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Highly Selective Addition of Chiral, Sulfonimidoyl Substituted Bis(allyl)titanium Complexes to *N*-Sulfonyl α-Imino Esters: Asymmetric Synthesis of γ,δ-Unsaturated α-Amino Acids Bearing a Chiral, Electron-Withdrawing Nucleofuge at the δ-Position

Marcel Schleusner, Hans-Joachim Gais,* Stefan Koep, and Gerhard Raabe

Contribution from the Institut für Organische Chemie der Rheinisch-Westfälischen Technischen Hochschule (RWTH) Aachen, Professor-Pirlet-Strasse 1, D-52056 Aachen, Germany

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Abstract: Selective addition of the chiral, sulfonimidoyl substituted bis(allyl)titanium complexes **5a**−**d**, which are configurationally labile in regard to the Cα-atoms, to *N*-toluenesulfonyl (Ts)-, *N*-2-trimethylsilylethanesulfonyl (SES)-, and *N*-*tert*-butylsulfonyl (Bus) α-imino ester (**9a**−**c**) in the presence of Ti(O*i*Pr)$_4$ and ClTi(O*i*Pr)$_3$ afforded with high regio- and diastereoselectivities in good yields the (*syn*, *E*)-configured β-alkyl-γ,δ-unsaturated α-amino acid derivatives **2a**−**g**, which carry a chiral, electron-withdrawing nucleofuge at the δ-position and a cyclohexyl, an isopropyl, a phenyl, and a methyl group at the β-position. Addition of the cyclic bis(allyl)titanium complex **14** to *N*-Bus α-imino ester **9c** afforded with similar high regio- and diastereoselectivities the (*E*)- and (*Z*)-configured amino acid derivatives (*E*)-**8** and (*Z*)-**8**. Reaction of complexes **5a**−**d** with α-imino esters **9a**−**c** in the presence of Ti(O*i*Pr)$_4$ occurs stepwise to give first the mono(allyl)titanium complexes containing **2a**−**g** as ligands, which react in the presence of ClTi(O*i*Pr)$_3$ with a second molecule of **9a**−**c** with formation of two molecules of **2a**−**g**. Formation of (*S*,*R*,*E*)-configured homoallylic amines **2a**−**g** entails *Si*,*Re*,*E* processes of α-imino esters **9a**−**c** with the (*R*,*R*)-configured bis(allyl)titanium complexes (*R*,*R*)-**5a**−**d** and (*R*)-configured mono(allyl)titanium complexes (*R*)-**17a**-**d**, both of which are most likely in rapid equilibrium with their (*S*,*S*)-diastereomers and (*S*)-diastereomers, respectively. Interestingly, in the reaction of **5a**−**d** with aldehydes, the (*S*,*S*)-configured complexes (*S*,*S*)-**5a**−**d** are the ones which react faster. Reaction of the N-titanated amino acid derivatives Ti-**2a** and Ti-**2b** with *N*-Ts α-imino ester **9a** led to the highly diastereoselective formation of imidazolidinones **15a** and **15b**, respectively. Cleavage of the sulfonamide group of the *N*-Bus amino acid derivative **2d** with CF_3SO_3H gave quantitatively the sulfonimidoyl functionalized amino acid H-**2d**. A Ni-catalyzed cross-coupling reaction of the amino acid derivative **2e** with $ZnPh_2$ led to a substitution of the sulfonimidoyl group by a phenyl group and furnished the enantiomerically pure protected α-amino acid Bus-**1**. Two new *N*-sulfonyl α-imino esters, the SES and the Bus α-imino esters **9b** and **9c**, respectively, have been synthesized from the corresponding sulfonamides by the Kresze method in medium to good yields. The *N*-SES α-imino ester **9b** and the *N*-Bus α-imino ester **9c** should find many synthetic applications, in particular, in cases where the *N*-Ts α-imino ester **9a** had been used before.

Introduction

γ,δ-Unsaturated α-amino acids **1** (Scheme 1) have received much synthetic attention[1−7] because of their utilization as starting material for the synthesis of complex amino acids and peptides,[8] isolation from natural sources,[9] and interesting biological activities.[10] Asymmetric synthesis of **1** has been accomplished by several methods including hydrogenation of dieneamides,[2] Claisen rearrangement of allylic ester enolates,[3] palladium-catalyzed allylic alkylation,[4] allylation of α-imino esters,[5] and ene reaction of α-imino esters.[5h,6,7] Although these methods are imaginative and frequently efficient, they allow only for the synthesis of **1** having either specific substituents R^1 to R^3 or a special substitution pattern. For example, the enantio- and diastereoselective synthesis of amino acids **1**, which bear sterically demanding substituents R^1 and possess a disubstituted double bond ($R^3 \neq H$), is a task not easily achieved by

* To whom correspondence should be addressed. E-mail: Gais@RWTH-Aachen.de.

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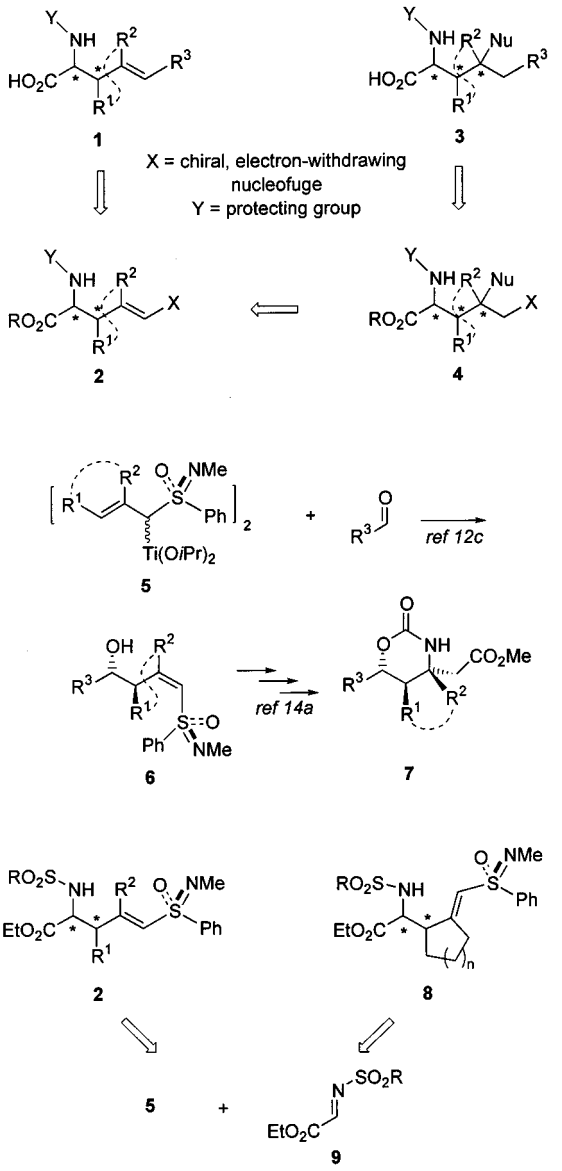
Scheme 1



existing methods.[2−7] Thus, it would be highly desirable to have a method which would give access to enantiomerically pure cyclic and acyclic amino acids **1** carrying the various groups R^1 to R^3. In our view, particularly attractive for the attainment of this goal would be unsaturated amino acids of type **2** bearing at the *δ*-position a chiral, electron-withdrawing nucleofuge that would not only permit a stereoselective addition of nucleophiles to the CC-double bond with formation of amino acids **4** but could also be replaced in **2** and **4** by various groups R^3. Thereby, both the unsaturated amino acids **1** and the saturated amino acids **3**, which are also of considerable interest,[1] would be accessible. Allylation of α-imino esters with properly functionalized chiral allylic metal reagents should be especially well suited for the synthesis of amino acids of type **2**. Up to now, however, only the addition of nonfunctionalized allyl-, crotyl-, and cinnamylmetal reagents to α-imino esters has been described.[5,11] We have recently shown that the chiral, sulfonimidoyl substituted bis(allyl)titanium complexes **5**, which are configurationally labile in regard to the Cα-atoms, selectively add to aldehydes with high regio- and diastereoselectivity, irrespective of the groups R^1 to R^3, to give the (*anti*, *E*)-configured cyclic and acyclic homoallylic alcohols **6**.[12,13] Alcohols **6** have served as versatile

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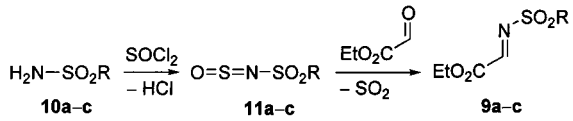
starting material for the synthesis of enantiomerically pure hydroxy substituted cyclic and acyclic β-amino acid derivatives **7**, the key steps of which are a stereoselective intramolecular nucleophilic amination of the double bond, activated by the sulfonimidoyl group and the replacement of the latter by a Cl-atom.[14b,c] We were thus interested to see whether bis(allyl)-titanium complexes **5** would also undergo a highly regio- and stereoselective selective addition to *N*-sulfonyl α-imino esters **9** with formation of the δ-sulfonimidoyl functionalized and *N*-sulfonyl protected unsaturated α-amino acids **2** and **8**. Because of the high synthetic versatility of vinylic sulfoximines, as exemplified, for example, by the conversion of **6** to **7**,[15] derivatives **2** and **8** should hold the prospect for serving as starting material for the stereoselective synthesis of a wide range of enantiomerically pure unsaturated and saturated acyclic and cyclic α-amino acids of type **1** and **3**, respectively. First, a stereoselective replacement of the sulfonimidoyl group of **2** and **8** by alkyl and aryl R^3 groups with formation of **1** can be envisaged by application of a transition-metal-catalyzed cross-coupling reaction with organozinc reagents.[16] Second, because of the ready inter- and intramolecular conjugate addition of C-,[14c,17a−c,g] O-,[17d,f,g] and N-nucleophiles[14,17e] to vinylic sulfoximines and the facile replacement of the sulfonimidoyl group, bound to a sp^3-C-atom, by a Cl-atom,[14b,c] synthesis of saturated amino acids **3** from **2** and **8** can be envisioned. Aside from being a potential starting material for the synthesis of **1** and **3**, amino acids of type **2** and **8** could perhaps also be developed into new analogues of buthionine sulfoximine and cysteine sulfoximine, which are intensively studied as inhibitors of γ-glutamylcysteine synthetase and asparagine synthetase contained in cancer cells for chemotherapy.[18] In this paper, we describe the highly selective addition of the bis(allyl)titanium complexes **5** to α-imino esters **9** leading to (*syn*, *E*)-configured amino acids of type **2** and **8**, the synthesis of an amino acid of type **1** from **2** (X = sulfonimidoyl), and the synthesis of two new *N*-sulfonyl α-imino esters **9**, both of which are expected to be of general synthetic interest.

Results and Discussion

Synthesis of SES and Bus α-Imino Esters. *N*-Toluenesulfonyl (Ts) α-imino ester **9a**,[19] which is readily available from ethyl glyoxylate and isothiocyanate **11a** or Ts isocyanate according to the method of Kresze and Albrecht[20] (Scheme 2), has found numerous applications in asymmetric synthesis, for example, through ene,[5h,6] Diels−Alder,[7i,j] allylation,[5b,g,h] alkylation,[5h,7h,i,j] Mannich,[21] Henry,[22] aromatic substitution,[23] and aziridination reactions.[24] However, a major drawback associated frequently with the utilization of *N*-Ts α-imino ester **9a** has been that the *N*-Ts group of the reaction products is difficult to remove.[25,26] Because it was thus uncertain whether a removal of the *N*-Ts group of amino acids **1**−**4** (X = sulfonimidoyl, Y = SO_2tol) could be achieved, the *N*-trimethylsilylethanesulfonyl (SES) and the *N*-*tert*-butylsulfonyl (Bus) α-imino esters **9b** and **9c**, respectively, were also included in the present study. These two new α-imino esters were selected because of the ready cleavage of SES and Bus protected amines with fluoride ion[27a−c] and anhydrous CF_3SO_3H,[27d] respectively. The *N*-SES α-imino ester **9b** and the *N*-Bus α-imino ester **9c** were prepared from amides **10b** and **10c**, respectively, according to the method of Kresze and Albrecht.[20] Thus, amide **10b**[28] was treated with $SOCl_2$ at reflux in toluene to afford the SES isothiocyanate **11b**, which was not isolated but reacted with ethyl glyoxylate at reflux to give the *N*-SES α-imino ester **9b** as a yellow oil in 38% isolated yield, based on **10b**. Similarly, treatment of amide **10c**[29] with $SOCl_2$ at reflux in toluene furnished the Bus isothiocyanate **11c**, which, without isolation, was reacted with ethyl glyoxylate at reflux to afford the *N*-Bus α-imino ester **9c** as a yellow oil in 63% isolated yield. In addition, amide **10c** was recovered in 23% yield. The overall yields of α-imino esters **9b** and **9c** from **10b** and **10c**, respectively, compare favorably with the one reported for the synthesis of **9a** from **10a**.[19,30] The intermediate SES thioisocyanate **11b**, the synthesis of which by other methods had already been described,[31] and the new Bus isothiocyanate **11c**, contaminated by 10% of **10c**, were also isolated in 54 and 57% yield, respectively.

