(±)-(2*R*,3*S*)-Methyl 2-(Bis(*tert*-butoxycarbonyl)amino)-3-neopentyloxypent-4-enoate (17b). (*E*)-3-Isopropoxyallyl 2-(bis(*tert*-butoxycarbonyl)amino)acetate **16b** (0.10 g, 0.31 mmol), TMSCl (0.08 mL, 0.61 mmol), and LiHMDS (0.61 mL, 0.61 mmol) were combined according to the general procedure. Treatment with diazomethane and purification by flash chromatography (15:1 pet./EtOAc + 1% NEt_3) afforded the title compound as a colorless oil (0.05 g, 50%). FTIR (film/cm^{-1}) υ_{max} 2979.2, 2937.1, 1798.7, 1750.2, 1698.2; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.09 (dd, 6H, J = 11.0, 6.1 Hz), 1.51 (s, 18H), 3.63 (sept, 1H, J = 6.1 Hz), 3.70 (s, 3H), 4.41−4.44 (m, 1H), 4.80 (d, 1H, J = 9.4 Hz), 5.24 (dq, 1H, J = 10.5, 0.8 Hz), 5.44 (dq, 1H, J = 15.4, 0.8 Hz), 6.03 (ddd, 1H, J = 15.4, 10.5, 6.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ:21.4, 23.3, 28.0, 47.2, 52.1, 62.1, 69.9, 74.9, 83.1, 117.1, 138.1, 152.2, 169.7; HRMS (ESI, +ve) m/z calcd for $C_{19}H_{33}NO_7Na$ 410.2154, found 410.2144 $(M + Na)^+$.

(±)-(2*R*,3*S*)-Methyl 2-(Bis(*tert*-butoxycarbonyl)amino)-3-ethoxypent-4-enoate (17c). (*E*)-3-Ethoxyallyl 2-(bis(*tert*-butoxycarbonyl)amino)acetate **16c** (0.10 g, 0.27 mmol), TMSCl (0.07 mL, 0.53 mmol), and LiHMDS (0.53 mL, 0.53 mmol) were combined according to the general procedure. Treatment with diazomethane and purification by flash chromatography (10:1 pet./EtOAc + 1% NEt_3) afforded the title compound as a colorless oil (0.07 g, 56%). FTIR (film/cm^{-1}) υ_{max} 2980.4, 2937.3, 1794.1, 1748.2, 1698.2; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.14 (t, 3H, J = 7.0 Hz), 1.52 (s, 18H), 3.30 (dq, 1H, J = 9.2, 7.0 Hz), 3.59 (dq, 1H, J = 9.2, 7.0 Hz), 3.71 (s, 3H), 4.32 (dd, 1H, J = 9.0 Hz), 4.86 (d, 1H, J = 9.0 Hz), 5.28 (dq, 1H, J = 10.4, 1.0 Hz), 5.42 (dq, 1H, J = 17.2, 1.0 Hz), 5.96 (ddd, 1H, J = 17.2, 10.4, 6.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.2, 28.0, 47.2, 51.9, 61.6, 64.6, 82.7, 117.7, 137.2, 152.24, 169.5; HRMS (ESI, +ve) m/z calcd for $C_{18}H_{31}NO_7Na$ 396.1998, found 396.2001 $(M + Na)^+$.

(±)-(2*R*,3*S*)-Methyl 2-(Bis(*tert*-butoxycarbonyl)amino)-3-(pentan-3-yloxy)pent-4-enoate (17d). (*E*)-3-(Pentan-3-yloxy)allyl 2-(bis(*tert*-butoxycarbonyl)amino)acetate **16d** (0.22 g, 0.55 mmol), TMSCl (0.14 mL, 1.10 mmol), and LiHMDS (1.10 mL, 1.10 mmol) were combined according to the general procedure. Treatment with diazomethane and purification by flash chromatography (15:1 pet./EtOAc + 1% NEt_3) afforded the title compound as a colorless oil

