JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Thio-Claisen Rearrangement Used in Preparing Anti-β-Functionalized γ,δ-Unsaturated Amino Acids: Scope and Limitations

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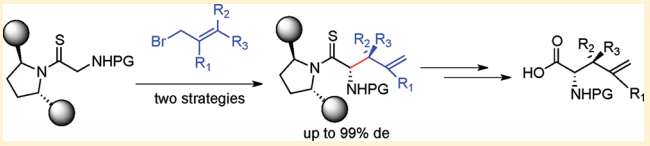
Supporting Information

ABSTRACT: Multifunctionalized amino acids, especially amino acids with unsaturation, are important, demanding building blocks in peptide chemistry. Here we present a summary of our most recent study using the thio-Claisen rearrangement for the synthesis of anti-β-functionalized γ,δ-unsaturated amino acids. Investigations on scope, limitations, chemoselectivities and stereoselectivities regarding an $FeBr_3$-catalyzed allylation strategy and a thio-enolate dianion formation strategy for asymmetric thio-Claisen rearrangement are documented. An explanation of the chirality crossover observed between the Eschenmoser−Claisen rearrangement and the thio-Claisen rearrangement is proposed. Novel optically active N^{α}-protected amino acids with biologically interesting functional groups were prepared for the first time.



INTRODUCTION

Peptides are among the most important modulators and information carriers throughout the human body. Their merits, such as high potency, high specificity, and low toxicity, make them appealing molecules for pharmaceutical applications. According to data in 2007, there are 67 peptides and peptidomimetics already marketed in the world targeting 29 disease indications, and these numbers are expected to have continuous growth in the next decade.[1] With this trend continuing, there is a concomitant demand to explore how to efficiently modify peptides and improve their bioavailability, stability, potency, receptor subtype selectivity, etc.[2] Because of the convenience of preparing peptides via solid phase chemistry,[3] it is inarguable that incorporating nonproteinogenic N^{α}-protected amino acids with required chemical, physical, and pharmacological properties during the synthesis is a straightforward solution.[4−8]

β-Functionalized γ,δ-unsaturated amino acids have drawn significant research interest, initially due to their natural occurrence and irreversible enzyme inhibitory activities.[9−12] More recently, their unique chemical and structural properties make them valuable tools in general peptide research. They carry β-position functionalization that could offer desired pharmacophores. The γ,δ-double bond, which is orthogonal to standard solid-phase peptide synthesis conditions, provides a wide selection of chemistries for on-resin and postcleavage modifications,[13−15] for example, site-specific peptide cyclization,[16,17] glycosylation,[18] and isotope labeling.[19] The Claisen rearrangement is one of the most efficient strategies to prepare these amino acids due to its high asymmetric selectivity.[20,21] Kazmaier and co-workers have developed a chelation ester−enolate Claisen rearrangement method which has been proven to be efficient in preparing syn-β-substituted γ,δ-unsaturated amino acids.[22−27] This method was further extended by Ohfune and co-workers.[28,29] Inspired by the seminal work from Welch[30,31] and Rawal[32] on the Claisen rearrangement, our group developed a highly asymmetric Eschenmoser−Claisen rearrangement[33,34] (ECR) and the thio-Claisen rearrangement[35,36] (TCR) methods for the synthesis of anti-β-functionalized, γ,δ-unsaturated amino acids. With the aim of examining the scope and limitations of these methodologies and their application in producing novel amino acids, we initiated an in-depth study with a focus on TCR methodology. This study includes both the $FeBr_3$-catalyzed allylation strategy and the thio-enolate dianion strategy.

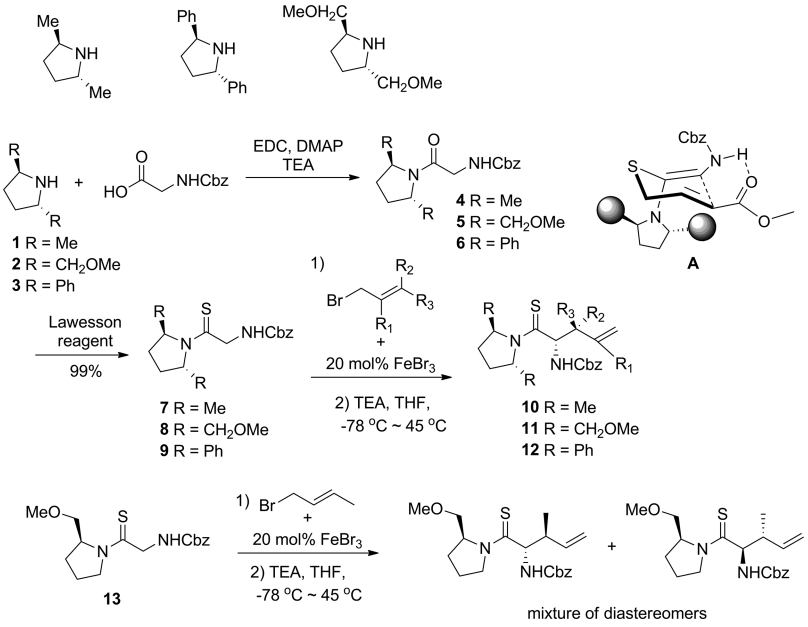
RESULTS AND DISCUSSION

Having successfully developed an $FeBr_3$-catalyzed allylation strategy for TCR methodology,[36] we were eager to examine the effectiveness of the reaction sequence in the preparation of optically active amino acids. Theoretically, it should transfer chirality with a high efficiency as we reported before. To avoid possible low asymmetric induction caused by rotomers, we chose a C_2-symmetric chiral auxiliary instead of nonsymmetric ones.[31] Three commercially available or easily accessible C_2-symmetric chiral pyrrolidine derivatives **1**−**3** were used.[37,38] They were first coupled to *N*-Cbz-protected glycine and then converted into thioamides **7**−**9** in almost quantitative yields.[39] The thioamides were S-allylated with a $FeBr_3$-catalyzed alkylation. Once the reaction was complete as monitored by TLC, the reaction mixture was cooled to −78 °C and the thio-

Received: September 6, 2011
Published: December 27, 2011

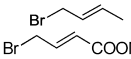
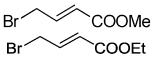
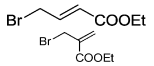
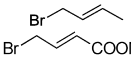
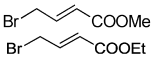
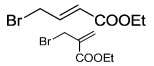
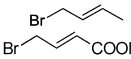
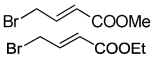
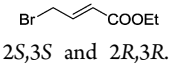
   dx.doi.org/10.1021/jo201753q | J. Org. Chem. 2012, 77, 1289−1300

Scheme 1. Asymmetric TCR Reaction with C_2-Symmetric Chiral Auxiliaries



Claisen rearrangement was initiated by deprotonation and raising the reaction temperature.[36] All reactions proceeded smoothly (Scheme 1) to give the desired products, and the results are summarized in Table 1. Chiral HPLC was used to analyze the diastereoselectivities of these reactions. We observed a trend of moderate diastereoselectivity increase as the size of R group on the chiral auxiliary was increased from CH_3 to CH_2OMe and Ph, suggesting sterically controlled asymmetric induction. We also noticed that when there is a conjugated carbonyl group in the allylic bromide, this method gave superior selectivity with only one diastereomer isolated in most cases. This observation offers further evidence for our previously reported bicyclic transition state model **A**,[36] which gives additional transition state stabilization. When the carbonyl group is at R_1 position, it is not possible to form the bicyclic transition state structure; there was no diastereoselectivity enhancement (entries **10a**, **11a**, **12a**). A non-C_2-symmetric chiral auxiliary coupled thioamide **13** was used as a control experiment, and a mixture of diastereomers was isolated showing very little or no diastereoselectivity.

Table 1. Results of Enantioselective TCR Reaction for Synthesis of Anti-β-Functionalized γ,δ-Unsaturated Thioamides

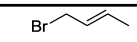
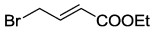
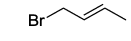
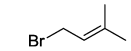
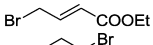
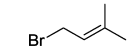
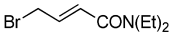
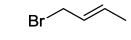
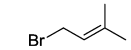
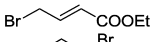
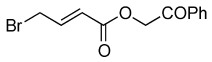
pdt	allylation reagent	R	anti:syn*	de(%)**	yield%[c]
10a		Me	n/a	56[b]	64
10b		Me	17:1[a]	78[a]	62
10c		Me	99:1[b]	99[b]	86
10d		Me	99:1[b]	99[b]	83
11a		CH_2OMe	n/a	90[b]	54
11b		CH_2OMe	30:1[b]	88[b]	52
11c		CH_2OMe	99:1[b]	99[b]	64
11d		CH_2OMe	99:1[b]	99[b]	65
12a		Ph	n/a	67[b]	60
12b		Ph	99:1[b]	91[b]	58
12c		Ph	99:1[b]	99[b]	63
12d		Ph	99:1[b]	99[b]	70

*Anti: 2*S*,3*S* and 2*R*,3*R*. Syn: 2*S*,3*R* and 2*R*,3*S*. **Diastereomeric excess between two anti isomers: anti major, 2*S*,3*S*; anti minor, 2*R*,3*R*. [a]Determined by weight. [b]Determined by chiral HPLC. [c]Isolated yield of total isomers.

We also studied the compatibility of different protecting groups for the α-amino group and this methodology. Our research group is interested in using these amino acids to make peptide dicarba analogues[17] with solid-phase peptide synthesis techniques. Therefore, we chose the four most commonly used carbamate protecting groups in solid-phase peptide synthesis: Fmoc, Boc, Cbz, and Alloc. The Fmoc-protected substrates gave a complex mixture of products after reaction and could not be identified, presumably due to the lack of stability of Fmoc group when exposed to bases at an elevated temperature overtime. The other carbamate protecting groups showed unequivocal compatibility with the $FeBr_3$-catalyzed allylation strategy for TCR. We noticed that the size of protecting group did not affect the diastereoselectivity, providing additional support for transition state model **A**, where the asymmetric introduction originated from the interaction between the chiral auxiliary and the allyl group, and not the carbamate protecting group. We were also delighted to see a moderate increase in the yield as the size of protecting group decreased. Presumably, this is caused by less steric repulsion between the allyl fragment and the N^{α} protecting group (**A** in Scheme 1). This effect is especially obvious when there is a *cis* substitution in the allyl bromide starting material (Table 2). Thus, in the case of 3,3-dimethylallyl bromide and 3-bromocyclohexene, we did not observe N^{α}-Boc protected rearrangement products **23b** and **23d**. However, by choosing a less sterically bulky Cbz group, we were able to isolate the desired products (Scheme 2). The least sterically bulky Alloc protecting group resulted in a further increase in yields. Notably, an amide functional group could be introduced (**24c**); anti/syn selectivity was excellent, presumably for reasons similar to those of ester substituents. However, **24c** was obtained with a lower yield presumably because of the steric hindrance of the tertiary amide group. In addition, the bromo enamide did show less reactivity than the bromo enester in the alkylation step.

dx.doi.org/10.1021/jo201753q | J. Org. Chem. 2012, 77, 1289–1300

Table 2. Results of Asymmetric TCR Reaction for Synthesis of Anti-β-Substituted γ,δ-Unsaturated Thioamide

pdt	Allylation Reagent	N^{α}-PG	anti:syn[a]	yield%[b]
22a		Fmoc	n/a	0
22b		Fmoc	n/a	0
23a		Boc	10/1	63
23b		Boc	n/a	0
23c		Boc	>49/1	79
23d		Boc	n/a	0
24a		Cbz	n/a	42
24b		Cbz	>49/1	15
24c		Cbz	>49/1	32
25a		Alloc	19/1	80
25b		Alloc	n/a	51
25c		Alloc	>49/1	82
25d		Alloc	>49/1	29
25e		Alloc	>49/1	51

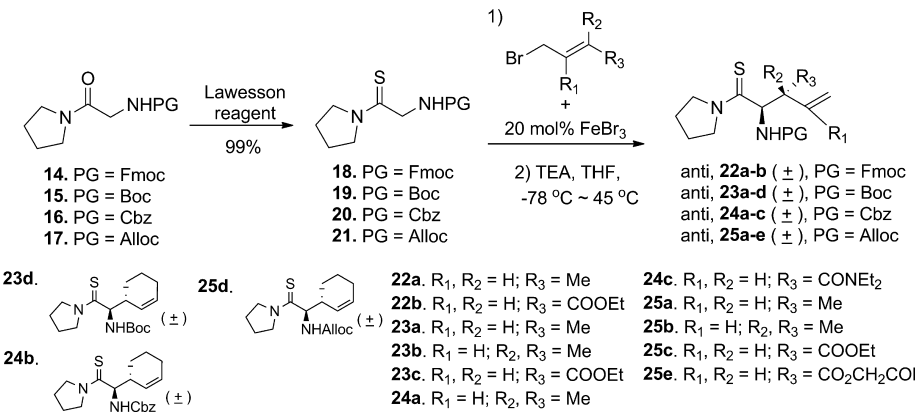
[a]Determined by ^{1}H NMR. [b]Isolated yield of total isomers.