Scheme 2



a: R = Tol, **b**: R = $CH_2CH_2SiMe_3$, **c**: R = *t*Bu

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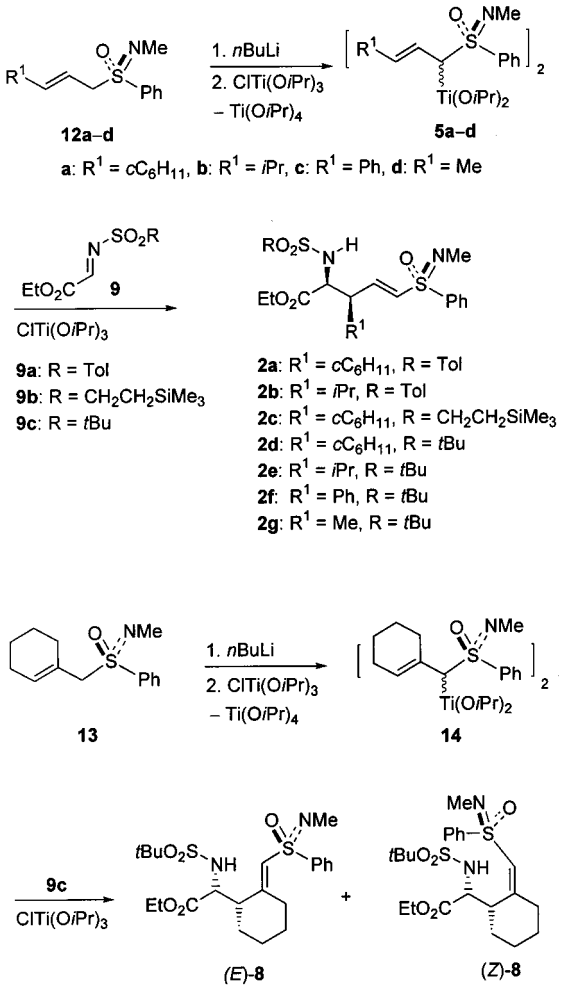
(29) (a) Netscher, T.; Prinzbach, H. *Synthesis* **1987**, 683. (b) Gontcharov, A. V.; Liu, H.; Sharpless, K. B. *Org. Lett.* **1999**, *1*, 783.
(30) For the synthesis of *N*-SES and *N*-Bus aldimines and ketimines from the corresponding oximes, see: Artman, G. D., III; Bartolozzi, A.; Franck, R. W.; Weinreb, S. M. *Synlett* **2001**, 232.
(31) (a) Sisko, J.; Weinreb, S. M. *J. Org. Chem*. **1990**, *55*, 393. (b) Stien, D.; Anderson, G. T.; Chase, C. E.; Koh, Y.; Weinreb, S. M. *J. Am. Chem. Soc*. **1999**, *121*, 9574.

Scheme 3



Addition to α-Imino Esters. We selected for the study of the addition of the bis(allyl)titanium complexes to the α-imino esters derivatives **5a**−**d**, which bear at the γ-position a cyclohexyl, an isopropyl, a phenyl, and a methyl group, respectively (Scheme 3). Because most methods for the synthesis of **1** are apparently limited to derivatives carrying small substituents R^1, it was especially interesting to see whether complexes **5a**−**c** would add selectively to α-imino esters **9a**−**c**. The enantiomerically pure allylic sulfoximines **12a**−**d**, required for the synthesis of **5a**−**d**, were prepared by the one-pot procedure, described recently,[12c] starting from enantiomerically pure (*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximine[32] and the corresponding aldehydes. Lithiation of **12a**−**d** in tetrahydrofuran followed by a lithium−titanium exchange through treatment with 1 equiv of $ClTi(OiPr)_3$ afforded bis(allyl)titanium complexes **5a**−**d**, respectively, admixed with equimolar amounts of $Ti(OiPr)_4$.[12c] Titanium complexes **5a**−**d** were not isolated but reacted directly with α-imino esters **9a**−**c**. Thus, treatment of cyclohexyl substituted complex **5a** with 1.12 equiv of *N*-Ts α-imino ester **9a** at −78 °C led to the highly regio- and diastereoselective formation of the vinylic sulfoximine **2a**. However, under these conditions, only one allylic sulfoximine moiety of the bis(allyl)-titanium complex **5a** was utilized in the reaction with the **9a** as revealed by a recovery of approximately 50% of the starting allylic sulfoximine **12a**. A similar observation had been made previously in the case of the reaction of complexes **5a**−**d** with aldehydes.[12c] In this case, treatment of **5a**−**d** before addition of the aldehyde with 1 equiv of $ClTi(OiPr)_3$ ensured a transfer of both allylic sulfoximine moieties with high regio- and diastereoselectivity. Thus, treatment of **5a**, derived from **12a**, with 1.1 equiv of *N*-Ts α-imino ester **9a** at −78 °C in tetrahydrofuran following the addition of 1 equiv of $ClTi(OiPr)_3$ led to a 79% conversion of **12a** and the highly regio- and diastereoselective formation of the vinylic sulfoximine **2a** in 75% chemical yield based on a ^{1}H NMR spectrum of the crude reaction mixture. Crystallization of crude **2a**, which contained the excess of **9a**, unconverted **12a**, and 5% of *N*-methyl-*S*-phenylsulfinamide, afforded pure **2a** with ≥98% de in 59% yield (Table 1). Formation of diastereomers and regioisomers of **2a** could not be detected by ^{1}H NMR spectroscopy of the crude reaction mixture. ^{1}H NMR spectroscopy indicated the (*syn*, *E*)-configuration for **2a**. The final proof for the configuration of **2a** was provided by an X-ray crystal structure analysis (Figure 1). Reaction of the isopropyl substituted complex **5b**, derived from **12b**, with 1.12 equiv of *N*-Ts α-imino ester **9a** in the presence of $ClTi(OiPr)_3$ resulted in an 85% conversion of **12b** and also occurred with high regio- and diastereoselectivity to give the vinylic sulfoximine **2b**, which was isolated with ≥98% de in 65% yield. Reaction of *N*-SES and *N*-Bus α-imino esters **9b** and **9c**, respectively, with **5a** and **5b** occurred with selectivities similar to that of *N*-Ts α-imino ester **9a**. Thus,

Table 1. Addition of Bis(allyl)titanium Complexes **5a**−**d** and **14** to α-Imino Esters **9a**−**c**

titanium complex	α-imino ester	convn of allylic sulfoximine[a](%)	amino acid derivative	dr[b]	yield (%)[c]	dr (%)
5a	**9a**	79	**2a**	≥95:5	59 (75)	≥98:2
5b	**9a**	85	**2b**	≥95:5	65 (80)	≥98:2
5a	**9b**	87	**2c**	≥95:5	61 (80)	≥98:2
5a	**9c**	97	**2d**	≥95:5	77 (92)	≥98:2
5b	**9c**	98	**2e**	≥95:5	82 (93)	≥98:2
5c	**9c**	99	**2f**	≥95:5	82 (96)	≥98:2
5d	**9c**	99	**2g**	≥95:5	67 (90)	≥98:2
14	**9c**	96	(*E*/*Z*)-**8**	≥95:5	70 (90)	≥98:2

[a] Including 3−9% decomposition with formation of *N*-methyl-*S*-phenylsulfinamide. [b] Only one diastereomer was detected in the crude reaction product by ^{1}H NMR spectroscopy. [c] Values in parentheses are chemical yields based on ^{1}H NMR spectroscopy of the crude product.

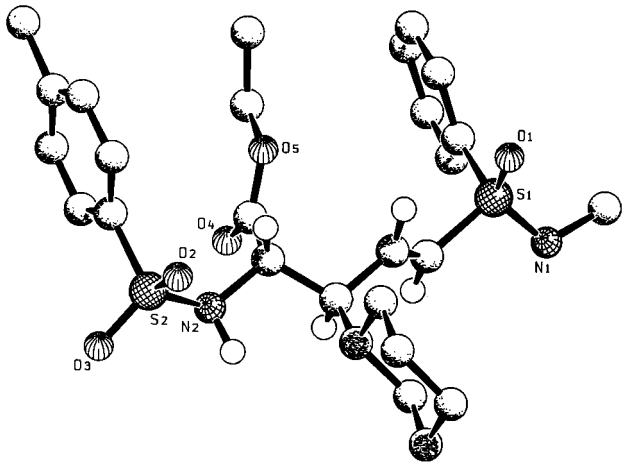


Figure 1. Structure of **2a** in the crystal.

(32) (a) Fusco, R.; Tericoni, F. *Chim. Ind.* **1965**, *47*, 61. (b) Johnson, C. R.; Schroeck, C. W. *J. Am. Chem. Soc*. **1973**, *95*, 7418. (c) Brandt, J.; Gais, H.-J. *Tetrahedron*: *Asymmetry* **1997**, *8*, 909.

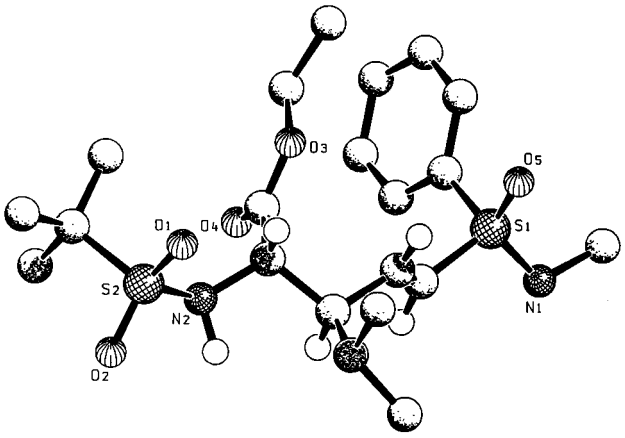


Figure 2. Structure of **2e** in the crystal.

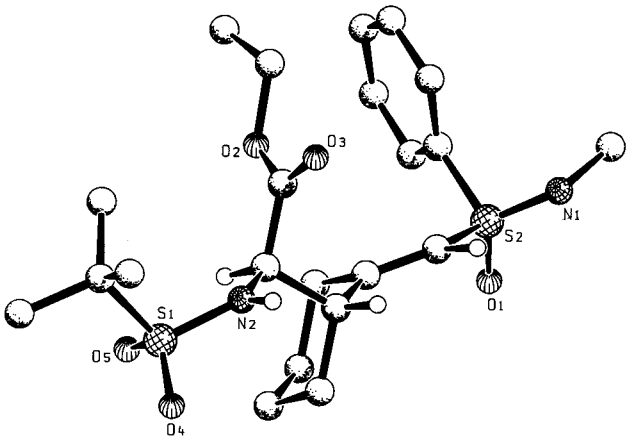


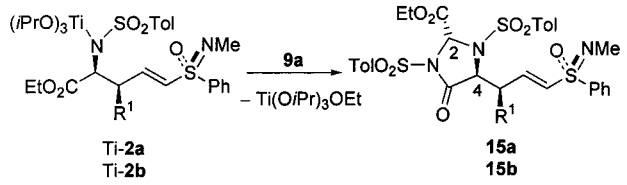
Figure 3. Structure of (*E*)-**8** in the crystal.

treatment of **5b** with 1.12 equiv of *N*-SES α-imino ester **9b** in the presence of ClTi(O*i*Pr)$_3$ saw an 80% conversion of **12b** and gave with high regio- and stereoselectivity the vinylic sulfoximine **2c**, which was isolated with ≥98% de in 61% yield. Similarly, reaction of **5a** with 1.12 equiv of *N*-Bus α-imino ester **9c** in the presence of ClTi(O*i*Pr)$_3$ led to a 92% conversion of **12a** and afforded the vinylic sulfoximine **2d** with ≥98% de in isolated 77% yield. Reaction of *N*-Bus α-imino ester **9c** with the isopropyl substituted complex **5b**, carried out in the same manner as with **5a**, also proceeded with high selectivities to give the vinylic sulfoximine **2e**, which was isolated with ≥98% de in 82% yield. In this case, the conversion of **12b** was 98%. The configuration of **2e** was determined by an X-ray crystal structure analysis (Figure 2). Finally, the reaction of the phenyl substituted complex **5c** with *N*-Bus α-imino ester **9c** was investigated. Treatment of **5c**, derived from **12c**, with 1.12 equiv of **9c** in the presence of ClTi(O*i*Pr)$_3$ gave a 99% conversion of **12c** and furnished with high regio- and diastereoselectivities the vinylic sulfoximine **2f**, which was isolated with ≥98% de in 82% yield. The attainment of high selectivity in the addition of **5** to **9** is not restricted to those titanium complexes carrying sterically demanding substituents at the γ-position. Thus, reaction of *N*-Bus α-imino ester **9c** with the methyl substituted complex **5d**,[12c] which was prepared from allylic sulfoximine **12d**, in the presence of ClTi(O*i*Pr)$_3$ proceeds with similar high regio- and diastereoselectivity as with **5a**−**c** and gave amino acid derivative **2d** in 67% isolated yield.