(0.10 g, 45%)FTIR (film/cm^{-1}) υ_{max} 2980.0, 2937.7, 2879.8, 1797.7, 1751.0, 1698.6; ^{1}H NMR (500 MHz, d_6-acetone) δ 0.84 (t, 6H, J = 7.6 Hz), 1.48−1.51 (m, 22H), 3.31 (quin, 1H, J = 5.9 Hz), 3.66 (s, 3H), 4.45 (dd, 1H, J = 9.2, 2.3 Hz), 4.84 (d, 1H, J = 9.2 Hz), 5.25 (dd, 1H, J = 10.5, 1.7 Hz), 5.39 (d, 1H, J = 17.1 Hz), 5.94 (ddd, 1H, J = 17.1, 10.5, 6.8 Hz); ^{13}C NMR (125 MHz, d_6-acetone) δ 8.0, 9.2, 24.2, 25.7, 27.3, 51.2, 61.8, 75.0, 78.2, 82.0, 117.3, 138.5, 152.2, 168; HRMS (ESI, +ve) m/z calcd for $C_{21}H_{38}NO_7$ 416.2648, found 416.2625 (M + H)$^+$.

(±)-(2*R*,3*S*)-Methyl 2-(Bis(*tert*-butoxycarbonyl)amino)-3-neopentyloxypent-4-enoate (17e). (*E*)-3-(Neopentyloxy)allyl 2-(bis(*tert*-butoxycarbonyl)amino)acetate **16e** (0.10 g, 0.25 mmol), TMSCl (0.06 mL, 0.49 mmol), and LiHMDS (0.49 mL, 0.49 mmol) were combined according to the general procedure. Treatment with diazomethane and purification by flash chromatography (15:1 pet./EtOAc + 1% NEt_3) afforded the title compound as a colorless oil (0.08 g, 80%). FTIR (film/cm^{-1}) υ_{max} 2979.6, 2955.0, 1796.3, 1749.2, 1698.4; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (s, 9H), 1.51 (s, 18H), 2.80 (d, 1H, J = 8.4 Hz), 3.23 (d, 1H, J = 8.4 Hz), 3.70 (s, 3H), 4.28 (dd, 1H, J = 9.0, 2.4 Hz) 4.94 (d, 1H, J = 9.0 Hz), 5.30 (dd, 1H, J = 10.3, 1.9 Hz), 5.43 (dt, 1H, J = 17.4, 1.9 Hz), 5.90 (ddd, 1H, J = 17.4, 10.3, 8.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.8, 28.1, 32.0, 51.9, 61.7, 77.3, 79.4, 82.8, 118.1, 137.6, 152.0, 169; HRMS (ESI, +ve) m/z calcd for $C_{21}H_{38}NO_7$ 416.2648, found 416.2620 (M + H)$^+$.

(±)-(2*R*,3*S*)-Methyl 2-(Bis(*tert*-butoxycarbonyl)amino)-3-allyloxypent-4-enoate(17f). (*E*)-3-Allyloxyallyl 2-(bis(*tert*-butoxycarbonyl)-amino)acetate **16f** (0.12 g, 0.21 mmol), TMSCl (0.05 mL, 0.41 mmol), and LiHMDS (0.41 mL, 0.41 mmol) were combined according to the general procedure. Treatment with diazomethane and purification by flash chromatography (10:1 pet./EtOAc + 1% NEt_3) afforded the title compound as a colorless oil (0.08 g, 65%). FTIR (film/cm^{-1}) υ_{max} 2981.7, 2935.6, 1747.9, 1698.3; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (s, 18H), 3.70 (s, 3H), 3.81 (ddt, 1H J = 12.9, 5.7, 1.6 Hz), 4.07 (ddt, 1H, J = 12.9, 5.1, 1.6 Hz), 4.36−4.40 (m, 1H), 4.91 (d, 1H, J = 8.9 Hz), 5.12 (dq, 1H, J = 10.4, 1.6 Hz), 5.24 (dq, 1H, J = 17.1, 1.6 Hz), 5.32 (dq, 1H, J = 10.5, 1.0 Hz), 5.43 (dq, 1H, J = 17.2, 1.0 Hz), 5.80−5.88 (m, 1H), 5.94 (ddd, 1H, J = 17.2, 10.5, 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ:28.0, 51.9, 61.5, 69.6, 74.9, 82.9, 116.4, 118.4, 134.7, 136.7, 152.2, 169.4; HRMS (ESI, +ve) m/z calcd for $C_{19}H_{31}NO_7Na$ 408.1998, found 408.1976 (M + Na)$^+$.