The TCR exploiting a thio-enolate dianion strategy also was investigated. According to our recent experiences with C_2-symmetric chiral auxiliary **3**, initial LDA or *n*-Bu-Li treatment of the thioamide should generate a thio-enolate dianion, which presumably would be *S*-allylated with addition of the allylic bromide and give the TCR product upon increasing the reaction temperature. To our surprise, the only major products identified and characterized were the *C*-allylation products **29**–**32** (Scheme 3). When we monitored the reaction progress involving auxiliaries **1** and **2** with TLC, we did not observe a transient intermediate spot as with auxiliary **3**, which was supposed to be the *S*-allylated rearrangement precursor. It is well established that the regioselectivity of the enolate ambident anion is affected by the solvent and the counterion.[40] At first, we assumed that the low reactivity of the sulfur anion might be caused by lithium metal chelation. With addition of HMPA or DMPU[41] aimed at reducing the enolate–metal chelation,[42,43] we hardly observed any improvement. We also tried several other bases to generate enolate with different counterions, and those efforts did not solve the problem either. C-Allylation products were isolated almost exclusively, and this process has poor stereocontrol as indicated by ^{1}H NMR and chiral HPLC studies. In any case, we conclude that *C*-allylation is a serious side reaction in the TCR reaction with the thio-enolate dianion strategy when certain substrates are used.

Despite the failure to obtain the expected rearrangement products from certain thioamide substrates, the TCR reaction using a thio-enolate dianion strategy is fast and clean: a typical TCR reaction expoiting this strategy takes about 4 h for completion, while one using the $FeBr_3$-catalyzed allylation strategy generally requires 2 days. As a side-by-side comparison of the two TCR strategies (Scheme 4, Table 3) reveals, the thio-enolate strategy gave slightly higher yields. When there are bulky substituents in the allyl bromide starting materials, the reaction was still valid and gave products with reasonable yields. The TCR reaction using the $FeBr_3$-catalyzed allylation strategy is inarguably a general method: the much more mild reaction conditions make it compatible with multiple functional groups, protecting groups, and auxiliaries. Both strategies provided excellent asymmetric introduction with no significant differences. The structure of compound **28c** was determined by an X-ray crystallography study, and this confirmed the absolute stereochemistry of the compound (Figure 1).

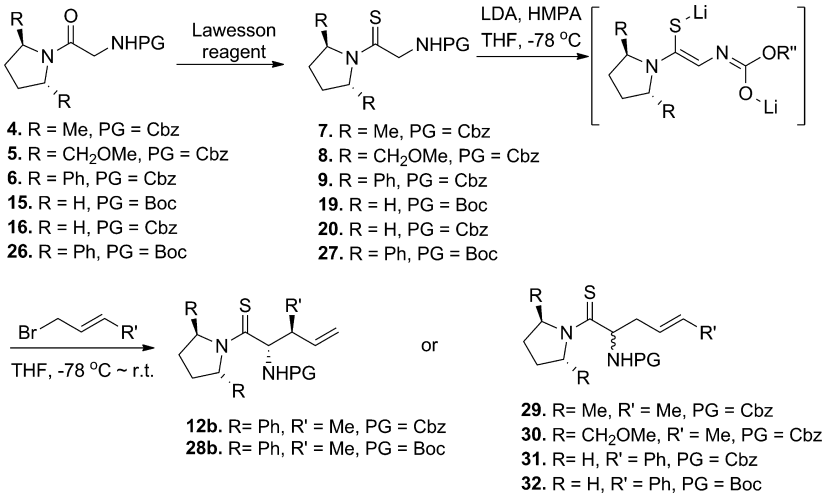
Converting the thioamide into the carboxylic acid has been studied by us previously.[35,36] For this work, we chose a three-step oxidation–iodolactonization–reduction method (Scheme 5) over a one-pot alkylation–reduction–oxidation method because it resulted in higher yields and was tolerant of those thioamides carrying alkylation-labile functional groups. After the thioamides were oxidized, the crude products were used without further purification to form iodolactones. The carboxylic acid was obtained from zinc reductive elimination with lactone ring-opening. The results are summarized in Table 4. Amino acids with assorted auxiliaries and protecting groups were selected for the study. All four auxiliaries could be removed smoothly, giving the desired amino acids with good yields. Little or no epimerization or racemization was detected during this process. It is worth pointing out that we could not covert compound **24c** into the desired amino acid because of the similar reactivities of the two tertiary amide functional groups in the molecule after oxidation.

Scheme 2. N^{α}-Protecting Group Compatibility Study with TCR Reaction



dx.doi.org/10.1021/jo201753q | J. Org. Chem. 2012, 77, 1289–1300

Scheme 3. *C*-Alkylation vs *S*-Alkylation in TCR Reaction with Thio-enolate Strategy



Scheme 4. Comparison between TCR Reactions Exploiting Thio-Enolate Strategy and $FeBr_3$-Catalyzed Allylation Strategy

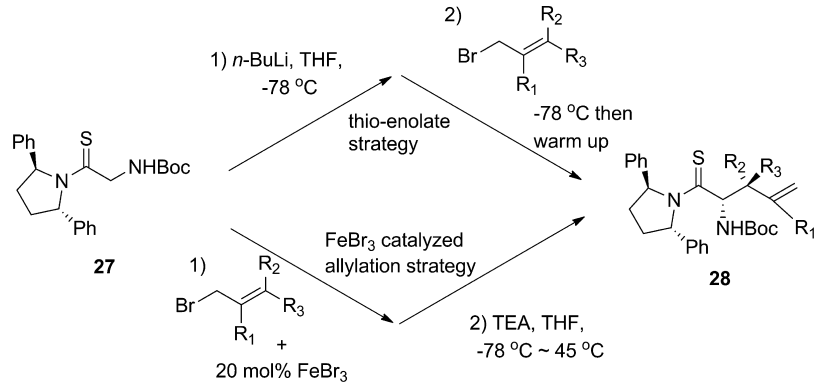
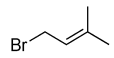
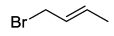
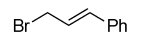
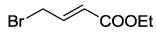


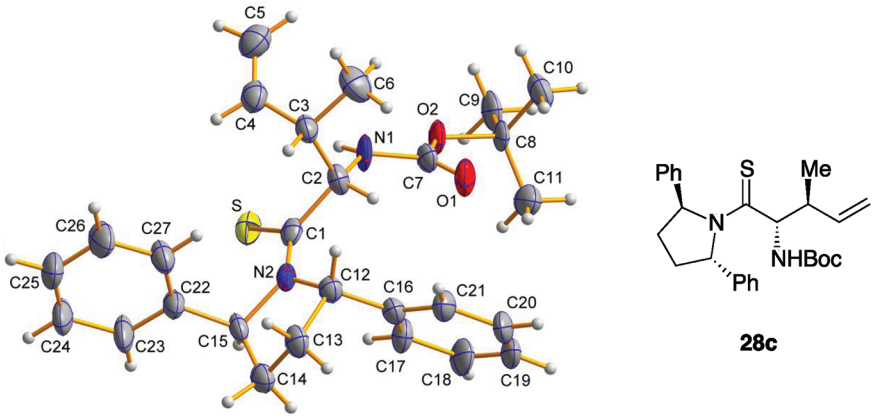
Table 3. Results of Comparing Thio-enolate Strategy and $FeBr_3$-Catalyzed Allylation Strategy Used in Asymmetric TCR Reaction for Synthesis of Anti-β-Substituted γ,δ-Unsaturated Thioamide

pdt	allylation Reagent	Thio-enolate strategy			$FeBr_3$ catalyzed allylation strategy		
		anti:syn*	de**	yield%[c]	anti:syn*	de**	yield%[c]
28a		n/a	99[b]	75	n/a	95[b]	55
28b		n/a	99[b]	55	n/a	n/a	0
28c		20:1[a]	94[b]	65	18:1[a]	88[b]	48
28d		99:1[b]	90[b]	89	99:1[b]	82[b]	52
28e		n/a	n/a	0	99:1[b]	99[b]	54

*Anti: 2*S*,3*S* and 2*R*,3*R*. Syn: 2*S*,3*R* and 2*R*,3*S*. **Diastereomeric excess between two anti isomers: anti major, 2*S*,3*S*; anti minor, 2*R*,3*R*. [a]Determined by weight. [b]Determined by chiral HPLC. [c]Isolated yield of total isomers.

We noticed that the absolute configuration of the TCR products is the opposite of the ECR reaction products when the same chiral auxiliary was used (Figure 2-I). Both reactions have similar rearrangement intermediates, and the only difference between them is the oxygen and sulfur. Interestingly enough, they give products of opposite chirality with excellent selectivities, respectively. This could be of great value in organic synthesis: the more expensive amino acids enantiomer could be prepared from the cheaper chiral auxiliary enantiomer. To understand and take advantage of these phenomena, we started by looking at X-ray crystallography studies data. In the crystal structure of phenoxathiin,[44] the bond length of C−O single bond is 1.40 Å, and the bond length of C−S single bond is 1.75 Å. The bond angle of C−O−C is measured 20° larger than the bond angle of C−S−C. The more acute C−S−C bond angle suggests the participation of *d* orbitals in the bonding of S, which has also been observed in multiple crystal structure determinations.[45] Base on these studies, we hypothesized that the shorter C−O bond length and larger C−O−C bond angle brought the CH_2 group from crotyl alcohol close to the dimethylpyrrolidinyl auxiliary in ECR transition state, making model **B** less favored than model **B′** (Figure 2-II, left). In TCR transition state, model **C** would be more favored than model **C′** in which the more acute C−S−C bond angle and longer bond

dx.doi.org/10.1021/jo201753q | J. Org. Chem. 2012, 77, 1289−1300



tert-butyl (2*S*,3*S*)-1-((2*S*,5*S*)-2,5-diphenylpyrrolidin-1-yl)-3-methyl-1-thioxopent-4-en-2-ylcarbamate

Figure 1. X-ray crystal structure of compound **28c**.

Scheme 5. Amino Acid Generation from Thioamides

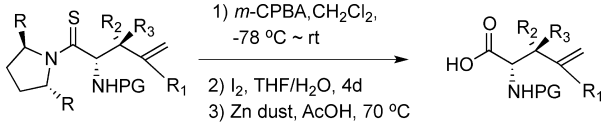


Table 4. Results of Preparing Optically Active Anti-β-Functionalized γ,δ-unsaturated amino acids

s.m.	pdt	R_1, R_2, R_3	R	PG	*anti/syn**	ee**	yields[c]
10a	**33a**	COOEt, H, H	Me	Cbz	n/a	59[b]	75
10b	**33b**	H, H, Me	Me	Cbz	9:1[a]	80[a]	72
10c	**33c**	H, H, COOMe	Me	Cbz	99:1[b]	99[b]	79
10d	**33d**	H, H, COOEt	Me	Cbz	99:1[b]	99[b]	76
11d	**33d**	H, H, COOEt	CH_2OMe	Cbz	99:1[b]	98[b]	74
12d	**33d**	H, H, COOEt	Ph	Cbz	99:1[b]	99[b]	71
23c	**34c**	H, H, COOEt	H	Boc	>49:1[c]	n/a	68
24c	**33e**	H, H, $CON(Et)_2$	H	Cbz	-	-	0
25c	**35c**	H, H, COOEt	H	Alloc	>49:1[c]	n/a	80
25d	**35d**		H	Alloc	>49:1[c]	n/a	68
25e	**35e**	H, H, $COOCH_2COPh$	H	Alloc	>49:1[c]	n/a	30
32c	**34b**	H, H, Me	Ph	Boc	99:1[b]	96[b]	70

*Anti: 2*S*,3*S* and 2*R*,3*R*; syn: 2*S*,3*R* and 2*R*,3*S*. **Enantiomeric excess between two anti isomers: anti major: 2*S*,3*S*; anti minor: 2*R*,3*R*. [a]Determined by weight. [b]Determined by chiral HPLC. [c]Isolated yield of total isomers.

length made the alkene moiety from crotyl bromide clash with the methyl group from chiral auxiliary (Figure 2-II, right).

To prove this hypothesis, we thought that by comparing the diastereoselectivities from both reactions when a *cis* substitution is presented could provide new insights. This is because when a *cis* substitution is presented in the ECR reaction, both **B** and **B′** would have stereic clashes, resulting in lower diastereoselectivity (Figure 2-III, left). On the contrary, when a *cis* substituion is presented for TCR reaction, this makes **C** still favored since the proximal methyl group on the auxiliary is pointing away from the allylic group moiety, creating an empty space that accommodates *cis* substitution. **C′** is further disfavored because an increased steric clash is introduced from the *cis* substitution with the methyl group from pyrrolidine ring. This should result in an enhanced diastereoselectivity in the TCR reaction (Figure 2-III, right). The experimental validation of this hypothesis was presented in Table 5. The TCR reaction gave better diastereoselectivities (compound **10e** and **28f**), and only one diastereopure compound was isolated in each case, which is consistent with **C** being the transition-state model. The ECR lost selectivities significantly, which suggests the reaction was struggling in both disfavored **B** and **B′** transition state models (Figure 2-III, left). It has to be pointed out here that compounds **36b** and **28f** are the closest compounds we can make for comparison. We have mentioned in our previous studies that the diphenylpyrrolidinyl auxiliary was not compatible with the ECR reaction.[33]

SUMMARY

Herein we have elaborated on our studies of the thio-Claisen rearrangement in the synthesis of anti-β-functionalized γ,δ-unsaturated amino acids. In the course of this investigation, the TCR methodologies gave excellent diastereoselectivities and enantioselectivities with both the thio-enolate dianion strategy and the $FeBr_3$-catalyzed allylation strategy. Except for Fmoc-protected amino acids, other commonly used *N*-protected amino acids were readily prepared with excellent optical purities. The TCR reaction using the thio-enolate dianion strategy is limited by *C*-alkylation, but it is a fast and clean reaction that is generally complete in around 4 h and gives excellent yields even for substrates with significant steric hindrance. The TCR reaction using the $FeBr_3$-catalyzed allylation strategy is a mild and general method that allows us to introduce multiple new functional groups into the products and does not suffer from *C*-alkylation side reaction problems. However, its efficiency can be sensitive to the steric environment of the reaction. We also gained a preliminary understanding of the chirality cross over problem between TCR and ECR reactions. Research on using these novel amino acids studying peptide dicarba analogues and β-turn structures are ongoing.