As a last example, the feasibility of a regio- and stereoselective addition of the cyclic bis(allyl)titanium complex **14**[12c] to an α-imino ester was probed. Treatment of complex **14**, which was prepared from allylic sulfoximine **13** in the usual manner,[12c,33] with 1.12 equiv of *N*-Bus α-imino ester **9c** in the presence of ClTi(O*i*Pr)$_3$ resulted in a 96% conversion of **13** and furnished with high regio- and diastereoselectivity a mixture of the cyclic amino acid derivatives (*E*)-**8** and (*Z*)-**8** in a ratio of 87:13 in 70% isolated yield.[34] The configuration of (*E*)-**8** was determined by X-ray crystal structure analysis (Figure 3).

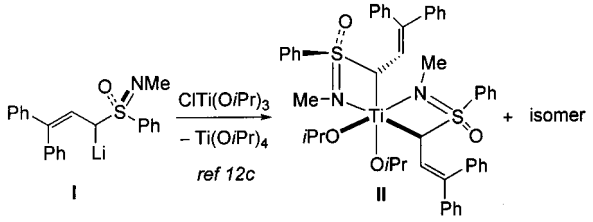
In the course of the study of the reaction of *N*-Ts α-imino ester **9a** with complexes **5a** and **5b**, the highly diastereoselective

Scheme 4



2a, **15a**: R^1 = *c*C_6H_{11}, **2b**, **15b**: R^1 = *i*Pr

Scheme 5



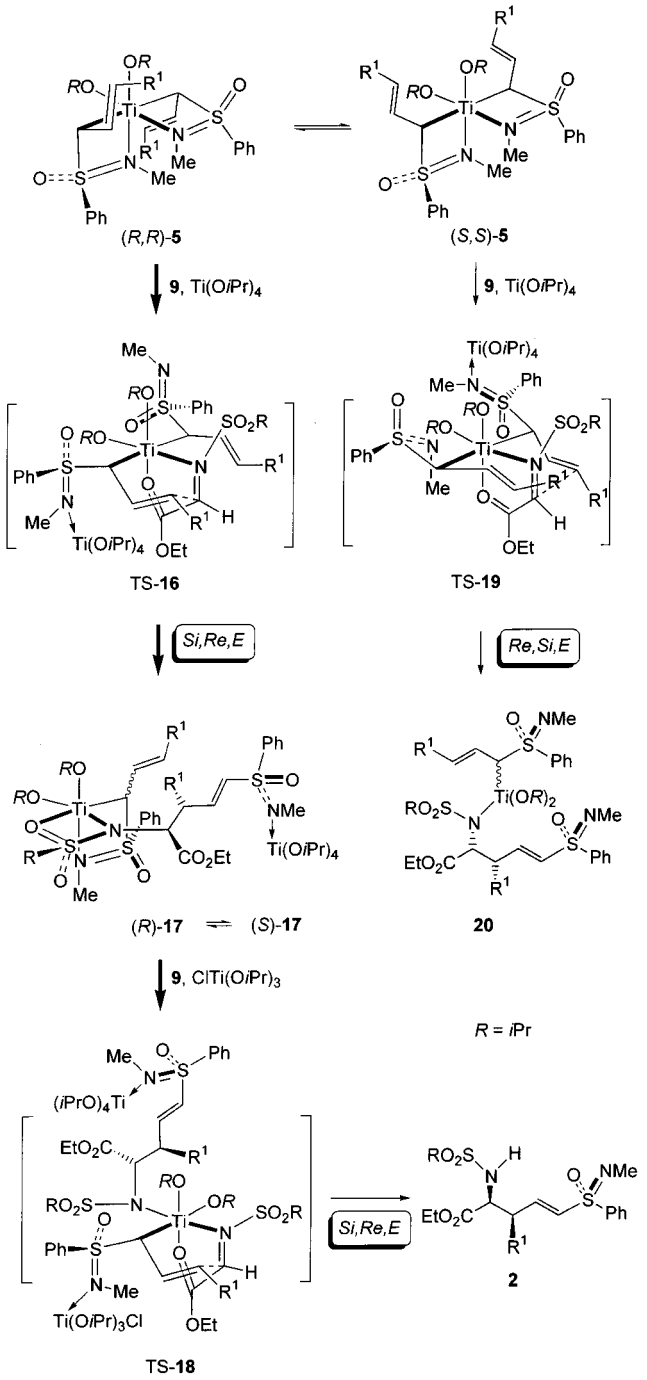
formation of the imidazolidinones **15a** and **15b**, respectively, as side products, besides **2a** and **2b**, was observed if 2 or more equiv of the α-imino ester was used (Scheme 4). Formation of **15a** and **15b** can be rationalized by assuming an addition of the intermediate N-titanated amino esters Ti-**2a** and Ti-**2b** to *N*-Ts α-imino ester **9a** followed by a cyclization under elimination of titanium ethoxide. We tentatively assign the trans configuration to **15a** and **15b** on the basis of the results of ^{1}H NOE experiments and, in particular, because of the lack of a NOE effect between 2-H and 4-H. This assignment is corroborated by the observation of a small coupling constant ^4J(2-H,4-H) < 0.5 Hz in the NMR spectra of **15a** and **15b**.

Stereochemical Considerations. Reaction of the racemic lithiated allylic sulfoximine **I** with ClTi(O*i*Pr)$_3$ led to the formation of two isomeric bis(allyl)titanium complexes in a ratio of 1:1 together with equimolar amounts of Ti(O*i*Pr)$_4$ (Scheme 5).[12c] Isolation and structure determination of one of these complexes in the crystal and in solution revealed an asymmetric (*cis*, *cis*, *cis*)-configured octahedral complex of type **II**, the ($S_{C\alpha}$,R_S)-configured allylic sulfoximine ligands of which are coordinated in a bidentate fashion via the Cα-atom and the N-atom to the Ti-atom. Complex **II** shows in solution a rapid exchange of the diastereotopic isopropoxy groups and of the diastereotopic allylic moieties, each of which gives rise to the formation of two sets of signals in the NMR spectra at low temperatures. This exchange of the allylic moieties at the Ti-atom of **II**, which can occur either in an intra- or in an

(33) Gais, H.-J.; Müller, H.; Bund, J.; Scommoda, M.; Brandt, J.; Raabe, G. *J. Am. Chem. Soc.* **1995**, *117*, 2453.

(34) Formation of a mixture of (*E*)-**8** and (*Z*)-**8** should pose no problem to its use as starting material for the synthesis of amino acids of type **2** and **3** because *Z*-vinylic sulfoximines can be isomerized quantitatively to the corresponding *E*-isomers (refs 12c and 16d).

Scheme 6



intermolecular fashion,[12c] proceeds under retention of configuration at the Cα-atom. NMR spectroscopy of bis(allyl)titanium complexes **5a** and **5d** admixed with Ti(O*i*Pr)$_4$ in d_8-THF and d_8-toluene solution had revealed in both cases the presence of two bis(allyl)titanium complexes in ratios of 1:2, which are in a fast equilibrium at low temperatures. We had assigned the structures of the C_2-symmetric (*cis*, *cis*, *trans*)-configured octahedral complexes (*R*,*R*)-**5** and (*S*,*S*)-**5** (Scheme 6) to the two species and thus proposed that titanium complexes of this type are configurationally labile in regard to the Cα-atoms.[35a−c] Their C_2-symmetry was followed from the observation of only one set of signals in the NMR spectra of both for the allylic moieties even at low temperatures. The isomerization of (*R*,*R*)-**5** and (*S*,*S*)-**5** proceeds perhaps through a fast reversible 1,3-C/N-shift of the Ti-atom containing group.[12c] In the case of the mono(allyl)trisdimethylaminotitanium complexes derived from allylic sulfoximines **12a**, **12b**, and **12d**, the occurrence of such a shift and, as a consequence, configurational lability of the Cα-atom had been unequivocally demonstrated by NMR spectroscopy.[12c,35a,d] Reaction of complexes **5** with α-imino esters **9** in the presence of Ti(O*i*Pr)$_4$ takes place stepwise to give first the mono(allyl)titanium complexes **17**, which react in a highly selective manner with a second molecule of **9** with formation of two molecules of **2** only, however, if ClTi(O*i*Pr)$_3$ is present (vide supra). Formation of (*S*,*R*,*E*)-configured homoallylic amines **2** entails *Si*,*Re*,*E* processes of α-imino esters **9** with titanium complexes **5** and **17**. This could be rationalized on the basis of the Curtin−Hammett principle[36] by assuming that equilibration of bis(allyl)titanium complexes (*R*,*R*)-**5** and (*S*,*S*)-**5** and of mono(allyl)titanium complexes (*R*)-**17** and (*S*)-**17** is faster than their reaction with **9** and that the α-imino esters react preferentially with the (*R*)-configured complexes (*R*,*R*)-**5** and (*R*)-**17** through the chairlike six-membered transition states TS-**16** and TS-**18**, respectively. These TSs feature, besides a bidentate coordination of (*E*)-configured α-imino esters **9** through the N-atom and the ester group to the Ti-atom, a pseudoaxial ester group, a pseudoaxial sulfonyl group, a pseudoequatorial sulfoximine group, and such a Cα-S conformation of the sulfonimidoyl group, which places the S-phenyl group and the N-methyl group in sterically unencumbered positions in regard to the isopropoxy groups. The corresponding *Re*,*Si*,*E* transition states TS-**19** derived from the (*S*)-configured bis(allyl)titanium complexes (*S*,*S*)-**5** and α-imino esters **9**, which would lead to formation of the (*syn*)-configured diastereomers **20**, are expected to be less favorable because of the placement of the N-methyl groups in the sterically encumbered position syn to the isopropoxy groups. The alternative *Re*,*Re*,*E* mode of bond formation between α-imino esters **9** and (*R*,*R*)-**5** (cf. TS-**16**) is also considered to be less favorable because of the boatlike transition state which would be involved. The essential role exerted by Ti(O*i*Pr)$_4$ in the reaction of six coordinated bis(allyl)-titanium complexes **5** with **9** may be that of providing free coordination sites at the Ti-atom, which are required for the binding of the α-imino ester, through complexation of a sulfoximine group. Although the structure of the mono(allyl)-titanium complexes **17** is not known, it seems conceivable that the α-sulfoximine group and the sulfonyl group are both coordinated to the Ti-atom to form a six-coordinate complex of the type depicted in Scheme 6. An intramolecular Ti−O coordination of this kind involving sulfonyl groups, being attached either to a C-atom[37] or to a N-atom,[38] has been observed previously in the case of bis(sulfonylalkylide) titanium bis-(isopropoxide) complexes[37] and bis(sulfonamido) titanium bis-(alkoxide) complexes[38] in the crystal. Thus, the essential role exerted by ClTi(O*i*Pr)$_3$ in the reaction of (*R*)-**17** with α-imino

(35) (a) Gais, H.-J.; Hainz, R.; Schleusner, M.; Bruns, P., unpublished results. (b) Hainz, R. Ph.D. Thesis, RWTH Aachen, 1998. (c) Schleusner, M. Ph.D. Thesis, RWTH Aachen, 2002. (d) Bruns, P. Ph.D. Thesis, RWTH Aachen, 2002.

(36) For reviews, see: (a) Curtin, D. Y. *Rec. Chem. Prog.* **1954**, *15*, 111. (b) Seemann, J. I. *Chem. Rev.* **1983**, *83*, 83.

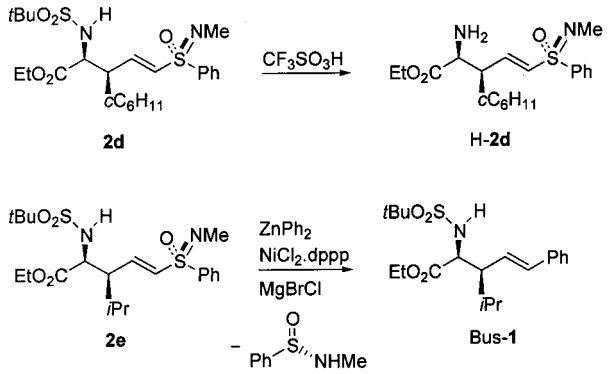
(37) (a) Gais, H.-J.; Vollhardt, J.; Lindner, H. J.; Paulus, H. *Angew. Chem.* **1988**, *100*, 1598; *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1540. (b) Hess, T. Ph.D. Thesis, RWTH Aachen, 1998.