+(±)-(2*R*,3*S*)-Methyl 2-(Bis(*tert*-butoxycarbonyl)amino)-3-(3-(trimethylsilyl)prop-2-ynyloxy)pent-4-enoate (17g). (*E*)-3-(Prop-2-yn-1-yloxy)allyl 2-(bis(*tert*-butoxycarbonyl)amino)acetate **16g** (0.10 g, 0.30 mmol, 1 equiv), TMSCl (0.10 mL, 0.89 mmol, 3 equiv), and LiHMDS (0.89 mL, 0.89 mmol, 3 equiv) were combined according to the general procedure. Treatment with diazomethane and purification by flash chromatography (10:1 pet./EtOAc + 1% NEt_3) afforded the title compound as a colorless oil (0.10 g, 71%). FTIR (film/cm^{-1}) υ_{max} 2979.7, 2867.7, 2182.2, 1794.0, 1749.6, 1700.7; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.16 (s, 9H), 1.52 (s, 18H), 3.70 (s, 3H), 4.05 (d, 1H, J = 15.6 Hz), 4.17 (d, 1H, J = 15.6 Hz), 4.51 (t, 1H, J = 8.0 Hz), 4.93 (d, 1H, J = 8.0 Hz), 5.36 (d, 1H, J = 10.6 Hz), 5.48 (d, 1H, J = 17.2 Hz), 5.86 (ddd, 1H, J = 17.2, 10.6, 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ −0.2, 28.0, 51.9, 56.6, 61.2, 76.5, 82.9, 90.9, 101.6, 119.8, 135.7, 152.1, 169.2; HRMS (ESI, +ve) m/z calcd for $C_{22}H_{37}NO_7SiNa$ 478.2237, found 478.2222 (M + Na)$^+$.

(±)-(2*R*,3*S*)-Methyl 2-(Bis(*tert*-butoxycarbonyl)amino)-3-(benzyloxy)pent-4-enoate (17h). (*E*)-3-Benzyloxyallyl 2-(bis(*tert*-butoxycarbonyl)amino)acetate **16h** (0.09 g, 0.22 mmol), TMSCl (0.05 mL, 0.43 mmol), and LiHMDS (0.43 mL, 0.43 mmol) were combined according to the general procedure. Treatment with diazomethane and purification by flash chromatography (10:1 pet./EtOAc + 1% NEt_3) afforded the title compound as a colorless oil (0.05 g, 55%). FTIR (film/cm^{-1}) υ_{max} 2980.7, 2890.6, 1750.9, 1700.6; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.45 (s, 18H), 3.71 (s, 3H), 4.33 (d, 1H, J = 11.6 Hz), 4.47 (dd, 1H, J = 9.1, 2.1 Hz), 4.61 (d, 1H, J = 11.6 Hz), 4.99 (d, 1H, J = 9.1 Hz), 5.38 (dd, 1H, J = 10.4, 1.4 Hz), 5.49 (dd, 1H, J = 17.3, 1.4 Hz), 5.89 (ddd, 1H, J = 17.3, 10.4, 7.0 Hz), 7.23−7.39 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.9, 52.0, 61.6, 70.5, 77.2, 82.9, 118.9, 127.3, 127.7, 128.1, 136.6, 138.3, 152.3, 169.3; HRMS (ESI, +ve) m/z calcd for $C_{23}H_{33}NO_7Na$ 458.2155, found 458.2161 (M + Na)$^+$.