EXPERIMENTAL SECTION

General Procedure for the Preparation of Compounds 7−9, 13, 18−21, and 27. A 250 mL round-bottom flask was charged with compound **4**, **5**, **14**−**17**, and **26** (10.0 mmol) dissolved in toluene (100 mL) with Lawesson's reagent (4.8 g, 12.0 mmol) and sodium bicarbonate (8.4 g, 100.0 mmol). The reaction was stirred and refluxed at 120 °C until starting material was no longer present by TLC analysis (about 3 h). Then the reaction was cooled to ambient temperature and diluted with 200 mL of EtOAc. The solution was filtered and washed with a 5% citric acid solution (50 mL × 2 and brine (50 mL × 1), and the organic layer was collected and dried over anhydrous $MgSO_4$. The dry solution was filtered and concentrated under reduced pressure. The residues collected were purified by flash

dx.doi.org/10.1021/jo201753q | *J. Org. Chem.* 2012, 77, 1289−1300

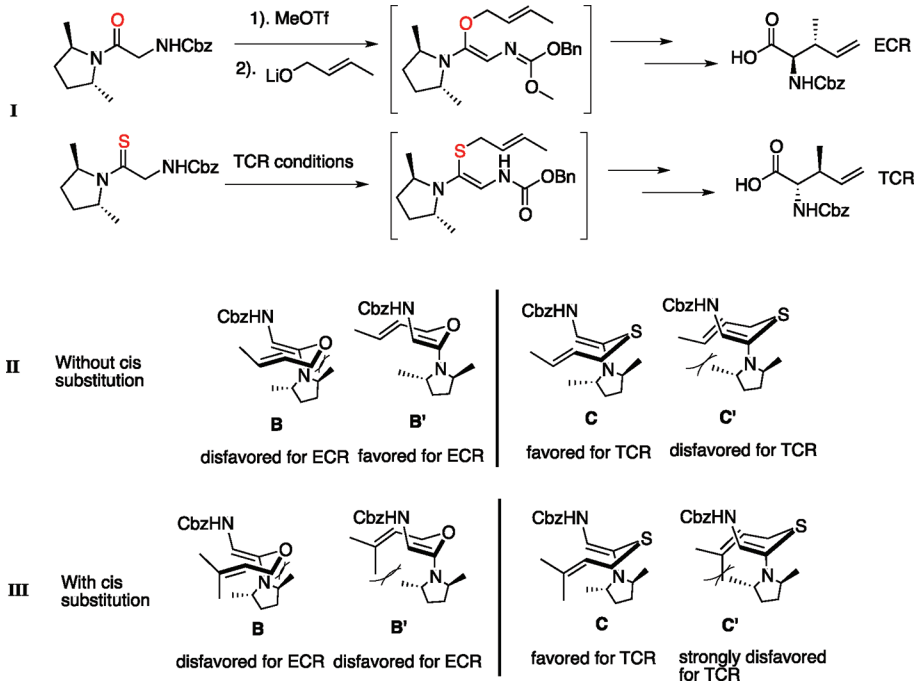
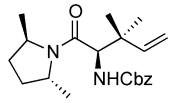
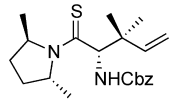
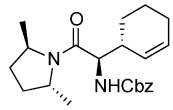
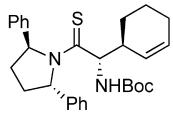


Figure 2. Proposed transition-state models for TCR and ECR reactions.

Table 5. Results of Comparing ECR and TCR Diastereoselectivities

pdt	structure	*anti/syn**	de**	yields
36a		n/a	49[c]	81[c]
10e		n/a	99[b]	66[d]
36b		-[a]	-[a]	32[d]
28f		99:1[b]	99[b]	44[d]

*Anti: 2*S*,3*S* and 2*R*,3*R*; syn: 2*S*,3*R* and 2*R*,3*S*. **Diastereomeric excess between two anti isomers: anti major: 2*S*,3*S*; anti minor: 2*R*,3*R*. [a]Inseparable diastereomeric mixtures. [b]Determined by chiral HPLC. [c]Results from previous publications. [d]Isolated yield of total isomers.

column chromatography to give thioamide products **7**–**9**, **18**–**21**, and **27** using a gradient solvent mixture eluate.

*Benzyl (2-((2R,5R)-2,5-Dimethylpyrrolidin-1-yl)-2-thioxoethyl)carbamate (**7**).* Amide **4** (983 mg, 3.39 mmol), Lawesson's reagent (1640 mg, 4.07 mmol), and sodium bicarbonate (2850 mg, 34.0 mmol) were reacted and worked up as described above. Product **22**: yellow solid, 1031 mg, yield 99%; R_f = 0.40 (hexanes/EtOAc = 2:1); $[\alpha]^{24.7}_D$ +79.0 (*c* 1.26, MeOH); IR (NaCl) 2968, 1719, 1465, 1208; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.26 (m, 5H), 6.35 (br, 1H), 5.19–5.08 (m, 2H), 4.78 (p, *J* = 6.6 Hz, 1H), 4.36–4.29 (m, 1H), 4.21 (dd, *J* = 16.6, 4.4 Hz, 1H), 4.08 (dd, *J* = 16.6, 4.8 Hz, 1H), 2.42–2.15 (m, 2H), 1.74 (dd, *J* = 11.8, 5.4 Hz, 1H), 1.68 (dd, *J* = 12.0, 5.7 Hz, 1H), 1.35 (d, *J* = 6.4 Hz, 3H), 1.30 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.4, 155.8, 136.4, 128.3, 127.8, 127.8, 66.7, 59.9, 57.3, 48.6, 31.2, 28.5, 20.8, 16.8; HRMS (ESI) calcd for $C_{16}H_{23}N_2O_2S$ (MH^+) 307.1475, found 307.1472.

*Benzyl (2-((2S,5S)-2,5-Bis(methoxymethyl)pyrrolidin-1-yl)-2-thioxoethyl)carbamate (**8**).* Amide **5** (541.4 mg, 1.55 mmol), Lawesson's reagent (751 mg, 1.86 mmol), and sodium bicarbonate (1300 mg, 15.5 mmol) were reacted and worked up as described above. Product **8**: colorless oil, 566 mg, yield 99%; R_f = 0.40 (hexanes/EtOAc = 1:1); $[\alpha]^{24.6}_D$ +39.1 (*c* 1.14, MeOH); IR (NaCl) 2928, 1720, 1447, 1113; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58–7.05 (m, 5H), 6.22 (br, 1H), 5.12 (s, 2H), 4.79 (t, *J* = 6.0 Hz, 1H), 4.34 (dd, *J* = 16.5, 5.0 Hz, 2H), 4.10 (dd, *J* = 16.7, 5.0 Hz, 1H), 3.77 (dd, *J* = 9.5, 2.4 Hz, 1H), 3.66 (dd, *J* = 9.4, 6.6 Hz, 1H), 3.45 (dd, *J* = 9.5, 4.5 Hz, 1H), 3.38–3.12 (m, 6H), 2.27 (dd, *J* = 13.2, 6.3 Hz, 1H), 2.12 (td, *J* = 12.9, 6.8 Hz, 1H), 2.07–1.86 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.5, 155.8, 136.4, 128.3, 127.9, 127.8, 73.4, 69.1, 66.7, 63.2, 61.2, 59.0, 58.8, 49.3, 27.9, 25.4; HRMS (ESI) calcd for $C_{18}H_{27}N_2O_4S$ (MH^+) 367.1686, found 367.1687.

*(S)-Benzyl (2-(2-(methoxymethyl)pyrrolidin-1-yl)-2-thioxoethyl)-carbamate (**13**):* IR (NaCl) 3322, 2930, 1717, 1456, 1215, 1109; $[\alpha]^{24.3}_D$ −49.4 (*c* 0.60, MeOH); HRMS (ESI) calcd for $C_{16}H_{23}N_2O_3S$ (MH^+) 323.1424, found 323.1430.

*(9H-Fluoren-9-yl)methyl (2-(Pyrrolidin-1-yl)-2-thioxoethyl)-carbamate (**18**).* Amide **14** (887 mg, 2.47 mmol), Lawesson's reagent (1200 mg, 2.96 mmol), and sodium bicarbonate (2000 mg, 24.7 mmol) were reacted and worked up as described above. Product **18**: white solid, 813 mg, yield 90%; R_f = 0.55 (hexanes/EtOAc = 1:1); IR (NaCl) 1491, 1448; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.5 Hz, 2H), 7.65 (d, *J* = 7.4 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 2H), 6.46 (s, 1H), 4.37 (d, *J* = 7.4 Hz, 2H), 4.26 (t, *J* = 7.3 Hz, 1H), 4.08 (d, *J* = 4.4 Hz, 2H), 3.87 (t, *J* = 6.9 Hz, 2H), 3.60 (t, *J* = 6.8 Hz, 2H), 2.11–2.05 (m, 2H), 1.97 (p, *J* = 6.9 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.6, 155.9, 143.8, 141.1, 127.5, 127.0, 125.2, 119.8, 67.1, 54.0, 49.5, 48.5, 47.0, 26.0, 23.6; HRMS (ESI) calcd for $C_{21}H_{23}N_2O_2S$ (MH^+) 367.1475, found 367.1480.

*tert-Butyl (2-(Pyrrolidin-1-yl)-2-thioxoethyl)carbamate (**19**).* Amide **15** (761 mg, 3.34 mmol), Lawesson's reagent (1640 mg, 4.07 mmol), and sodium bicarbonate (2800 mg, 33.4 mmol) were reacted and worked up as described above. Product **19**: yellow solid, 780 mg, yield 96%; R_f = 0.30 (hexanes/EtOAc = 2:1); IR (NaCl) 2972, 1716, 1484; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.09 (s, 1H), 4.01 (d, *J* = 4.4 Hz, 2H), 3.86 (t, *J* = 7.0 Hz, 2H), 3.61 (t, *J* = 6.9 Hz, 2H), 2.11 (p, *J* = 6.9

dx.doi.org/10.1021/jo201753q | J. Org. Chem. 2012, 77, 1289–1300

Hz, 2H), 1.99 (p, J = 7.0 Hz, 2H), 1.45 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.0, 155.4, 79.5, 53.9, 49.5, 48.4, 28.3, 26.0, 23.7; HRMS (ESI) calcd for $C_{11}H_{20}N_2NaO_2S$ (MNa^+) 267.1138, found 267.1135.

*Allyl (2-(Pyrrolidin-1-yl)-2-thioxoethyl)carbamate (**21**).* Amide **17** (505 mg, 2.38 mmol), Lawesson's reagent (1150 mg, 2.86 mmol), and sodium bicarbonate (1999 mg, 23.8 mmol) were reacted and worked up as described above. Product **21**: white solid, 496 mg, yield 95%; R_f = 0.20 (hexanes/EtOAc = 2:1); IR (NaCl) 1721, 1490; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.36 (s, 1H), 5.93 (ddd, J = 22.7, 10.8, 5.6 Hz, 1H), 5.32 (dd, J = 17.0, 1.4 Hz, 1H), 5.21 (dt, J = 11.7, 1.2 Hz, 1H), 4.59 (d, J = 5.5 Hz, 2H), 4.06 (d, J = 4.5 Hz, 2H), 3.85 (t, J = 7.1 Hz, 2H), 3.63 (t, J = 6.9 Hz, 2H), 2.16–2.07 (m, 2H), 2.05–1.95 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.3, 155.5, 132.5, 117.3, 65.5, 53.8, 49.5, 48.4, 25.9, 24.5, 23.5; HRMS (ESI) calcd for $C_{10}H_{17}N_2O_2S$ (MH^+) 229.1005, found 229.1006.

