Asymmetric Synthesis of Protected β-Substituted and β,β-Disubstituted β-Amino Acids Bearing Branched Hydroxyalkyl Side Chains and of Protected 1,3-Amino Alcohols with Three Contiguous Stereogenic Centers from Allylic Sulfoximines and Aldehydes

Hans-Joachim Gais,*^[a] Ralf Loo,^[a] Daniel Roder,^[a] Parthasarathi Das,^[a] and Gerhard Raabe^[a]

Keywords: Amino alcohols / Amino acids / Asymmetric synthesis

We describe a new method for the asymmetric synthesis, from allylic sulfoximines and aldehydes, of N,O-protected, cyclic and acyclic, β -substituted and β , β -disubstituted δ -hydroxy-β-amino acids and of N,O-protected 1,3-amino alcohols, both possessing three contiguous stereogenic centers. Treatment of enantiomerically pure, acyclic allylic sulfoximines with aldehydes after successive lithiation and titanation afforded sulfonimidoyl-substituted homoallylic alcohols with high regio- and diastereoselectivities. Diastereomerically pure, cyclic, sulfonimidoyl-substituted homoallylic alcohols were synthesized in a similar manner from the corresponding enantiomerically pure, cyclic allylic sulfoximines and isobutyraldehyde. A highly diastereoselective amination of the sulfonimidoyl-substituted homoallylic alcohols with the generation of secondary and tertiary C atoms and formation of the sulfonimidoyl-substituted, protected 1,3-amino alcohols (oxazinones) was achieved by the carbamate method, through cyclization of the corresponding carbamates after their lithiation with nBuLi. The sulfonimidoyl-substituted, monocyclic and bicyclic oxazinones were converted into protected, acyclic and cyclic, β -substituted and β , β -disubstituted β-amino acids and protected 1,3-amino alcohols by two different routes: the carbanion route and the substitution route. The carbanion route involves: (1) a double lithiation of the protected β -amino sulfoximines, (2) treatment of the dilithiated sulfoximines with electrophiles, and (3) reductive removal of the sulfonimidoyl group. By the carbanion route, double lithiation of the sulfonimidoyl-substituted oxazinones with *n*BuLi gave the corresponding dilithium salts, which reacted readily with a number of electrophiles to give the corresponding a-substituted sulfoximines in good yields. Reduction of the sulfoximines with Raney nickel afforded the corresponding protected monocyclic and bicyclic 1,3-amino alcohols and the protected acyclic and cyclic β -amino acids in good yields. The substitution route involves: (1) a facile substitution of the sulfonimidoyl group by a Cl atom, and (2) a substitution of the Cl atom of the protected β-amino chlorides by a cyano group. Treatment of the sulfoximines with ClCO₂Me readily afforded the corresponding β -amino chlorides in good yields, and so treatment of alkyl sulfoximines with chloroformates seems to be a general method for the replacement of an N-methylsulfonimidoyl group by a Cl atom. Introduction of a cyano group was achieved through treatment of chlorides with NaCN, which gave the corresponding β -amino nitriles in good yields. Finally, hydrolysis of the nitriles afforded the protected acyclic and cyclic, β substituted and $\beta_{\beta}\beta_{\beta}$ -disubstituted β_{β} -amino acids. Treatment of the protected β -amino sulfoximines with ClCO₂Me gave – besides the corresponding chlorides – methyl (S)-N-phenylsulfinylcarbamate with \geq 99% ee in good yield. Treatment of the sulfinamide with MeMgCl afforded (S)-methyl phenyl sulfoxide with 97% ee, and this could be converted with complete retention of configuration into (S)-N,S-dimethyl-Sphenylsulfoximine, the starting material for the synthesis of the allylic sulfoximines used in this work.

(© Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, Germany, 2003)

Background and Synthetic Concept

 β -Amino acids have attracted much attention^[1] because of their incorporation in naturally occurring peptides and other biologically active compounds and their utilization as starting materials for the synthesis of β -lactams^[2] and β peptides,^[3] oligomers of β -amino acids. This has resulted in ever-growing interest in the asymmetric synthesis of β -amino acids.^[4] Cyclic and acyclic β , β -disubstituted β -amino acids are currently of much interest because of anticipated unusual structural and pharmacological properties of their derived β -peptides.^[1i,3b,3c,3e] While numerous imaginative and efficient asymmetric syntheses of β -substituted β -amino acids have been described,^[1,4] methods for the asymmetric synthesis of β , β -disubstituted β -amino acids are scarce.^[5] The well established Arndt–Eistert homologation of α amino acids, for example, fails in the case of α , α -disubstituted α -amino acids.^[1i] Methods described for the asymmetric synthesis of β , β -disubstituted β -amino acids include the

 [[]a] Institut für Organische Chemie der Rheinisch-Westfälischen Technischen Hochschule-(RWTH) Aachen, Prof.-Pirlet-Str. 1, 52056 Aachen, Germany Fax (internat.) +49-(0)241/8092665 E-mail: Gais@RWTH-Aachen.de

addition of nucleophiles to N-sulfinvlimines,^[5a-5c] the hydrogenation of N-sulfinylimine-derived aziridines,^[5d] and the functionalization of aspartic acid derivatives.^[5e] While the sulfinylimine method has been restricted to the synthesis of β -methyl-substituted derivatives and seems to be limited by syn and anti isomerization of ketosulfinimines, the selectivities of the aziridine method tend to be variable, while the aspartic acid method is confined to particular examples. As well as β , β -disubstituted derivatives, β -amino acids bearing hydroxy groups in their side chains are of particular interest. Hydroxy-β-amino acids occur as structural motifs in natural products and have been used as starting materials for the synthesis of biologically active compounds.[6a-6i,6k] The most interesting application of these functionalized β -amino acids, however, should be in the field of β -peptides,^[6j] in particular in the synthesis of glycosylated β -peptides.^[6],6m] Glycosylated α -peptides,^[7] oligomers of α -amino acids, are of high biological relevance, and so their glyco-β-peptide analogues may also exhibit interesting biological activities and structures.

We felt that β -substituted and β , β -disubstituted δ hydroxy- β -amino acids of type I, with three contiguous stereogenic centers (Figure 1), ought to be particularly attractive as starting materials for the synthesis of glyco-Bpeptides and peptide mimetics. Variation of R^1 to R^3 and the incorporation of R^1 and R^2 of I into a cyclic skeleton should provide a high degree of synthetic and structural flexibility. Asymmetric syntheses of acyclic derivatives of I bearing hydroxy groups at their γ -positions (R¹ = OH)^[6a-6c] had been accomplished previously by use of the corresponding δ -hydroxy- α , β -unsaturated esters as starting materials and application of a stereoselective amination by the Hirma-Itô carbamate method. The asymmetric synthesis of β -amino acids of type I bearing functions other than a hydroxy group at the γ -position by this route, however, has with a few exemptions not been achieved.^[6c,6i] This is perhaps due to the lack of direct methods for the asymmetric synthesis of the required γ -substituted δ hydroxy- α , β -unsaturated esters from aldehydes,^[8,9] which necessitates the use of indirect, albeit efficient, methods such as aldol or allylation reactions and Wittig homologation.[10]

Structurally closely related to I are the 1,3-amino alcohols IV, which have also aroused much attention because of their occurrence as structural motifs in natural products,^[11] their use as starting materials for the synthesis of, for example, analgesics,^[12] and their demonstrated or potential application as chiral auxiliaries and ligands in asymmetric synthesis.^[13] As a consequence, much activity has been directed towards the asymmetric synthesis of 1,3-amino alcohols. While a number of methods have been developed,^[14,15] those suitable for the asymmetric synthesis of type IV compounds with three contiguous stereogenic centers, situated either in a cyclic or in an acyclic carbon skeleton, are much less abundant.^[16] Known methods include: (1) the addition of amino-substituted allenylindium,^[16f] allylindium,^[16g] and allyltitanium^[16c] compounds (derived from α -amino acids, for example) to aldehydes, (2) the re-



Figure 1. The carbanion and the substitution routes from δ -hydroxy- α , β -unsaturated sulfoximines to β -amino acids and 1,3-amino alcohols

duction of β -amino ketones,^[16a,16b,16e] prepared through reduction of chiral dihydropyrimidines^[16a,16b] or by asymmetric Mannich-type reactions,^[17] and (3) asymmetric 1,3-dipolar cycloadditions with alkenes.^[14b,14f,16d] While the selectivities of the allenylmetal and allylmetal routes tend to be variable, access to β -amino ketones with two stereogenic C atoms and a broad range of substituents is limited at present, and the 1,3-dipolar cycloaddition gives access only to 1,3-amino alcohols with particular substituents. Thus, in view of the current strong interest both in β -amino acids and in 1,3-amino alcohols, we considered it desirable to have a method for the asymmetric synthesis of the β -amino acids I and the 1,3-amino alcohols IV, both with three contiguous stereogenic centers. In our view, sulfonimidoyl-substituted homoallylic alcohols of type VIII should be particularly attractive as starting materials for the asymmetric synthesis of I and IV.^[18,19] Firstly, cyclic and acyclic derivatives of VIII with various substituents, including sterically demanding ones, are readily available enantiomerically and diastereomerically pure through treatment of the corresponding chiral, sulfonimidoyl-substituted bis(allyl)titanium complexes IX with aldehydes.^[18] Secondly, the sulfonimidoyl group, because of its almost unique array of features - including nucleofugacity, basicity, nucleophilicity, carbanion-stabilizing and electron-withdrawing character, and favorable redox potential - offers a number of synthetic possibilities for the introduction of substituents and also for its replacement.^[20] Some of these properties of the sulfonimidoyl group have already been advantageously exploited in the conversion of VIII ($R^2 = H$) into the corresponding enantiomerically and diastereomerically pure branched homopropargylic alcohols.^[21] Synthesis of both the β-amino acids I and the 1,3-amino alcohols IV from VIII would require in a first step the installation of the amino group of the target molecules with the stereoselective generation of a secondary or tertiary C atom. This transformation could perhaps be accomplished through cyclization of the carbamates^[6b] derived from the hydroxyalkenyl sulfoximines VIII with formation of N,O-protected δ -hydroxy- β -amino sulfoximines VII, since alkenyl sulfoximines are known to be good Michael acceptors for N-nucleophiles.^[22] In a second step, the sulfonimidoyl group of VII would have to be replaceable by various groups, including a carboxy group. Because of the ability of the sulfonimidoyl group to act not only to stabilize a carbanion but also as a nucleofuge,^[20] two different but complementary routes, the carbanion route and the substitution route, for the achievement of this goal could be envisaged. The carbanion route would include: (1) double deprotonation of the protected β -amino sulfoximines VII at the N atom and at the C α atom with formation of the dilithiated sulfoximines III, (2) treatment of III with electrophiles including ClCO₂R with formation of the substituted sulfoximines II, and (3) reduction of II with formation of I or IV after deprotection. While the feasibility of (1) lithiation of alkyl sulfoximines, (2) the facile reaction of lithiated alkyl sulfoximines with electrophiles, and (3) the reduction of alkyl sulfoximines have been amply demonstrated,^[20] nothing is known, however, about the stability of the lithioalkyl sulfoximines III with potential nucleofuges at their β -positions. The substitution route would encompass: (1) substitution of the sulfonimidoyl group of VII, with formation of the protected β -amino chlorides VI by the chloroformate method developed recently in our laboratories,^[23,24] and (2) the replacement of the Cl atom of VI, with the formation of derivatives V, upon treatment with various nucleophiles, including cyanide, to afford either I or IV after deprotection. Although the substitution of a

sulfonimidoyl group by a Cl atom by treatment with ClCO₂R works well for simple alkyl and allyl sulfoximines, nothing is known about the feasibility of the substitution of sulfoximines of type **VII** with secondary or tertiary carbon atoms at their β -positions. The nucleophilic substitution of chlorides **VI** by cyanide, for example, should pose no problem in the case of $R^2 = H$,^[4a] but might face one in the case of $R^2 \neq H$ and the cyclic derivatives of **VI**.

In this paper we describe a new method for the asymmetric synthesis of *N*,*O*-protected, cyclic and acyclic δ -hydroxy β -amino acids of type **I** and of *N*,*O*-protected, cyclic and acyclic 1,3-amino alcohols of type **IV** from the bis(allyl)titanium complexes **IX** and aldehydes.^[25] This adds considerably to the synthetic usefulness of complexes **IX**, which have previously been shown to be excellent reagents not only for the asymmetric synthesis of branched homopropargylic alcohols from aldehydes,^[21] but also for that of branched γ , δ unsaturated α -amino acids from *N*-sulfonyl α -imino esters.^[26]

Results and Discussion

I. Stereoselective Synthesis and Amination of δ -Hydroxy- α , β -Unsaturated Sulfoximines

Treatment of the enantiomerically and diastereomerically pure homoallylic alcohols 2a-c, synthesized in good yields from the allylic sulfoximines $1a-c^{[18c,27-29]}$ and the corresponding aldehydes as described previously, with trichloroacetyl isocyanate and subsequent cleavage of the N-trichloroacetyl carbamates 3a-c with aqueous ammonia gave a mixture of the (Z)-configured carbamate (Z)-4a and the (E)-configured carbamate (E)-4a in a ratio of 3:1, the pure (Z)-configured carbamate (Z)-4b, and a mixture of the (Z)configured carbamate (Z)-4c and the (E)-configured carbamate (E)-4c in a ratio of 4.7:1, in 85%, 90% and 92% yields, respectively (Scheme 1). Carbamates $4\mathbf{a} - \mathbf{c}$ were purified by chromatography, which also allowed separation of carbamates (Z)-4c and (E)-4c. The N-trichloroacetyl carbamates 3a-c were not generally isolated, but ¹H NMR spectroscopy of the reaction product derived from alcohol 2b and the isocyanate showed the formation of a mixture of (Z)-3b and (E)-3b in a ratio of approximately 11:1. This indicates that the isomerization of the C=C double bond has already taken place at the stage of the N-trichloroacetyl carbamates. Isomerization of the (Z) isomer to the more stable (E) isomer perhaps occurs through a reversible addition of the N atom of the fairly acidic trichloroacetyl carbamate group to the activated double bond after proton transfer to the basic sulfonimidoyl group. Treatment of the mixture of carbamates (Z)-4a and (E)-4a, and also of the pure carbamates (Z)-4b and (Z)-4c, each with 2-3 equiv. of *n*BuLi at -78 °C and warming of the reaction mixtures to room temperature resulted in highly diastereoselective cyclization reactions ($\geq 95\%$ de) and afforded the oxazinones 5a-c after aqueous workup, each as a single diastereomer, in 93%, 94%, and 83% yields, respectively.^[30] The configuration of the newly generated stereogenic center of

oxazinone **5b** was determined indirectly by X-ray crystal structure analysis of a derivative (vide infra). ¹H NMR spectroscopy of oxazinones **5a**–**c** showed that oxazinones **5a** and **5c** also have the same configuration as **5b**. Oxazinones **5a**–**c** are characterized by high magnitudes of the vicinal coupling constants for all protons in their oxazinone rings, which clearly demonstrates their *trans-trans* relationships. In solution, according to the NMR and IR data, oxazinones **5a**–**c** preferentially if not exclusively adopt a structure of type **5-A**, characterized by an intramolecular hydrogen bond between the N atoms of the oxazinone ring and the sulfonimidoyl group and a conformation of the oxazinone ring in which all substituents are in pseudoequatorial positions. A structure of the type was also found in the crystal in the case of the derivative of **5b** (vide infra).