(2*R*,3*S*)-Methyl 2-(Bis(*tert*-butoxycarbonyl)amino)-3-(4-methoxybenzyloxy)pent-4-enoate (17i). (*E*)-3-(4-Methoxybenzyloxy)allyl 2-(bis(*tert*-butoxycarbonyl)amino)acetate **16i** (0.14 g, 0.31 mmol), TMSCl (0.08 mL, 0.62 mmol), and LiHMDS (0.62 mL, 0.62 mmol) were combined according to the general procedure. Treatment with diazomethane and purification by flash chromatography (15:1 pet./EtOAc + 1% NEt_3) afforded the title compound as a colorless oil (0.06 g, 40%). FTIR (film/cm^{-1}) υ_{max} 3010.5, 2955.0, 1794.7, 1751.3, 1697.4; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.45 (s, 18H), 3.70 (s, 3H), (s, 3H), 4.26 (d, 1H, J = 9.7 Hz), 4.44 (dd, 1H, J = 8.5, 6.9 Hz), 4.53 (d, 1H, J = 9.7 Hz), 4.95 (d, 1H, J = 8.5 Hz), 5.37 (dd, 1H, J = 10.4, 1.1 Hz), 5.47 (dd, 1H, J = 17.7, 1.1 Hz), 5.98 (ddd, 1H, J = 17.7, 10.4, 6.9 Hz), 6.84 (d, 2H, J = 8.4 Hz), 7.23 (d, 2H, J = 8.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.9, 51.9, 55.2, 61.7, 65.8, 70.2, 82.9, 113.6, 118.7, 129.3, 130.2, 130.5, 136.7, 152.2, 159.0, 169.3; HRMS (ESI, +ve) m/z calcd for $C_{24}H_{35}NO_8Na$ 488.2260, found 488.2243 (M + Na)$^+$.

(±)-(2*R*,3*S*)-Methyl 2-(Bis(*tert*-butoxycarbonyl)amino)-3-(2,6-dichlorobenzyloxy)pent-4-enoate (17j). (*E*)-2,6-Dichlorobenzyloxyallyl 2-(bis(*tert*-butoxycarbonyl)amino)acetate **16j** (0.07 g, 0.15 mmol), TMSCl (0.04 mL, 0.30 mmol), and LiHMDS (0.30 mL, 0.30 mmol) were combined according to the general procedure. Treatment with diazomethane and purification by flash chromatography (15:1 pet./EtOAc + 1% NEt_3) afforded the title compound as a colorless oil (0.06 g, 78%). FTIR (film/cm^{-1}) υ_{max} 2979.9, 2933.7, 1796.6, 1749.3, 1697.7; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.38 (s, 18H), 3.70 (s, 3H), 4.51−4.54 (m, 2H), 4.89 (dd, 2H, J = 36.6, 9.6 Hz), 5.42 (dd, 1H, J = 10.7, 0.6 Hz), 5.61 (dq, 1H, J = 17.4, 0.6 Hz), 6.05 (ddd, 1H, J = 17.4, 10.7, 6.9 Hz), 7.15 (dd, 1H, J = 8.7, 0.9 Hz), 7.28 (d, 2H, J = 8.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.8, 51.9, 62.0, 65.3, 77.7, 82.6, 118.9, 128.1, 129.7, 133.7, 136.5, 137.1, 152.0, 169.1; HRMS (ESI, +ve) m/z calcd for $C_{23}H_{32}Cl_2NO_7$ 504.1556, found 504.1562 (M + H)$^+$.

(2*R*,3*S*)-Methyl 2-(Bis(*tert*-butoxycarbonyl)amino)-3-((*S*)-1-phenylethoxy)pent-4-enoate (17k). (*S*,*E*)-3-(1-Phenylethoxy)-allyl 2-(bis(*tert*-butoxycarbonyl)amino)acetate **16k** (0.24 g, 0.54 mmol), TMSCl (0.14 mL, 1.08 mmol), and LiHMDS (1.08 mL, 1.08 mmol) were combined according to the general procedure. Treatment with diazomethane and purification by flash chromatography (15:1 pet./EtOAc + 1% NEt_3) afforded the title compound as a colorless oil (0.10 g, 42%). $[\alpha]^{20}_D$ = −55 (*c* 1, CH_2Cl_2); FTIR (film/cm^{-1}) υ_{max} 2982.7, 1789.2, 1745.6, 1696.4; ^{1}H NMR (500 MHz, $CDCl_3$) major δ 1.38 (d, 3H, J = 6.3 Hz), 1.52 (s, 18H), 3.71 (s, 3H), 4.35 (d, 1H, J = 6.2 Hz), 4.56 (q, 1H, J = 6.3 Hz), 4.92−4.95 (m, 1H), 5.16−5.34 (m, 2H), 5.90 (ddd, 1H, J = 17.1, 10.8, 6.7 Hz), 7.21 −7.36 (m, 5H); minor δ 1.35 (d, 1H, J = 6.3 Hz), 1.52 (s, 18H), 3.64 (s, 3H),4.34 (d, 1H, J = 6.2 Hz), 4.56 (q, 1H, J = 6.3 Hz), 4.92−4.95 (m, 1H), 5.37−5.42 (m, 2H), 5.97 (ddd, 1H, J = 13.8, 10.0, 6.7 Hz), 7.21−7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ Major δ 22.3, 28.0, 51.9, 61.8, 73.2, 75.2, 83.0, 118.0, 126.2, 126.7, 128.0, 128.5, 137.4, 152.3, 169.4; Minor δ 22.1, 27.9, 51.7, 62.2,73.3, 75.6, 82.8, 118.0, 126.1, 126.8, 128.1, 128.4, 137.5, 151.8, 168.4; HRMS (ESI, +ve) m/z calcd for $C_{24}H_{35}NO_7Na$, 472.2311 found 472.2293 (M + Na)$^+$.