*tert-Butyl (2-((2S,5S)-2,5-Diphenylpyrrolidin-1-yl)-2-thioxoethyl)-carbamate (**27**).* Amide **26** (1216 mg, 3.20 mmol), Lawesson's reagent (751 mg, 1.86 mmol), and sodium bicarbonate (1550 mg, 3.84 mmol) were reacted and worked up as described above. Product **27**: light yellow solid, 945 mg, yield 75%; R_f = 0.40 (hexanes/EtOAc = 3:1); $[\alpha]^{24.7}_D$ −12.9 (c 1.39, MeOH); IR (NaCl) 1709.47, 1447.44, 1165.50; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44–7.10 (m, 10H), 6.04 (d, J = 8.4 Hz, 1H), 5.83 (s, 1H), 5.70 (d, J = 8.1 Hz, 1H), 4.28 (dd, J = 17.2, 4.5 Hz, 1H), 3.44 (d, J = 17.2 Hz, 1H), 2.69–2.62 (m, 1H), 2.53 (tdd, J = 14.1, 8.4, 6.0 Hz, 1H), 1.90 (dd, J = 12.4, 5.9 Hz, 1H), 1.84 (dd, J = 12.5, 6.0 Hz, 1H), 1.40 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.3, 155.5, 141.2, 140.6, 129.2, 128.5, 127.8, 126.8, 125.4, 125.1, 79.5, 68.6, 68.6, 65.9, 65.8, 49.3, 32.9, 30.0, 28.3, 28.2; HRMS (ESI) calcd for $C_{23}H_{28}N_2NaO_2S$ (MNa^+) 419.1764, found 419.1757.

General Procedure for the Preparation of Compounds 10–12. Thioamide (1.00 mmol), $FeBr_3$ (45 mg, 0.20 mmol), and allylic bromide (2.00 mmol) were dissolved in a minimum amount of dry MeCN (about 1 mL) in a 25 mL pear-shaped flask at ambient temperature under argon atmosphere. The mixture was stirred at 45–50 °C for 24–48 h. Dry THF (15 mL) was added to dilute the reaction and the mixture cooled to −78 °C. TEA (173 μL, 1.20 mmol) was added slowly to the reaction mixture, and the mixture was allowed to warm slowly to ambient temperature and then heated slowly to 45 °C for completion. The reaction was quenched by the addition of a saturated ammonium chloride solution (1 mL), and the volatiles were removed under reduced pressure; the residue was extracted twice with hexanes and diethyl ether. The combined organic layers were washed with a saturated ammonium chloride solution (10 mL × 1) and a saturated sodium bicarbonate solution (10 mL × 1) and dried over anhydrous $MgSO_4$. The dry solution was filtered and concentrated under reduced pressure, and the crude product was purified by flash column chromatography to afford compounds **10–12** using a gradient solvent mixture eluate.

*(S)-Ethyl 4-(Benzyloxycarbonylamino)-5-((2R,5R)-2,5-dimethyl-pyrrolidin-1-yl)-2-methylene-5-thioxopentanoate (**10a, major**).* Compound **7** (82 mg, 0.27 mmol), $FeBr_3$ (16 mg, 0.05 mmol), allylic bromide (0.53 mmol), and TEA (46 μL, 0.32 mmol) were reacted and worked up as described above. Product **10a, major** + **minor**: yellow oil, 71 mg, yield 64%; R_f = 0.45 (hexanes/EtOAc = 2: 1); IR (NaCl) 1717, 1461, 1134; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41–7.21 (m, 5H), 6.15 (s, 1H), 6.11 (d, J = 9.5 Hz, 1H), 5.63 (s, 1H), 5.20–5.07 (m, 2H), 4.97 (d, J = 12.3 Hz, 1H), 4.83–4.75 (m, 1H), 4.71–4.63 (m, 1H), 4.25 (q, J = 7.1 Hz, 2H), 2.62 (dd, J = 13.3, 3.7 Hz, 1H), 2.44 (dd, J = 13.3, 9.7 Hz, 1H), 2.39–2.16 (m, 2H), 1.79 (dd, J = 12.0, 5.7 Hz, 1H), 1.69 (dd, J = 12.2, 5.9 Hz, 1H), 1.37 (d, J = 6.4 Hz, 3H), 1.32 (dd, J = 13.4, 6.6 Hz, 6H); ^{13}C (125 MHz, $CDCl_3$) δ 199.3, 166.6, 155.4, 136.4, 135.3, 128.7, 128.3, 127.8, 127.8, 66.6, 60.9, 59.4, 57.8, 55.4, 41.8, 31.1, 28.5, 21.6, 16.6, 14.2; HRMS (ESI) calcd for $C_{22}H_{31}N_2O_4S$ (MH^+) 419.1995, found 419.1993. HPLC analysis: de =56%. Chiralpak AD-RH column (CH_3CN/H_2O 50/50 to 75/25, in 30 min, 0.4 mL/min, 254 nm); retention times of the diastereomers observed: 14.3 min, 15.9 min (**10a**).

*Benzyl (2S,3S)-1-((2R,5R)-2,5-dimethylpyrrolidin-1-yl)-3-methyl-1-thioxopent-4-en-2-ylcarbamate (**10b, major**).* Compound **7** (154 mg, 0.50 mmol), $FeBr_3$ (30 mg, 0.10 mmol), allylic bromide (1.01 mmol) and TEA (87 μL, 0.60 mmol) were reacted and worked up as described above. Product **10b, major**: yellow oil, 92.1 mg, yield 51%; R_f = 0.50 (hexanes/EtOAc = 2:1); $[\alpha]^{23.1}_D$ +67.7 (c 1.03, MeOH); IR (NaCl) 2970, 1714, 1497, 1456, 1215; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40–7.28 (m, 5H), 6.02 (d, J = 9.8 Hz, 1H), 5.78 (ddd, J = 17.3, 10.0, 8.6 Hz, 1H), 5.10 (dd, J = 32.4, 14.7 Hz, 2H), 5.01 (dd, J = 11.1, 7.6 Hz, 2H), 4.86 (p, J = 6.6 Hz, 1H), 4.69 (t, J = 9.3 Hz, 1H), 4.46 (p, J = 6.6 Hz, 1H), 2.63–2.56 (m, 1H), 2.34 (tt, J = 13.1, 6.7 Hz, 1H), 2.25 (ddd, J = 20.4, 13.5, 6.9 Hz, 1H), 1.80 (dd, J = 12.2, 5.8 Hz, 1H), 1.71 (dd, J = 12.3, 6.1 Hz, 1H), 1.36 (d, J = 3.0 Hz, 3H), 1.35 (d, J = 3.1 Hz, 3H), 0.97 (d, J = 6.8 Hz, 3H); ^{13}C (150 MHz, $CDCl_3$) δ 199.2, 155.3, 139.1, 136.5, 128.3, 127.9, 127.8, 116.3, 66.6, 60.3, 59.6, 58.4, 46.8, 31.0, 28.3, 21.2, 16.6, 16.1; HRMS (ESI) calcd for $C_{20}H_{29}N_2O_2S$ (MH^+) 361.1944, found 361.1943.

*Benzyl (2R,3R)-1-((2R,5R)-2,5-Dimethylpyrrolidin-1-yl)-3-methyl-1-thioxopent-4-en-2-ylcarbamate (**10b, minor**).* Compound **7** (154 mg, 0.50 mmol), $FeBr_3$ (30 mg, 0.10 mmol), allylic bromide (1.01 mmol) and TEA (87 μL, 0.60 mmol) were reacted and worked up as described above. Product **10b, minor**: yellow oil, 11.4 mg, yield 6%; R_f = 0.55 (hexanes/EtOAc = 2:1); $[\alpha]^{24.9}_D$ +100.3 (c 0.44, MeOH); IR (NaCl) 2970, 1714, 1497, 1456, 1215; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40–7.27 (m, 5H), 6.14 (d, J = 9.7 Hz, 1H), 5.66 (ddd, J = 17.3, 10.3, 8.0 Hz, 1H), 5.17–4.98 (m, 4H), 4.83–4.78 (m, 1H), 4.65 (t, J = 9.5 Hz, 1H), 4.35 (p, J = 6.6 Hz, 1H), 2.65–2.56 (m, 1H), 2.32–2.17 (m, 2H), 1.74 (dd, J = 11.8, 5.4 Hz, 1H), 1.66 (dd, J = 11.7, 5.4 Hz, 1H), 1.33 (d, J = 6.6 Hz, 3H), 1.31 (d, J = 6.4 Hz, 3H), 1.13 (d, J = 6.8 Hz, 3H); ^{13}C (150 MHz, $CDCl_3$) δ 199.2, 155.5, 138.0, 136.4, 128.4, 128.0, 127.9, 116.4, 66.7, 60.6, 59.6, 58.5, 46.5, 30.8, 28.5, 21.2, 16.5, 15.9; HRMS (ESI) calcd for $C_{20}H_{29}N_2O_2S$ (MH^+) 361.1944, found 361.1943.

*(S)-Methyl 2-((S)-1-(Benzyloxycarbonylamino)-2-((2R,5R)-2,5-dimethylpyrrolidin-1-yl)-2-thioxoethyl)but-3-enoate (**10c**).* Compound **7** (75.5 mg, 0.25 mmol), $FeBr_3$ (15 mg, 0.05 mmol), allylic bromide (0.62 mmol), and TEA (43 μL, 0.30 mmol) were reacted and worked up as described above. Product **10c**: yellow oil, 86 mg, yield 86%; R_f = 0.40 (hexanes/EtOAc = 2:1); $[\alpha]^{25.0}_D$ −0.3 (c 0.64, MeOH); IR (NaCl) 1729, 1498, 1464, 1196; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45–7.24 (m, 5H), 5.88–5.80 (m, 2H), 5.30–4.94 (m, 5H), 4.85–4.72 (m, 2H), 3.77–3.64 (m, 1H), 3.61 (s, 3H), 2.39–2.16 (m, 2H), 1.75 (dd, J = 12.3, 5.9 Hz, 1H), 1.67 (dd, J = 12.3, 6.1 Hz, 1H), 1.30 (d, J = 6.6 Hz, 3H), 1.23 (d, J = 6.4 Hz, 3H); ^{13}C (150 MHz, $CDCl_3$) δ 196.6, 171.7, 154.9, 136.3, 132.0, 128.3, 127.9, 127.8, 121.0, 66.7, 59.8, 59.6, 58.6, 57.0, 51.9, 30.9, 28.5, 21.4, 16.0; HRMS (ESI) calcd for $C_{21}H_{29}N_2O_4S$ (MH^+) 405.1843, found 405.1836. HPLC analysis: de >99%. Chiralpak AD-RH column (CH_3CN/H_2O 55/45, 0.5 mL/min, 254 nm); retention times of the only diastereomer observed: 12.8 min (**10c**).

*(S)-Ethyl 2-((S)-1-(Benzyloxycarbonylamino)-2-((2R,5R)-2,5-dimethylpyrrolidin-1-yl)-2-thioxoethyl)but-3-enoate (**10d**).* Compound **7** (127 mg, 0.42 mmol), $FeBr_3$ (25 mg, 0.08 mmol), allylic bromide (0.83 mmol), and TEA (72 μL, 0.50 mmol) were reacted and worked up as described above. Product **10d**: yellow oil, 144 mg, yield 83%; R_f = 0.50 (hexanes/EtOAc = 2:1); $[\alpha]^{24.7}_D$ +20.0 (c 1.26, MeOH); IR (NaCl) 2974, 1726, 1464, 1184; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40–7.27 (m, 5H), 5.88–5.79 (m, 2H), 5.28–4.98 (m, 4H), 4.86–4.76 (m, 2H), 4.10–4.01 (m, 2H), 3.69 (t, J = 9.4 Hz, 1H), 2.38–2.30 (m, 1H), 2.22 (ddd, J = 20.4, 13.4, 6.9 Hz, 1H), 1.75 (dd, J = 12.3, 6.0 Hz, 1H), 1.67 (dd, J = 12.4, 6.2 Hz, 1H), 1.30 (d, J = 6.6 Hz, 3H), 1.26–1.17 (m, 6H); ^{13}C (150 MHz, $CDCl_3$) δ 196.7, 171.3, 155.0, 136.3, 132.1, 128.3, 128.0, 127.9, 120.9, 66.7, 60.9, 59.9, 59.6, 58.6, 56.9, 30.9, 28.5, 21.4, 16.0, 14.0; HRMS (ESI) calcd for $C_{22}H_{30}N_2NaO_4S$ (MNa^+) 441.1818, found 441.1811. HPLC analysis: de >99%. Chiralpak AD-RH column (CH_3CN/H_2O 55/45, 0.5 mL/min, 254 nm); retention times of the only diastereomer observed: 15.3 min (**10d**).