(38) Pritchett, S.; Woodmansee, D. H.; Gantzel, P.; Walsh, P. J. *J. Am. Chem. Soc.* **1998**, *120*, 6423.

esters **9** may also be that of providing the free sites at the Ti-atom, which are required for the binding of the α-imino ester, through a complexation of the sulfoximine group. A key feature of the TSs depicted in Scheme 6 is the coordination of **9** to the Ti-atom through both the N-atom and the ester group. This is, however, an assumption, which is based on the known ability of **9** to form chelate complexes with metal ions[39] and on the proposal of TSs for other metal mediated additions to **9a**, featuring a chelation of this type.[5h,6d,21] Alternatively, the sulfonyl group of **9** could engage instead the ester group or even together with this group in a coordination of the α-imino ester to the Ti-atom.[7i,j,37,38] The reaction of bis(allyl)titanium complexes **5** with aldehydes proceeds in a stepwise manner similar to that with α-imino esters **9** with formation of mono-(allyl)titanium complexes and also requires the presence of Ti-(O*i*Pr)$_4$ in the first and ClTi(O*i*Pr)$_3$ in the second step.[12c] Most interestingly, however, **5** and the corresponding mono(allyl)-titanium complexes derived from the bis(allyl)titanium complexes and the aldehydes react with aldehydes with formation of the (*S*,*R*,*Z*)-configured homoallylic alcohols **6**. This requires *Re*,*Re*,*Z* processes, which were rationalized by proposing that in this case not the (*R*,*R*)- but the (*S*,*S*)-configured complexes (*S*,*S*)-**5** react with the aldehyde via similar chairlike six-membered TSs, the sulfoximine group of which adopts, however, a pseudoaxial position and is coordinated via the N-atom to the Ti-atom.[12c,15] The difference in stereoselectivity of the addition of **5** to aldehydes and **9** originates, according to these TS models, primarily from the *N*-sulfonyl group of the latter, which adopts in the TSs a pseudoaxial position and thus hinders the sulfoximine group from adopting also a pseudoaxial position because of a steric interference of both.

Deprotection and Substitution. Synthesis of amino acids **1** and **3** from **2** requires, besides a substitution of the sulfonimidoyl group, a deprotection of the amino group. Unfortunately, all attempts to cleave the toluenesulfonamide group of **2a** and **2b** (cf. Scheme 3) with either HBr in acetic acid,[40] sodium in liquid ammonia,[41a] or sodium naphthalenide[41b] failed. While **2a** and **2b** were unaffected at room temperature by HBr in acetic acid, complex mixtures of reaction products were obtained at higher temperatures. Surprisingly, similar results were encountered in the attempted cleavage of *N*-SES protected **2c**. While treatment of **2c** with CsF or Bu$_4$NF in dimethylformamide or acetonitrile below 50 °C saw no conversion, a number of unidentified products were formed at higher temperatures. Similar results were obtained by treatment of **2c** with tris(diethylamino)-sulfonium difluorotrimethylsiliconate.[27c] However, we were delighted to see that the *tert*-butylsulfonamide group of the *N*-Bus amino acid derivative **2d** suffered a ready and clean cleavage with formation of H-**2d** upon treatment with 0.1 M CF_3SO_3H (approximately 10 equiv) in anhydrous methylene chloride, first at 0 °C and then at room temperature (Scheme 7). The amino acid derivative H-**2d** was isolated in 96% yield. For the cleavage of *N*-Bus protected **2d** to occur, the presence of anisole, which has been reported to be necessary as a cation scavenger in the case of the cleavage of other Bus amines,[27a,b,d] was not required.

Scheme 7



Finally, the feasibility of a substitution of the sulfonimidoyl group of **2** by a phenyl group through a Ni-catalyzed cross-coupling reaction was probed. Thus, treatment of **2e** with $ZnPh_2$ in the presence of 30 mol % Ni(dppp)Cl$_2$ (dppp = bis-(diphenylphosphino)propane) as precatalyst and MgBrCl as cocatalyst[16] afforded stereoselectively the Bus amino acid Bus-**1** in a nonoptimized isolated yield of 48%. The starting material **2e** was recovered in 32% yield. Formation of side products was not observed. Previous results with Ni-catalyzed cross-coupling reactions of vinylic sulfoximines suggest[16,42] that a more efficient substitution of **2e** with formation of Bus-**1** might be achieved by using a more active catalyst. Besides Bus-**1**, (*S*)-*N*-methyl-*S*-phenylsulfinamide was formed in the cross-coupling reaction. We had previously shown that the Ni-catalyzed cross-coupling reaction of vinylic *N*-methyl-*S*-phenyl sulfoximines proceeds with complete retention of configuration at the S-atom.[16,42] The stereoselective conversion of (*S*)-*N*-methyl-*S*-phenylsulfinamide to (*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximine, the starting material for the synthesis of allylic sulfoximines, has already been described.[43]

Conclusion

Reaction of *N*-Bus, *N*-SES, and *N*-Ts α-imino esters with bis(allyl)titanium complexes, being most likely configurationally labile, in the presence of Ti(O*i*Pr)$_4$ and ClTi(O*i*Pr)$_3$ gives with high regio- and stereoselectivity δ-sulfonimidoyl functionalized β-alkyl-γ,δ-unsaturated amino acids.[44] The regio- and diastereoselectivity of the addition is neither influenced by the steric size of the *N*-sulfonyl group of the α-imino esters nor by that of the substituent at the γ-position of the bis(allyl)titanium complex. The reaction of the bis(allyl)titanium complexes with the α-imino esters takes a stereochemical course being different from that with aldehydes. While the former yields in a *Re*,*Re*,*E* process the (*syn*, *E*)-configured amino acid derivatives, the latter gives in a *Si*,*Re*,*Z* process the (*anti*, *Z*)-configured homoallylic alcohols. This result can be rationalized by proposing that the (*R*,*R*)-configured bis(allyl)titanium complexes react faster with α-imino esters, while their (*S*,*S*)-configured diastereomers react faster with aldehydes.

(39) van Vliet, R. P.; van Koten, G.; Modder, J. F.; van Beek, J. A.; Klaver, W. J. *J. Organomet. Chem.* **1987**, *319*, 285.
(40) (a) Weisblat, D. L.; Magerlein, B. J.; Myers, D. R. *J. Am. Chem. Soc.* **1953**, *75*, 3630. (b) Li, G.; Sharpless, K. B. *Acta Chem. Scand.* **1996**, *50*, 649.
(41) (a) du Vigneaud, V.; Behrens, O. K. *J. Biol. Chem.* **1937**, *117*, 27. (b) Ji, S.; Gortler, L. B.; Waring, A.; Battisti, A.; Bank, S.; Closson, W. D.; Wriede, P. *J. Am. Chem. Soc.* **1967**, *89*, 5311.
(42) (a) Woo, C.-W. Ph.D. Thesis, RWTH Aachen, 2000. (b) Decker, J. Ph.D. Thesis, RWTH Aachen, 1996. (c) Bülow, G. Ph.D. Thesis, Universität Freiburg, 1992.
(43) Johnson, C. R.; Jonsson, E. U.; Wambsgans, A. *J. Org. Chem.* **1979**, *44*, 2061.
(44) No addition of titanium complex **5a** to *N*-Boc α-imino ester could be observed.

A selective and quantitative deprotection of the amino group of the sulfonimidoyl functionalized amino acid derivatives was achieved only in the case of the Bus derivatives. Whether a conversion of the *N*-Ts derivatives to the corresponding *N*-Boc derivatives by the method described recently[26] will be possible remains to be seen. The ability of the sulfonimidoyl group of the *N*-Bus amino acid derivatives to act as a nucleofuge has been demonstrated through a Ni-catalyzed cross-coupling reaction with $ZnPh_2$.

For the *N*-Bus and *N*-SES α-imino esters, many synthetic applications can be foreseen, in particular, in those cases where the *N*-Ts α-imino ester had been used before[5b,g,h,6,7i,j,21−24,45,46] and where deprotection of the amino group of the reaction product posed problems.

Experimental Section

General. All reactions were carried out in absolute solvents under argon with syringe and Schlenk techniques in oven-dried glassware. THF and ether were distilled under argon from potassium/benzophenone and sodium/benzophenone, respectively. CH_2Cl_2 and MeCN were distilled from calcium hydride, and toluene and benzene were distilled from sodium−lead/benzophenone. $ClTi(OiPr)_3$[47] of ≥96% purity (^{1}H NMR) was prepared according to the literature. (*S*,*E*)-*S*-(3-Cyclohexyl-2-propenyl)-*N*-methyl-*S*-phenylsulfoximine (**12a**) of ≥98% ee,[12c] (*S*,*E*)-*N*-methyl-*S*-(4-methyl-2-pentenyl)-*S*-phenylsulfoximine (**12b**) of ≥98% ee,[12c] (*S*,*E*)-*N*-methyl-*S*-(3-phenyl-2-propenyl)-*S*-phenylsulfoximine (**12c**) of ≥98% ee,[12c] (*S*,*E*)-*N*-methyl-*S*-(2-butenyl)-*S*-phenylsulfoximine (**12d**) of ≥98% ee,[12c] and (*R*)-*S*-(1-cyclohexen-1-ylmethyl)-*N*-methyl-*S*-phenylsulfoximine (**13**)[33] were synthesized from (*S*)-*S*-methyl-*S*-phenylsulfoximine and (*R*)-*S*-methyl-*S*-phenylsulfoximine, respectively, according to the literature. Enantiomerically pure (*S*)- and (*R*)-*S*-methyl-*S*-phenylsulfoximine, which are also commercially available, were synthesized as described previously.[32c] *N*-Ts α-imino ester **9a** was prepared from ethyl glyoxylate and *p*-toluenesulfonyl isocyanate according to the literature.[19,20] Commercially obtained ethyl glyoxylate was distilled from P_2O_5, stored under argon, and freshly distilled prior to its use. $ZnPh_2$ was freshly prepared from PhMgBr and anhydrous $ZnCl_2$ in ether. All other chemicals were obtained from commercial sources used without further purification. TLC: Merck silica gel 60 F_{254} plates. Column chromatography: Merck silica gel 60 (0.063−0.200 mm). HPLC: Merck Nova Prep 5000, Merck Hibar LiChrosorb Si 60 (7 μm). Melting points were determined using a Büchi apparatus SMP-20 and are uncorrected. Optical rotations: Perkin-Elmer Model 241, measurements were made at approximately 22 °C, specific rotations are in grad × mL/dm × g, *c* in g/100 mL. ^{1}H and ^{13}C NMR: Varian Inova 400 and Varian Unity 500. The following abbreviations are used to designate the multiplicity of the peaks in the ^{1}H NMR spectra: s = singlet, sb = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and combinations thereof. Peaks in the ^{13}C NMR spectra are denoted as "u" for carbons with zero or two attached protons or "d" for carbons with one or three attached protons, as determined from APT pulse sequence. ^1J(C,H) coupling constants were extracted from the traces of HET2DJ experiments, and multiplicity is given instead of "u" or "d". Assignments in the ^{1}H NMR spectra were made by COSY, GMQCOSY, or 1D-GNOE experiments, and those in the ^{13}C NMR spectra were made by GHSQC or HMQC experiments. Assignment of the signals of quaternary C atoms was made by GHMBC experiments. GC analyses: Chrompack CP-9000 (DB-5, 30 m × 0.32 mm; 50 kPa H_2). IR spectra were taken with a Perkin-Elmer PE 1759 FT instrument, and only peaks of ν > 600 cm^{-1} are listed. GC-MS: Magnum Finnigan (HT-5, 25 m, 0.25 mm; 50 kPa He, CI, 40 eV, MeOH). Low-resolution MS were recorded with a Varian MAT 212S (EI, 70 eV) instrument, and only peaks of *m*/*z* > 70 and an intensity > 10%, except decisive ones, are listed. High-resolution MS: Varian MAT 95. Elemental analysis: Microanalytical Laboratories of the Institut für Organische Chemie and of the Institut für Anorganische Chemie, RWTH Aachen.