Scheme 1. Amination of acyclic δ -hydroxy- α , β -unsaturated sulfoximines with formation of a secondary C atom

Formation of the diastereomerically pure oxazinone 5a from the mixture of carbamates (Z)-4a and (E)-4a points to a stereoselective cyclization of both carbamates with the same sense and with similar degrees of asymmetric induction (stereoconvergence). In order to test this hypothesis, the cyclization of the (E)-configured carbamate (E)-4c was

also studied. Treatment of (E)-4c with *n*BuLi under the same conditions as used in the case of (Z)-4c resulted in a highly stereoselective cyclization reaction ($\geq 95\%$ de) to give oxazinone 5c as a single diastereomer in 82% yield. These results indicate that the formation of (E/Z) mixtures in the case of 4a and 4c is not detrimental to the success of the highly stereoselective amination of 2a and 2c.

Sulfoximines 5a-c can serve as starting materials only for the synthesis of acyclic β -amino acids of type I (R² = H) and of acyclic 1,3-amino alcohols of type IV ($R^2 = H$) (cf. Figure 1). Synthesis of acyclic β , β -disubstituted β -amino acids of type I ($\mathbb{R}^2 \neq H$) and of acyclic 1.3-amino alcohols of type IV ($\mathbb{R}^2 \neq H$) requires the successful extension of the highly selective hydroxyalkylation of the monosubstituted bis(allyl)titanium complexes IX ($R^2 = H$) with aldehydes to that of the disubstituted titanium complexes IX ($R^2 \neq H$). The hydroxyalkylation of the allylic sulfoximine (E)-6^[27] was therefore studied (Scheme 2). Titanation of the allylic sulfoximine (E)-6 with ClTi(OiPr)3 after deprotonation with *n*BuLi furnished the corresponding bis(allyl)titanium complex, which upon treatment with isobutyraldehyde gave the *anti*-configured homoallylic alcohol (Z)-7 with high regioselectivity ($\geq 95\%$) and diastereoselectivity $(\geq 95\% de)$, isolated as a single diastereomer in 59% yield. The allylic sulfoximine (E)-6 was recovered in 25% yield. The depicted configuration of (Z)-7 was determined by Xray crystal structure analysis (Figure 2).



Scheme 2. Amination of acyclic (*E*)-configured δ -hydroxy- α , β -unsaturated sulfoximines with formation of a tertiary C atom

Successive treatment of alcohol (Z)-7 with trichloroacetyl isocyanate and aqueous ammonia afforded carbamate (Z)-8 in 89% yield. Besides (Z)-8, a small amount of the corresponding N-trichloroacetyl carbamate was also isolated. To our delight, cyclization of carbamate (Z)-8 upon treatment with *n*BuLi also proceeded with high diastereoselectivity (\geq 95% *de*) to give the oxazinone 9 as a single diastereomer in 84% yield after aqueous workup. The configuration of 9 was verified by X-ray crystal structure analysis (Figure 3). Interestingly, sulfoximine 9 features an intramolecular hydrogen bond in the crystal, between the N atom of the oxazinone ring and the O atom of the sulfoximine group incorporated in a six-membered ring. In the absence of a steri-



Figure 2. Structure of the δ -hydroxy- α , β -unsaturated sulfoximine (*Z*)-7 in the crystal

cally demanding substituent at the N atom of the sulfonimidoyl group^[19a] it is normally the N atom and not the O atom that engages in hydrogen bonding with hydroxy groups, as demonstrated by 2a-c, 5a-c, a derivative of **5b** (vide infra), and other sulfoximines.^[18c] Formation of a hydrogen bond to the N atom of **9** is perhaps less favorable than to the O atom because of an otherwise resulting steric 1,3-interaction between the methyl group at the C atom and the *S*-phenyl group.



Figure 3. Structure of sulfonimidoyl-substituted 1,3-amino alcohol derivative 9 in the crystal; H···O1 223.3, N2···O1 297.9(3), N2–H 97.1 pm, N2–H···O1 132.7°

The cyclization of both carbamates (Z)-4c and (E)-4c, each possessing a disubstituted double bond, occurred with the same sense and with the same high degree of asymmetric induction. Although the synthesis of carbamate (Z)-8, with a trisubstituted double bond, was not accompanied by formation of the isomeric carbamate (E)-8, we were interested in whether (E)-8 would also selectively give oxazinone 9 upon treatment with *n*BuLi. The synthesis of (E)-8 was accomplished as shown in Scheme 3. Thus, treatment of the silyl ether (Z)-10, derived from alcohol (Z)-7, with MeLi in Et_2O at -35 °C initially afforded the alkenyllithium derivative (Z)-11, which rapidly isomerized to (E)-11. Protonation of (E)-11 with water yielded the (E)-configured alkenyl sulfoximine (E)-10 in 93% yield based on (Z)-10. Deprotection of the silyl ether (E)-10 gave alcohol (E)-7, which was converted in two steps into carbamate (E)-8 (78% yield based on (E)-10). Cyclization of carbamate (E)-8 under the same conditions as employed for that of (Z)-8 delivered a mixture of the oxazinones 9 and *epi*-9 in a ratio of 4.4:1 in 76% yield. Thus, cyclization of (E)-8 occurred with a lower diastereoselectivity than that of the isomer (Z)-8.



Scheme 3. Amination of acyclic (*Z*)-configured δ -hydroxy- α , β -unsaturated sulfoximines with formation of a tertiary C atom

Having been shown that a stereoselective amination of acyclic homoallylic alcohols of type VIII with generation of secondary and tertiary carbon atoms can be accomplished efficiently by the carbamate method, its extension to cyclic homoallylic alcohols of type VIII was studied. Firstly, the feasibility of a regio- and stereoselective synthesis of the cyclic five-membered homoallylic alcohol 13a was examined (Scheme 4). Treatment of a mixture of $Ti(OiPr)_4$ and the corresponding bis(allyl)titanium complex, prepared from the cyclopentenyl sulfoximine $12a^{[29]}$ by lithiation and subsequent titanation with one equivalent of ClTi(OiPr)₃, with isobutyraldehyde proceeded with high regioselectivity $(\geq 95\%)$ and diastereoselectivity $(\geq 95\% de)$ to give the homoallylic alcohol 13a, which was purified through conversion into the corresponding triethylsilyl ether, as a single diastereomer in 68% yield. The diastereomerically pure cyclic six-membered homoallylic alcohol 13b was obtained from the allylic sulfoximine 12b^[31] as described previously.^[18c] Successive treatment of alcohols 13a and 13b



Scheme 4. Amination of cyclic sulfonimidoyl-substituted homoallylic alcohols with formation of a tertiary C atom

with trichloroacetyl isocyanate and aqueous ammonia gave carbamates **14a** and **14b**, respectively, both in 90% yield; small amounts of the corresponding *N*-trichloroacetyl carbamates were also isolated. The cyclizations of carbamates **14a** and **14b** also occurred with high diastereoselectivities (\geq 95% *de*) upon treatment with 2 equiv. of *n*BuLi and gave the bicyclic oxazinones **15a** and **15b**, respectively, each as a single diastereomer, in 80% and 84% yields. The configuration of **15b** was determined indirectly by X-ray crystal structure analysis of derivatives (vide infra).

Stereochemical Consideration of the Intramolecular Amination

The formation of the oxazinones from the corresponding carbamates (cf. Schemes 1-4) most probably starts with deprotonation of the amino groups, with formation of the lithium salts 4-Li, 8-Li, and 14-Li, respectively (Figure 4).^[32] These lithium salts then undergo cyclization to give the C-lithiated sulfoximines 5-Li_C, 9-Li_C, and 15-Li_C, respectively.^[33,34] Since the acidity of the carbamates is much higher than that of alkyl sulfoximines,^[35] the lithiated sulfoximines 5-Li_C, 9-Li_C, and 15-Li_C would be expected to undergo transmetalation, with formation of the O-lithiated oxazinones 5-Lio, 9-Lio, and 15-Lio, respectively. This transmetalation may be crucial to the success of the intramolecular amination, since the lithiated oxazinones should be much less prone to *retro*-Michael reaction than the lithiated sulfoximines because of the poorer leaving groups in their β -positions.

The generation of the new stereogenic centers in the monocyclic oxazinones and the bicyclic oxazinones occurs with the same sense and with the same high degree of asymmetric induction. The highly selective formation of the oxazinones 5a-c from (Z)-4a-Li, (E)-4a-Li, (Z)-4b-Li, (Z)-4c-Li, and (E)-4c-Li, of oxazinone 9 from (Z)-8-Li, and of oxazinones 15a and 15b from 14a-Li and 14b-Li, respectively, implies that the C=C double bond of the lithiated carbam-



Figure 4. Cyclization of sulfonimidoyl-substituted lithiated homoallylic carbamates



Figure 5. Transition state models for the intramolecular amination

ates is attacked by the N atom from the Si face. This can be explained by invoking transition state models of type **TS-1** for the acyclic (Z) isomers and **TS-3** for the acyclic (E) isomers, in which the substituents R^1 and R^2 and the C=C double bond adopt pseudoequatorial positions (Figure 5). The alternative transition states TS-2 and TS-4, which would feature attack of the N atom at the double bond from the Re face and afford the epimeric oxazinones, seem to be less favorable because of severe steric 1,3-interactions involving the sulfonimidoyl group and the double bond. Similar arguments can be applied to the transition states TS-5 and TS-6 for the cyclization of the (Z)-configured methyl-substituted lithiated carbamate and to TS-7 and TS-8 for the cyclization of the (E)-configured isomer. Why the selectivity is lower in the case of the cyclization of the latter salt is difficult to ascertain by these models. For the cyclization of the cyclic lithiated carbamates, transition state model TS-9 has to be invoked, resulting in the bicyclic oxazinones with the cis ring fusion. The alternative transition state model TS-10, which would give isomeric bicyclic oxazinones with a trans ring fusion, is highly strained and destabilized by an unfavorable interaction between the sulfonimidoyl group and the lithiated carbamoyl group.

II. The Carbanion Route

Synthesis of Protected Dilithiated β-Amino Sulfoximines and Treatment with Electrophiles

We were delighted to see that the protected β -amino sulfoximines 5a and 5b readily afforded the dilithiated sulfoximines 5a-Li2 and 5b-Li2, respectively, upon treatment with 2.1 equiv. of *n*BuLi in THF at -10 °C (Scheme 5). The dilithiated sulfoximines 5a-Li2 and 5b-Li2 were stable in THF solution at -78 °C for at least 2 h. Treatment of 5a-Li₂ with MeI gave a mixture of 16a and epi-16a in a ratio of 9:1, chromatography delivering the diastereomerically pure derivative 16a in 68% yield. No C,N-dimethylation of 5a-Li₂ was observed under these conditions, within the limits of detection by ¹H NMR spectroscopy. Deuteration of **5b**-Li₂ with CD₃OD afforded a mixture of sulfoximines 16b and *epi*-16b in a ratio of 3:1, with a D-content of \geq 98%, in 99% yield. Methylation of 5b-Li₂ yielded a mixture of 16c and epi-16c in a ratio of 5:1 in 82% yield, chromatography furnishing diastereomerically pure 16c in 75% yield. Similarly, treatment of 5b-Li2 with PhCH2OCH2Cl proceeded readily and diastereoselectively to give the diastereomerically pure sulfoximine 16d in 70% yield after chromatography of the crude reaction mixture. As a final example, treatment of **5b**-Li₂ with acetaldehyde was carried out, yielding a mixture consisting of alcohols 16e and epi-16e in a ratio of 1.7:1 (67% yield) and of starting material **5b** (27% yield).

The configurations both of the newly generated stereogenic C atom of **16c**, at the position α to the sulfonimidoyl group, and, of no less importance, of the stereogenic C atom bearing the N atom were determined by X-ray crystal structure analysis (Figure 6). The structure of **16c** in the crystal is characterized by an intramolecular hydrogen bond between the N atoms of the oxazinone ring and of the sul-



Scheme 5. Synthesis and reactivity of dilithium salts of protected β -amino sulfoximines having a secondary C atom

fonimidoyl group incorporated in a six-membered ring. The methyl group and the phenyl group adopt pseudoaxial positions. From the magnitudes of the vicinal coupling constants of the protons of the oxazinone ring and the proton in the α -position in the ¹H NMR spectrum and NOE experiments, **16c** in solution preferentially adopts a structure similar to that in the crystal. On the basis of the unambiguous assignment of the configuration of **16c**, we tentatively assign the configurations depicted in Scheme 5 to the major diastereomers of sulfoximines **16a**–**d**. Treatment of **5b**-Li₂ with MeCHO gave a mixture of two diastereomers in a ratio of 1.7:1. Because of the almost unselective reaction between lithiated alkyl sulfoximines and aldehydes in general^[20] and the observation of a 5:1 selectivity in the methylation of this dilithium salt with MeI, we tentatively assign

the structures **16e** and *epi*-**16e**, which differ in the configuration of the C atom bearing the hydroxy group.