(2*R*,3*S*)-Methyl 2-(Bis(*tert*-butoxycarbonyl)amino)-3-hydroxypent-4-enoate (*syn*-18). To a stirred solution of **17k** (0.08 g, 0.17 mmol) in methanol (20 mL) was added catalytic palladium on carbon (0.02 g), and the mixture was stirred under 1 atm of hydrogen for 16 h. The solution was filtered through Celite and washed with another 20 mL of methanol, dried over Na_2SO_4,

filtered, and concentrated *in vacuo* to afford the title compound as a colorless oil (0.04 g, 73%). FTIR (film/cm^{-1}) υ_{max} 3428.0, 2980.0, 1737.2, 1693.7; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.00 (t, 3H, J = 7.6 Hz), 1.49−1.52 (m, 2H), 1.53 (s, 18H), 3.78 (s, 3H), 3.96 (d, 1H, J = 9.0 Hz), 4.11−4.17 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.2, 27.5, 27.9, 52.4, 62.4, 83.6, 1534.0, 169.7; HRMS (ESI, +ve) m/z calcd for $C_{16}H_{30}NO_7$ 348.2022, found 348.1986 $(M + H)^+$.

(2*R*,3*S*)-Methyl 2-(*tert*-Butoxycarbonyl)amino)-3-hydroxypentanoate (*syn*-19).[45] To a stirred solution of *syn*-**18** (0.07 g, 0.19 mmol, 1 equiv) in CH_2Cl_2 (5 mL) was added TFA (0.03 mL, 0.38 mmol, 2 equiv) at 0 °C. The mixture was stirred for 30 min before being concentrated *in vacuo*. The residue was taken up in saturated sodium bicarbonate solution (10 mL) and extracted with EtOAc (4 × 20 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification was achieved by flash chromatography (2:1 pet./EtOAc) to afford the title compound as a colorless oil (0.04 g, 78%). $[\alpha]^{20}_D$ = +3.2 (*c* 0.85, EtOH abs); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94 (t, 3H, J = 7.0 Hz), 1.42 (s, 9H), 1.51−1.55 (m, 2H), 3.71 (s, 3H), 3.97−3.99 (m, 1H), 4.19 (br, 1H), 4.23 (d, 1H, J = 9.0 Hz), 5.72 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.0, 27.8, 28.3, 52.2, 58.3, 73.7, 80.1, 155.5, 173.7.

(*Z*)-*tert*-Butyl (2-Methoxy-2-((trimethylsilyl)oxy)vinyl)(methyl)carbamate (21a). To a stirred solution of methyl 2-((*tert*-butoxycarbonyl)(methyl)amino)acetate (0.06 g, 0.26 mmol, 1 equiv) in THF (0.5 mL) at −95 °C was added TMSCl (0.06 mL, 0.52 mmol, 2 equiv), and the mixture was stirred for 10 min. LiHMDS (1 M in THF, 0.52 mL, 0.52 mmol, 2 equiv) was added *via* syringe pump, and then the solution was allowed to warm to room temperature. Rapid concentration *in vacuo* afforded the title compound as a yellow oil (0.05 g, 81%, Z/E 2:1, 2:1 rotamers). FTIR (film/cm^{-1}) υ_{max} 2955.1, 1756.9, 1698.7; ^{1}H NMR (400 MHz, $CDCl_3$) *Z* δ 0.22 and 0.26 (2s, 9H), 1.49 and 1.51 (2s, 9H), 2.99 and 3.00 (2s, 3H), 3.58 and 3.60 (2s, 3H), 4.88 and 4.93 (2br, 1H); *E* δ 0.22 and 0.26 (2s, 9H) 1.49 and 1.51 (2s, 9H), 2.99 and 3.00 (2s, 3H), 3.58 and 3.60 (2s, 3H), 4.99 and 5.08 (2br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *Z* δ 5.5, 28.5, 55.2, 87.7, 164.1, 179.3; HRMS (ESI, +ve) m/z calcd for $C_{12}H_{26}NO_4Si$ 276.1631, found 276.1627 $(M + H)^+$.