X-ray Analyses. The crystal data and the most salient experimental parameters used in the X-ray measurements and in the crystal structure analyses are reported in Table 2. The crystal structures of **2a**, **2e**, and (*E*)-**8** were solved using direct methods as implemented in the XTAL3.4 package of crystallographic routines.[48] The absolute configurations of **2a**, **2e**, and (*E*)-**8** depicted in Figures 1−3 were determined by the method of Flack.[49] Molecular structures were visualized with the program SCHAKAL 92.[50]

***N*-2-Trimethylsilylethanesulfonylthioisocyanate (11b).** To a solution of **10b** (1.87 g, 10.3 mmol) in benzene (15 mL) was added at room temperature freshly distilled $SOCl_2$ (0.87 mL, 11.9 mmol), and the resulting slightly turbid yellow mixture was heated at reflux for 2 d. Concentration of the solution in vacuo and kugelrohr distillation (80−125 °C, 0.15 mbar) of the residue gave **11b** (1.50 g, 54%) of 97% purity (^{1}H NMR) as pale yellow crystals: mp 87−90 °C. Spectroscopic data of **11b** were in accordance with those reported in the literature.[31]

Ethyl *N*-2-Trimethylsilylethanesulfonylimino Acetate (9b). Freshly distilled $SOCl_2$ (6.92 g, 95.0 mmol) was added at room temperature to a solution of amide **10b** (17.21 g, 94.5 mmol) in toluene (125 mL), and the mixture was heated at reflux for 2 d. Evaporation of the solvent in vacuo gave crude **11b** as a brown oil, which was used without purification in the next step. Thus, obtained SES thioisocyanate **11b** was added to a solution of ethyl glyoxylate (6.80 g, 77.2 mmol) in toluene (200 mL), and the resulting mixture was heated at reflux for 1.5 d. Concentration of the mixture in vacuo and fractional kugelrohr distillation (125−175 °C, 0.10 mbar) of the residue afforded **9b** (9.45 g, 38%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.05 (s, 9H, $Si(CH_3)_3$), 1.03 (m, 2H, 2-H), 1.38 (t, J = 7.1 Hz, 3H, OCH_2CH_3), 3.19 (m, 2H, 1-H), 4.41 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 8.35 (s, 1H, N=CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ −1.8 (d), 9.3 (u), 14.2 (d), 49.1 (u), 63.5 (u), 161.0 (u), 162.9 (d). MS (CI, 100 eV): *m*/*z* (relative intensity, %) 266 [M^+ + 1] (100), 202 (13), 174 (20), 101 (13). IR (capillary) ν 3293 (w), 2954 (m), 2901 (w), 1752 (s), 1639 (w), 1334 (s), 1252 (s), 1173 (m), 1150 (s), 861 (s), 843 (s) cm^{-1}.

***N*-2-Methylpropane-2-sulfonylthioisocyanate (11c).** Freshly distilled $SOCl_2$ (1.25 mL, 16.75 mmol) was added at room temperature to a solution of **10c** (1.99 g, 14.5 mmol) in benzene (15 mL), and the resulting slightly turbid yellow mixture was heated at reflux for 4 d. Concentration of the solution in vacuo and kugelrohr distillation (90−130 °C, 0.20 mbar) of the residue gave **11c** (1.52 g, 57%) of 90% purity (^{1}H NMR), containing 10% of **9c**, as pale yellow crystals: mp 86−87 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.45 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.7 (d, $C(CH_3)_3$), 61.9 (u, $C(CH_3)_3$). IR (KBr): ν 3345 (s), 3248 (s), 3106 (w), 2986 (m), 2945 (w), 2879 (w), 1562 (m), 1477 (m), 1376 (m), 1307 (s), 1211 (m), 1145 (s), 1117 (s), 902 (m), 672 (m) cm^{-1}.

Ethyl *N*-2-Methylpropane-2-sulfonylimino Acetate (9c). Freshly distilled $SOCl_2$ (7.15 mL, 97.9 mmol) was added at room temperature to a solution of **10c** (12.22 g, 89 mmol) in toluene (200 mL), and the resulting slightly turbid yellow mixture was heated at reflux for 8 h. After the mixture was cooled to approximately 80 °C, ethyl glyoxylate (7.84 g, 89 mmol) was added, and the mixture was heated at reflux for 2.5 d. Concentration of the mixture at 25 °C and 0.5 mbar by using a cooling trap (−100 °C) gave a brown oil, which was submitted first to a kugelrohr sublimation at 70 °C and 0.20 mbar to separate amide **10c**

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Table 2. Crystal Data and Parameters of Data Collection for **2a**, **2e**, and (*E*)-**8**

	2a	**2e**	(*E*)-**8**
formula	$C_{27}H_{36}N_2O_5S_2$	$C_{21}H_{34}N_2O_5S_2$	$C_{22}H_{34}N_2O_5S_2$
M_r	532.73	458.60	470.66
color and habit	colorless, irregular	colorless, irregular	colorless, rod
crystal size, ca. mm	0.6 × 0.6 × 0.2	0.56 × 0.2 × 0.2	0.4 × 0.4 × 0.4
crystal system	orthorhombic	orthorhombic	monoclinic
space group (No.)	$P2_12_12_1$ (19)	$P2_12_12_1$ (19)	P_{21} (4)
a [Å]	10.800(2)	8.371(1)	11.108(3)
b [Å]	11.084(4)	13.892(6)	9.688(3)
c [Å]	21.870(5)	21.229(2)	11.282(4)
α [deg]	90.0	90.0	90.0
β [deg]	90.0	90.0	90.25(1)
γ [deg]	90.0	90.0	90.00
V [Å^3]	2830.5	2468.72	1214.1(7)
Z	4	4	2
D_{calcd} [g cm^{-3}]	1.250	1.234	1.287
μ [mm^{-1}]	2.015	2.22	2.274
diffractometer	CDA4 Enraf-Nonius	CAD4 Enraf-Nonius	CAD4 Enraf-Nonius
T [K]	150	150	150
radiation	Cu Kα	Cu Kα	Cu Kα
λ [Å]	1.54179	1.54179	1.54179
monochromator	graphite	graphite	graphite
scan method	*ω*/2*θ*	*ω*/2*θ*	*ω*/2*θ*
Θ_{max} [deg]	75.5	79.9	72.76
no. of data colld.	6520	6003	7129
no. of unique data	5405	5052	4297
obsn. criterion	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$
no. of params. refd.	325	271	280
no. of data obsd.	4660	3137	4266
R, R_w	0.061, 0.067	0.10, 0.11	0.036, 0.048
Δ(*ρ*) [e Å^{-3}]	−0.63/0.83	−5.06/2.99	−0.68/0.42
GOF	2.174	1.980	2.798

(2.78 g, 23%, colorless solid) and then to a kugelrohr distillation at 100 °C and 0.20 mbar, which gave *N*-Bus α-imino ester **9c** (12.45 g, 63%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 1.36 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.46 (s, 9H, $C(CH_3)_3$), 4.38 (q, *J* = 7.1 Hz, 2H, OCH_2CH_3), 8.36 (s, 1H, N═CH). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 14.0 (d, OCH_2CH_3), 23.8 (d, $C(CH_3)_3$), 59.2 (u, $C(CH_3)_3$), 63.2 (u, OCH_2CH_3), 161.0 (u, C═O), 163.2 (d, N═C). IR (capillary): *ν* 3266 (w), 2986 (m), 2940 (w), 2877 (w), 1752 (s), 1734 (s), 1638 (m), 1480 (w), 1466 (w), 1371 (m), 1319 (s), 1212 (m), 1133 (s), 1026 (m), 808 (m), 734 (m) cm^{-1}. MS (CI, 100 eV): *m*/*z* (relative intensity, %) 222 [M$^+$ + 1] (100), 158 (24), 138 (36), 102 (44). Anal. Calcd for $C_8H_{15}NO_4S$ (221.27): C, 43.42; H, 6.83; N, 6.33. Found: C, 43.35; H, 7.02; N, 6.51.

General Procedure for the Synthesis of Sulfoximine Substituted Amino Acids 2 (*GP1*). *n*BuLi (1.37 mL of 1.6 M solution in *n*-hexane, 2.2 mmol) was added dropwise at −78 °C to a solution of allylic sulfoximine **12** (2 mmol) in THF (20 mL). After the mixture was stirred at −78 °C for 30 min, $ClTi(OiPr)_3$ (4 mmol) was added, and stirring at this temperature was continued for 30 min. The mixture was then warmed to room temperature within 1 h, recooled to −78 °C, and treated with α-imino ester **9** (2.25 mmol). After the mixture was stirred at −78 °C for 3 h, it was allowed to warm to room temperature within 16 h. The mixture was then poured into saturated aqueous $(NH_4)_2CO_3$ (150 mL) and extracted with ethyl acetate (150 mL). The combined organic phase was dried ($MgSO_4$), concentrated in vacuo, and the remaining yellow oil was taken up in ether (75 mL). Evaporation of the ether in vacuo afforded the crude vinylic sulfoximine **2** of ≥95:5 dr (^{1}H NMR) contaminated by the excess of **9**, unconverted **12**, and 3−9% of *N*-methyl-phenylsulfinamide, as a colorless solid. Recrystallization from ether or washing with *n*-hexane/ether gave the pure vinylic sulfoximine **2** of ≥98:2 dr.

(+)-(*E*,*S*$_S$,2*S*,3*R*)-5-(*N*-Methyl-*S*-phenylsulfonimidoyl)-3-cyclohexyl-2-(toluene-4-sulfonylamino)-pent-4-enoic Acid Ethyl Ester (2a). Following *GP1*, the reaction of sulfoximine **12a** (695 mg, 2.5 mmol) with *N*-Ts α-imino ester **9a** (700 mg, 2.75 mmol) resulted in a 79% conversion of **12a** under formation of the crude sulfoximine **2a** in approximately 75% chemical yield (^{1}H NMR). Crystallization from ether afforded **2a** (794 mg, 59%) as colorless crystals: mp 134−138 °C. $[\alpha]_D$ +4.4 (*c* 1.21, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 0.8−1.25 (m, 5H, cC_6H_{11}), 0.90 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.54−1.75 (m, 6H, cC_6H_{11}), 2.21 (m, 1H, 3-H), 2.38 (s, 3H, *p*-tol), 2.71 (s, 3H, NCH_3), 3.37 (dq, *J* = 7.1, *J* = 10.7 Hz, 1H, OCH_2CH_3), 3.56 (dq, *J* = 7.1, *J* = 10.7 Hz, 1H, OCH_2CH_3), 3.95 (dd, *J* = 8.1, *J* = 10.2 Hz, 1H, 2-H), 4.97 (d, *J* = 10.1 Hz, 1H, N−H), 6.24 (d, *J* = 14.9 Hz, 1H, 5-H), 6.53 (dd, *J* = 10.7, *J* = 14.9 Hz, 1H, 4-H), 7.24 (m, 2H, *p*-tol), 7.51 (m, 2H, *m*-Ph), 7.56 (m, 1H, *p*-Ph), 7.62 (m, 2H, *p*-tol), 7.82 (m, 2H, *o*-Ph). ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 13.7 (d, OCH_2CH_3), 21.5 (d, *p*-tol), 26.0 (u, cC_6H_{11}), 26.05 (u, cC_6H_{11}), 26.15 (u, cC_6H_{11}), 28.5 (u, cC_6H_{11}), 29.4 (d, NCH_3), 31.4 (u, cC_6H_{11}), 37.2 (d, cC_6H_{11}), 51.7 (d, C-3), 55.9 (d, C-2), 61.5 (u, OCH_2CH_3), 127.3 (d, *p*-tol), 128.5 (d, *o*-Ph), 129.3 (d, *m*-Ph), 129.6 (d, *p*-tol), 132.7 (d, *p*-Ph), 133.9 (d, C-5), 136.3 (u, *i*-Ph), 139.2 (u, *i*-Ph), 142.4 (d, C-4), 143.8 (u, *i*-Ph), 170.2 (u, C-1). IR (KBr): *ν* 3213 (m), 3056 (m), 2931 (s), 2856 (m), 2808 (w), 2212 (w), 1743 (w), 1725 (s), 1449 (m), 1339 (s), 1241 (s), 1161 (s), 1093 (m), 666 (m) cm^{-1}. MS (CI, isobutane): *m*/*z* (relative intensity, %) 533 [M$^+$ + 1] (100), 377 (38), 256 (18). Anal. Calcd for $C_{27}H_{36}N_2O_5S_2$ (532.76): C, 60.86; H, 6.81; N, 5.27. Found: C, 60.58; H, 6.73; N, 5.17.

(+)-(*E*,*S*$_S$,2*S*,3*R*)-5-(*N*-Methyl-*S*-phenylsulfonimidoyl)-3-isopropyl-2-(toluene-4-sulfonylamino)-pent-4-enoic Acid Ethyl Ester (2b). Following *GP1*, the reaction of sulfoximine **12b** (306 mg, 1.29 mmol) with *N*-Ts α-imino ester **9a** (361 mg, 1.42 mmol) resulted in a 85% conversion of **12b** under formation of the crude sulfoximine **2b** in approximately 80% chemical yield (^{1}H NMR). Crystallization from ether afforded **2b** (414 mg, 65%) as colorless crystals: mp 186−188 °C. $[\alpha]_D$ +8.7 (*c* 0.97, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 0.87 (d, *J* = 6.9 Hz, 3H, $CH(CH_3)_2$), 0.89 (t, *J* = 7.4 Hz, 3H, OCH_2CH_3), 0.92 (d, *J* = 6.9 Hz, 3H, $CH(CH_3)_2$, 2.08−2.19 (m, 1H, $CH(CH_3)_2$), 2.17−2.24 (m, 1H, 3-H), 2.39 (s, 3H, *p*-tol), 2.72 (s, 3H, NCH_3), 3.36 (dq, *J* = 7.1, *J* = 10.7 Hz, 1H, OCH_2CH_3), 3.56 (dq, *J* = 7.1, *J* = 10.7

Hz, 1H, OCH_2CH$_3$), 3.93 (dd, J = 8.2, J = 10.2 Hz, 2-H), 4.92 (d, J = 10.2 Hz, 1H, N−H), 6.24 (d, J = 15.1 Hz, 1H, 5-H), 6.54 (dd, J = 10.7, J = 15.0 Hz, 4-H), 7.25 (m, 2H, *p*-tol), 7.49−7.60 (m, 3H, *m*-, *p*-Ph), 7.63 (m, 2H, *p*-tol), 7.84 (m, 2H, *o*-Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9 (d), 17.9 (d), 21.3 (d), 21.7 (d), 27.8 (d), 29.6 (d), 52.4 (d), 56.9 (d), 61.7 (u), 127.4 (d), 128.6 (d), 129.4 (d), 129.7 (d), 132.8 (d), 134.5 (d), 136.4, 139.4 (u), 141.6 (d), 143.9 (u), 170.2 (u). MS (CI, isobutane): *m*/*z* (relative intensity, %) 493 [M^+ + 1] (100), 337 (22), 291 (24), 155 (19). IR (KBr): ν 3475 (w), 3077 (m), 2965 (m), 2930 (w), 2872 (m), 2807 (w), 1748 (s), 1597 (w), 1449 (m), 1375 (m), 1338 (s), 1237 (s), 1155 (s), 1092 (s), 864 (m) cm^{-1}. Anal. Calcd for $C_{24}H_{32}N_2O_5S_2$ (492.70): C, 58.51; H, 6.55; N, 5.69. Found: C, 58.32; H, 6.49; N, 5.55.