Figure 6. Structure of the sulfonimidoyl-substituted 1,3-amino alcohol derivative **16c** in the crystal; H···N2 198.8, N2···N1 280.5(5), N1-H 100.5 pm, N1-H···N2 136.7°

From previous structural investigations of lithiated alkyl and allyl sulfoximines,^[33,34] a transition state model of type TS-11 is proposed for the reaction of the dilithiated sulfoximines 5a-Li2 and 5b-Li2 giving rise to the major diastereomer. This transition state model is characterized by the lack of a C-Li bond and by the coordination of one of the two Li atoms by the two N atoms of the oxazinone ring and of the sulfonimidoyl group. Coordination of the N atom of the sulfonimidoyl group to the Li atom results in a C_{α} -S conformation of the carbanion, in which the lone pair orbital at the C_{α} atom and the S-Ph bond are approximately in one plane.^[36] Theoretical calculations on α -sulfonimidoyl carbanions predict that this conformation should be energetically preferred because of a stabilizing $n_{\rm C} - \sigma_{\rm SPh}^{*}$ interaction.^[33c] The preferential formation of the (R)-configured methyl derivative 16c in the reaction between 5b-Li2 and MeI may be interpreted by assuming a preferential attack of MeI from the Re face of the carbanionic centers as depicted in TS-11 because of steric shielding of the Si face by R^1 and the phenyl group. It is proposed that the reactions between 5a-Li₂ and 5b-Li₂ and the other electrophiles take a similar stereochemical course.

It is not only sulfoximines **5a** and **5b**, each with a secondary C atom in the β -position, that can be deprotonated twice; the procedure is also successful with sulfoximines incorporating tertiary C atoms. Treatment of sulfoximine **9** with 2 equiv. of *n*BuLi and trapping of the dilithium salts **9**-Li₂ with CD₃OD thus afforded a mixture of the deuterated sulfoximine **9**-D and *epi*-**9**-D in a ratio of approximately 1.1:1 in 99% yield (Scheme 6).

Synthesis of Protected 1,3-Amino Alcohols

The above results show that substituents at the α -positions of protected β -amino sulfoximines **5a** and **5b** can readily be introduced through formation of the corresponding



Scheme 6. Synthesis and reactivity of dilithium salts of protected β -amino sulfoximines having a tertiary C atom

dilithiated sulfoximines and their treatment with electrophiles. Completion of the asymmetric synthesis of 1,3-amino alcohols by this route requires replacement of the sulfonimidoyl group, which should be possible either by reduction or by Cl-substitution (cf. Figure 1). Thus, treatment of the monocyclic sulfoximines **5b** and **16c** with Raney nickel^[37] readily afforded the 1,3-amino alcohol derivatives **17a** and **17b**, respectively, each in 88% yield (Scheme 7). Similarly, reduction of the bicyclic sulfoximine **15b** furnished the cyclic 1,3-amino alcohol derivative **18** in 86% yield. The configuration of **18** and hence that of the oxazinone **15b** was determined by X-ray crystal structure analysis (Figure 7). The reductive substitution of the sulfonimidoyl groups of the β -hydroxy sulfoximines **16e** and *epi*-**16e**



Scheme 7. Synthesis of protected acyclic and cyclic 1,3-amino alcohols by reduction

was accomplished with the generation of a double bond. Thus, treatment of **16e** and *epi*-**16e** (admixed with **15b**) with Al/Hg^[38] afforded a mixture of the unsaturated protected 1,3-amino alcohols (*E*)-**19** and (*Z*)-**19** in a ratio of 1:1 in 85% yield, together with **17a** in 46% yield.



Figure 7. Structure of the protected 1,3-amino alcohol 18 in the crystal



Scheme 8. Synthesis of protected acyclic β -substituted β -amino acids and protected 1,3-amino alcohols by the carbanion route

Synthesis of Protected β-Amino Acids

Conversion of the sulfonimidoyl-substituted monocyclic and bicyclic oxazinones to β -amino acid derivatives by the carbanion route first requires the introduction of a carboxy group into the molecules. Thus, treatment of the dilithiated sulfoximine **5b**-Li₂, derived from **5b**, with ClCO₂Me furnished a mixture of the esters **20** and *epi*-**20** in a ratio of 5.2:1 in 64% yield (Scheme 8). The configurations of the esters **20** and *epi*-**20** were tentatively assigned as depicted. Finally, reduction of the sulfoximines **20** and *epi*-**20** with Raney nickel gave the protected β -amino acid **21** in 87% yield.

It was now of particular interest to see whether the carbanion route could also be successfully implemented for the synthesis of protected cyclic and acyclic β -amino acids with tertiary C_{β} atoms. Deprotonation of sulfoximine 9 with *n*BuLi in THF at -78 °C gave the dilithiated sulfoximine 9-Li₂, which upon treatment with ClCO₂R (R = Me, *i*Pr, *i*Bu, and CH_2tBu) furnished mixtures of esters 22a-d and epi-22a-d and the starting sulfoximine 9, the last of which was separated by chromatography (Scheme 9). Because of partial transmetalation between 9-Li2 and the esters formed, conversion of sulfoximine 9 was incomplete and 7-18% of the sulfoximine was recovered. Reduction of sulfoximines 22a - d and *epi*-22a - d with Raney nickel afforded the protected β , β -disubstituted β -amino acids 23a-d in 48% to 74% yields, based on 9. The highest overall yield in the conversion of sulfoximine 9 into one of the β -amino ester derivatives was achieved in the case of ester 23c (74%), for which isobutyl chloroformate was used for the introduction of the ester group into 9-Li₂.

Finally, the conversion of the bicyclic sulfoximine 15b into the amino acid derivative 25 by this route was investigated. Double deprotonation of sulfoximine 15b with *n*BuLi



Scheme 9. Synthesis of protected acyclic β , β -disubstituted β -amino acids and protected 1,3-amino alcohols by the carbanion route

in THF at -78 °C cleanly gave the dilithiated sulfoximine **15b**-Li₂ (Scheme 10), which upon treatment with ClCO₂Me delivered ester **24** as a single diastereomer in 70% yield. Reduction of sulfoximine **24** with Raney nickel furnished the protected cyclic β -amino acid **25** in 86% yield. The

structure of **25** was verified by X-ray crystal structure analysis (Figure 8).



Scheme 10. Synthesis of protected cyclic β , β -disubstituted β -amino acids and protected 1,3-amino alcohols by the carbanion route



Figure 8. Structure of the protected cyclic β -amino ester **25** in the crystal; O3…H 214.9, N1…O3 285.5(8), N1–H 101.9 pm, N1–H…O3 124.7°

III. The Substitution Route

Synthesis of Protected β-Amino Chlorides and Protected β-Amino Acids

The carbanion route allows access to protected cyclic and acyclic β -amino acids of type I and to protected cyclic and acyclic 1,3-amino alcohols of type IV. This route ought to be particularly well suited for the synthesis of 1,3-amino alcohols IV with various substitution patterns, because of the potential for the introduction of a wide range of substituents R^4 through the reaction between the dilithiated sulfonimidoyl-substituted oxazinones and electrophiles. A principle shortcoming of the carbanion route may be seen, however, in the fact that the chirality of the sulfonimidoyl group is lost in the reduction step. The envisaged substitution route from sulfoximines VII to amino acids I and 1,3-amino alcohols IV via protected β -amino chlorides VI would not have this shortcoming, since we had found previously that the sulfonimidoyl groups of alkyl and allyl sulfoximines can readily be replaced by chlorine, proceeding with complete retention of configuration at the S atom, by treatment with ClCO₂Me.^[23,24] The substitution route could perhaps therefore provide a valuable alternative to the carbanion route and at the same time open new synthetic possibilities, in particular for the synthesis of functionalized 1,3-amino alcohols. We were delighted to see that treatment of sulfoximines $5\mathbf{a}-\mathbf{c}$ with ClCO₂Me at room temperature in CH₂Cl₂ for 3 days gave clean substitution of the sulfonimidoyl group and afforded the β -chloroamines $27\mathbf{a}-\mathbf{c}$ in 84%, 85% and 81% yields, respectively (Scheme 11). In addition, the sulfinamide **26** was isolated (vide infra). Treatment of chloride **27c** with NaCN in DMF readily gave the β -amino nitrile **28** in 87% yield.



Scheme 11. Synthesis of protected acyclic β -amino chlorides and nitriles by the substitution route

The sulfoximine **5c** having successfully been converted into the nitrile **28** by double substitution, it was of particular interest to see whether such transformations would also be feasible in the cases of sulfoximines **9**, **15a**, and **15b** and the corresponding chlorides with tertiary C atoms at their β -positions. To our delight, treatment of sulfoximine **9** with CICO₂Me in CH₂Cl₂ at room temperature for 2.5 days gave (besides sulfinamide **26**) the protected β -amino chloride **29** in 81% yield (Scheme 12). Treatment of chloride **29** with NaCN in DMF for 2 h furnished nitrile **30** in 87% yield, hydrolysis of nitrile **30** delivering the protected acyclic β amino acid **31** in 72% yield. Interestingly, the oxazinone ring of **31** was not cleaved under these conditions. The structure of acid **31** was confirmed by X-ray crystal structure analysis (Figure 9).

Finally, the extension of the substitution route to the conversion of sulfoximines **15a** and **15b** into amino acid derivatives **34a** and **34b**, respectively, was attempted in order to study the scope and limitation of the substitution route. Substitution of the cyclic sulfoximines **15a** and **15b** proceeded uneventfully on treatment with ClCO₂Me and gave, besides **26**, the protected β -amino chlorides **32a** in 83% yield and **32b** in 86% yield, respectively (Scheme 13). The structure of chloride **32b** was confirmed by X-ray crystal structure analysis (Figure 10). Treatment of chlorides **32a** and **32b** with NaCN in DMF readily furnished the nitrile **33a** in 92% yield and the nitrile **33a** and **33b** with aque-



Scheme 12. Synthesis of protected acyclic β , β -disubstituted β -amino acids by the substitution route



Figure 9. Structure of the protected acyclic $\beta\text{-amino}$ acid 31 in the crystal



Scheme 13. Synthesis of protected cyclic β , β -disubstituted β -amino acids by the substitution route



Figure 10. Structure of the chlorine-substituted cyclic 1,3-amino alcohol derivative **32b** in the crystal

ous NaOH at reflux afforded the protected cyclic β -amino acids **34a** in 70% yield and **34b** in 69% yield, respectively.

Recycling of the Chiral Auxiliary

Treatment of sulfoximines 5a-c, 9, 15a, and 15b with ClCO₂Me in all cases delivered – in addition to the chlorides 27a-c, 29, 32a, and 32b, respectively – the sulfinamide 26 as a second reaction product, isolated in the case of – for example – the synthesis of 29 with $\ge 99\%$ ee in 73% yield (Scheme 14). These results, together with those obtained previously,^[23,24] indicate that treatment of *S*-alkyl-*N*-methyl-*S*-phenylsulfoximines with a chloroformate seems to be a general method for the replacement of the sulfonimidoyl group by a Cl atom. We assume that the substitution proceeds through the intermediate formation of the aminooxosulfonium chlorides 35. It was now of interest to see whether the sulfoxide $36^{[39]}$ could be prepared from the sulfinamide 26 with complete inversion of configuration,



Scheme 14. Substitution of the sulfonimidoyl group and recycling of the chiral auxiliary

since a two-step conversion of **36** to sulfoximine **37** with complete retention of configuration had already been described.^[40,41] Sulfoximine **37**, which is normally prepared through an efficient resolution,^[29,42,43] can readily be methylated to give sulfoximine **38**,^[44] the starting material for the synthesis of the allylic sulfoximines used in this work. Treatment of sulfinamide **26** with methylmagnesium chloride in THF at -78 °C resulted in the isolation of the sulfoxide **36** with 97% *ee* in 70% yield, so the synthesis of **36** from **26** represents a recycling of the chiral auxiliary.

Substitution of an α-Methylated Sulfoximine

Substitution of the sulfonimidoyl groups of 5a-c, 9, 15a, and 15b, without further substituents at their α -positions, by a Cl atom having been achieved, it was now of interest to study the reactivity of the α -methylated sulfoximine 16a towards chloroformates (Scheme 15). Interestingly, treatment of sulfoximine 16a with ClCO₂CH(Cl)Me in the presence of pyridine in CH₂Cl₂ at room temperature for 1 h afforded a mixture of the unsaturated 1,3-amino alcohol derivative 39 and the chloride 40 in a ratio of 8:1 in 91% yield. This transformation could perhaps open a further route to synthetically highly valuable unsaturated 1,3-amino alcohols (cf. Scheme 7).



Scheme 15. Substitution of an α -methylated sulfoximine

Conclusion

We have presented a new method for the asymmetric synthesis of protected cyclic and acyclic β -substituted and β , β disubstituted δ -hydroxy β -amino acids from aldehydes through the use of sulfonimidoyl-substituted bis(allyl)titanium complexes. The δ -hydroxy- β -amino acids are potentially useful not only for the synthesis of glycosylated β peptides, but also for further derivatization of the amino acids. The method described also permits the asymmetric synthesis of protected cyclic and acyclic, unfunctionalized and sulfonimidoyl-, chlorine-, and cyano-functionalized 1,3-amino alcohols with three contiguous stereogenic C atoms and a secondary or tertiary C atom bearing the amino group. The key steps of this method are: (1) the highly regio- and stereoselective addition of the cyclic and acyclic sulfonimidoyl-substituted bis(allyl)titanium complexes to aldehydes, (2) the stereoselective intramolecular amination of sulfonimidoyl-substituted homoallylic alcohols by the carbamate method, (3) the substitution of protected β -amino sulfoximines with formation of protected β -amino chlorides, (4) the generation of lithiated alkyl sulfoximines with protected lithiated β -amino groups, (5) their treatment with electrophiles, and (6) the reduction of the substituted sulfoximines. The δ -hydroxy- β -amino acids and 1,3-amino alcohols described in this paper have protecting groups at the O and the N atom. We are currently studying the conversion of the β -amino nitriles into differently protected δ hydroxy- β -amino acids.