(*Z*)-2-(2-Methoxy-2-((trimethylsilyl)oxy)vinyl)isoindoline-1,3-dione (21b). To a stirred solution of methyl 2-(1,3-dioxoisoindolin-2-yl)acetate (0.05 g, 0.24 mmol, 1 equiv) in THF (0.5 mL) at −95 °C was added TMSCl (0.06 mL, 0.48 mmol, 2 equiv), and the mixture was stirred for 10 min. LiHMDS (1 M in THF, 0.48 mL, 0.48 mmol, 2 equiv) was added *via* syringe pump, and then the solution was allowed to warm to room temperature. Rapid concentration *in vacuo* afforded the title compound as a yellow solid (0.06 g, 87%, Z/E 12:1). FTIR (film/cm^{-1}) υ_{max} 3119.3, 3024.9, 2977.4, 1780.6, 1719.1, 1669.9, 1659.7; ^{1}H NMR (400 MHz, $CDCl_3$) *Z* δ 0.22 (s, 9H), 3.80 (s, 3H), 4.69 (s, 1H), 7.73−7.75 (m, 2H), 7.88−7.90 (m, 2H); *E* δ 0.22 (s, 9H), 3.81 (s, 3H), 4.74 (s, 1H), 7.73−7.75 (m, 2H), 7.88−7.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *Z* δ 5.5, 55.5, 71.8, 123.1, 132.4, 133.8, 159.6, 168.1; HRMS (ESI, +ve) m/z calcd for $C_{14}H_{17}NO_4SiNa$ 314.0825, found 314.0837 $(M + Na)^+$.

(*Z*)-Bis(*tert*-butyl (2-methoxy-2-((trimethylsilyl)oxy)vinyl))carbamate (21c). To a stirred solution of methyl 2-(bis(*tert*-butoxycarbonyl) amino)acetate (0.06 g, 0.22 mmol, 1 equiv) in THF (0.5 mL) at −78 °C was added TMSCl (0.06 mL, 0.44 mmol, 2 equiv), and the mixture was stirred for 10 min. LiHMDS (1 M in THF, 0.44 mL, 0.44 mmol, 2 equiv) was added *via* syringe pump, and then the solution was allowed to warm to room temperature. Rapid concentration *in vacuo* afforded the title compound as a yellow oil (0.05 g, 51%, Z/E > 25:1). FTIR (film/cm^{-1}) υ_{max} 2980.5, 2900.9, 1736.9, 1739.8, 1700.0; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.19 (s, 9H), 1.47 (s, 18H), 3.72 (s, 3H), 4.33 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 5.6, 28.1, 55.2, 81.7, 156.9, 168.1, 178.4; HRMS (ESI, +ve) m/z calcd for $C_{16}H_{31}NO_6SiNa$ 384.1818, found 384.1822 $(M + Na)^+$.

(*Z*)-Methyl 3-Methoxyacrylate (*Z*-4a). To a stirred solution of silver(I) trifluoromethanesulfonate (0.29 g, 1.12 mmol, 0.1 equiv) in methanol (15 mL) was added methyl propiolate (0.95 g, 11.2 mmol, 1 equiv). The solution was stirred at room temperature for 20 h and concentrated *in vacuo*. The solution was taken up in chloroform, filtered through Celite, and concentrated to afford the title compound as a pale brown oil (1.10 g, 71%) FTIR (film/cm^{-1}) υ_{max} 2990.0, 2950.5, 2877.1, 2833.7, 1709.4, 1646.2, 1626.2; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.65 (s, 3H), 3.84 (s, 3H), 4.82 (d, 1H, J = 7.1 Hz), 6.43 (d, 1H, J = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 50.8, 62.5, 95.9, 160.1, 165.6; HRMS (ESI, +ve) m/z calcd for $C_5H_8O_3Na$ 139.0371, found 139.0378 $(M + Na)^+$.