(+)-(*E*,*S*$_S$,2*S*,3*R*)-5-(*N*-Methyl-*S*-phenylsulfonimidoyl)-3-cyclohexyl-2-(trimethylsilylethanesulfonylamino)-pent-4-enoic Acid Ethyl Ester (2c). Following *GP1*, the reaction of sulfoximine **12a** (1.83 g, 6.61 mmol) with *N*-SES α-imino ester **9b** (1.92 g, 7.27 mmol) resulted in an 87% conversion of **12a** under formation of the crude sulfoximine **2c** in approximately 80% chemical yield (^{1}H NMR). Washing with ether/*n*-hexane (1:1) afforded **2c** (2.18 g, 61%) as colorless crystals: mp 121−122 °C. $[\alpha]_D$ +4.9 (*c* 0.90, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ −0.10 (s, 9H, Si(CH_3)$_3$), 0.90 (m, 2H, SiCH_2CH$_3$), 1.00−1.18 (m, 5H, *c*C$_6$H$_{11}$), 1.14 (t, J = 7.1 Hz, 3H, OCH$_2$CH_3), 1.60−1.80 (m, 6H, *c*C$_6$H$_{11}$), 2.29 (m, 1H, 3-H), 2.72 (s, 3H, NCH$_3$), 2.74−2.88 (m, 2H, SO$_2$CH$_2$), 3.75 (dq, J = 7.1, J = 10.7 Hz, 1H, OCH_2CH$_3$), 3.98 (dq, J = 7.1, J = 10.7 Hz, 1H, OCH_2CH$_3$), 4.12 (dd, J = 7.4, J = 10.2 Hz, 1H, 2-H), 4.58 (d, J = 9.9 Hz, 1H, NH), 6.33 (d, J = 14.8 Hz, 1H, 5-H), 6.58 (dd, J = 10.8, J = 15.0 Hz, 1H, 4-H), 7.48−7.58 (m, 3H, *m*-Ph, *p*-Ph), 7.85 (m, 2H, *o*-Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ −2.0 (d, Si(CH_3)$_3$), 10.4 (u, SiCH_2), 14.1 (d, OCH$_2$CH_3), 26.1 (u, *c*C$_6$H$_{11}$), 26.2 (u, *c*C$_6$H$_{11}$), 29.1 (u, *c*C$_6$H$_{11}$), 29.5 (d, NCH$_3$), 31.5 (u, *c*C$_6$H$_{11}$), 37.5 (d, *c*C$_6$H$_{11}$), 49.8 (u, SO$_2$CH$_2$), 52.2 (d, C-3), 56.2 (d, C-2), 61.9 (u, OCH$_2$CH$_3$), 128.5 (d, *o*-Ph), 129.3 (d, *m*-Ph), 132.6 (d, *p*-Ph), 134.1 (d, C-5), 139.2 (u, *i*-Ph), 142.2 (d, C-4), 170.8 (u, C-1). IR (KBr): ν 3225 (m), 3050 (w), 2925 (s), 2851 (m), 2801 (w), 1741 (s), 1633 (w), 1447 (m), 1329 (s), 1249 (s), 1177 (s), 1150 (s), 862 (m), 841 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (relative intensity, %) 542 [M^+] (3), 527 (18), 469 (6), 377 (9), 276 (100), 150 (43), 125 (50), 73 (51). HRMS (EI, 70 eV) calcd for $C_{25}H_{42}N_2O_5S_2$: 542.230447. Found: 542.230368.

(+)-(*E*,*S*$_S$,2*S*,3*R*)-5-(*N*-Methyl-*S*-phenylsulfonimidoyl)-3-cyclohexyl-2-(2-methylpropane-2-sulfonylamino)-pent-4-enoic Acid Ethyl Ester (2d). Following *GP1*, the reaction of sulfoximine **12a** (1.88 g, 6.78 mmol) with *N*-Bus α-imino ester **9c** (1.65 g, 7.45 mmol) resulted in a 97% conversion of **12a** under formation of the crude sulfoximine **2d** in approximately 92% chemical yield (^{1}H NMR). Washing with ether/*n*-hexane (1:1) afforded **2d** (2.60 g, 77%) as colorless crystals: mp 155−156 °C. $[\alpha]_D$ +13.4 (*c* 0.99, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90−1.25 (m, 5H, *c*C$_6$H$_{11}$), 1.16 (t, J = 7.1 Hz, 3H, OCH$_2$CH_3), 1.25 (s, 9H, C(CH_3)$_3$), 1.56−1.78 (m, 6H, *c*C$_6$H$_{11}$), 2.25 (dt, J = 6.6, J = 11.0 Hz, 1H, 3-H), 2.73 (s, 3H, NCH$_3$), 3.85 (dq, J = 7.1, J = 10.7 Hz, 2H, OCH_2CH$_3$), 4.01 (dq, J = 7.1, J = 10.7 Hz, 2H, OCH_2CH$_3$), 4.14 (d, J = 10.3 Hz, 1H, NH), 4.19 (dd, J = 6.5, J = 10.3 Hz, 1H, 2-H), 6.33 (d, J = 14.8 Hz, 1H, 5-H), 6.49 (dd, J = 11.0, J = 14.8 Hz, 1H, 4-H), 7.48−7.58 (m, 3H, *m*-Ph, *p*-Ph), 7.83−7.87 (m, 2H, *o*-Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (d, OCH$_2$CH_3), 24.1 (d, C(CH_3)$_3$), 26.0 (u, *c*C$_6$H$_{11}$), 26.1 (u, *c*C$_6$H$_{11}$), 29.6 (d, NCH$_3$), 29.8 (u, *c*C$_6$H$_{11}$), 31.3 (u, *c*C$_6$H$_{11}$), 37.6 (d, *c*C$_6$H$_{11}$), 53.3 (d, C-3), 57.0 (d, C-2), 60.0 (u, *C*(CH$_3$)$_3$), 61.7 (u, OCH$_2$CH$_3$), 128.4 (d, *o*-Ph), 129.3 (d, *m*-Ph), 132.6 (d, *p*-Ph), 134.1 (d, C-5), 139.4 (u, *i*-Ph), 142.7 (d, C-4), 170.4 (u, C-1). IR (KBr): ν 3247 (s), 3055 (w), 2979 (m), 2929 (s), 2853 (m), 2801 (w), 1740 (s), 1449 (s), 1323 (s), 1246 (s), 1147 (s), 1130 (s), 1083 (m), 607 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (relative intensity, %) 498 [M^+] (5), 425 (6), 362 (5), 276 (100), 150 (54), 125 (62), 107 (29), 57 (39). HRMS (EI, 70 eV) calcd for $C_{24}H_{38}N_2O_5S_2$: 498.222218. Found: 498.222430.

(+)-(*E*,*S*$_S$,2*S*,3*R*)-5-(*N*-Methyl-*S*-phenylsulfonimidoyl)-3-isopropyl-2-(2-methylpropane-2-sulfonylamino)-pent-4-enoic Acid Ethyl Ester (2e). Following *GP1*, the reaction of sulfoximine **12b** (1.16 g, 4.89 mmol) with *N*-Bus α-imino ester **9c** (1.19 g, 5.38 mmol) resulted in a 98% conversion of **12a** under formation of the crude sulfoximine **2e** in approximately 93% chemical yield (^{1}H NMR). Washing with ether/hexanes (1:1) afforded **2e** (1.84 g, 82%) as colorless crystals: mp 124−124.5 °C. $[\alpha]_D$ +19.0 (*c* 1.10, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (d, J = 6.6 Hz, 3H, CH(CH_3)$_2$), 0.97 (d, J = 6.6 Hz, 3H, CH(CH_3)$_2$), 1.15 (t, J = 7.1 Hz, 3H, OCH$_2$CH_3), 1.26 (s, 9H, C(CH_3)$_3$), 2.03 (oct, J = 6.8 Hz, 1H, CH(CH$_3$)$_2$), 2.33 (dt, J = 6.8, J = 10.7 Hz, 1H, 3-H), 2.73 (s, 3H, NCH$_3$), 3.80 (dq, J = 7.1, J = 10.7 Hz, 1H, OCH_2CH$_3$), 4.01 (dq, J = 7.1, J = 10.7 Hz, 1H, OCH_2CH$_3$), 4.14 (dd, J = 7.1, J = 10.2 Hz, 1H, 2-H), 4.21 (d, J = 10.4 Hz, 1H, NH), 6.34 (d, J = 15.1 Hz, 1H, 5-H), 6.57 (dd, J = 10.9, J = 15.0 Hz, 1H, 4-H), 7.48−7.58 (m, 3H, *m*-Ph, *p*-Ph), 7.85 (m, 2H, *o*-Ph). ^{13}C NMR (100 MHz, $CDCl_3$); δ 14.1 (d, OCH$_2$CH_3), 18.9 (d, CH(CH_3)$_2$), 21.1 (d, CH(CH_3)$_2$), 24.1 (d, C(CH_3)$_3$), 27.9 (d, CH(CH$_3$)$_2$), 29.5 (d, NCH$_3$), 53.9 (d, C-3), 57.8 (d, C-2), 60.1 (u, *C*(CH$_3$)$_3$), 61.7 (u, OCH$_2$-CH$_3$), 128.4 (d, *o*-Ph), 129.3 (d, *m*-Ph), 132.6 (d, *p*-Ph), 134.6 (d, C-5), 139.4 (u, *i*-Ph), 142.0 (d, C-4), 170.5 (u, C-1). MS (CI, isobutane): *m*/*z* (relative intensity, %) 459 [M^+ + 1] (100). IR (KBr): ν 3128 (m), 3056 (m), 2977 (m), 2956 (m), 2909 (s), 2870 (m), 2797 (w), 1747 (s), 1629 (w), 1478 (s), 1448 (m), 1371 (m), 1330 (s), 1313 (s), 1223 (s), 1180 (s), 1144(s), 1020 (m) cm^{-1}. Anal. Calcd for $C_{21}H_{34}N_2O_5S_2$ (458.64): C, 55.00; H, 7.47; N, 6.11. Found: C, 54.90; H, 7.53; N, 6.08.