Experimental Section

General: The enantiomerically and diastereomerically pure homoallylic alcohols 2a-c and 13b were synthesized from the allylic sulfoximines 1a-c and 12b, respectively, by literature procedures.^[18c] The enantiomerically pure allylic sulfoximines 1a-c,^[27] (E)-6,^[27] 12a,^[31] and 12b^[31] were prepared from sulfoximine 38 by the onepot procedure described previously.^[18c] All reactions were carried out in absolute solvents under an argon atmosphere by use of syringe and Schlenk techniques in oven-dried glassware. THF and Et₂O were distilled under argon from lead/sodium/benzophenone. CH₂Cl₂ and DMF were distilled from CaH₂. TLC: Merck silica gel 60 F254 plates. Column chromatography: Merck silica gel 60 (0.063-0.200 mm. Melting points: Büchi, melting points are uncorrected. Optical rotations: Perkin-Elmer Model 241, measurements were made at approximately 22 °C, specific rotations are in grad·mL/dm·g, and c is in g/100 mL. ¹H and ¹³C NMR: Varian VXR 300, Varian Gemini 300, Varian Inova 400, and Varian Unity 500. Peaks in the ¹³C 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 sequences. The following abbreviations are used to designate the multiplicity of the peaks in ¹H NMR spectra: s = singlet, d = doublet, t = doublettriplet, q = quadruplet, quin = quintet, sept = septet, m = multiplet, br. = broad, symm. = symmetrical and combinations thereof. IR spectra: Perkin–Elmer PE 1759 FT, only peaks of $\tilde{v} >$ 1000 cm⁻¹ are listed, vs = very strong, s = strong, m = medium, and w = weak. GC-MS (CI): Magnum Finnigan (HT-5: 25 m, 0.25 mm; 50 kPa He, 40 eV, MeOH). MS (EI): Varian MAT 212S, 70 eV. MS (CI): Finnigan SSQ 7000, 100 eV; only peaks of m/z >80 and intensity > 10%, except for decisive ones, are listed.

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 1. The crystal structures were solved by direct methods as implemented in the XTAL3.7 package of crystallographic routines.^[45] The molecular structures were illustrated by use of the SCHAKAL 92 program.^[46,47]

General Procedure for the Conversion of Alcohols into Carbamates (*GP1*): Trichloroacetyl isocyanate (1.05 mmol) was added at room temperature to a solution of the alcohol (1.00 mmol) in THF (20 mL). After the mixture had been stirred at room temperature for 2 h, concentrated aqueous ammonia (3 mL) was added. Stirring of the mixture was continued at room temperature for 1 h. Saturated aqueous NH₄Cl (20 mL) was then added, and the mixture was extracted with CH₂Cl₂. The combined organic phases were

Table 1. (Crystal data a	nd parameters of d	ata collection for	or (Z)-7, 9,	16c, 18, 25, 31, and 32b
------------	----------------	--------------------	--------------------	--------------	--------------------------

[a]	(Z)-7	9	16c	18	25	31	32b
Empirical formula	C ₂₁ H ₂₇ NO ₂ S	C ₂₂ H ₂₈ N ₂ O ₃ S	$C_{17}H_{26}N_2O_3S$	$2 imes (C_{12}H_{21}NO_2)^{[a]}$	C ₁₄ H ₂₃ NO ₄	C ₁₆ H ₂₁ NO ₄	C ₁₂ H ₂₀ ClNO ₂
$M_{\rm r}$	357.52	400.54	338.47	2×211.31	269.34	291.35	245.75
Color and habit	colorless,	colorless,	colorless,	Colorless,	colorless,	Colorless,	Colorless,
	irregular	irregular	irregular	irregular	irregular	block	irregular
Crystal size, ca. mm	$0.6 \times 0.5 \times 0.2$	$0.13 \times 0.24 \times 0.56$	$0.3 \times 0.3 \times 0.3$	0.3 imes 0.3 imes 0.3	$0.3 \times 0.3 \times 0.3$	$0.18 \times 0.28 \times 0.44$	$0.3 \times 0.3 \times 0.3$
Crystal system	orthorhombic	monoclinic	orthorhombic	monoclinic	monoclinic	trigonal	orthorhombic
space group	$P2_{1}2_{1}2_{1}$	$P2_1$	$P2_{1}2_{1}2_{1}$	$P2_1$	$P2_1$	<i>P</i> 3 ₁ 21	$P 2_1 2_1 2_1$
a, A	7.394(2)	11.625(1)	8.338(1)	11.494(2)	5.8447(7)	9.9834(7)	9.138(4)
b, Å	10.175(3)	8.230(1)	9.397(1)	9.266(1)	12.713(2)	9.9834(7)	11.581(4)
<i>c</i> , Å	26.481(5)	12.144(2)	23.093(4)	11.685(3)	9.6417(9)	27.063(3)	12.053(5)
α, °	90.0	90.0	90.0	90.0	90.0	90.0	90.0
β, °	90.0	114.952(2)	90.0	101.69(2)	103.696(1)	90.0	90.0
γ, °	90.0	90.0	90.0	90.0	90.0	120.0	90.0
$V, Å^3$	1992.3(9)	1053.4(2)	1809.4(4)	1218.7(4)	696.9(2)	2336.0(4)	1275.5(9)
Z	4	2	4	2×2	2	6	4
$D_{\rm calcd}$, g cm ⁻³	1.192	1.263	1.242	1.152	1.283	1.243	1.280
μ , mm ⁻¹	1.537	0.178	1.677	0.615	0.764	0.089	2.544
Data collection							
Diffractometer	CDA4	Bruker	CDA4	CDA4	CDA4	Bruker	CDA4
	Enraf-Nonius	SMART APEX	Enraf-Nonius	Enraf-Nonius	Enraf-Nonius	SMART APEX	Enraf-Nonius
Т, К	150	298	298	200	150	293	150
Radiation	Cu-K _a	$Mo-K_{\alpha}$	Cu-Ka	Cu-Ka	Cu-Ka	Mo-K _a	Cu-Ka
λ. Å	1.54179	0.71073	1.54179	1.54179	1.54179	0.71073	1.54179
Scan method	ω/2θ	ω	ω/2θ	ω/2θ	ω/2θ	ω	ω/2θ
Omax.°	74.8	28.3	74.8	74.9	75.0	26.1	74.9
No. of data colld	4612	14686	4148	5373	3000	34565	3038
No. of unique data	3967	5232	3591	4848	2678	3100	2599
Obsevation criterion	$I \ge 2\sigma(I)$	$F > 4\sigma(F)$	$I \ge 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$F > 4\sigma(F)$	$I > 2\sigma(I)$
Refinement	1 · 20(1)	1 * 10(1)	1 · 20(1)	1. 20(1)	1 = 20(1)	1 • 10(1)	1 20(1)
No of parameters refined	226	253	209	270	172	190	145
No of data observed in	3548	3668	2149	4478	2662	1886	2239
refinement	5510	2000	21.12		2002	1000	2207
R R ^[b]	0.059.0.069	$0.042/0.042^{[c]}$	0.057 0.061[°]	0 056/0 070	0 073/0 088	0 090/0 101 ^[d]	0.056/0.076
$\Lambda(0) e^{-3}$	$-0.90/\pm0.70$	$-0.24/\pm0.32$	$-1.73/\pm0.88$	-0.33/+0.37	$-0.53/\pm0.52$	$-0.58/\pm0.74$	$-0.63/\pm0.65$
GOF	1.969	0.944	1.351	2.700	4.675 ^[e]	1.031	2.908

^[a] Two symmetrically independent molecules. ^[b] $R = \Sigma ||F_o| - |F_c| |\Sigma|F_o|$; $Rw = [\Sigma w(|F_o| - |F_c|)^2 / \Sigma w |F_o|^2]^{0.5}$; $w = 1/\sigma^2(F_o)$ where F_o and F_c are observed and calculated structure factors. ^[c] $w = 1/[\sigma^2(F_o) + 0.0004 \cdot F_o^2]$. ^[d] $w = 1/[11 \cdot \sigma^2(F_o)]$. ^[e] Poor crystal quality.

dried (MgSO₄) and concentrated in vacuo. Purification of the residue by chromatography or crystallization afforded the carbamate.

General Procedure for the Conversion of Carbamates into Oxazinones (*GP2*): *n*BuLi in hexane (1.05–1.30 mmol) was added at -78 °C to a solution of the carbamate (1.0 mmol) in THF (40 mL). The reaction mixture was then allowed to warm to room temperature over 18 h. Saturated aqueous NH₄Cl (40 mL) was added, and the aqueous phase was extracted with CH₂Cl₂. The combined organic phases were dried (MgSO₄) and concentrated in vacuo. Purification of the residue by chromatography or crystallization afforded the oxazinone.

General Procedure for the Introduction of Substituents at the α -Positions of Sulfoximines (*GP3*): *n*BuLi in hexane (3.00 mmol) was added at -50 °C to a solution of the sulfoximine (1.00 mmol) in THF (40 mL). The mixture was allowed to warm to -10 °C over 1 h, cooled to -50 °C, and then treated with the electrophile. The mixture was then allowed to warm to room temperature over 6 h, and saturated aqueous NH₄Cl (50 mL) was added. The aqueous phase was extracted with CH₂Cl₂, and the combined organic phases were dried (MgSO₄). Concentration in vacuo gave the sulfoximine, which was purified by chromatography or crystallization.

General Procedure for the Reduction of Sulfoximines with Raney Nickel (*GP4*): Raney nickel was prepared as follows: nickel aluminium alloy powder (50:50, 2.5 g) was suspended in desalted H₂O (100 mL) and treated with KOH until the evolution of hydrogen ceased. Subsequently, the suspension was heated at 80 °C for 30 min. After the mixture had cooled to room temperature, the aqueous layer was decanted, and the Raney nickel was washed with desalted H₂O (10 × 50 mL) and suspended in THF/H₂O (4:1, 50 mL).

The suspension was then added at room temperature to a solution of the sulfoximine (0.71 mmol) in THF/H₂O (4:1, 5 mL). Subsequently, the reaction mixture was stirred at room temperature until TLC or GC indicated complete conversion of the sulfoximine. The solution was then filtered, and the Raney nickel was washed with THF (5×25 mL). The combined organic phases were concentrated in vacuo, and the residue was dissolved in CH₂Cl₂. The aqueous phase was extracted with CH₂Cl₂ and the combined organic phases were dried (MgSO₄) and concentrated in vacuo. Purification of the residue by chromatography or crystallization afforded the reduction product.

General Procedure for the Conversion of Sulfoximines into Esters by the Carbanion Route (GP5): nBuLi in hexane (2.1 mmol) was added at -78 °C to a solution of the sulfoximine (1.0 mmol) in THF (35 mL). After the mixture had been stirred at this temperature for 2 h, the chloroformate (2.1 mmol) was added and stirring was continued for 90 min. Subsequently, saturated aqueous NH₄Cl was added, and the aqueous phase was extracted with CH₂Cl₂. The combined organic phases were concentrated in vacuo, and the ester and the remaining starting sulfoximine were separated by chromatography (EtOAc). The obtained functionalized sulfoximine was reduced with Raney nickel as in *GP4*, and the ester was purified by chromatography (EtOAc/cyclohexane, 4:1).

General Procedure for the Conversion of Sulfoximines into Chlorides (*GP6*): $ClCO_2Me$ (15.0 mmol) was added at room temperature to a solution of the sulfoximine (1.00 mmol) in CH_2Cl_2 (12 mL). The mixture was stirred at room temperature until TLC or GC indicated almost complete conversion of the sulfoximine. Concentration in vacuo and purification of the residue by chromatography afforded the chloride.

General Procedure for the Conversion of Chlorides into Nitriles (*GP7*): NaCN (2.00 mmol) was added at room temperature to a solution of the chloride (1.00 mmol) in DMF (15 mL), and the resulting mixture was heated with stirring at 105 °C for 2 h. After the mixture had cooled to room temperature, the solvent was removed in vacuo. The remaining solid was purified by chromatography or recrystallization.

General Procedure for the Conversion of Nitriles into Acids (*GP8*): Aqueous NaOH (2 N, 2 mL) was added to a solution of the nitrile (0.32 mmol) in EtOH (8 mL), and the mixture was heated at reflux for 3 h. After the mixture had cooled to room temperature, EtOH was removed in vacuo and the solution was acidified with aqueous $3 \times$ HCl until a colorless solid precipitated. The mixture was then extracted with CHCl₃, whereupon the solid dissolved, and the combined organic phases were concentrated in vacuo. Purification by chromatography or crystallization afforded the amino acid.

(3*S*,4*R*,5*Z*)- and (3*S*,4*R*,5*E*)-4-Methyl-6-[(*S*)-*N*-methyl-*S*-phenylsulfonimidoyl]-5-hexen-3-yl Carbamate [(*Z*)-4a and (*E*)-4a]: Treatment of alcohol 2a (560 mg, 2.09 mmol) with trichloroacetyl isocyanate (0.26 mL, 2.19 mmol) according to *GP1* and purification by chromatography (EtOAc) gave a mixture of carbamates (*Z*)-4a and (*E*)-4a (550 mg, 85%) in a ratio of 3:1 as a colorless solid:

Compound (Z)-4a: ¹H NMR (300 MHz, CDCl₃): $\delta = 0.68$ (d, J = 6.7 Hz, 3 H, CH*Me*), 0.93 (t, J = 7.4 Hz, 3 H, Et), 1.42–1.70 (m, 2 H, Et), 2.69 (s, 3 H, NMe), 3.67 (m, 1 H, CHMe), 4.63 (m, 1 H, CHO), 4.95 (br. s, 2 H, NH₂), 6.14 (t, J = 11.1 Hz, 1 H, SCH= CH), 6.39 (d, J = 11.1 Hz, 1 H, SCH=CH), 7.56 (m, 3 H, Ph), 7.91 (m, 2 H, Ph) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 9.62$ (d), 15.96 (d), 26.12 (u), 29.27 (d), 35.27 (d), 78.37 (d), 128.88 (d), 129.34 (d), 131.71 (d), 132.69 (d), 146.82 (d), 140.50 (u), 157.23 (u) ppm.

Compound (E)-4a: ¹H NMR (300 MHz, CDCl₃): $\delta = 0.84$ (t, J = 7.4 Hz, 3 H, Et), 1.09 (d, J = 6.9 Hz, 3 H, CH*Me*), 1.42–1.70 (m, 2 H, Et), 2.74 (s, 3 H, NMe), 2.60 (m, 1 H, CHMe), 4.63 (m, 1 H, CHO), 4.82 (br. s, 2 H, NH₂), 6.39 (d, J = 15.0 Hz, 1 H, SCH=CH), 6.81 (dd, J = 15.0, J = 8.2 Hz, 1 H, SCH=CH), 7.56 (m, 3 H, Ph), 7.91 (m, 2 H, Ph) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 9.68$ (d), 15.66 (d), 25.05 (u), 29.47 (d), 39.79 (d), 77.74 (d), 128.76 (d), 129.38 (d), 131.23 (d), 132.63 (d), 147.16 (d), 139.44 (u), 156.80 (u) ppm.