(*Z*)-3-(Methoxy)prop-2-enol (*Z*-5a). (*Z*)-Methyl 3-(methoxy)-acrylate *Z*-**4a** (0.51 g, 4.39 mmol) was reduced according to general procedure to afford the title compound as a colorless oil (0.13 g, 33%). FTIR (film/cm^{-1}) υ_{max} 3337.8, 3046.0, 2936.2, 2859.6, 1662.9; ^{1}H NMR (300 MHz, d_6-acetone) δ 1.85 (br, 1H), 3.63 (s, 3H), 4.16 (dd, 2H, J = 6.9, 1.1 Hz), 4.64 (q, 1H, J = 6.9 Hz), 6.02 (dt, 1H, J = 6.3, 1.2 Hz); ^{13}C NMR (75 MHz, d_6-acetone) δ 56.9, 60.6, 106.3, 149.2.

(*Z*)-3-Methoxyallyl 2-(Bis(*tert*-butoxycarbonyl)amino)acetate (*Z*-10a). EDCi·HCl (1.06 g, 5.45 mmol), triethylamine (0.76 mL, 5.45 mmol), 2-(bis(*tert*-butoxycarbonyl)amido)-acetic acid (1.52 g, 5.45 mmol), catalytic DMAP, and (*Z*)-3-methoxyprop-2-enol *Z*-**5a** (0.24 g, 2.72 mmol) were combined according to general procedure to afford a yellow oil. Purification by flash chromatography (Al_2O, 15:1 pet./EtOAc) afforded the title compound as colorless oil (0.28 g, 30%). FTIR (film/cm^{-1}) υ_{max} 2979.6, 2937.6, 1799.3, 1756.9, 1736.0, 1697.7, 1666.7; ^{1}H NMR (500 MHz, d_6-acetone) δ 1.48 (s, 18H), 3.65 (s, 3H), 4.28 (s, 2H), 4.54−4.58 (m, 1H), 4.67 (dd, 2H, J = 7.8, 0.9 Hz), 6.21 (dt, 1H, J = 6.3, 1.1 Hz); ^{13}C NMR (125 MHz, d_6-acetone) δ 32.4, 52.2, 63.3, 64.6, 87.3, 104.6, 156.0, 157.0, 174.1; HRMS (ESI, +ve) m/z calcd for $C_{16}H_{27}NO_7Na$ 368.1685, found 368.1684 $(M + Na)^+$.

(±)-(2*R*,3*R*)-Methyl 2-(Bis(*tert*-butoxycarbonyl)amino)-3-methoxypent-4-enoate (*anti*-17a). (*Z*)-3-Methoxyallyl 2-(bis-(*tert*-butoxycarbonyl)amino)acetate *Z*-**10a** (0.10 g, 0.29 mmol), TMSCl (0.07 mL, 0.58 mmol), and LiHMDS (0.58 mL, 0.58 mmol) were combined according to general procedure. Treatment with diazomethane and purification by flash chromatography (15:1 pet./EtOAc + 1% NEt_3) afforded the title compound as a colorless oil (0.06 g, 55%, dr 1.5:1). A small fraction of the major *anti* product was isolated for identification. FTIR (film/cm^{-1}) υ_{max} 2983.1, 2932.2, 1788.9, 1745.9, 1695.6; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.49 (s, 18H), 3.37 (s, 3H), 3.76 (s, 3H), 4.28 (t, 1H, J = 8.2 Hz), 4.86 (d, 1H, J = 8.2 Hz), 5.25−5.32 (m, 2H), 5.61 (ddd, 1H, J = 17.9, 9.5, 1.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.0, 52.2, 56.5, 60.5, 82.1, 83.3, 120.1, 133.8, 151.6, 170.0; HRMS (ESI, +ve) m/z calcd for $C_{17}H_{30}NO_7$ 360.2022, found 360.2032 $(M + H)^+$.