*(S)-Ethyl 4-(((Benzyloxy)carbonyl)amino)-5-((2S,5S)-2,5-bis-(methoxymethyl)pyrrolidin-1-yl)-2-methylene-5-thioxopentanoate (**11a**).* Compound **8** (70 mg, 0.19 mmol), $FeBr_3$ (23 mg, 0.08 mmol), allylic bromide (0.38 mmol), and TEA (40 μL, 0.27 mmol) were reacted and worked up as described above. Product **11a**: clear oil, 47

dx.doi.org/10.1021/jo201753q | J. Org. Chem. 2012, 77, 1289–1300

mg, yield 54%; R_f = 0.40 (hexanes/EtOAc = 2:1); $[\alpha]^{24.8}_D$ +64.3 (*c* 0.10, MeOH); IR (NaCl) 1716, 1500, 1447, 1115; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.24 (m, 5H), 6.17 (s, 1H), 6.08 (d, *J* = 9.5 Hz, 1H), 5.63 (s, 1H), 5.26−4.97 (m, 3H), 4.80 (t, *J* = 8.5 Hz, 1H), 4.68 (td, *J* = 7.8, 3.8 Hz, 1H), 4.28−4.20 (m, 2H), 3.72−3.62 (m, 2H), 3.58−3.51 (m, 1H), 3.42 (dd, *J* = 17.4, 8.7 Hz, 1H), 3.32 (t, *J* = 10.4 Hz, 6H), 2.64 (dd, *J* = 13.4, 3.7 Hz, 1H), 2.43 (dd, *J* = 13.3, 9.8 Hz, 1H), 2.31 (ddd, *J* = 19.8, 12.3, 7.4 Hz, 1H), 2.11 (dddd, *J* = 35.1, 19.3, 12.6, 6.9 Hz, 3H), 1.35−1.30 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.92, 166.61, 155.36, 136.52, 135.38, 128.76, 128.37, 127.95, 127.90, 99.95, 73.14, 69.21, 66.59, 62.89, 61.27, 61.00, 58.99, 58.90, 56.16, 42.06, 27.57, 25.44, 14.15; HRMS (ESI) calcd for $C_{24}H_{35}N_2O_6S$ (MH^+) 479.2210, found 479.2211. HPLC analysis: de = 90%. Chiralpak AD-RH column (CH_3CN/H_2O 60/40 to 70/30, in 30 min, 0.5 mL/min, 254 nm); retention times of the diastereomeric mixture observed: 8.8 min (**11a**) and 14.3.

*Benzyl (2S,3S)-1-((2S,5S)-2,5-Bis(methoxymethyl)pyrrolidin-1-yl)-3-methyl-1-thioxopent-4-en-2-ylcarbamate13C (**11b**).* Compound **8** (90 mg, 0.25 mmol), $FeBr_3$ (30 mg, 0.10 mmol), crotyl bromide (0.49 mmol), and TEA (50 μL, 0.34 mmol) were reacted and worked up as described above. Product **11b**: yellow oil, 54 mg, yield 52%; R_f = 0.60 (hexanes/EtOAc = 2:1); $[\alpha]^{24.1}_D$ +40.8 (*c* 0.34, MeOH); IR (NaCl) 1792, 1498, 1455, 1199, 1113; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42−7.22 (m, 5H), 5.99 (d, *J* = 9.7 Hz, 1H), 5.83−5.72 (m, 1H), 5.15−4.98 (m, 1H), 4.83 (t, *J* = 5.6 Hz, 4H), 4.76−4.72 (m, 1H), 4.37 (td, *J* = 8.2, 3.5 Hz, 1H), 3.82 (dd, *J* = 9.4, 5.8 Hz, 1H), 3.63 (dd, *J* = 9.4, 2.6 Hz, 1H), 3.54 (dd, *J* = 9.7, 3.6 Hz, 1H), 3.30 (s, 7H), 2.61−2.52 (m, 1H), 2.39−2.22 (m, 1H), 2.10 (dddd, *J* = 31.9, 25.2, 12.5, 7.1 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.5, 155.2, 138.9, 136.5, 128.3, 127.8, 127.8, 116.3, 72.7, 69.5, 66.6, 63.0, 62.0, 61.0, 58.9, 58.7, 46.5, 27.7, 25.4, 16.3; HRMS(ESI) calcd for $C_{22}H_{33}N_2O_4S$ (MH^+) 421.2156, found 421.2152. HPLC analysis: de = 88%. Chiralpak AD-RH column (CH_3CN/H_2O 30/70, 0.5 mL/min, 254 nm); the diastereomeric mixture: 19.5 min, 21.6 min (**11b**).

*(S)-Methyl 2-((S)-1-(Benzyloxycarbonylamino)-2-((2S,5S)-2,5-bis-(methoxymethyl)pyrrolidin-1-yl)-2-thioxoethyl)but-3-enoate (**11c**).* Compound **8** (102 mg, 0.28 mmol), $FeBr_3$ (30 mg, 0.10 mmol), allylic bromide (0.56 mmol), and TEA (55 μL, 0.38 mmol) were reacted and worked up as described above. Product **11c**: yellow oil, 83 mg, yield 64%; R_f = 0.45 (hexanes/EtOAc = 2:1); $[\alpha]^{24.3}_D$ −21.8 (*c* 0.32, MeOH); IR (NaCl) 1729, 1451; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.23 (m, 5H), 5.90 (d, *J* = 9.9 Hz, 1H), 5.83 (dt, *J* = 17.0, 9.7 Hz, 1H), 5.21 (dt, *J* = 16.8, 7.0 Hz, 3H), 5.07 (s, 2H), 4.82 (td, *J* = 7.5, 2.7 Hz, 1H), 4.73 (td, *J* = 7.8, 4.2 Hz, 1H), 3.64 (s, 3H), 3.46−3.38 (m, 2H), 3.32 (s, 3H), 3.25 (s, 3H), 2.31−2.20 (m, 1H), 2.17−1.99 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.4, 171.3, 154.9, 136.4, 131.8, 128.4, 128.0, 127.9, 121.0, 72.9, 68.7, 66.8, 62.9, 62.1, 59.9, 58.8, 58.6, 57.5, 52.0, 27.3, 25.1; HRMS (ESI) calcd for $C_{23}H_{33}N_2O_6S$ (MH^+) 465.2054, found 465.2052. HPLC analysis: de >99%. Chiralpak AD-RH column (CH_3CN/H_2O 50/50, 0.5 mL/min, 254 nm); retention times of the only diastereomer observed: 21.4 min (**11c**).

*(S)-Ethyl 2-((S)-1-(Benzyloxycarbonylamino)-2-((2S,5S)-2,5-bis-(methoxymethyl)pyrrolidin-1-yl)-2-thioxoethyl)but-3-enoate (**11d**).* Compound **8** (88 mg, 0.24 mmol), $FeBr_3$ (30 mg, 0.10 mmol), allylic bromide (0.73 mmol) and TEA (50 μL, 0.34 mmol) were reacted and worked up as described above. Product **11d**: yellow oil, 75 mg, yield 65%; R_f = 0.55 (hexanes/EtOAc = 2:1); $[\alpha]^{23.7}_D$ −24.2 (*c* 0.61, MeOH); IR (NaCl) 1726, 1115; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39−7.26 (m, 5H), 5.93−5.80 (m, 2H), 5.27−5.16 (m, 2H), 5.09−5.05 (m, 2H), 4.82 (dd, *J* = 7.4, 4.6 Hz, 1H), 4.75 (dd, *J* = 11.7, 7.9 Hz, 1H), 4.23−4.02 (m, 2H), 3.69−3.59 (m, 2H), 3.47−3.21 (m, 8H), 2.24 (dd, *J* = 16.8, 9.6 Hz, 1H), 2.18−1.84 (m, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.3, 170.9, 154.8, 136.3, 131.8, 128.3, 128.0, 127.9, 120.9, 72.9, 68.7, 66.8, 62.9, 62.0, 61.0, 60.0, 58.8, 58.6, 57.5, 27.3, 25.0, 14.0; HRMS (ESI) calcd for $C_{24}H_{35}N_2O_6S$ (MH^+) 479.2210, found 479.2208. HPLC analysis: de >99%. Chiralpak AD-RH column (CH_3CN/H_2O 50/50, 0.5 mL/min, 254 nm); retention times of the only diastereomer observed: 17.0 min (**11d**).

*(S)-Methyl 2-((S)-1-(Benzyloxycarbonylamino)-2-((2S,5S)-2,5-diphenylpyrrolidin-1-yl)-2-thioxoethyl)but-3-enoate (**12c**).* Compound **9** (200 mg, 0.47 mmol), $FeBr_3$ (30 mg, 0.10 mmol), allylic bromide (112 μL, 0.94 mmol), and TEA (82 μL, 0.57 mmol) were reacted and worked up as described above. Product **12c**: yellow oil, 173 mg, yield 63%; R_f = 0.50 (hexanes/EtOAc = 2:1); $[\alpha]^{24.5}_D$ +126.0 (*c* 0.55, MeOH); IR (NaCl) 3029, 2950, 1728, 1447; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41−7.10 (m, 15H), 6.23 (d, *J* = 7.9 Hz, 1H), 5.91 (d, *J* = 8.6 Hz, 1H), 5.75−5.66 (m, 1H), 5.27 (d, *J* = 9.4 Hz, 1H), 5.17−5.04 (m, 2H), 4.72 (d, *J* = 12.3 Hz, 1H), 4.57 (d, *J* = 12.3 Hz, 1H), 3.76 (t, *J* = 9.4 Hz, 1H), 3.68 (s, 3H), 2.83−2.70 (m, 1H), 2.46 (tt, *J* = 16.2, 8.8 Hz, 1H), 1.91 (dd, *J* = 12.5, 5.8 Hz, 1H), 1.75 (dd, *J* = 12.6, 6.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.2, 172.5, 153.5, 141.5, 141.2, 136.3, 131.7, 128.4, 128.2, 128.1, 127.7, 127.7, 127.2, 126.7, 125.5, 125.5, 120.8, 68.8, 67.0, 66.2, 58.9, 57.0, 52.0, 32.9, 30.1; HRMS (ESI) calcd for $C_{31}H_{33}N_2O_4S$ (MH^+) 529.2156, found 529.2164. HPLC analysis: de >99%. Chiralpak AD-RH column (CH_3CN/H_2O 60/40, 0.5 mL/min, 254 nm); retention times of the only diastereomer observed: 19.7 min (**12c**).

*(S)-ethyl 2-((S)-1-(benzyloxycarbonylamino)-2-((2S,5S)-2,5-diphenylpyrrolidin-1-yl)-2-thioxoethyl)but-3-enoate (**12d**).* Compound **9** (124 mg, 0.29 mmol), $FeBr_3$ (19 mg, 0.06 mmol), allylic bromide (78 μL, 0.58 mmol), and TEA (51 μL, 0.35 mmol) were reacted and worked up as described above. Product **12d**: yellow oil, 109 mg, yield 70%; R_f = 0.55 (hexanes/EtOAc = 3:1); $[\alpha]^{24.8}_D$ +127.0 (*c* 1.05, MeOH); IR (NaCl) 1718, 1448, 1187; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45−7.08 (m, 15H), 6.24 (d, *J* = 8.0 Hz, 1H), 5.91 (d, *J* = 8.6 Hz, 1H), 5.75−5.65 (m, 1H), 5.28 (d, *J* = 9.5 Hz, 1H), 5.17−5.04 (m, 2H), 4.73 (d, *J* = 12.3 Hz, 1H), 4.57 (d, *J* = 12.3 Hz, 1H), 4.31−4.01 (m, 2H), 3.74 (t, *J* = 9.4 Hz, 1H), 2.81−2.69 (m, 1H), 2.54−2.39 (m, 1H), 1.91 (dd, *J* = 12.5, 5.8 Hz, 1H), 1.75 (dd, *J* = 12.6, 6.0 Hz, 1H), 1.24−1.18 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.3, 172.1, 153.5, 141.5, 141.2, 136.3, 131.9, 128.4, 128.2, 128.1, 127.8, 127.7, 127.2, 126.7, 125.5, 120.7, 68.9, 67.0, 66.2, 60.9, 59.0, 57.0, 33.0, 30.1, 14.0; HRMS (ESI) calcd for $C_{32}H_{35}N_2O_4S$ (MH^+) 543.2312, found 543.2310. HPLC analysis: de >99%. Chiralpak AD-RH column (CH_3CN/H_2O 60/40, 0.5 mL/min, 254 nm); retention times of the only diastereomer observed: 21.2 min (**12d**).

*tert-Butyl 3-Methyl-1-(pyrrolidin-1-yl)-1-thioxopent-4-en-2-ylcarbamate (**23a**).* Compound **19** (127 mg, 0.56 mmol), $FeBr_3$ (20 mg, 0.06 mmol), crotyl bromide (168 μL, 1.40 mmol), and TEA (96 μL, 0.67 mmol) were reacted and worked up as described above. Product **23a**: yellow oil, 105 mg, yield 63%; R_f = 0.65 (hexanes/EtOAc = 2:1); IR (NaCl) 2974, 1710, 1487, 1165; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.82 (ddd, *J* = 17.2, 10.3, 8.1 Hz, 1H), 5.44 (d, *J* = 9.6 Hz, 1H), 5.09 (ddd, *J* = 11.3, 9.1, 3.6 Hz, 2H), 4.56 (dd, *J* = 11.6, 6.9 Hz, 1H), 4.06−3.99 (m, 1H), 3.94−3.78 (m, 2H), 3.75−3.67 (m, 1H), 2.74−2.62 (m, 1H), 2.16−1.86 (m, 4H), 1.41 (s, 9H), 0.99 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.9, 155.2, 139.2, 116.1, 79.4, 60.2, 53.7, 51.0, 44.3, 28.3, 26.0, 23.9, 16.8; HRMS (ESI) calcd for $C_{15}H_{27}N_2O_2S$ (MH^+) 299.1788, found 299.1788.