(2*S*,3*R*,4*Z*)-3-(1-Methylethyl)-5-[(*S*)-*N*-methyl-*S*-phenylsulfonimidoyl]-4-penten-2-yl Carbamate [(*Z*)-4b]: Treatment of alcohol 2b (2.02 g, 7.18 mmol) with trichloroacetyl isocyanate (0.89 mL, 7.54 mmol) according to GP1 and purification by crystallization (Et₂O/CH₂Cl₂, 25:1) gave carbamate (Z)-4b (2.09 g, 90%) as a colorless solid: M.p. 209 °C. ¹H NMR (300 MHz, CDCl₃): $\delta = 0.47$ (d, J = 6.9 Hz, 3 H, *i*Pr), 0.80 (d, J = 6.7 Hz, 3 H, *i*Pr), 1.33 (d, J = 6.4 Hz, 3 H, Me), 1.60 (m, 1 H, *i*Pr), 2.68 (s, 3 H, NMe), 3.31 (ddd, J = 11.5, J = 6.7, J = 4.4 Hz, 1 H, CHiPr), 4.78 (br. s, 2 H, NH₂), 5.04 (qd, J = 6.4, J = 4.4 Hz, 1 H, CHO) 6.13 (t, J =11.5 Hz, 1 H, SCH=CH), 6.52 (d, J = 11.5 Hz, 1 H, SCH=CH), 7.50-7.60 (m, 3 H, Ph), 7.90 (m, 2 H, Ph) ppm. ¹³C NMR $(75 \text{ MHz}, \text{ CDCl}_3)$: $\delta = 19.10 \text{ (d)}, 19.47 \text{ (d)}, 20.63 \text{ (d)}, 28.61 \text{ (d)},$ 29.24 (d), 47.41 (d), 70.90 (d), 129.13 (d), 129.31 (d), 132.71 (d), 133.38 (d), 145.03 (d), 140.12 (u), 156.55 (u) ppm. IR (KBr): $\tilde{v} =$ 3856 (w), 3437 (s), 3328 (s), 3290 (s), 3201 (m), 3052 (m), 2999 (m), 2966 (s), 2926 (m), 2903 (m), 2862 (s), 2792 (m), 1735 (vs), 1701 (vs), 1627 (m), 1611 (m), 1582 (w), 1474 (m), 1446 (s), 1391 (s), 1360 (s), 1333 (s), 1317 (s), 1253 (vs), 1214 (s), 1144 (vs), 1103 (s), 1081 (s), 1070 (s), 1048 (vs), 1010 (m) cm⁻¹. MS (EI): *m/z* (relative intensity, %) = $325 [M^+ + 1] (2)$, $324 [M^+] (8)$, 265 (10), 264 (54), 236 (17), 156 (58), 126 (16), 125 (100), 111 (14), 109 (28), 108 (23), 107 (25), 97 (22), 96 (14), 93 (35), 91 (41), 83 (19), 81 (38). C16H24N2O3S (324.44): calcd. C 59.23, H 7.46, N 8.63; found C 58.77, H 7.22, N 8.75.

(2*S*,3*R*,4*Z*)- and (2*S*,3*R*,4*E*)-3-(1-Methylethyl)-5-[(*S*)-*N*-methyl-*S*-phenylsulfonimidoyl]-5-penten-2-yl *N*-Trichloroacetylcarbamate [(*Z*)-3b and (*E*)-3b]: Trichloroacetyl isocyanate (49 μ L, 0.41 mmol) was added at 0 °C to a solution of alcohol (*Z*)-2b (78 mg, 0.28 mmol) in CH₂Cl₂ (8 mL). After the mixture had been stirred at 0 °C for 3.5 h, it was concentrated in vacuo to give a mixture of (*Z*)-3b and (*E*)-3b in a ratio of 11:1, together with trichloroacetyl isocyanate (¹H NMR). Purification by chromatography (EtOAc/hexane, 4:1) afforded a mixture of carbamates (*Z*)-3b and (*E*)-3b (75 mg, 58%) in a ratio of 6:1 as a colorless solid.

Compound (Z)-3b: ¹H NMR (300 MHz, CDCl₃): $\delta = 0.63$ (d, J = 6.7 Hz, 3 H, *i*Pr), 0.78 (d, J = 6.7 Hz, 3 H, *i*Pr), 1.45 (d, J = 6.3 Hz, 3 H, Me), 1.74 (m, 1 H, *i*Pr), 2.67 (s, 3 H, NMe), 3.52 (dt, J = 11.1, J = 6.3 Hz, 1 H, CH*i*Pr), 5.08 (quin, J = 6.3 Hz, 1 H, CHO), 6.17 (t, J = 11.1 Hz, 1 H, SCH=CH), 6.50 (d, J = 11.1 Hz, 1 H, SCH=CH), 7.54–7.66 (m, 3 H, Ph), 7.86 (m, 2 H, Ph), 9.65 (br. s, 1 H, NH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 17.71$ (d), 18.90 (d), 21.01 (d), 28.01 (d), 29.46 (d), 47.50 (d), 73.92 (d), 77.38 (u), 129.27 (d), 129.70 (d), 133.24 (d), 133.97 (d), 143.56 (d), 139.07 (u), 150.30 (u), 158.56 (u) ppm, signal of CCl₃ was not observed.

Compound (E)-3b: ¹H NMR (300 MHz, CDCl₃): $\delta = 0.88$ (d, J = 6.7 Hz, 3 H, *i*Pr), 0.98 (d, J = 6.7 Hz, 3 H, *i*Pr), 1.19 (d, J = 6.3 Hz, 3 H, Me), 1.85 (m, 1 H, *i*Pr), 2.06 (m, 1 H, CH*i*Pr), 2.77 (s, 3 H, NMe), 5.22 (quin, J = 6.3, J = 4.4 Hz, 1 H, CHO), 6.42 (d, J = 15.0 Hz, 1 H, SCH=CH), 6.78 (dd, J = 15.0, J = 10.4 Hz, 1 H, SCH=CH), 7.50–7.64 (m, 3 H, Ph), 7.88 (m, 2 H, Ph), 8.50 (br. s, 1 H, NH) ppm.

(+)-(3*S*,4*R*,5*Z*)-2-Methyl-6-[(*S*)-*N*-methyl-*S*-phenylsulfonimidoyl]-4-phenyl-5-hexen-3-yl Carbamate [(*Z*)-4c)] and (+)-(3*S*,4*R*,5*E*)-2-Methyl-6-[(*S*)-*N*-methyl-*S*-phenylsulfonimidoyl]-4phenyl-5-hexen-3-yl Carbamate [(*E*)-4c]: Treatment of alcohol 2c (1.47 g, 4.28 mmol) with trichloroacetyl isocyanate (0.53 mL, 4.49 mmol) according to *GP1* and purification by chromatography (EtOAc/*i*PrOH, 4:1) gave carbamates (*Z*)-4c (1.26 g, 76%) and (*E*)-4c (270 mg, 16%) as colorless solids.

Compound (Z)-4c: M.p. 46–49 °C. $[\alpha]_D = +68.6$ (c = 0.60, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): $\delta = 0.89$ (d, J = 6.9 Hz, 3 H, *i*Pr), 0.91 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.57 (septd, 1 H, J = 6.9, J = 3.5 Hz, *i*Pr), 2.68 (s, 3 H, NMe), 4.86 (m, 1 H, CHPh), 4.97

(br. s, 2 H, NH₂), 4.98 (dd, J = 9.4, J = 3.5 Hz, 1 H, CHO), 6.39 (d, J = 11.0 Hz, 1 H, SCH=CH), 6.47 (dd, J = 11.0, J = 11 Hz, 1 H, SCH=CH), 6.93-6.96 (m, 2 H, Ph), 7.15-7.21 (m, 3 H, Ph), 7.43-7.57 (m, 3 H, Ph), 7.82-7.86 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 15.52 (d), 19.75 (d), 28.90 (d), 29.18 (d), 45.03 (d), 79.82 (d), 126.96 (d), 127.66 (d), 128.58 (d), 128.60 (d), 128.97 (d), 131.17 (d), 132.32 (d), 138.16 (u), 139.90 (u), 144.98 (d), 157.16 (u) ppm. IR (KBr): $\tilde{v} = 3428$ (m), 3356 (m), 3171 (w), 3061 (w), 3030 (w), 2965 (m), 2935 (m), 2875 (m), 2803 (w), 1724 (s), 1600 (m), 1495 (m), 1448 (m), 1390 (s), 1331 (m), 1305 (m), 1246 (s), 1214 (m), 1184 (w), 1147 (s), 1110 (m), 1080 (m), 1041 (s) cm⁻¹. MS (EI): m/z (relative intensity, %) = 387 [M⁺ + 1] (4), 386 (16), 343 (35), 326 (32), 300 (10), 271 (18), 171 (42), 170 (97), 156 (43), 155 (60), 146 (11), 145 (21), 144 (21), 143 (17), 129 (15), 128 (11), 127 (13), 125 (68), 118 (12), 117 (77), 116 (28), 115 (100), 109 (19), 97 (13), 91 (32). C21H26N2O3S (386.51): calcd.C 65.26, H 6.78, N 7.25; found C 64.97, H 6.79, N 7.24.

Compound (E)-4c: M.p. 56–58 °C. $[\alpha]_D$ +62.1 (c = 0.38, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): $\delta = 0.81$ (d, J = 6.7 Hz, 3 H, *i*Pr), 0.82 (d, J = 6.7 Hz, 3 H, *i*Pr), 1.57 (septd, 1 H, J = 6.7, J = 3.7 Hz, *i*Pr), 2.70 (s, 3 H, NMe), 3.65 (7, J = 9.1, 1 H, CHPh), 4.64 (s, 2 H, NH₂), 5.00 (dd, J = 9.1, J = 3.7 Hz, 1 H, CHO), 6.35 (dd, J =15.1, J = 0.8 Hz, 1 H, SCH=CH), 7.04 (dd, J = 15.1, J = 9.1 Hz,1 H, SCH=CH), 7.19–7.34 (m, 5 H, Ph), 7.48–7.56 (m, 3 H, Ph), 7.85–7.89 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta =$ 15.39 (d), 19.62 (d), 28.99 (d), 29.30 (d), 50.88 (d), 78.97 (d), 127.36 (d), 127.93 (d), 128.64 (d), 128.91 (d), 129.04 (d), 131.39 (d), 132.33 (d), 137.94 (u), 138.97 (u), 145.75 (d), 156.34 (u) ppm. IR (KBr): $\tilde{v} = 3840$ (m), 3426 (s), 3060 (w), 3030 (w), 2965 (m), 2935 (m), 2875 (m), 2804 (w), 2373 (w), 1725 (s), 1602 (m), 1563 (w), 1545 (w), 1496 (w), 1448 (m), 1385 (s), 1331 (m), 1243 (s), 1184 (w), 1150 (m), 1109 (w), 1081 (w), 1040 (s) cm⁻¹. MS (EI): *m/z* (relative intensity, %) = 387 [M⁺ + 1] (3), 386 (17), 271 (18), 270 (33), 261 (10), 248 (14), 225 (24), 200 (42), 193 (12), 191 (10), 171 (24), 170 (32), 158 (24), 156 (23), 146 (14), 145 (44), 144 (60), 125 (62), 117 (28), 116 (39), 115 (100), 107 (19), 106 (10), 91 (38). C₂₁H₂₆N₂O₃S (386.51): calcd. C 65.26, H 6.78, N 7.25; found C 65.00, H 6.87, N 7.02.

(+)-(4S,5R,6S)-Tetrahydro-6-ethyl-5-methyl-4-{[(S)-Nmethyl-S-phenylsulfonimidoyl]methyl}-2H-1,3-oxazin-2-one (5a): Treatment of a mixture of carbamates (Z)-4a and (E)-4a (928 mg, 2.99 mmol, in a ratio of 3:1) with nBuLi (2.43 mL of 1.60 м in hexane, 3.89 mmol) according to GP2 and purification by crystallization (Et₂O) gave oxazinone 5a (863 mg, 93%) as a colorless solid. M.p. 240 °C, $[\alpha]_D = +179.1$ (c = 0.45, CH₂Cl₂). ¹H NMR $(300 \text{ MHz}, \text{CDCl}_3)$: $\delta = 0.75 \text{ (d, } J = 6.7 \text{ Hz}, 3 \text{ H}, \text{CH}Me), 0.99 \text{ (t,}$ J = 7.4 Hz, 3 H, Et), 1.53 (m, 2 H, CHMe, Et), 1.80 (dqd, J =14.4, J = 7.4, J = 3.0 Hz, 1 H, Et), 2.71 (s, 3 H, NMe), 3.09 (dd, J = 14.0, J = 10.3 Hz, 1 H, CH₂S), 3.26 (dd, J = 14.0, J = 1.0 Hz, 1 H, CH₂S), 3.31 (td, J = 10.3, J = 1.0 Hz, 1 H, CHNH), 3.85 (ddd, J = 10.0, J = 7.4, J = 3.0 Hz, 1 H, CHO), 7.48 (s, 1 H, NH), 7.60-7.72 (m, 3 H, Ph), 7.86 (m, 2 H, Ph) ppm. ¹³C NMR $(75 \text{ MHz}, \text{ CDCl}_3)$: $\delta = 8.24 \text{ (d)}, 12.61 \text{ (d)}, 24.93 \text{ (u)}, 29.32 \text{ (d)},$ 34.63 (d), 52.74 (d), 59.66 (u), 81.11 (d), 129.44 (d), 129.98 (d), 133.80 (d), 136.89 (u), 153.20 (u) ppm. IR (KBr): $\tilde{v} = 3271$ (s), 3061 (w), 2973 (m), 2929 (m), 2877 (m), 2802 (w), 1710 (vs), 1581 (w), 1529 (w), 1469 (s), 1445 (s), 1418 (m), 1403 (m), 1386 (m), 1362 (m), 1341 (m), 1310 (m), 1271 (m), 1242 (vs), 1143 (vs), 1106 (s), 1078 (s), 1018 (s) cm⁻¹. MS (EI): m/z (relative intensity, %) = $311 [M^+ + 1]$ (2), 282 (12), 281 (21), 157 (13), 156 (75), 154 (14), 140 (42), 126 (18), 125 (100), 112 (26), 107 (39), 106 (27), 105 (38), 98 (10), 97 (24), 96 (32), 95 (24), 94 (15), 91 (31), 88 (40), 83 (11),

82 (18), 81 (10). $C_{15}H_{22}N_2O_3S$ (310.41): calcd. C 58.04, H 7.14, N 9.02; found C 57.86, H 7.05, N 8.97.