(+)-(*E*,*S*$_S$,2*S*,3*S*)-5-(*N*-Methyl-*S*-phenylsulfonimidoyl)-3-phenyl-2-(2-methylpropane-2-sulfonylamino)-pent-4-enoic Acid Ethyl Ester (2f). Following *GP1*, the reaction of sulfoximine **12c** (1.15 g, 4.24 mmol) with *N*-Bus α-imino ester **9c** (1.03 g, 4.66 mmol) resulted in a 99% conversion of **12c** under formation of the crude sulfoximine **2f** in approximately 96% chemical yield (^{1}H NMR). Washing with ether/*n*-hexane (1:1) afforded **2f** (1.15 g, 55%) as a fine white solid. The mother liquor was concentrated in vacuo, and the residue was purified by chromatography (ethyl acetate/*n*-hexane, 4:1). Crystallization from ethyl acetate/*n*-hexane, 1:4, provided additional **2f** (570 mg, 27%): mp 153 °C. $[\alpha]_D$ +44.6 (*c* 0.60, CH_2Cl_2). ^{1}H NMR (500 MHz, d_6-benzene): δ 0.96 (s, 9H, C(CH$_3$)$_3$), 1.00 (t, J = 7.0 Hz, 3H, OCH$_2$CH_3), 2.85 (s, 3H, NCH$_3$), 3.72 (dq, J = 7.3, J = 10.7 Hz, 1H, OCH_2CH$_3$), 3.84−3.95 (m, 2H, OCH_2CH$_3$, 3-H), 4.35 (dd, J = 10.4 Hz, 1H, 2-H), 5.62 (d, J = 10.4 Hz, 1H, NH), 6.77 (d, J = 14.6 Hz, 1H, 5-H), 6.91−7.05 (m, Ph), 7.47 (dd, J = 14.9 Hz, 1H, 4-H), 7.95−7.99 (m, 2H, *o*-Ph). ^{13}C NMR (125 MHz, d_6-benzene): δ 13.96 (d, C-11), 23.81 (d, C-17), 29.40 (d, NCH$_3$), 50.93 (d, C-3), 59.94 (u, C-16), 61.90 (u, C-10), 62.26 (d, C-2), 127.91 (d), 128.78 (d), 129.09 (d), 129.26 (d), 129.29 (d), 132.26 (d), 137.85 (u), 140.32 (u) (Ph), 142.40 (d, C-4), 172.54 (u, C-1). IR (KBr): ν 3676 (w), 3653 (w), 3446 (w), 3297 (s), 3065 (w), 3031 (w), 2984 (s), 2932 (m), 2905 (m), 2875 (m), 2804 (w), 2370 (w), 2175 (w), 1734 (s), 1630 (w), 1603 (w), 1448 (s), 1370 (m), 1322 (s), 1306 (s), 1235 (s), 1172 (s), 1132 (s), 1089 (s), 1024 (m), 989 (w), 901 (s), 861 (s), 829 (w), 775 (w), 754 (m), 735 (m), 704 (m), 675 (m), 611 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (relative intensity, %) 492 [M^+] (6), 419 (5), 273 (5), 272 (17), 271 (94), 270 (100), 225 (6), 218 (25), 217 (7), 216 (6), 193 (8), 192 (5), 191 (8), 156 (8), 146 (16), 145 (10), 144 (75), 143 (8), 126 (5), 125 (63), 117 (39), 116 (17), 115 (42), 109 (6), 107 (10), 102 (13), 97 (5), 91 (7), 78 (5), 77 (7), 57 (73). Anal. Calcd for $C_{24}H_{32}N_2O_5S_2$ (492.65): C, 58.51; H, 6.55; N, 5.69. Found: C, 58.46; H, 6.71; N, 5.59.

(+)-(*E*,*S*$_S$,2*S*,3*R*)-5-(*N*-Methyl-*S*-phenylsulfonimidoyl)-3-methyl-2-(2-methylpropane-2-sulfonylamino)-pent-4-enoic Acid Ethyl Ester (2g). Following *GP1*, the reaction of sulfoximine **12d** (970 mg, 4.63 mmol) with *N*-Bus α-imino ester **9c** (1.13 g, 5.11 mmol) resulted in a 99% conversion of **12d** with formation of the crude sulfoximine **2g** as a light brownish solid. Repeated crystallization from ethyl acetate/*n*-pentane (1:4) afforded **2g** (1.35 g, 67%) as a fine white solid: mp

152 °C. $[\alpha]_D$ +32.9 (*c* 0.62, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.08 (d, J = 6.9 Hz, 3H, CH_3), 1.14 (t, J = 7.1 Hz, 3H, OCH_2CH_3), 1.26 (s, 9H, $C(CH_3)_3$), 2.67 (s, 3H, NCH_3), 2.71−2.82 (m, 1H, CH_3-CH), 3.89−4.01 (m, 2H, OCH_2, COCH), 4.01−4.12 (m, 1H, OCH_2), 4.74 (d, J = 10.2 Hz, 1H, NH), 6.38 (d, J = 15.1 Hz, 1H, SCH), 6.75 (dd, J = 15.0, J = 7.8 Hz, 1H, SCHCH), 7.43−7.56 (m, 3H, *m*-Ph, *p*-Ph), 7.81 (m, 2H, *o*-Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.46 (d, C-8), 15.32 (d, C-6), 24.50 (d, C-10), 29.66 (d, NCH_3), 40.27 (d, C-3), 60.71 (u, C-9), 60.85 (d, C-2), 62.29 (u, C-7), 129.02, 129.57 (d, *m*-Ph, *o*-Ph), 132.19 (d, C-5), 132.96 (d, *p*-Ph), 139.00 (u, *i*-Ph), 145.64 (d, C-4), 170.96 (u, C-1). IR (KBr): ν 3064 (s), 2990 (s), 2936 (m), 2874 (m), 2807 (m), 2724 (w), 1736 (s), 1634 (w), 1467 (m), 1446 (m), 1395 (w), 1370 (m), 1316 (s), 1265 (m), 1239 (s), 1209 (m), 1177 (s), 1156 (s), 1124 (s), 1081 (m), 1023 (m), 973 (w), 937 (s), 896 (w), 867 (s), 828 (s), 754 (s), 731 (w), 694 (m), 650 (m), 607 (s), 550 (s), 513 (m), 479 (w) cm^{-1}. MS (EI, 70 eV): *m*/*z* (relative intensity, %) 430 [M^+] (7), 209 (36), 208 (100), 163 (18), 156 (13), 131 (16), 126 (11), 125 (76), 107 (21), 102 (20), 82 (42), 57 (62). Anal. Calcd for $C_{19}H_{30}N_2O_5S_2$ (430.58): C, 53.00; H, 7.02; N, 6.51. Found: C, 52.95; H, 7.22; N, 6.50.

(+)-(*E*,R_S,2*R*,3*S*)- and (+)-(*Z*,R_S,2*R*,3*S*)-[2-(*N*-Methyl-*S*-phenylsulfonimidoyl-methylene-cyclohexyl)-(2-methylpropane-2-sulfonylamino) Acetic Acid Ethyl Ester ((*E*)-8 and (*Z*)-8). Following *GP1*, the reaction of sulfoximine **13** (610 mg, 2.45 mmol) with *N*-Bus α-imino ester **9c** (570 mg, 2.57 mmol) resulted in a 96% conversion of **13** under formation of a crude mixture of sulfoximines (*E*)-**8** and (*Z*)-**8** in a ratio of 83:17 in approximately 90% chemical yield (^{1}H NMR). Recrystallization from ether gave (*E*)-**8** (642 mg, 56%) of 94% de as colorless crystals. Preparative HPLC (ethyl acetate) of the mother liquor afforded (*Z*)-**8** (150 mg, 13%) as a colorless solid.

(*E*)-8. mp 99−101 °C. $[\alpha]_D$ +45.5 (*c* 1.11, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.04 (t, J = 7.1 Hz, 3H, 11-H), 1.33 (s, 9H, 17-H), 1.43 (m, 1H, 6-H), 1.58−1.74 (m, 3H, 5-H/5′-H/4-H), 1.83 (m, 1H, 6′-H), 2.02 (dt, J = 13.3, J = 3.8 Hz, 1H, 7-H), 2.21 (m, 1H, 4′-H), 2.29 (m, 1H, 3-H), 2.65 (s, 3H, NCH_3), 3.45 (m, 1H, 7′-H), 3.49 (dq, J = 7.1, J = 10.7 Hz, 1H, 10-H), 3.93 (dq, J = 7.1, J = 10.7 Hz, 1H, 10′-H), 4.24 (t, J = 10.4 Hz, 1H, 2-H), 4.45 (d, J = 10.2 Hz, 1H, N−H), 6.19 (s, 1H, 9-H), 7.48−7.60 (m, 3H, 14-H/15-H), 7.85 (m, 2H, 13-H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 13.9 (d, C-11), 20.6 (u, C-5), 24.2 (d, C-17), 25.6 (u, C-7), 27.3 (u, C-6), 28.6 (u, C-4), 29.2 (d, NCH_3), 50.0 (d, C-3), 57.2 (d, C-2), 60.1 (u, C-16), 61.4 (u, C-10), 126.7 (d, C-9), 128.6 (d, C-13), 129.2 (d, C-14), 132.4 (d, C-15), 140.5 (u, C-12), 157.2 (u, C-8), 171.3 (u, C-1). MS (EI, 70 eV): *m*/*z* (relative intensity, %) 470 [M^+] (2), 397 (5), 270 (100), 200 (66), 169 (72), 125 (37), 57 (41). IR (KBr): ν 3457 (w), 3061 (m), 2986 (m), 2947 (m), 2906 (m), 2874 (m), 2804 (m), 1740 (s), 1621 (m), 1473 (m), 1448 (m), 1420 (w), 1307 (s), 1239 (s), 1188 (s), 1129 (s), 1107 (s), 1081 (s), 848 (s), 762 (m) cm^{-1}. Anal. Calcd for $C_{22}H_{34}N_2O_5S_2$ (470.66): C, 56.14; H, 7.28; N, 5.95. Found: C, 55.94; H, 7.40; N, 5.75.

(*Z*)-8. mp 57−58 °C. $[\alpha]_D$ +169.1 (*c* 0.51, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.74 (m, 1H, 4-H_{eq}), 1.25 (m, 1H, 6-H_{ax}), 1.29 (t, J = 7.1 Hz, 3H, 11-H), 1.34−1.39 (m, 1H, 5-H_{eq}), 1.36 (s, 9H, 17-H), 1.70 (m, 3H, 5-H_{ax}), 1.89 (m, 1H, 6-H_{eq}), 2.02 (m, 1H, 4-H_{ax}), 2.13 (m, 1H, 7-H_{eq}), 2.50 (m, 1H, 7-H_{ax}), 2.56 (s, 3H, NCH_3), 3.52 (dd, J = 2.5, J = 10.5 Hz, 1H, 3-H), 4.26 (m, 2H, 10-H/10′-H), 4.32 (t, J = 10.3 Hz, 1H, 2-H), 4.87 (d, J = 10.1 Hz, 1H, N−H), 6.34 (d, J = 1.2 Hz, 1H, 9-H), 7.49−7.57 (m, 3H, 14-H/15-H), 7.82 (m, 2H, 13-H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.1 (d, C-11), 19.5 (u, C-5), 24.1 (d, C-17), 27.6 (u, C-4), 28.8 (u, C-6), 29.0 (d, NCH_3), 33.9 (u, C-7), 41.0 (d, C-3), 56.8 (d, C-2), 60.3 (u, C-16), 62.0 (u, C-10), 126.8 (d, C-9), 128.5 (d, C-13), 129.2 (d, C-14), 132.3 (d, C-15), 140.8 (u, C-12), 158.9 (u, C-8), 170.4 (u, C-1). MS (EI, 70 eV): *m*/*z* (relative intensity, %) 470 [M^+] (2), 397 (2), 349 (9), 194 (100), 166 (26), 122 (28), 57 (20). IR (KBr): ν 3284 (m), 3060 (m), 2937 (s), 2871 (m), 2801 (m), 1744 (s), 1624 (m), 1447 (m), 1369 (m), 1313 (s), 1238 (s), 1185 (m), 1124 (s), 1080 (m), 1024 (m), 917 (m), 851 (m), 756 (m) cm^{-1}.

General Procedure for the Synthesis of Imidazolidinones 15 (*GP2*). *n*BuLi (1.37 mL of 1.6 M solution in *n*-hexane, 2.2 mmol) was added dropwise at −78 °C to a solution of the allylic sulfoximine **12** (2 mmol) in THF (20 mL). After the mixture was stirred at −78 °C for 30 min, $ClTi(OiPr)_3$ (4 mmol) was added, and stirring at this temperature was continued for 30 min. The mixture was then warmed to room temperature within 1 h, recooled to −78 °C, and treated with the *N*-Ts α-imino ester **9a** (4.4 mmol). The mixture was slowly warmed to room temperature within 16 h, poured into saturated aqueous $(NH_4)_2CO_3$ (300 mL), and extracted with ethyl acetate (200 mL). The combined organic phase was dried ($MgSO_4$), concentrated in vacuo, and the remaining yellow oil was taken up in ether (75 mL). Evaporation of the ether in vacuo afforded a mixture of the amino acid derivative **2** and the imidazolidinone **15** in a ratio of approximately 2:3 (^{1}H NMR) as a solid material. Preparative HPLC (cyclohexane/ethyl acetate, 1:4) gave the pure amino acid derivative and the pure imidazolidinone derivative.