*Ethyl 2-(1-(tert-Butoxycarbonylamino)-2-(pyrrolidin-1-yl)-2-thioxoethyl)but-3-enoate (**23c**).* Compound **19** (167 mg, 0.68 mmol), $FeBr_3$ (25 mg, 0.07 mmol), allylic bromide (198 μL, 1.47 mmol), and TEA (108 μL, 0.75 mmol) were reacted and worked up as described above. Product **23c**: yellow oil, 183 mg, yield 79%; R_f = 0.60 (hexanes/EtOAc = 2: 1); IR (NaCl) 2978, 1724, 1168; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.82 (d, *J* = 16.9 Hz, 1H), 5.35−5.24 (m, 2H), 5.22−5.09 (m, 2H), 4.14−4.04 (m, 3H), 4.04−3.97 (m, 1H), 3.87 (t, *J* = 9.3 Hz, 1H), 3.82−3.71 (m, 2H), 2.15−1.89 (m, 4H), 1.40 (s, 9H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.2, 171.6, 154.8, 132.1, 120.5, 79.9, 60.9, 56.9, 56.2, 53.8, 51.2, 28.2, 25.9, 24.0, 14.0; HRMS (ESI) calcd for $C_{17}H_{29}N_2O_4S$ (MH^+) 357.1843, found 357.1844.

*Benzyl 1-(Cyclohex-2-enyl)-2-(pyrrolidin-1-yl)-2-thioxoethylcarbamate (**24b**).* Compound **20** (180 mg, 0.79 mmol), $FeBr_3$ (48 mg, 0.16 mmol), allylic bromide (181 μL, 1.57 mmol), and TEA (137 μL, 0.95 mmol) were reacted and worked up as described above. Product **24b**: yellow oil, 34 mg, yield 15%; R_f = 0.40 (hexanes/EtOAc = 3:1); IR (NaCl) 2924, 1717, 1489, 1450; ^{1}H NMR (500 MHz, $CDCl_3$) δ

7.41−7.22 (m, 5H), 5.86−5.77 (m, 2H), 5.34 (d, J = 8.0 Hz, 1H), 5.15−5.10 (m, 1H), 5.04 (d, J = 12.3 Hz, 1H), 4.65 (t, J = 9.8 Hz, 1H), 3.94−3.70 (m, 3H), 2.56 (s, 1H), 2.12−1.91 (m, 6H), 1.83−1.53 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.3, 199.5, 156.0, 136.3, 130.7, 128.4, 128.0, 127.8, 125.9, 66.8, 60.2, 53.6, 51.2, 41.4, 25.9, 25.3, 24.8, 24.0, 20.2; HRMS (ESI) calcd for $C_{20}H_{27}N_2O_2S$ (MH^+) 359.1788, found 359.1788.

*Benzyl ((2S,3S)-3-(Diethylcarbamoyl)-1-(pyrrolidin-1-yl)-1-thioxopent-4-en-2-yl)carbamate (**24c**).* Compound **20** (81 mg, 0.29 mmol), $FeBr_3$ (36 mg, 0.12 mmol), allylic bromide (0.59 mmol), and TEA (60 μL, 0.41 mmol) were reacted and worked up as described above. Product **24b**: yellow oil, 63 mg, yield 51%; R_f = 0.65 (hexanes/EtOAc = 1: 2); IR (NaCl) 2974, 1720, 1626; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39−7.27 (m, 5H), 5.94−5.82 (m, 1H), 5.40 (d, J = 10.3 Hz, 1H), 5.29−4.99 (m, 5H), 4.34−4.26 (m, 1H), 4.01 (dt, J = 13.0, 8.0 Hz, 2H), 3.81−3.43 (m, 4H), 3.39−3.13 (m, 3H), 2.12−1.85 (m, 4H), 1.21 (t, J = 7.1 Hz, 3H), 1.02 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.05, 170.10, 155.55, 136.21, 133.95, 128.41, 128.04, 127.88, 119.94, 114.67, 66.95, 57.85, 54.38, 53.82, 51.55, 42.56, 40.69, 25.94, 24.10, 14.37, 12.69; HRMS (ESI) calcd for $C_{22}H_{32}N_3O_3S$ (MH^+) 418.2159, found 418.2166.

*Allyl 3-Methyl-1-(pyrrolidin-1-yl)-1-thioxopent-4-en-2-ylcarbamate (**25a**).* Compound **21** (94 mg, 0.41 mmol), $FeBr_3$ (25 mg, 0.08 mmol), crotyl bromide (107 μL, 0.83 mmol), and TEA (71 μL, 0.49 mmol) were reacted and worked up as described above. Product **25a**: yellow oil, 92 mg, yield 80%; R_f = 0.50 (hexanes/EtOAc = 2:1); IR (NaCl) 2973, 1716, 1495; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 (dtdd, J = 25.2, 18.2, 10.4, 6.8 Hz, 2H), 5.68 (d, J = 9.6 Hz, 1H), 5.34−5.06 (m, 4H), 4.63−4.47 (m, 3H), 4.10−4.03 (m, 1H), 3.94−3.80 (m, 2H), 3.78−3.70 (m, 1H), 2.78−2.68 (m, 1H), 2.15−1.91 (m, 4H), 1.01 (d, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.4, 155.6, 139.0, 132.5, 117.4, 116.3, 65.6, 60.6, 53.8, 51.1, 44.0, 26.0, 23.9, 16.7; HRMS (ESI) calcd for $C_{14}H_{23}N_2O_2S$ (MH^+) 283.1475, found 283.1471.

*Allyl 3,3-Dimethyl-1-(pyrrolidin-1-yl)-1-thioxopent-4-en-2-ylcarbamate (**25b**).* Compound **21** (138 mg, 0.60 mmol), $FeBr_3$ (35 mg, 0.12 mmol), allylic bromide (140 μL, 1.20 mmol), and TEA (104 μL, 0.72 mmol) were reacted and worked up as described above. Product **25b**: yellow oil, 90 mg, yield 51%; R_f = 0.60 (hexanes/EtOAc = 2:1); IR (NaCl) 2969, 1721, 1218; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.00 (dd, J = 17.8, 10.5 Hz, 1H), 5.90 (tt, J = 13.1, 5.6 Hz, 2H), 5.30 (dd, J = 17.2, 1.4 Hz, 1H), 5.19 (ddd, J = 8.0, 6.8, 1.4 Hz, 1H), 5.10−5.03 (m, 2H), 4.71 (d, J = 10.0 Hz, 1H), 4.62−4.46 (m, 2H), 3.95−3.84 (m, 2H), 3.75 (tt, J = 13.7, 6.7 Hz, 2H), 2.09−1.88 (m, 4H), 1.17 (s, 3H), 1.14 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.0, 156.0, 143.5, 132.6, 117.5, 113.3, 65.7, 62.5, 53.7, 51.8, 41.6, 26.0, 24.4, 23.9, 23.5; HRMS (ESI) calcd for $C_{15}H_{25}N_2O_2S$ (MH^+) 297.1631, found 297.1628.

*Ethyl 2-(1-(Allyloxycarbonylamino)-2-(pyrrolidin-1-yl)-2-thioxoethyl)but-3-enoate (**25c**).* Compound **21** (110 mg, 0.48 mmol), $FeBr_3$ (30 mg, 0.10 mmol), allylic bromide (173 μL, 0.96 mmol), and TEA (84 μL, 0.58 mmol) were reacted and worked up as described above. Product **25c**: yellow oil, 135 mg, yield 82%; R_f = 0.60 (hexanes/EtOAc = 2:1); IR (NaCl) 1725, 1504, 1451; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.94−5.76 (m, 2H), 5.41 (d, J = 10.2 Hz, 1H), 5.37−5.10 (m, 5H), 4.53 (ddd, J = 33.6, 13.3, 5.5 Hz, 2H), 4.19−4.00 (m, 4H), 3.90 (t, J = 9.5 Hz, 1H), 3.78 (dtt, J = 21.1, 14.0, 7.0 Hz, 2H), 2.15−1.91 (m, 4H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.0, 171.5, 155.4, 132.4, 131.9, 120.9, 117.6, 65.8, 61.0, 56.6, 56.6, 53.8, 51.3, 25.9, 24.0, 13.9; HRMS (ESI) calcd for $C_{16}H_{25}N_2O_4S$ (MH^+) 341.1530, found 341.1530.

*Allyl 1-(Cyclohex-2-enyl)-2-(pyrrolidin-1-yl)-2-thioxoethylcarbamate (**25d**).* Compound **21** (151 mg, 0.66 mmol), $FeBr_3$ (40 mg, 0.13 mmol), allylic bromide (153 μL, 1.33 mmol), and TEA (115 μL, 0.80 mmol) were reacted and worked up as described above. Product **25d**: yellow oil, 58 mg, yield 29%; R_f = 0.60 (hexanes/EtOAc = 2: 1); IR (NaCl) 2928, 1695, 1252; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.93 (ddd, J = 22.5, 10.8, 5.6 Hz, 1H), 5.88−5.83 (m, 1H), 5.62 (dd, J = 8.0, 1.8 Hz, 1H), 5.38−5.19 (m, 3H), 4.61 (d, J = 5.5 Hz, 2H), 4.28−4.22 (m, 1H), 4.11 (d, J = 6.0 Hz, 2H), 2.12−1.94 (m, 4H), 1.81−1.73 (m, 1H), 1.72−1.62 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.1, 155.9, 132.4, 131.3, 125.7, 117.9, 66.1, 50.5, 39.6, 29.4, 24.6, 19.8; HRMS (ESI) calcd for $C_{16}H_{25}N_2O_2S$ (MH^+) 309.1631, found 309.1629.

*2-Oxo-2-phenylethyl 2-(1-(((Allyloxy)carbonyl)amino)-2-(pyrrolidin-1-yl)-2-thioxoethyl)but-3-enoate (**25e**).* Compound **21** (194 mg, 0.85 mmol), $FeBr_3$ (77 mg, 0.34 mmol), allylic bromide (283 mg, 1.70 mmol), and TEA (147 μL, 1.02 mmol) were reacted and worked up as described above. Product **25d**: yellow oil, 186 mg, yield 51%; R_f = 0.50 (hexanes/EtOAc = 2:1); IR (NaCl) 2925, 1716; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96−7.81 (m, 2H), 7.63−7.55 (m, 1H), 7.47 (dd, J = 10.7, 4.8 Hz, 2H), 5.98−5.82 (m, 2H), 5.56 (d, J = 10.1 Hz, 1H), 5.48−5.14 (m, 7H), 4.54 (ddd, J = 34.0, 13.4, 5.5 Hz, 1H), 4.11 (t, J = 9.5 Hz, 1H), 4.03 (t, J = 6.8 Hz, 2H), 3.91 (dt, J = 13.3, 6.6 Hz, 1H), 3.81 (dt, J = 14.2, 7.2 Hz, 1H), 2.08−1.91 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.44, 191.16, 170.89, 155.36, 133.91, 133.77, 132.37, 131.56, 128.75, 127.64, 121.39, 117.57, 66.59, 65.78, 56.53, 56.27, 53.98, 51.35, 25.86, 23.91; HRMS (ESI) calcd for $C_{22}H_{27}N_2O_5S$ (MH^+) 431.1635, found 431.1632.

General Procedure for the Preparation of Compounds 28−32. LDA was prepared freshly in a 25 mL flask at 0 °C under argon atmosphere by mixing diisopropylamine (140 μL, 1.0 mmol) with *n*-butyllithium (1.6 M in hexanes, 0.63 mL, 1.0 mmol) in dry THF (10 mL) for 15 min. Then the LDA solution was transferred into a 50-mL flask which had thioamide **4**−**6**, **19**, **20**, or **27** (0.33 mmol) dissolved in dry THF (10 mL) at −78 °C. The mixture was stirred for 30 min at −78 °C before HMPA (180 μL, 1.0 mmol) was added and another 5 min before the allylic bromide (0.66 mmol) was added, respectively. The reaction was allowed to warm slowly to room temperature (or other temperatures found in Table 1) over a period of 4 h. Then the reaction was quenched by the addition of a saturated ammonium chloride solution (1 mL). THF was removed under reduced pressure; the residue was extracted twice with hexanes and diethyl ether. The combined organic layers were pooled and washed with a saturated sodium bicarbonate solution (10 mL × 1) and a saturated ammonium chloride solution (10 mL × 1) and dried over anhydrous $MgSO_4$. The dry solution was concentrated under reduced pressure, and the crude product was purified by flash column chromatography to afford C-allylation compounds **28**−**32**.

*(E)-Benzyl 5-Phenyl-1-(pyrrolidin-1-yl)-1-thioxopent-4-en-2-ylcarbamate (**31**).* Thioamide **20** (113 mg, 0.41 mmol), *n*-butyllithium (1.6 M in hexanes, 0.56 mL, 0.89 mmol), and cinnamyl bromide (72 μL, 0.48 mmol) were reacted and worked up as described above. Product **31**: light yellow solid, 118 mg, yield 74%; R_f = 0.50 (hexanes/EtOAc = 2:1); IR (NaCl) 1715, 1491, 1449; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38−7.13 (m, 10H), 6.47 (d, J = 15.8 Hz, 1H), 6.17−6.09 (m, 1H), 6.02 (d, J = 9.1 Hz, 1H), 5.11 (d, J = 12.3 Hz, 1H), 5.02 (d, J = 12.2 Hz, 1H), 4.89 (dd, J = 15.9, 7.4 Hz, 1H), 3.87 (dd, J = 13.0, 6.3 Hz, 2H), 3.82−3.75 (m, 1H), 3.70−3.63 (m, 1H), 2.66 (t, J = 7.2 Hz, 2H), 2.11−1.82 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.0, 155.5, 136.9, 136.2, 133.6, 128.4, 128.3, 127.9, 127.8, 127.3, 126.0, 124.0, 66.8, 56.9, 53.9, 50.9, 40.0, 26.0, 23.8; HRMS (ESI) calcd for $C_{23}H_{27}N_2O_2S$ (MH^+) 395.1788, found 395.1787.