(+)-(4S,5R,6S)-Tetrahydro-6-methyl-5-(1-methylethyl)-4-{[(S)-N-methyl-S-phenylsulfonimidoyl]methyl}-2H-1,3-oxazin-2-one (5b): Treatment of carbamate 4b (1.63 g, 5.02 mmol) with nBuLi (4.10 mL of 1.60 M in hexane, 6.56 mmol) according to GP2 and purification by crystallization (Et₂O) gave oxazinone 5b (1.54 g, 94%) as a colorless solid. M.p. 113 °C, $[\alpha]_D = +130.5$ (c = 0.55, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): $\delta = 0.66$ (d, J =7.1 Hz, 3 H, *i*Pr), 0.79 (d, J = 7.1 Hz, 3 H, *i*Pr), 1.32 (m, 1 H, CHiPr), 1.35 (d, J = 6.2 Hz, 3 H, Me), 1.63 (m, 1 H, *i*Pr), 2.73 (s, 3 H, NMe), 3.14-3.26 (m, 2 H, CH₂S), (td, J = 8.5, J = 2.7 Hz, 1 H, CHNH), 4.15 (dq, J = 9.4, J = 6.2 Hz, 1 H, CHO), 7.22 (s, 1 H, NH), 7.60–7.73 (m, 3 H, Ph), 7.87 (m, 2 H, Ph) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 18.80$ (d), 18.98 (d), 20.02 (d), 27.29 (d), 29.20 (d), 47.42 (d), 48.16 (d), 62.21 (u), 74.30 (d), 129.35 (d), 129.90 (d), 133.69 (d), 137.13 (u), 154.03 (u) ppm. IR (KBr): $\tilde{v} =$ 3451 (m), 3241 (s), 3156 (s), 3046 (m), 3007 (m), 2971 (vs), 2930 (s), 2899 (s), 2874 (s), 2809 (m), 1733 (vs), 1579 (m), 1551 (w), 1465 (m), 1445 (s), 1425 (m), 1414 (m), 1394 (s), 1385 (s), 1369 (m), 1354 (m), 1345 (m), 1321 (m), 1294 (s), 1232 (s), 1187 (m), 1173 (m), 1157 (s), 1147 (s), 1127 (m), 1110 (s), 1079 (s), 1066 (s), 1045 (m), 1007 (m) cm⁻¹. MS (EI): m/z (relative intensity, %) = 325 [M⁺ + 1] (3), 296 (10), 295 (15), 171 (10), 170 (62), 156 (20), 154 (12), 140 (48), 128 (16), 127 (27), 126 (39), 125 (100), 112 (29), 110 (20), 109 (37), 107 (41), 106 (30), 105 (14), 97 (27), 94 (16), 91 (34), 88 (25), 84 (23), 83 (50), 82 (22), 81 (10). C₁₆H₂₄N₂O₃S (324.44): calcd. C 59.23, H 7.46, N 8.63; found C 58.89, H 7.46, N 8.63.

(+)-(4*S*,5*R*,6*S*)-Tetrahydro-6-(1-methylethyl)-4-{[(*S*)-*N*-methyl-*S*-phenylsulfonimidoyl]methyl}-5-phenyl-2*H*-1,3-oxazin-2-one (5c). From Carbamate (*Z*)-4c: Treatment of carbamate (*Z*)-4c (1.63 g, 4.21 mmol) with *n*BuLi (2.76 mL of 1.60 M in hexane, 4.42 mmol) according to *GP2* and purification by crystallization (EtOAc/*i*PrOH, 1:1) and chromatography (EtOAc) of the remaining mother liquor gave oxazinone 5c (1.34 g, 83%) as a colorless solid, together with sulfoximine 1c (20 mg, 2%).

From Carbamate (E)-4c: Treatment of carbamate (*E*)-**4c** (221 mg, 0.57 mmol) with *n*BuLi (0.37 mL of 1.60 M in hexane, 0.60 mmol) according to *GP2* and purification by crystallization (EtOAc/*i*P-rOH, 1:1) and chromatography (EtOAc) of the mother liquor gave oxazinone **5c** (183 mg, 82%) as a colorless solid, together with sulfoximine **1c** (5 mg, 3%).

5c: M.p. 180 °C (dec.). $[\alpha]_D = +98.6 (c = 0.70, CH_2Cl_2)$. ¹H NMR (300 MHz, CDCl₃): δ = 0.83 (d, J = 6.9 Hz, 3 H, *i*Pr), 0.96 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.40 (septd, J = 6.9, J = 1.7 Hz, 1 H, *i*Pr), 2.62 (t, J = 10.6 Hz, 1 H, CHPh), 2.71 (s, 3 H, NMe), 2.76 (dd, J = 14.1, J = 1.2 Hz, 1 H, CH₂S), 3.06 (dd, J = 14.1, J = 10.7 Hz, 1 H, CH₂S), 3.65 (ddd, J = 10.7, J = 10.6, J = 1.2 Hz, 1 H, CHNH), 4.20 (dd, J = 10.6, J = 1.7 Hz, 1 H, CHO), 6.75-6.78 (m, 2 H, Ph), 7.12-7.24 (m, 3 H, Ph), 7.49-7.56, 7.60-7.67 (m, 6 H, Ph, NH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 14.12$ (d), 20.01 (d), 29.04 (d), 29.58 (d), 46.43 (d), 52.93 (d), 58.83 (u), 84.01 (d), 127.97 (d), 128.49 (d), 129.41 (d), 129.60 (d), 129.85 (d), 133.65 (d), 134.97 (u), 136.51 (u), 153.12 (u) ppm. IR (KBr): $\tilde{v} = 3822$ (s), 3278 (m), 3089 (w), 3066 (w), 3028 (w), 3003 (w), 2969 (m), 2916 (m), 2880 (m), 2809 (w), 2734 (w), 2659 (w), 2579 (w), 2373 (w), 2343 (w), 2183 (w), 2106 (w), 2001 (w), 1956 (w), 1931 (w), 1906 (w), 1708 (s), 1604 (m), 1583 (m), 1525 (w), 1497 (w), 1449 (s), 1420 (w), 1373 (m), 1326 (m), 1298 (w), 1246 (s), 1143 (s), 1105 (m), 1080 (m), 1037 (m), 1001 (w) cm⁻¹. MS (CI): *m/z* (relative intensity, %) = $387 [M^+ + 1] (29), 235 (13), 234 (69), 233 (15), 132 (74), 156$ (100). $C_{21}H_{26}N_2O_3S$ (386.51): calcd. C 65.26, H 6.78, N 7.25; found C 65.09, H 6.84, N 7.17.

(+)-(3S,4R,5Z)-2,5-Dimethyl-6-[(S)-N-methyl-S-phenylsulfonimidoyl]-4-phenyl-5-hexen-3-ol [(Z)-7]: nBuLi (10.7 mL of 1.60 M in hexane, 17.0 mmol) was added at -78 °C to a solution of the allylic sulfoximine (E)-6 (4.42 g, 15.5 mmol) in THF (85 mL). After the mixture had been stirred at this temperature for 10 min, ClTi(OiPr)₃ (4.44 mL, 18.6 mmol) was added. The mixture was then stirred at -78 °C for 10 min, allowed to warm to 0 °C, and stirred at this temperature for 45 min. Subsequently, the mixture was cooled to -78 °C and isobutyraldehyde (2.8 mL, 31.0 mmol) was added dropwise. After the mixture had been stirred at -78 °C for 80 min, it was poured into saturated aqueous $(NH_4)_2CO_3$ and extracted with EtOAc. The combined organic phases were dried (MgSO₄) and concentrated in vacuo. Purification by chromatography (EtOAc/cyclohexane, 4:1) gave alcohol (Z)-7 (3.27 g, 59%) as a colorless solid, together with sulfoximine (E)-6 (1.01 g, 25%). M.p. 105 °C. $[\alpha]_D = +194.7$ (c = 1.02, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): $\delta = 0.90$ (d, J = 6.9 Hz, 3 H, *i*Pr), 1.05 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.68 (septd, J = 7.3, J = 1.1 Hz, 1 H, *i*Pr), 1.74 (d, J = 1.4 Hz, 3 H, Me), 2.64 (s, 3 H, NMe), 4.10 (dd, J =11.1, J = 1.3 Hz, 1 H, CHO), 5.04 (br. s, 1 H, OH), 5.21 (d, J =11.1 Hz, 1 H, CHPh), 6.32 (p, J = 1.1 Hz, 1 H, C=CH), 7.00-7.03 (m, 2 H, Ph), 7.17-7.28 (m, 3 H, Ph), 7.57-7.68 (m, 3 H, Ph), 7.94–7.98 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta =$ 13.80 (d), 19.64 (d), 20.94 (d), 29.36 (d), 29.74 (d), 50.68 (d), 74.74 (d), 126.87 (d), 128.34 (d), 128.82 (d), 128.90 (d), 128.94 (d), 129.29 (d), 132.66 (d), 138.00 (u), 139.59 (u), 156.94 (u) ppm. IR (KBr): $\tilde{v} = 3222$ (m), 3067 (m), 3032 (w), 2960 (s), 2935 (m), 2903 (s), 2869 (s), 2769 (m), 2319 (w), 1619 (m), 1601 (m), 1582 (w), 1494 (m), 1467 (m), 1444 (s), 1385 (m), 1298 (w), 1217 (s), 1159 (m), 1139 (s), 1100 (s), 1079 (s), 1034 (m), 1009 (m) cm⁻¹. MS (EI): m/ z (relative intensity, %) = $358 [M^+ + 1] (5)$, 314 (42), 206 (14), 205(18), 202 (12), 185 (12), 184 (54), 160 (15), 159 (65), 158 (13), 156 (73), 132 (12), 131 (100), 130 (30), 129 (57), 128 (23), 127 (11), 125 (79), 116 (12), 115 (33), 91 (40). C₂₁H₂₇NO₂S (357.51): calcd. C 70.55, H 7.61, N 3.92; found C 70.88, H 7.63, N 3.89.

(+)-(3S,4R,5Z)-2,5-Dimethyl-6-[(S)-N-methyl-S-phenylsulfonimidoyl]-4-phenyl-5-hexen-3-yl Carbamate [(Z)-8]: Treatment of alcohol (Z)-7 (4.21 g, 11.78 mmol) with trichloroacetyl isocyanate (1.47 mL, 12.37 mmol) according to GP1 and purification by chromatography (EtOAc/iPrOH, 8:1) gave carbamate (Z)-8 (4.31 g, 89%) as a colorless solid, together with the corresponding N-trichloroacetyl carbamate (450 mg, 7%). M.p. 62-64 °C. $[\alpha]_{D} = +169.1$ $(c = 0.72, CH_2Cl_2)$. ¹H NMR (400 MHz, CDCl₃): $\delta = 0.90$ (d, J =6.9 Hz, 3 H, *i*Pr), 0.96 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.75 (septd, J =6.9, J = 1.8 Hz, 1 H, i Pr, 1.81 (d, J = 1.1 Hz, 3 H, Me), 2.68 (s,)3 H, NMe), 5.15 (br. s, 2 H, NH₂), 5.31 (d, J = 11.1 Hz, 1 H, CHPh), 5.38 (dd, J = 11.1, J = 1.8 Hz, 1 H, CHO), 6.25 (d, J =1.4 Hz, 1 H, C=CH), 6.84–6.87 (m, 2 H, Ph), 7.16–7.18 (m, 3 H, Ph), 7.57–7.66 (m, 3 H, Ph), 7.97–7.99 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 14.76$ (d), 20.01 (d), 20.88 (d), 29.07 (d), 29.18 (d), 46.66 (d), 75.86 (d), 126.99 (d), 128.17 (d), 128.34 (d), 128.83 (d), 128.91 (d), 129.27 (d), 132.36 (d), 137.36 (u), 140.42 (u), 154.59 (u), 157.32 (u) ppm. IR (KBr): $\tilde{v} = 3421$ (s), 3357 (s), 3179 (m), 3061 (m), 3030 (m), 2965 (s), 2932 (m), 2875 (m), 2803 (w), 1724 (s), 1615 (s), 1601 (s), 1496 (m), 1467 (m), 1446 (s), 1393 (s), 1383 (s), 1334 (m), 1308 (m), 1236 (s), 1147 (s), 1105 (s), 1081 (s), 1047 (s), 1001 (w) cm⁻¹. MS (EI): m/z (relative intensity, %) = $401 [M^+ + 1] (3), 185 (24), 184 (100), 169 (30), 159 (17), 156 (25),$ 141 (11), 131 (12), 129 (25), 128 (16), 125 (23), 115 (11), 191 (14). C₂₂H₂₈N₂O₃S (400.54): calcd. C 65.67, H 7.05, N 6.99; found C 65.63, H 7.12, N 6.91.

7.12, N 6.91.

N-**Trichloroacetyl Carbamate:** ¹H NMR (400 MHz, CDCl₃): δ = 0.94 (d, J = 6.9 Hz, 3 H, *i*Pr), 0.99 (d, J = 7.1 Hz, 3 H, *i*Pr), 1.72 (d, J = 1.4 Hz, 3 H, Me), 1.87 (septd, J = 6.9, J = 1.9 Hz, 1 H, *i*Pr), 2.73 (s, 3 H, NMe), 5.39 (dd, J = 11.0, J = 1.9 Hz, 1 H, CHO), 5.62 (d, J = 11.0 Hz, 1 H, CHPh), 6.19 (d, J = 1.4 Hz, 1 H, C=CH), 7.05–7.09 (m, 2 H, Ph), 7.20–7.29 (m, 3 H, Ph), 7.56–7.66 (m, 3 H, Ph), 7.94–7.98 (m, 2 H, Ph), 9.24 (br. s, 1 H, NH) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.71 (d), 20.20 (d), 20.65 (d), 29.01 (d), 29.22 (d), 46.23 (d), 77.78 (d), 127.22 (d), 128.50 (d), 128.55 (d), 128.87 (d), 128.92, (d), 129.35 (d), 132.51 (d), 136.90 (u), 139.69 (u), 152.57 (u), 154.17 (u), 154.62 (u) ppm, signal of CCl₃ was not observed.