(+)-(*E*,S_S,4*S*,1′*R*)-4-[3′-(*N*-Methyl-*S*-phenylsulfonimidoyl)-1′-cyclohexyl-allyl]-5-oxo-1,3-bis-(toluene-4-sulfonyl)-imidazolidine-2-carboxylic Acid Ethyl Ester (15a). Following *GP2*, the reaction of sulfoximine **12a** (530 mg, 1.91 mmol) with *N*-Ts α-imino ester **9a** (1.07 g, 4.20 mmol) resulted in a 100% conversion of **12a** under formation of a mixture of the amino acid **2a** and imidazolidinone **15a** in a ratio of 1:1. Preparative HPLC afforded **2a** (159 mg, 30%) and **15a** (282 mg, 20%) as colorless crystals. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.8−0.93 (m, 1H, *c*C_6H_{11}), 0.98−1.08 (m, 2H, *c*C_6H_{11}), 1.18−1.35 (m, 3H, *c*C_6H_{11}), 1.30 (t, J = 7.0 Hz, 3H, OCH_2CH_3), 1.54−1.94 (m, 5H, *c*C_6H_{11}), 2.35 (m, 1H, 1′-H), 2.39 (s, 3H, *p*-tol), 2.44 (s, 3H, *p*-tol), 2.75 (s, 3H, NCH_3), 4.09 (d, J = 10.4 Hz, 1H, 4-H), 4.25 (q, J = 7.0 Hz, 2H, OCH_2CH_3), 5.91 (s, 1H, 2-H), 5.93 (d, J = 14.9 Hz, 1H, 3′-H), 6.60 (dd, J = 10.8, J = 14.9 Hz, 2′-H), 7.10 (m, 2H, *p*-tol), 7.34 (m, 2H, *p*-tol), 7.52 (m, 2H, *m*-Ph), 7.59 (m, 1H, *p*-Ph), 7.61 (m, 2H, *p*-tol), 7.70 (m, 2H, *p*-tol), 7.89 (m, 2H, *o*-Ph). ^{13}C NMR (125 MHz, $CDCl_3$, partial signal set, determined by GHSQC pulse sequence): δ 13.7 (OCH_2CH_3), 21.6 (*p*-tol), 26.0 (*c*C_6H_{11}), 26.7 (*c*C_6H_{11}), 29.2 (NCH_3), 31.9 (*c*C_6H_{11}), 37.4 (*c*C_6H_{11}), 49.8 (C-1′), 61.8 (C-4), 63.3 (OCH_2CH_3), 127.6 (*p*-tol), 128.5 (*o*-Ph, *p*-tol), 128.9 (*m*-Ph), 129.2 (*p*-tol), 130.7 (*p*-tol), 132.3 (*p*-Ph).

(+)-(*E*,S_S,4*S*,1′*R*)-4-[3′-(*N*-Methyl-*S*-phenylsulfonimidoyl)-1′-isopropyl-allyl]-5-oxo-1,3-bis-(toluene-4-sulfonyl)-imidazolidine-2-carboxylic Acid Ethyl Ester (15b). Following *GP2*, the reaction of sulfoximine **12b** (305 mg, 1.29 mmol) with the *N*-Ts α-imino ester **9a** (640 mg, 2.84 mmol) resulted in a 100% conversion of **12b** under formation of a mixture of the amino acid **2b** and imidazolidinone **15b** in a ratio of 7:13. Preparative HPLC afforded **2b** (85 mg, 24%) and **15b** (315 mg, 35%) as colorless crystals: mp 128−129.5 °C. $[\alpha]_D$ +40.1 (*c* 0.61, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.81 (d, J = 6.7 Hz, 3H, $CH(CH_3)_2$), 0.90 (d, J = 6.7 Hz, 3H, $CH(CH_3)_2$), 1.29 (t, J = 7.2 Hz, 3H, OCH_2CH_3), 2.24 (dsept, J = 3.0, J = 6.7 Hz, 1H, $CH(CH_3)_2$), 2.37 (m, 1H, 1′-H), 2.37 (s, 3H, *p*-tol), 2.42 (s, 3H, *p*-tol), 2.74 (s, 3H, NCH_3), 4.05 (d, J = 10.7 Hz, 4-H), 4.24 (dq, J = 1.7, J = 7.1 Hz, 2H, OCH_2CH_3), 5.89 (s, 1H, 2-H), 5.94 (d, J = 14.9 Hz, 1H, 3′-H), 6.59 (dd, J = 10.4, J = 14.9 Hz, 2′-H), 7.08 (m, 2H, *p*-tol), 7.33 (m, 2H, *p*-tol), 7.49−7.54 (m, 2H, *m*-Ph), 7.55−7.59 (m, 1H, *p*-Ph), 7.60 (m, 2H, *p*-tol), 7.69 (m, 2H, *p*-tol), 7.88 (m, 2H, *o*-Ph). ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.9 (q, J = 127 Hz, OCH_2CH_3), 15.9 (q, J = 124 Hz, $CH(CH_3)_2$), 21.3 (q, J = 124 Hz, $CH(CH_3)_2$), 21.70 (q, J = 127 Hz, *p*-tol), 21.72 (q, J = 127 Hz, *p*-tol), 27.4 (d, J = 131 Hz, $CH(CH_3)_2$), 29.4 (q, J = 138 Hz, NCH_3), 50.0 (d, J = 134 Hz, C-1′), 62.4 (d, J = 148 Hz, C-4), 63.3 (t, J = 150 Hz, OCH_2CH_3), 71.6 (d, J = 162 Hz, C-2), 127.7 (d, J = 166 Hz, *p*-tol), 128.5 (d, J = 169 Hz, *o*-Ph), 128.6 (d, J = 169 Hz, *p*-tol), 128.9 (d, J = 162 Hz, *m*-Ph), 129.2 (d, J = 162 Hz, *p*-tol), 130.7 (d, J = 162 Hz, *p*-tol), 131.9 (s,

i-Ph), 131.9 (d, $J = 162$ Hz, *p*-Ph), 133.8 (s, *i*-Ph), 133.8 (d, $J = 180$ Hz, C-3′), 139.5 (s, *i*-Ph), 140.9 (d, $J = 159$ Hz, C-2′), 145.8 (s, *i*-Ph), 146.0 (s, *i*-Ph), 166.2 (s, C-5), 166.9 (s, $COOC_2H_5$). MS (FAB): *m*/*z* (relative intensity, %) 702 [$M^+ + 1$] (14), 397 (50), 303 (64), 133 (100). IR (KBr): ν 3061 (w), 2963 (m), 2931 (m), 2874 (w), 2804 (w), 1758 (s), 1631 (w), 1597 (m), 1448 (m), 1374 (s), 1246 (s), 1203 (s), 1172 (s), 1150 (s), 1087 (m), 668 (s) cm^{-1}. Anal. Calcd for $C_{33}H_{39}N_3O_8S_3$ (701.88): C, 56.47; H, 5.60; N, 5.99. Found: C, 56.13; H, 5.48; N, 5.73.

(+)-(*E*)-(*S*$_S$,2*S*,3*R*)-2-Amino-5-(*N*-methyl-*S*-phenylsulfonimidoyl)-3-cyclohexyl-pent-4-enoic Acid Ethyl Ester (H-2d). *N*-Bus amino acid **2d** (350 mg, 0.70 mmol) was added to 0.1 M CF_3SO_3H in CH_2Cl_2 (40 mL, 4 mmol), and the resulting mixture was stirred first at 0 °C for 1 h and then at room temperature for 16 h. The mixture was then poured into 2 N NaOH (2 mL)/aqueous $(NH_4)Cl$ (20 mL), and the resulting mixture was extracted with CH_2Cl_2. Concentration of the organic phases in vacuo gave amino acid H-**2d** (255 mg, 96%) of 99% purity (^{1}H NMR) as pale yellow crystals: mp 67−69 °C. $[\alpha]_D$ +13.5 (*c* 1.28, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.75−1.25 (m, 5H, *c*C_6H_{11}), 1.05 (t, $J = 7.1$ Hz, 3H, OCH_2CH_3), 1.46 (sb, 2H, NH_2), 1.52−1.72 (m, 6H, *c*C_6H_{11}), 2.17 (dt, $J = 6.6$, $J = 10.7$ Hz, 1H, 3-H), 2.68 (s, 3H, NCH_3), 3.45 (d, $J = 7.1$ Hz, 1H, 2-H), 3.68 (dq, $J = 7.1$, $J = 10.7$ Hz, 1H, OCH_2CH_3), 3.86 (dq, $J = 7.1$, $J = 10.7$ Hz, 1H, OCH_2CH_3), 6.26 (d, $J = 15.1$ Hz, 1H, 5-H), 6.62 (dd, $J = 10.8$, $J = 15.0$ Hz, 1H, 4-H), 7.42−7.52 (m, 3H, *m*-, *p*-Ph), 7.80 (m, 2H, *o*-Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (d, OCH_2CH_3), 26.2 (u, *c*C_6H_{11}), 26.3 (u, *c*C_6H_{11}), 29.3 (u, *c*C_6H_{11}), 29.5 (d, NCH_3), 31.5 (u, *c*C_6H_{11}), 37.4 (d, *c*C_6H_{11}), 52.8 (d, C-3), 54.9 (d, C-2), 60.7 (u, OCH_2CH_3), 128.3 (d, *o*-Ph), 129.1 (d, *m*-Ph), 132.3 (d, *p*-Ph), 132.6 (d, C-5), 139.4 (u, *i*-Ph), 144.6 (d, C-4), 174.1 (u, C-1). MS (CI, isobutane): *m*/*z* (relative intensity, %) 379 ($M^+ + 1$, 100). MS (EI, 70 eV): *m*/*z* (relative intensity, %) 378 [M^+] (0.5), 350 (5), 305 (38), 277 (56), 248 (87), 231 (37), 156 (95), 125 (100). IR (KBr): ν 3384 (m), 3320 (w), 3052 (m), 2927 (s), 2853 (s), 2798 (m), 1710 (s), 1620 (m), 1582 (m), 1448 (m), 1383 (m), 1243 (s), 1196 (s), 1144 (s), 1104 (s), 1081 (s), 1023 (m) cm^{-1}. HRMS (EI, 70 eV) calcd for $C_{17}H_{25}N_2OS$: 305.168761. Found: 305.168800.

(+)-(*E*)-(*S*$_S$,2*S*,3*R*)-3-Isopropyl-5-phenyl-2-(2-methylpropane-2-sulfonylamino)-pent-4-enoic Acid Ethyl Ester (Bus-1). Ni(dppp)Cl_2 (125 mg, 0.23 mmol) was added at room temperature to a stirred solution of $ZnPh_2$/2MgBrCl (0.97 mL of 3.5 M solution in ether, 3.4 mmol) in ether (20 mL). After the mixture was stirred at room temperature for 30 min, a solution of sulfoximine **2e** (320 mg, 0.7 mmol) in ether (20 mL) was added, and stirring of the heterogeneous reaction mixture at room temperature was continued for 4.5 d. The mixture was then poured into saturated aqueous NH_4Cl (150 mL) and extracted with ethyl acetate (150 mL). The combined organic phases were filtered through Celite, dried ($MgSO_4$), and concentrated in vacuo. Preparative HPLC (cyclohexane/ethyl acetate, 1:1) of the residue afforded **2e** (103 mg, 32%) and amino acid Bus-**1** (156 mg, 48%) as colorless crystals: mp 99−101 °C. $[\alpha]_D$ +45.5 (*c* 1.11, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (d, $J = 6.6$ Hz, 3H, $CH(CH_3)_2$), 1.04 (d, $J = 6.6$ Hz, 3H, $CH(CH_3)_2$), 1.20 (t, $J = 7.1$ Hz, 3H, OCH_2CH_3), 1.48 (s, 9H, $C(CH_3)_3$), 1.97 (oct, $J = 6.6$ Hz, 1H, $CH(CH_3)_2$), 2.19 (dt, $J = 6.9$, $J = 10.0$ Hz, 1H, 3-H), 4.15 (dq, $J = 2.6$, $J = 7.1$ Hz, 2H, OCH_2CH_3), 4.23 (dd, $J = 6.7$, $J = 10.6$ Hz, 1H, 2-H), 4.52 (d, $J = 10.7$ Hz, 1H, NH), 5.89 (dd, $J = 10.3$, $J = 15.8$ Hz, 1H, 4-H), 6.42 (d, $J = 15.7$ Hz, 1H, 5-H), 7.19−7.25 (m, 1H, *p*-Ph), 7.27−7.35 (m, 4H, *o*-, *m*-Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4 (d, OCH_2CH_3), 19.7 (d, $CH(CH_3)_2$), 21.4 (d, $CH(CH_3)_2$), 24.4 (d, $C(CH_3)_3$), 28.5 (d, $CH(CH_3)_2$), 56.1 (d, C-3), 58.5 (d, C-2), 60.2 (u, $C(CH_3)_3$), 61.5 (u, OCH_2CH_3), 126.0 (d, C-4), 126.4 (d, *o*-Ph), 128.1 (d, *p*-Ph), 128.6 (d, *m*-Ph), 134.6 (d, C-5), 136.7 (u, *i*-Ph), 171.5 (u, C-1). MS (CI, methane): *m*/*z* (relative intensity, %) 382 [$M^+ + 1$] (17), 262 (100), 159 (11). IR (KBr): ν 3260 (s), 3060 (w), 3029 (w), 2964 (s), 2931 (m), 2897 (m), 2875 (m), 1721 (s), 1600 (w), 1452 (m), 1394 (m), 1374 (m), 1330 (s), 1310 (s), 1270 (s), 1132 (s), 1092 (s), 1033 (s), 908 (s), 752 (m) cm^{-1}. Anal. Calcd for $C_{20}H_{31}N_1O_4S_1$ (381.53): C, 62.96; H, 8.19; N, 3.67. Found: C, 62.77; H, 8.29; N, 3.43.

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Supporting Information Available: X-ray crystallographic data of **2a**, **2e**, and (*E*)-**8**, and NMR spectra of **2c**, **2d**, H-**2d**, **9b**, **11c**, and **15a** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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