*(E)-tert-Butyl 5-Phenyl-1-(pyrrolidin-1-yl)-1-thioxopent-4-en-2-ylcarbamate (**32**).* Thioamide **19** (133 mg, 0.55 mmol), *n*-butyllithium (1.6 M in hexanes, 0.75 mL, 1.2 mmol), and cinnamyl bromide (121 μL, 0.82 mmol) were reacted and worked up as described above. Product **32**: yellow oil, 128 mg, yield 65%; R_f = 0.60 (hexanes/EtOAc = 2:1); IR (NaCl) 1709, 1486, 1166; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38−7.19 (m, 5H), 6.50 (d, J = 15.8 Hz, 1H), 6.22−6.11 (m, 1H), 5.77 (d, J = 9.1 Hz, 1H), 4.85 (dd, J = 16.0, 7.2 Hz, 1H), 3.96−3.86 (m, 2H), 3.85−3.75 (m, 1H), 3.73−3.64 (m, 1H), 2.66 (t, J = 7.2 Hz, 2H), 2.11−1.84 (m, 4H), 1.42 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.6, 154.9, 137.0, 133.3, 128.4, 127.2, 126.0, 124.3, 79.6, 56.4, 53.8, 50.7, 40.0, 28.2, 26.0, 23.7; HRMS (ESI) calcd for $C_{20}H_{29}N_2O_2S$ (MH^+) 361.1944, found 361.1945.

*tert-Butyl ((S)-1-((2S,5S)-2,5-Diphenylpyrrolidin-1-yl)-1-thioxopent-4-en-2-yl)carbamate (**28a**).* Product **28a**: yellow oil, R_f = 0.65 (hexanes/EtOAc = 3:1); IR (NaCl) 1711, 1493, 1437; $[\alpha]^{25.8}_D$ −46.3 (c 0.16, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.08 (m, 10H),

6.01 (d, J = 8.6 Hz, 1H), 5.77 (ddt, J = 17.3, 10.1, 7.3 Hz, 1H), 5.60 (dd, J = 36.9, 8.2 Hz, 2H), 5.18−5.08 (m, 2H), 4.66 (dd, J = 14.9, 6.9 Hz, 1H), 2.75−2.65 (m, 1H), 2.59−2.31 (m, 3H), 1.96 (dd, J = 12.5, 6.0 Hz, 1H), 1.80 (dd, J = 12.5, 6.1 Hz, 1H), 1.23 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.40, 153.34, 141.31, 141.03, 133.30, 128.90, 128.36, 127.68, 126.92, 125.77, 125.26, 118.54, 78.75, 68.33, 66.70, 56.76, 42.64, 33.20, 30.02, 28.25; HRMS (ESI) calcd for $C_{26}H_{33}N_2O_2S$ (MH^+) 437.2257, found 437.2250. HPLC analysis: de >99%. Chiralpak AD-RH column (CH_3CN/H_2O 60/40 to 70/30, in 30 min 0.5 mL/min, 254 nm); retention times of the only diastereomer observed: 13.1 min (**28a**).

*tert-Butyl ((S)-1-((2S,5S)-2,5-Diphenylpyrrolidin-1-yl)-3,3-dimethyl-1-thioxopent-4-en-2-yl)carbamate (**28b**).* Product **28b**: yellow oil, R_f = 0.70 (hexanes/EtOAc = 3:1); IR (NaCl) 2975, 1720, 1489, 1422; $[\alpha]^{26.0}_D$ −19.5 (c 0.12, MeOH); ^{1}H NMR (600 MHz) δ 7.40−7.04 (m, 6H), 5.95−5.89 (m, 1H), 5.74 (d, J = 7.8 Hz, 1H), 5.63 (d, J = 9.1 Hz, 0H), 5.15−5.07 (m, 1H), 4.53 (d, J = 9.2 Hz, 0H), 2.80 (dq, J = 20.4, 6.9 Hz, 1H), 2.46−2.38 (m, 1H), 1.96 (dd, J = 12.6, 6.2 Hz, 1H), 1.75 (dd, J = 12.8, 6.4 Hz, 1H), 1.21 (s, 4H), 1.04 (s, 1H), 1.02 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 202.4, 153.4, 145.1, 142.2, 141.7, 129.0, 128.2, 127.6, 127.0, 126.5, 125.1, 112.8, 78.5, 69.0, 62.2, 43.7, 33.6, 30.0, 28.2, 25.0, 23.1; HRMS (ESI) calcd for $C_{28}H_{37}N_2O_2S$ (MH^+) 465.2570, found 465.2556. HPLC analysis: de >99%. Chiralpak AD-RH column (CH_3CN/H_2O 60/40 to 80/20, in 40 min, 0.5 mL/min, 254 nm); retention times of the only diastereomer observed: 15.0 min (**12c**).

*tert-butyl (2S,3S)-1-((2S,5S)-2,5-diphenylpyrrolidin-1-yl)-3-methyl-1-thioxopent-4-en-2-ylcarbamate (**28c**).* Product **28c**: yellow oil, R_f = 0.65 (hexanes/EtOAc = 3:1); $[\alpha]^{24.2}_D$ −42.4 (c 0.24, MeOH); IR (NaCl) 2975, 1716, 1426; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42−7.11 (m, 10H), 6.00 (d, J = 8.8 Hz, 1H), 5.77−5.64 (m, 2H), 5.38 (d, J = 9.3 Hz, 1H), 4.94 (dd, J = 22.4, 13.7 Hz, 2H), 4.49−4.45 (m, 1H), 2.85−2.75 (m, 1H), 2.66−2.57 (m, 1H), 2.47 (ddd, J = 20.4, 11.5, 7.6 Hz, 1H), 1.99 (dd, J = 12.5, 6.0 Hz, 1H), 1.79 (dd, J = 12.6, 6.2 Hz, 1H), 1.19 (s, 9H), 1.04 (d, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.3, 153.4, 141.6, 141.2, 139.2, 128.8, 128.4, 127.7, 127.0, 125.9, 125.3, 115.6, 78.5, 68.7, 66.8, 60.5, 46.4, 33.4, 29.8, 28.2, 17.2; HRMS (ESI) calcd for $C_{27}H_{35}N_2O_2S$ (MH^+) 451.2414, found 451.2413. HPLC analysis: de = 94%. Chiralpak AD-RH column (CH_3CN/H_2O 50/50 to 90/10 in 40 min, 0.5 mL/min, 254 nm); retention times of the diastereomeric mixture observed: 22.5 min (**28c**), 25.6 min.

*tert-Butyl (2S,3R)-1-((2S,5S)-2,5-Diphenylpyrrolidin-1-yl)-3-phenyl-1-thioxopent-4-en-2-ylcarbamate (**28d**).* Product **28d**: yellow oil, R_f = 0.60 (hexanes/EtOAc = 2:1); $[\alpha]^{24.6}_D$ −75.1 (c 0.30, MeOH); IR (NaCl) 2976, 1716, 1170; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53−7.02 (m, 15H), 6.23 (d, J = 7.1 Hz, 2H), 6.05−5.92 (m, 1H), 5.80 (dd, J = 21.2, 8.0 Hz, 1H), 5.41−5.28 (m, 2H), 5.03−4.86 (m, 3H), 3.82 (dd, J = 27.1, 17.3 Hz, 1H), 2.42−2.11 (m, 2H), 1.71 (dd, J = 12.2, 5.5 Hz, 1H), 1.55 (dd, J = 12.3, 5.7 Hz, 1H), 1.21 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.2, 153.1, 140.9, 140.6, 140.2, 138.4, 128.9, 128.6, 128.3, 127.6, 126.9, 126.2, 125.2, 125.2, 116.7, 78.6, 68.7, 67.1, 60.2, 59.8, 32.7, 30.0, 28.2; HRMS (ESI) calcd for $C_{32}H_{37}N_2O_2S$ (MH^+) 513.2570, found 513.2577. HPLC analysis: de = 82%. Chiralpak AD-RH column (CH_3CN/H_2O 55/45, 0.5 mL/min, 254 nm); retention times of the diastereomeric mixture observed: 29.7 min (**28d**), 33.9 min.

*(S)-Ethyl 2-((S)-1-((tert-Butoxycarbonyl)amino)-2-((2S,5S)-2,5-diphenylpyrrolidin-1-yl)-2-thioxoethyl)but-3-enoate (**28e**).* Product **28e**: clear oil, R_f = 0.60 (hexanes/EtOAc = 3:1); $[\alpha]^{26.0}_D$ −79.8 (c 0.06, MeOH); IR (NaCl) 1723, 1447; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48−7.01 (m, 10H), 6.27 (d, J = 8.0 Hz, 1H), 5.91 (d, J = 8.6 Hz, 1H), 5.71 (dt, J = 16.9, 9.7 Hz, 1H), 5.31−4.97 (m, 4H), 4.33−4.19 (m, 1H), 4.16−4.06 (m, 1H), 3.69 (t, J = 9.4 Hz, 1H), 2.76 (ddd, J = 20.3, 10.9, 6.9 Hz, 1H), 2.53−2.44 (m, 1H), 1.90 (dd, J = 12.4, 5.9 Hz, 1H), 1.75 (dd, J = 12.5, 6.0 Hz, 1H), 1.23 (t, J = 7.1 Hz, 3H), 1.16 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.87, 172.41, 152.89, 141.59, 141.45, 132.45, 128.62, 128.26, 127.59, 126.77, 125.61, 125.53, 120.50, 78.85, 68.93, 67.08, 60.96, 59.77, 56.44, 33.01, 30.20, 28.18, 14.05; HRMS (ESI) calcd for $C_{29}H_{37}N_2O_4S$ (MH^+) 509.2469, found 509.2462. HPLC analysis: de >97%. Chiralpak AD-RH column (CH_3CN/H_2O 75/25 to 90/10 in 30 min, 0.5 mL/min, 254 nm); retention times of the diastereomeric mixture observed: 5.6 min, 6.9 min(**28e**).

*tert-Butyl ((S)-1-((S)-Cyclohex-2-en-1-yl)-2-((2S,5S)-2,5-diphenylpyrrolidin-1-yl)-2-thioxoethyl)carbamate (**28f**).* Compound **27** (51 mg, 0.13 mmol), n-butyllithium (1.6 M in hexanes, 0.18 mL, 0.28 mmol), and cinnamyl bromide (20 μL, 0.155 mmol) were reacted and worked up as described above. Product **28f**: yellow oil, 54 mg, yield 52%; R_f = 0.50 (hexanes/EtOAc = 3:1); $[\alpha]^{26.0}_D$ +70.1 (c 0.12, MeOH); IR (NaCl) 1716, 1493, 1432; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48−7.04 (m, 10H), 5.97 (d, J = 8.8 Hz, 1H), 5.91 (d, J = 9.5 Hz, 1H), 5.67 (d, J = 8.1 Hz, 1H), 5.49 (t, J = 9.9 Hz, 2H), 4.48 (t, J = 9.2 Hz, 1H), 2.82 (tt, J = 13.7, 7.0 Hz, 1H), 2.51−2.36 (m, 2H), 2.12−1.91 (m, 3H), 1.77 (dd, J = 12.6, 6.2 Hz, 1H), 1.67−1.45 (m, 5H), 1.21 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.96, 153.57, 141.80, 141.64, 130.30, 128.99, 128.35, 127.70, 127.41, 127.06, 126.31, 125.15, 78.50, 68.89, 66.92, 59.61, 44.02, 33.43, 29.80, 28.26, 25.36, 24.17, 20.20; HRMS (ESI) calcd for $C_{29}H_{37}N_2O_2S$ (MH^+) 477.2570, found 477.2570. HPLC analysis: de >99%. Chiralpak AD-RH column (CH_3CN/H_2O 60/40 to 70/30, in 30 min, 0.5 mL/min, 254 nm); retention times of the only diastereomer observed: 21.9 min (**28f**).

General Procedure for the Oxidation−Iodolactonization−Zinc Reduction To Generate Amino Acids 33−35. Compounds **3** (0.2 mmol) were dissolved in DCM (2 mL) and cooled to −78 °C. *m*-CPBA (148 mg, 0.6 mmol) was added, and the suspension was stirred and allowed to warm to ambient temperature in 1 h. The reaction was diluted with ether and hexanes, washed with a saturated sodium bicarbonate solution (5 mL × 3) and brine, and dried with anhydrous $MgSO_4$. The dry solvent was filtered and concentrated under reduced pressure, and the residue was dissolved in 10 mL of THF/H_2O (1.5:1). To the solution was added iodine (152 mg, 0.6 mmol), and the resultant mixture was stirred in the dark at ambient temperature for 4 d. The reaction was quenched by the addition of 10% aqueous $Na_2S_2O_3$ (3 mL) and was extracted with DCM (5 mL × 3). The combined organic layers were washed with 10% aqueous $Na_2S_2O_3$ (3 mL × 2) and brine (3 mL) and dried over $MgSO_4$. The dry solution was concentrated under reduced pressure, and the crude product was purified by flash column chromatography using a gradient solvent mixture eluate (Hex/EtOAc = 8:1 to 4:1) to afford the iodolactone compounds. The purified iodolactones were dissolved in glacial acetic acid (10 mL) and treated with zinc dust (195 mg, 3 mmol). The mixture was stirred for 2 h at 70 °C and then cooled to ambient temperature. HCl (0.5 M, 10 mL) was added, the reaction mixture was filtered and extracted with DCM (10 mL × 3), and the combined organic layers were dried over $MgSO_4$. The dry solution was concentrated under reduced pressure, and the crude product was purified by flash column chromatography to afford compounds **33−35** using a gradient solvent mixture eluate (hexanes/EtOAc = 2:1 to hexanes/EtOAc/AcOH = 75:25:1).