(+)-(4S,5R,6S)-Tetrahydro-4-methyl-6-(1-methylethyl)-4-{[(S)-N-methyl-S-phenylsulfonimidoyl]methyl}-5-phenyl-2H-**1,3-oxazin-2-one** (9): Treatment of carbamate (Z)-8 (2.19 g, 5.47 mmol) with *n*BuLi (3.76 mL of 1.60 M in hexane, 6.02 mmol) according to GP2 and purification by crystallization (Et₂O) and chromatography (EtOAc/iPrOH, 8:1) of the mother liquor gave oxazinone 9 as a colorless solid (1.83 g, 84%), together with the allylic sulfoximine (*E*)-6 (160 mg, 10%). M.p. 178 °C. $[\alpha]_D = +59.8$ (*c* = 1.01, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): $\delta = 0.75$ (d, J =7.0 Hz, 3 H, *i*Pr), 1.05 (d, J = 7.0 Hz, 3 H, *i*Pr), 1.52–1.59 (m, 1 H, *i*Pr), 1.53 (s, 3 H, Me), 2.64 (s, 3 H, NMe), 3.03 (d, *J* = 11.4 Hz, 1 H, CHPh), 3.19 (d, J = 14.3 Hz, 1 H, CH₂S), 3.25 (d, J =14.3 Hz, 1 H, CH_2S), 4.66 (dd, J = 11.4, J = 1.8 Hz, 1 H, CHO), 7.10-7.12 (m, 2 H, Ph), 7.30-7.36 (m, 3 H, Ph), 7.71 (br. s, 1 H, NH), 7.54–7.65 (m, 3 H, Ph), 7.78–7.82 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 14.43$ (d), 19.78 (d), 23.90 (d), 28.79 (d), 28.59 (d), 50.85 (d), 56.53 (u), 64.83 (u), 79.42 (d), 128.15 (d), 128.54 (d), 128.77 (d), 129.54 (d), 133.12 (d), 133.76 (u), 139.45 (u), 154.59 (u) ppm. IR (KBr): $\tilde{v} = 3676$ (m), 3653 (w), 3404 (s), 3067 (w), 3027 (w), 2971 (s), 2930 (m), 2878 (m), 2806 (m), 2285 (w), 1978 (w), 1706 (s), 1607 (m), 1583 (m), 1498 (m), 1459 (s), 1426 (s), 1390 (s), 1361 (m), 1333 (s), 1304 (m), 1240 (s), 1226 (s), 1184 (s), 1136 (s), 1097 (s), 1046 (s) cm⁻¹. MS (CI): m/z (relative intensity, % = 401 [M⁺ + 1] (13), 249 (18), 248 (85), 246 (30), 156 (100). C₂₂H₂₈N₂O₃S (400.54): calcd. C 65.97, H 7.05, N 6.99; found C 65.90, H 6.72, N 6.92.

(+)-(S)-S-[(1Z,3R,4S)-2,5-dimethyl-3-phenyl-4-(triethylsilyloxy)hex-1-enyl]-N-methyl-S-phenylsulfoximine [(Z)-10]: Imidazole (1.34 g, 19.65 mmol) and ClSiEt₃ (1.0 mL, 5.9 mmol) were successively added at room temperature to a solution of alcohol (Z)-7 (1.76 g, 4.92 mmol) in DMF (35 mL). After the mixture had been stirred at room temperature for 12 h, half-saturated aqueous NaHCO3 was added and the resulting mixture was extracted with diethyl ether. The combined organic layers were dried (MgSO₄) and concentrated in vacuo. Chromatography (EtOAc/cyclohexane, 1:1) gave silvl ether (Z)-10 (2.30 g, 99%) as a colorless oil. $[\alpha]_{\rm D}$ = +123.6 (c = 2.04, EtOAc). ¹H NMR (400 MHz, CDCl₃): $\delta = 0.55$ (q, J = 8.0 Hz, 6 H, Et), 0.80 (d, J = 6.9 Hz, 3 H, iPr), 0.93 (t,J = 8.0 Hz, 9 H, Et), 1.02 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.66 (septd, J = 6.9, J = 3.1 Hz, 1 H, *i*Pr), 1.96 (d, J = 1.4 Hz, 3 H, Me), 2.74 (s, 3 H, NMe), 4.21 (dd, J = 8.7, J = 3.2 Hz, 1 H, CHO), 5.33 (qd, J = 8.7 Hz, 1 H, CHPh), 6.11 (q, J = 1.1 Hz, 1 H, C=CH), 6.98-7.02 (m, 2 H, Ph), 7.10-7.16 (m, 3 H, Ph), 7.35-7.44 (m, 3 H, Ph), 7.46-7.51 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, $CDCl_3$): $\delta = 5.93$ (u), 7.59 (d), 17.15 (d), 20.46 (d), 22.41 (d), 29.72 (d), 32.47 (d), 47.63 (d), 78.78 (d), 126.67 (d), 128.48 (d), 128.60 (d), 128.81 (d), 128.98 (d), 129.10 (d), 132.22 (d), 139.81 (u), 141.13 (u), 156.26 (u) ppm. IR (KBr): $\tilde{v} = 3060$ (m), 3027 (w), 2958 (s), 2912 (s), 2876 (s), 2802 (m), 1614 (m), 1600 (m), 1583 (w), 1582 (w), 1494 (w), 1446 (m), 1415 (w), 1385 (w), 1373 (w), 1243 (s), 1182 (w), 1147 (s), 1107 (s), 1079 (s), 1010 (s) cm⁻¹. MS (EI): m/z

(relative intensity, %) = 471 [M⁺] (1), 442 (24), 429 (17), 428 (56), 316 (17), 301 (14), 287 (21), 274 (10), 273 (43), 206 (11), 205 (14), 187 (16), 185 (22), 184 (55), 159 (17), 156 (27), 129 (19), 125 (11), 116 (12), 115 (100), 103 (19). CI 472 [M⁺ + 1] (100). C₂₇H₄₁NO₂SSi (471.77): calcd. C 68.74. H 8.76, N 2.97; found C 68.36, H 8.93, N 3.15.

(+)-(S)-S-[(1E,3R,4S)-2,5-Dimethyl-3-phenyl-4-(triethylsilyloxy)-1-hexenyl]-N-methyl-S-phenylsulfoximine [(*E*)-10]: MeLi $(0.40 \text{ mL of } 1.60 \text{ M in Et}_2\text{O}, 0.64 \text{ mmol})$ was added at $-78 \text{ }^\circ\text{C}$ to a solution of silyl ether (Z)-10 (200 mg, 0.42 mmol) in Et₂O (20 mL). The mixture was warmed to -35 °C and stirred at this temperature for 2 h. It was then cooled to $-78\,$ °C, and saturated aqueous NH₄Cl was added. The aqueous phase was extracted with diethyl ether and the combined organic layers were dried (MgSO₄) and concentrated in vacuo. Chromatography (EtOAc/cyclohexane, 1:1) afforded silvl ether (E)-10 (186 mg, 93%) as a colorless oil. $[\alpha]_{\rm D} =$ +27.4 (c = 0.90, Et₂O). ¹H NMR (400 MHz, CDCl₂): δ = 0.30-0.46 (m, 6 H, Et), 0.73 (d, J = 6.7 Hz, 3 H, *i*Pr), 0.82 (t, J =8.0 Hz, 9 H, Et), 0.89 (d, J = 6.7 Hz, 3 H, *i*Pr), 1.68–1.73 (m, 1 H, *i*Pr), 1.99 (d, J = 1.1 Hz, 3 H, Me), 2.64 (s, 3 H, NMe), 3.42 (d, J = 7.4 Hz, 1 H, CHPh), 4.02 (dd, J = 7.4, J = 4.0 Hz, 1 H,CHO), 6.70 (br. s, 1 H, C=CH), 7.07-7.11 (m, 2 H, Ph), 7.16-7.26 (m, 3 H, Ph), 7.46-7.56 (m, 3 H, Ph), 7.86-7.89 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 5.55$ (u), 7.35 (d), 17.03 (d), 17.74 (d), 20.48 (d), 29.54 (d), 31.92 (d), 59.70 (d), 79.47 (d), 127.251 (d), 128.343 (d), 128.75 (d), 128.84 (d), 128.94 (d), 129.16 (d), 132.35 (d), 139.94 (u), 140.90 (u), 156.19 (u) ppm. IR (CHCl₃): $\tilde{v} = 3061$ (m), 3026 (m), 2957 (s), 2912 (s), 2876 (s), 2801 (m), 2732 (w), 1626 (m), 1600 (w), 1584 (w), 1494 (w), 1448 (m), 1416 (m), 1382 (m), 1243 (s), 1145 (s), 1106 (s), 1080 (s), 1009 (s) cm⁻¹. MS (EI): m/z (relative intensity, %) = 272 [M⁺ + 1] (3), 442 (21), 428 (10), 287 (12), 286 (11), 285 (50), 273 (24), 270 (10), 245 (11), 244 (26), 237 (17), 214 (17), 206 (38), 205 (43), 187 (55), 185 (14), 184 (15), 160 (17), 159 (56), 158 (14), 157 (11), 156 (24), 143 (10), 131 (17), 130 (29), 129 (40), 128 (15), 125 (19), 116 (15), 115 (100), 103 (23), 91 (16), 87 (69). C₂₇H₄₁NO₂SSi (471.77): calcd. C 68.74, H 8.76, N 2.97; found C 68.40, H 8.71, N 3.19.

(+)-(3S,4R,5E)-2,5-Dimethyl-6-[(S)-N-methyl-S-phenylsulfonimidoyl]-4-phenyl-5-hexen-3-ol [(E)-7]: Aqueous HCl (0.15 M, 13 mL) was added at room temperature to a vigorously stirred solution of the silvl ether (E)-10 (1.06 g, 2.25 mmol) in THF (15 mL) and acetic acid (3 mL). Stirring of the mixture was continued at this temperature for 2 h. The mixture was then neutralized by the addition of saturated aqueous NaHCO₃ and extracted with EtOAc. The combined organic phases were dried (MgSO₄) and concentrated in vacuo. Chromatography (EtOAc/cyclohexane, 4:1) afforded alcohol (E)-7 (660 mg, 82%) as a colorless solid. M.p. 135 °C. $[\alpha]_{D} = +4.0 \ (c = 0.60, CH_{2}Cl_{2})$. ¹H NMR (400 MHz, CDCl₃): $\delta = 0.81$ (d, J = 7.0 Hz, 3 H, *i*Pr), 0.92 (d, J = 7.0 Hz, 3 H, *i*Pr), 1.51 (septd, J = 7.0, J = 2.8 Hz, 1 H, *i*Pr), 1.89 (d, J = 1.1 Hz, 3 H, Me), 2.60 (br. s, 1 H, OH), 2.65 (s, 3 H, NMe), 3.41 (d, J =9.9 Hz, 1 H, CHPh), 3.96 (dd, J = 9.9, J = 2.8 Hz, 1 H, CHO), 6.74 (br. s, 1 H, C=CH), 7.09-7.13 (m, 2 H, Ph), 7.18-7.28 (m, 3 H, Ph), 7.46-7.55 (m, 3 H, Ph), 7.89-7.92 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 14.16$ (d), 16.78 (d), 20.52 (d), 29.22 (d), 29.27 (d), 59.42 (d), 75.16 (d), 127.12 (d), 127.40 (d), 128.18 (d), 128.37 (d), 128.54 (d), 128.83 (d), 132.00 (d), 138.21 (u), 140.26 (u), 156.17 (u) ppm. IR (KBr): $\tilde{v} = 3676$ (w), 3652 (w), 3400 (m), 3256 (m), 3062 (w), 3039 (w), 2967 (s), 2930 (m), 2905 (m), 2873 (m), 2802 (m), 2370 (w), 2343 (w), 1736 (w), 1703 (w), 1617 (m), 1493 (m), 1465 (m), 1446 (s), 1381 (m), 1335 (w), 1302 (m), 1229 (s), 1135 (s), 1108 (s), 1083 (s), 1004 (s) cm⁻¹. MS (CI): m/z(relative intensity, %) = $358 [M^+ + 1] (41), 287 (14), 286 (69), 187$

(11), 160 (18), 156 (100), 140 (12), 133 (29), 132 (38), 131 (50), 129 (13). C $_{21}H_{27}NO_2S$ (357.51): calcd. C 70.55, H 7.61, N 3.92; found C 70.55, H 7.75, N 3.78.

(+)-(3S,4R,5E)-2,5-Dimethyl-6-[(S)-N-methyl-S-phenylsulfonimidovl]-4-phenyl-5-hexen-3-vl Carbamate ((E)-8): Treatment of alcohol (E)-7 (418 mg, 1.17 mmol) in THF (15 mL) with trichloroacetyl isocyanate (0.15 mL, 1.23 mmol) according to GP1 and purification by chromatography (EtOAc/iPrOH, 8:1) gave carbamate (E)-8 (443 mg, 95%) as a colorless solid. M.p. 64–70 °C. $[\alpha]_{\rm D} = +23.6$ $(c = 0.95, \text{Et}_2\text{O})$. ¹H NMR (400 MHz, CDCl₃): $\delta = 0.77$ (d, J =6.9 Hz, 3 H, *i*Pr), 0.87 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.70 (septd, J =6.9, J = 2.7 Hz, 1 H, *i*Pr), 1.88 (d, J = 0.8 Hz, 3 H, Me), 2.67 (s, 3 H, NMe), 3.59 (d, J = 10.5 Hz, 1 H, CHPh), $4.69 (s, 2 H, NH_2)$, 5.28 (dd, J = 10.5, J = 2.7 Hz 1 H, CHO), 6.61 (br. d, J = 0.8 Hz, 1 H, C=CH), 7.16-7.19 (m, 2 H, Ph), 7.21-7.31 (m, 3 H, Ph), 7.47-7.56 (m, 3 H, Ph), 7.89-7.92 (m, 2 H, Ph) ppm. ¹³C NMR $(100 \text{ MHz}, \text{CDCl}_3)$: $\delta = 14.88 \text{ (d)}, 14.98 \text{ (d)}, 19.94 \text{ (d)}, 29.14 \text{ (d)},$ 29.18 (d), 57.86 (d), 76.14 (d), 127.43 (d), 127.92 (d), 128.40 (d), 128.43 (d), 128.61 (d), 128.81 (d), 132.05 (d), 137.05 (u), 140.34 (u), 154.73 (u), 156.31 (u) ppm. IR (KBr): $\tilde{v} = 3428$ (m), 3175 (w), 3061 (w), 3029 (w), 2965 (m), 2934 (m), 2874 (m), 2802 (w), 1724 (s), 1620 (m), 1496 (m), 1448 (m), 1389 (s), 1333 (s), 1236 (s), 1144 (s), 1107 (s), 1081 (m), 1043 (s) cm⁻¹. MS (EI): *m/z* (relative intensity, %) = 401 $[M^+ + 1]$ (3), 400 (30), 340 (40), 298 (14), 285 (12), 265 (32), 260 (19), 259 (14), 237 (18), 236 (14), 217 (11), 214 (17), 206 (40), 205 (52), 204 (11), 194 (11), 185 (11), 184 (23), 183 (10), 172 (12), 169 (28), 159 (11), 158 (30), 157 (11), 156 (33), 145 (31), 143 (18), 142 (100), 141 (21), 131 (24), 130 (47), 129 (100), 128 (64), 127 (18), 126 (11), 125 (64), 117 (16), 116 (11), 115 (43), 109 (12), 107 (10), 105 (25), 103 (10), 97 (10), 91 (72). C₂₂H₂₈N₂O₃S (400.54): calcd. C 65.97, H 7.05, N 6.99; found C 65.82, H 7.21, N 6.94.