(±)-(2*R*,3*S*)-Methyl 2-((*tert*-Butoxycarbonyl)amino)-3-methoxypent-4-enoate (*syn*-22). To a stirred solution of (±)-(2*R*,3*S*)-methyl 2-(bis(*tert*butoxycarbonyl)amino)-3-methoxypent-4-enoate (0.07 g, 0.19 mmol, 1 equiv) in CH_2Cl_2 (5 mL) was added TFA (0.03 mL, 0.38 mmol, 2 equiv) at 0 °C. The mixture was stirred for 30 min before concentratinmg in vacuo. The residue was taken up in saturated sodium bicarbonate solution (10 mL) and extracted with EtOAc (4 × 20 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification was achieved by flash chromatography (6:1 pet./EtOAc) to afford the title compound as a colorless oil (0.04 g, 78%). FTIR (film/cm^{-1}) υ_{max} 3372.0, 2980.6, 2940.1, 1756.0, 1718.8, 1502.9; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.45 (s, 9H), 3.26 (s, 3H), 3.78 (s, 3H), 4.12 (d, 1H, J = 6.8 Hz), 4.38 (dd, 1H, J = 9.9, 2.8 Hz), 5.24 (d, 1H, J = 9.9 Hz), 5.34−5.39 (m, 2H), 5.75 (ddd, 1H, J = 17.6, 9.9, 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.3, 52.4, 56.9, 57.5,

79.9, 82.0, 119.6, 133.8, 155.9, 171.1; HRMS (ESI, +ve) m/z calcd for $C_{12}H_{21}NO_5Na$ 282.1317, found 282.1304 $(M + Na)^+$.

(±)-(2*S*,3*S*)-2-Bis(*tert*-butoxycarbonyl)amino-3-methoxypent-4-en-1-ol (*syn*-23). To a stirred solution of lithium aluminum hydride (0.01 g, 0.26 mmol, 2 equiv) in ether (7 mL) at −78 °C was added a solution of (±)-(2*R*,3*S*)-methyl 2-(bis(*tert*-butoxycarbonyl)-amino)-3-methoxypent-4-enoate (0.05 g, 0.13 mmol) in ether (3 mL). The mixture was stirred at −78 °C for 5 h before being quenched by the addition of EtOAc and then poured onto ice-cold saturated Rochelle salt solution (100 mL) followed by the addition of further EtOAc (100 mL). The biphasic mixture was vigorously stirred at 0 °C for 2 h before being separated and extracted with EtOAc (3 × 10 mL). The organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification was achieved by flash chromatography (pet./EtOAc 10:1) to afford the title compound as a colorless oil (0.03 g, 60%, 2:1 rotamers). FTIR (film/cm^{-1}) υ_{max} 3338.7, 2967.3, 2928.0, 2882.8, 1705.4, 1596.4; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.49 and 1.56 (2s, 18H), 3.29−3.32 (m, 1H), 3.34 (s, 3H), 3.72 (t, 1H, J = 3.2 Hz), 3.94 (t, 1H, J = 7.9 Hz), 4.14 (dd, 1H, J = 7.9, 3.2 Hz), 4.67 (br, 1H), 5.27−5.34 (m, 2H), 5.76 (ddd, 1H, J = 17.5, 9.9, 7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.8, 28.4 (× 2), 57.0, 57.3, 79.4, 80.5, 119.5, 127.5, 127.6, 133.9, 135.8, 135.9, 152.8; HRMS (ESI, +ve) m/z calcd for $C_{16}H_{30}NO_6Na$ 332.2073, found 332.2064 $(M + H)^+$.

(*Z*)-Methyl 2-(Bis(*tert*-butoxycarbonyl)amino)penta-2,4-dienoate (24). FTIR (film/cm^{-1}) υ_{max} 2914.3, 2851.5, 1796.6, 1727.8, 1644.8; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.45 (s, 18H), 3.81 (s, 3H), 5.58 (d, 1H, J = 10.8 Hz), 5.71 (d, 1H, J = 17.3 Hz), 6.50 (dt, 1H, J = 17.3, 10.8 Hz), 7.17 (d, 1H, J = 10.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.8, 52.3, 83.0, 126.9, 128.0, 130.2, 136.8, 150.4, 165.0; HRMS (ESI, +ve) m/z calcd for $C_{16}H_{25}NO_6Na$ 350.1580, found 350.1578 $(M + Na)^+$.

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Supporting Information Available: Full experimental details and NMR spectra of novel compounds. This material is available free of charge via the Internet at http://pubs.acs.org.