*(S)-2-(Benzyloxycarbonylamino)-4-(ethoxycarbonyl)pent-4-enoic Acid (**33a**).* Compound **10a** (112 mg, 0.27 mmol), *m*-CPBA (198 mg, 0.80 mmol), I_2 (203 mg, 0.80 mmol), and Zn dust (261 mg, 4.03 mmol) were reacted and worked up as described above. Product **33a**: a colorless oil, 64 mg, yield 75%; R_f = 0.20 (hexanes/EtOAc/AcOH = 25:25:1); IR (NaCl) 1716.66, 1524.74, 1215.66; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.26 (br, 1H), 7.41−7.27 (m, 5H), 6.27 (s, 1H), 5.69−5.63 (m, 2H), 5.09 (q, J = 12.3 Hz, 2H), 4.56 (dd, J = 13.0, 7.9 Hz, qH), 4.20 (q, J = 7.0 Hz, 2H), 2.92 (dd, J = 14.1, 4.8 Hz, 1H), 2.72 (dd, J = 14.1, 8.3 Hz, 1H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C (150 MHz, $CDCl_3$) δ 175.69, 166.91, 156.07, 136.19, 135.57, 129.02, 128.45, 128.13, 128.01, 67.09, 61.22, 53.53, 34.42, 14.03; HRMS (ESI) calcd for $C_{16}H_{19}NNaO_6$ (MNa^+) 344.1105, found 344.1106. HPLC analysis: de = 69%. Chiralpak AD-RH column (CH_3CN/H_2O 27.5/72.5, 0.5 mL/min, 254 nm); retention times the racemic mixture observed: 23.8 min, 26.3 min; retention time of the enantiorich product observed: 23.2 min (**33a**), 25.5 min.

*(2S,3S)-2-(Benzyloxycarbonylamino)-3-(methoxycarbonyl)pent-4-enoic Acid (**33c**).* Compound **10c** (78.8 mg, 0.20 mmol), *m*-CPBA (144 mg, 0.58 mmol), I_2 (148 mg, 0.58 mmol), and Zn dust (190 mg,

2.93 mmol) were reacted and worked up as described above. Product **33c**: a colorless oil, 47 mg, yield 79%; R_f = 0.30 (hexanes/EtOAc/AcOH = 25:25:1); $[\alpha]^{23.0}_D$ −31.4 (*c* 0.59, MeOH); IR (NaCl) 1732.69, 1524.79, 1258.23; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.43 (br, 1H), 7.38−7.27 (m, 5H), 5.97−5.86 (m, 1H), 5.58 (d, *J* = 8.6 Hz, 1H), 5.31−5.23 (m, 2H), 5.10 (s, 2H), 4.81 (dd, *J* = 8.3, 5.4 Hz, 1H), 3.69 (s, 3H), 3.61 (dd, *J* = 8.4, 5.4 Hz, 1H); ^{13}C (125 MHz, $CDCl_3$) δ 174.32, 171.36, 155.93, 135.84, 130.76, 128.46, 128.20, 128.04, 121.02, 67.37, 55.66, 52.53, 52.12; HRMS (ESI) calcd for $C_{15}H_{17}NNaO_6$ (MNa^+) 330.0948, found 330.0941. HPLC analysis: de = 99%. Chiralpak AD-RH column (CH_3CN/H_2O 27.5/72.5, 0.5 mL/min, 254 nm); retention times the racemic mixture observed: 15.5 min, 19.5 min; retention time of the enantiopure product observed: 15.7 min (**33c**).

*(2S,3S)-2-(Benzyloxycarbonylamino)-3-(ethoxycarbonyl)pent-4-enoic Acid (**33d**).* Compound **10d** (86 mg, 0.21 mmol), *m*-CPBA (152 mg, 0.62 mmol), I_2 (156 mg, 0.62 mmol), and Zn dust (205 mg, 3.15 mmol) were reacted and worked up as described above. Product **33d**: a colorless oil, 50 mg, yield 76%; R_f = 0.20 (hexanes/EtOAc/AcOH = 25:25:1), $[\alpha]^{24.8}_D$ −28.8 (*c* 0.38, MeOH); IR (NaCl) 1732.57, 1246.43, 1195.13; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.20 (br, 1H), 7.40−7.27 (m, 5H), 5.97−5.89 (m, 1H), 5.53 (d, *J* = 8.6 Hz, 1H), 5.28−5.23 (m, 2H), 5.11 (s, 2H), 4.82 (dd, *J* = 8.1, 5.5 Hz, 1H), 4.16 (dd, *J* = 13.9, 6.9 Hz, 2H), 3.59 (dd, *J* = 8.4, 5.4 Hz, 1H), 1.24 (t, *J* = 7.0 Hz, 3H); ^{13}C (150 MHz, $CDCl_3$) δ 174.61, 170.88, 155.95, 135.89, 130.90, 128.50, 128.24, 128.09, 120.97, 67.34, 61.59, 55.63, 52.18, 13.95; HRMS (ESI) calcd for $C_{16}H_{20}NO_6$ (MH^+) 322.1285, found 322.1284. HPLC analysis: de = 99%. Chiralpak AD-RH column (CH_3CN/H_2O 27.5:72.5, 0.5 mL/min, 254 nm); retention times the racemic mixture observed: 22.7 min, 28.1 min; retention time of the enantiopure product observed: 21.5 min (**33d**).

*(2S,3S)-2-((tert-Butoxycarbonyl)amino)-3-methylpent-4-enoic Acid (**34b**).* Compound **32c** (45 mg, 0.10 mmol), *m*-CPBA (75 mg, 0.30 mmol), I_2 (76 mg, 0.30 mmol), and Zn dust (98 mg, 1.50 mmol) were reacted and worked up as described above. Product **34b**: a colorless oil, 16 mg, yield 70%; R_f = 0.70 (hexanes/EtOAc/AcOH = 25:25:1); $[\alpha]^{25.6}_D$ +26.4 (*c* 0.06, MeOH); IR (NaCl) 2924, 1717, 1164; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77−5.70 (m, 1H), 5.20−5.11 (m, 2H), 4.95 (d, *J* = 8.6 Hz, 1H), 4.34 (dd, *J* = 8.5, 4.6 Hz, 1H), 2.85 (d, *J* = 5.6 Hz, 1H), 1.47 (s, 9H), 1.15 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.80, 155.89, 137.38, 117.18, 80.23, 57.63, 39.62, 28.27, 16.07; HRMS (ICR) calcd for $C_{11}H_{18}NO_4$ ($M - H^-$) 228.1241, found 228.1244. HPLC analysis: de = 96%. Chiralpak AD-RH column (CH_3CN/H_2O 27.5/72.5, 0.5 mL/min, 254 nm); retention times the racemic mixture observed: 20.1 min, 22.2 min; retention time of the enantiorich product observed: 21.7 min, 23.2 (**33d**).

*(2S,3S)-2-((tert-Butoxycarbonyl)amino)-3-(ethoxycarbonyl)pent-4-enoic Acid (**34c**).* Compound **23c** (84 mg, 0.24 mmol), *m*-CPBA (174 mg, 0.71 mmol), I_2 (180 mg, 0.71 mmol), and Zn dust (234 mg, 3.60 mmol) were reacted and worked up as described above. Product **34c**: a colorless oil, 57 mg, yield 68%; R_f = 0.75 (hexanes/EtOAc/AcOH = 25:25:1); IR (NaCl) 2924, 1717, 1161; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.23 (d, *J* = 7.4 Hz, 1H), 4.91 (t, *J* = 8.4 Hz, 1H), 4.83 (dd, *J* = 4.9, 2.4 Hz, 2H), 4.32−4.18 (m, 2H), 3.62 (dd, *J* = 9.1, 1.8 Hz, 1H), 3.43 (ddd, *J* = 18.3, 10.8, 6.2 Hz, 2H), 1.47 (s, 9H), 1.32 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, CDCl3) δ 172.10, 169.24, 155.18, 81.14, 78.35, 62.03, 50.77, 48.87, 28.21, 14.15, 4.75; HRMS (ICR) calcd for $C_{13}H_{20}NO_6$ ($M - H^-$) 286.1296, found 286.1297.

*(2S,3S)-2-((((Allyloxy)carbonyl)amino)-3-(ethoxycarbonyl)pent-4-enoic Acid (**35c**).* Compound **25c** (28 mg, 0.09 mmol), *m*-CPBA (80 mg, 0.33 mmol), I_2 (85 mg, 0.33 mmol), and Zn dust (98 mg, 1.50 mmol) were reacted and worked up as described above. Product **35c**: a colorless oil, 17 mg, yield 80%; R_f = 0.40 (hexanes/EtOAc/AcOH = 25:25:1); IR (NaCl) 2925, 1732; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.01−5.82 (m, 2H), 5.49 (d, *J* = 8.0 Hz, 1H), 5.29 (ddd, *J* = 38.7, 17.2, 6.0 Hz, 4H), 4.79 (s, 1H), 4.58 (d, *J* = 5.3 Hz, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.59 (s, 1H), 1.27 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.08, 170.92, 155.86, 132.29, 130.97, 120.99, 118.08, 66.21, 61.61, 52.16, 29.70, 14.01; HRMS (ICR) calcd for $C_{12}H_{16}NO_6$ ($M - H^-$) 270.0983, found 270.0983.

*(S)-2-(((Allyloxy)carbonyl)amino)-2-((S)-cyclohex-2-en-1-yl)acetic Acid (**35d**).* Compound **25d** (49 mg, 0.17 mmol), *m*-CPBA (128 mg, 0.48 mmol), I_2 (123 mg, 0.48 mmol), and Zn dust (156 mg, 2.40 mmol) were reacted and worked up as described above. Product **35d**: a colorless oil, 28 mg, yield 68%; R_f = 0.65 (hexanes/EtOAc/AcOH = 25:25:1); IR (NaCl) 2927, 1720; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.10 (br, 1H), 5.90 (ddd, *J* = 22.3, 10.7, 5.5 Hz, 1H), 5.85−5.80 (m, 1H), 5.54 (d, *J* = 9.8 Hz, 1H), 5.40−5.25 (m, 2H), 4.56 (d, *J* = 4.9 Hz, 2H), 4.47−4.39 (m, 1H), 2.85−2.65 (m, 1H), 2.05−1.90 (m, 2H), 1.85−1.75 (m, 1H), 1.75−1.62 (m, 1H), 1.58−1.46 (m, 1H), 1.34 (dd, *J* = 23.0, 11.1 Hz, 1H);^{13}C NMR (126 MHz, $CDCl_3$) δ 176.38, 156.27, 132.47, 130.51, 126.65, 117.94, 66.02, 57.30, 38.34, 29.68, 24.70, 23.85, 21.36; HRMS (ICR) calcd for $C_{12}H_{16}NO_4$ ($M - H^-$) 238.1085, found 238.1087.

*(2S,3S)-2-((((Allyloxy)carbonyl)amino)-3-((2-oxo-2-phenylethoxy)-carbonyl)pent-4-enoic Acid (**35e**).* Compound **25e** (70 mg, 0.16 mmol), *m*-CPBA (120 mg, 0.48 mmol), I_2 (120 mg, 0.48 mmol), and Zn dust (156 mg, 2.40 mmol) were reacted and worked up as described above. Product **35e**: a colorless oil, 18 mg, yield 30%; R_f = 0.65 (hexanes/EtOAc/AcOH = 25:25:1); IR (NaCl) 2924, 2853, 1700; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.6 Hz, 2H), 7.63 (t, *J* = 7.2 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 2H), 6.06 (dt, *J* = 19.0, 9.6 Hz, 1H), 5.94 (ddd, *J* = 22.6, 10.8, 5.7 Hz, 1H), 5.84 (d, *J* = 8.7 Hz, 1H), 5.37 (dd, *J* = 29.6, 18.2 Hz, 4H), 5.24 (d, *J* = 10.6 Hz, 1H), 4.86 (s, 1H), 4.62 (d, *J* = 5.3 Hz, 2H), 3.83 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.07, 176.18, 134.10, 133.94, 132.47, 130.92, 128.91, 127.89, 121.25, 117.92, 100.00, 66.71, 66.18, 29.74, 20.60; HRMS (ESI) calcd for $C_{18}H_{19}NNaO_7$ (MNa^+) 384.1054, found 384.1047.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Spectroscopic characterization (^{1}H NMR, ^{13}C NMR) of all new compounds and X-ray crystallography data. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENTS

This work was supported by US Public Health Service Grant No. DK 17420 and the National Institute of Drug Abuse (Grant Nos. DA 06284, DA 13449). We also thank Prof. Richard Glass (the University of Arizona) for useful discussions.

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