(+)-(4*S*,5*R*,6*S*)- and (-)-(4*R*,5*R*,6*S*)-Tetrahydro-4-methyl-6-(1methylethyl)-4-{[(*S*)-*N*-methyl-*S*-phenylsulfonimidoyl]methyl}-5-phenyl-2*H*-1,3-oxazin-2-one (9 and *epi*-9): Treatment of carbamate (*E*)-8 (453 mg, 1.13 mmol) with *n*BuLi (0.78 mL of 1.60 M in hexane, 1.24 mmol) according to *GP2* and purification by chromatography (EtOAc/*i*PrOH, 8:1) gave oxazinones 9 (279 mg, 62%) and *epi*-9 (65 mg, 14%) as colorless solids, together with (*E*)-6 (32 mg, 10%) and (*Z*)-6 (26 mg, 8%).

epi-9: M.p. 183–187 °C. $[\alpha]_D = -63.4$ (c = 0.55, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): $\delta = 0.75$ (d, J = 7.0 Hz, 3 H, *i*Pr), 1.03 (d, J = 7.0 Hz, 3 H, *i*Pr), 1.62 (septd, J = 7.0, J = 1.8 Hz, 1 H, *i*Pr), 1.67 (s, 3 H, Me), 2.59 (s, 3 H, NMe), 2.97 (m, 2 H, CH₂S), 3.56 (d, J = 13.7 Hz, 1 H, CHPh), 4.46 (dd, J = 11.4, J = 1.9 Hz, 1 H, CHO), 7.02-7.03 (m, 2 H, Ph), 7.30-7.34 (m, 3 H, Ph), 7.54-7.65 (m, 4 H, Ph, NH), 7.78-7.81 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 13.24$ (d), 19.74 (d), 27.04 (d), 28.59 (d), 29.39 (d), 53.72 (d), 56.01 (u), 63.31 (u), 79.34 (d), 128.14 (d), 128.69 (d), 128.74 (d), 129.54 (d), 132.99 (d), 133.44 (u), 138.97 (u), 152.85 (u) ppm. IR (KBr): $\tilde{v} = 3676$ (w), 3405 (m), 3060 (m), 3030 (w), 2967 (m), 2931 (m), 2875 (m), 2803 (w), 1710 (s), 1583 (w), 1498 (w), 1445 (m), 1384 (m), 1335 (w), 1302 (w), 1235 (s), 1182 (w), 1148 (m), 1105 (w), 1075 (m), 1044 (w) cm⁻¹. MS (CI): m/z(relative intensity, %) = $401 [M^+ + 1] (34), 248 (21), 247 (18), 246$ (100), 156 (73). C₂₂H₂₈N₂O₃S (400.54): calcd. C 65.97, H 7.05, N 6.99; found C 65.57, H 6.28, N 6.77.

(-)- $(\alpha S, 1R, 2Z)$ - α -(1-Methylethyl)-2-{[(S)-N-methyl-S-phenylsulfonimidoyl]methylene}cyclopentylmethanol (13a): *n*BuLi (16.1 mL of 1.6 M in hexane, 25.7 mmol) was added at -78 °C to a solution of the allylic sulfoximine 12a (5.77 g, 24.5 mmol) in THF (130 mL). After the mixture had been stirred at this temperature for 1 h, CITi(O*i*Pr)₃ (12.3 mL, 51.5 mmol) was added. The mixture was then stirred at -78 °C for 1 h, allowed to warm to 0 °C, and stirred at this temperature for 2 h. Subsequently the mixture was cooled to -78 °C, and isobutyraldehyde (4.7 mL, 51.5 mmol) was added dropwise. The mixture was then allowed to warm to room temperature over a period of 5 h and was then poured into saturated aqueous $(NH_4)_2CO_3$ and extracted with EtOAc. The combined organic phases were dried (MgSO₄) and concentrated in vacuo. Purification by chromatography (cyclohexane/EtOAc, 4:1) gave a mixture of alcohol 13a, sulfoximine 12a, and N-methyl-S-phenylsulfinamide in a ratio of 45:12:1. This mixture was dissolved in DMF (200 mL), and imidazole (7.06 g, 103.7 mmol) and ClSiEt₃ (6.4 mL, 38.4 mmol) were added successively. After the mixture had been stirred at room temperature for 12 h, half-saturated aqueous NaHCO₃ was added and the mixture was extracted with diethyl ether. The combined organic layers were dried (MgSO₄) and concentrated in vacuo. Chromatography (EtOAc/hexane, 3:1) gave silyl ether 13a-SiEt₃ (7.34 g, 71%) as a colorless oil, together with sulfoximine 12a (750 mg, 13%). The silyl ether 13a-SiEt₃ (7.34 g, 17.45 mmol) was dissolved in THF (200 mL), and acetic acid (40 mL) and aqueous HCl (0.15 M, 210 mL) were added to the vigorously stirred solution at room temperature. Stirring of the mixture was continued at this temperature for 2 h. The mixture was then neutralized by the addition of saturated aqueous NaHCO₃ solution and extracted with EtOAc. The combined organic phases were dried (MgSO₄) and concentrated in vacuo. Chromatography (EtOAc) afforded alcohol 13a (5.11 g, 68%, based on 12a) as a colorless solid.

Compound 13a–SiEt₃: $[\alpha]_D = -249.5 (c = 0.20, EtOAc)$. ¹H NMR $(400 \text{ MHz}, \text{ CDCl}_3)$: $\delta = 0.65 - 0.73 \text{ (m, 6 H, Et)}, 0.92 \text{ (d, } J =$ 6.9 Hz, 3 H, iPr), 0.96-1.02 (m, 12 H, Et, iPr), 1.41-1.53 (m, 1 H, CH₂), 1.63-1.81 (m, 3 H, *i*Pr, CH₂), 2.06-2.16 (m, 1 H, CH₂), 2.30-2.38 (m, 1 H, CH₂), 2.51-2.63 (m, 1 H, CH₂), 2.71 (s, 3 H, NMe), 3.54-3.62 (m, 1 H, CHC=C), 4.33-4.37 (m, 1 H, CHO), 6.17-6.19 (m, 1 H), 7.49-7.58 (m, 3 H, Ph), 7.88-7.92 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 5.51$ (u), 7.48 (d), 18.61 (d), 22.71 (d), 23.03 (u), 27.74 (u), 29.78 (d), 31.36 (d), 38.07 (u), 47.50 (d), 77.56 (d), 122.35 (d), 128.74 (d), 129.29 (d), 132.37 (d), 140.77 (u), 164.04 (u) ppm. IR (KBr): $\tilde{v} = 3062$ (m), 2957 (s), 2876 (s), 2801 (m), 1624 (m), 1461 (s), 1447 (s), 1416 (m), 1389 (w), 1374 (w), 1241 (s), 1152 (s), 1118 (s), 1080 (s), 1008 (s) cm⁻¹. MS (EI): m/z (relative intensity, %) = 422 [M⁺ + 1] (2), 394 (10), 393 (31), 392 (95), 391 (93), 379 (14), 378 (56), 345 (11), 344 (47), 270 (32), 266 (13), 251 (24), 238 (16), 237 (15), 235 (74), 235 (11), 223 (19), 191 (14), 189 (14), 188 (11), 187 (67), 159 (48), 157 (15), 156 (28), 155 (27), 149 (12.84), 135 (13), 125 (15), 125 (14), 116 (14), 115 (100), 110 (11), 109 (19), 107 (17), 105 (11), 103 (33), 97 (13), 93 (10), 91 (13), 87 (86), 85 (10), 81 (14). C₂₃H₃₉NO₂SSi (421.72): calcd. C 65.51, H 9.32, N 3.32; found C 65.38, H 9.23, N 3.65.

Compound 13a: M.p. 53 °C. $[\alpha]_D = -94.1$ (c = 1.70, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): $\delta = 0.99$ (d, J = 6.9 Hz, 3 H, *i*Pr), 1.07 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.61–1.89 (m, 5 H, *i*Pr, CH₂), 2.30–2.40 (m, 1 H, CH₂), 2.63 (s, 3 H, NMe), 2.64–2.74 (m, 1 H, CH₂), 3.22 (dd, J = 10.6, J = 2.0 Hz, 1 H, CHC=C), 3.87–3.93 (m, 1 H, CHO), 6.00 (br. s, 1 H, OH), 6.20–6.22 (m, 1 H, C=CH), 7.52–7.62 (m, 3 H, Ph), 7.88–7.92 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 14.67$ (d), 21.54 (d), 21.65 (u), 29.31 (d), 30.16 (u), 31.30 (d), 34.52 (u), 46.38 (d), 77.26 (d), 123.52 (d), 128.89 (d), 129.48 (d), 132.89 (d), 139.97 (u), 164.21 (u) ppm. IR (KBr): $\tilde{v} = 3144$ (s), 3024 (w), 2957 (s), 2870 (m), 2800 (w), 1627 (s), 1582 (w), 1447 (s), 1383 (w), 1365 (w), 1289 (w), 1218 (s), 1142 (s), 1101 (s), 1077 (s), 1020 (s) cm⁻¹. MS (CI): m/z (relative intensity, %) = 308 [M⁺ + 1] (100), 236 (43), 156 (48). C₁₇H₂₅NO₂S

Eur. J. Org. Chem. 2003, 1500-1526

(307.44): calcd. C 66.41, H 8.20, N 4.55; found C 66.51, H 8.36, N 4.55.

 $(-)-(\alpha S, 1R, 2Z)-\alpha-(1-Methylethyl)-2-{[(S)-N-methyl-S-phenyl$ sulfonimidoyl]-methylene]cyclopentylmethyl Carbamate (14a): Treatment of alcohol 13a (2.38 g, 7.44 mmol) with trichloroacetyl isocyanate (0.96 mL, 8.13 mmol) according to GP1 and purification by chromatography (EtOAc/iPrOH, 8:1) gave carbamate 14a (2.44 g, 90%) as a colorless solid, together with the corresponding N-trichloroacetyl carbamate (370 mg, 10%). M.p. 45–47 °C. $[\alpha]_D$ = -237.7 (*c* = 1.85, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ = 1.03 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.05 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.50–1.61 (m, 1 H, CH₂), 1.63-1.70 (m, 2 H, CH₂), 1.78-1.90 (m, 1 H, CH₂), 2.00 (septd, J = 6.9, J = 3.6 Hz, 1 H, *i*Pr), 2.21–2.31 (m, 1 H, CH₂), 2.61 (s, 3 H, NMe), 2.60-2.70 (m, 1 H, CH₂), 3.90-3.97 (m, 1 H, CHC=C), 4.42 (dd, J = 10.0, J = 3.6 Hz, 1 H, CHO), 5.85 (br. s, 2 H, NH₂), 6.35 (m, 1 H, C=CH), 7.52-7.58 (m, 3 H, Ph), 7.86–7.89 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 16.38$ (d), 20.37 (d), 20.98 (u), 29.28 (d), 29.66 (u), 30.46 (d), 34.51 (u), 42.28 (d), 76.80 (d), 122.80 (d), 128.76 (d), 128.17 (d), 132.10 (d), 139.56 (u), 158.38 (u), 161.59 (u) ppm. IR (KBr): $\tilde{v} =$ 3410 (m), 3159 (m), 3062 (m), 2964 (s), 2875 (m), 2803 (m), 1723 (s), 1609 (m), 1467 (w), 1446 (m), 1380 (s), 1333 (s), 1306 (m), 1235 (s), 1152 (s), 1104 (m), 1079 (s), 1047 (s) cm⁻¹. MS (EI): *m/z* (relative intensity, %) = 351 [M⁺ + 1] (2), 307 (29), 306 (81), 291 (20), 290 (100), 264 (14), 236 (13), 235 (87), 189 (12), 187 (15), 157 (12), 156 (39), 155 (37), 135 (25), 134 (26), 129 (12), 125 (60), 110 (10), 109 (26), 107 (17), 105 (11), 97 (12), 93 (11), 91 (17), 81 (16). C₁₈H₂₆N₂O₃S (350.48): calcd. C 61.69, H 7.48, N 7.99; found C 61.56, H 7.48, N 7.91.

N-Trichloroacetyl Carbamate: ¹H NMR (400 MHz, CDCl₃): δ = 1.07 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.09 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.55–1.88 (m, 4 H, CH₂), 2.08 (septd, 1 H, J = 6.9, J = 3.4 Hz, *i*Pr), 2.22–2.34 (m, 1 H, CH₂), 2.48–2.58 (m, 1 H, CH₂), 2.69 (s, 3 H, NMe), 4.38–4.42 (m, 1 H, CHC=C), 4.39 (dd, J = 10.0, J = 3.4 Hz, 1 H, CHO), 6.26 (br. d, J = 1.4 Hz, 1 H, C=CH), 7.49–7.62 (m, 3 H, Ph), 7.86–7.90 (m, 2 H, Ph), 10.43 (br. s, 1 H, NH) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 16.49 (d), 20.41 (d), 21.39 (u), 29.10 (d), 29.93 (u), 30.82 (d), 34.53 (u), 42.03 (d), 75.86 (d), 123.29 (d), 128.89 (d), 129.27 (d), 132.33 (u), 138.71 (u), 154.66 (u), 155.18 (u), 159.78 (u) ppm, signal of CCl₃ was not observed.

(-)-(αS,1R,2Z)-α-(1-Methylethyl)-2-{[(S)-N-methyl-S-phenylsulfonimidoyl|methylene}cyclohexylmethyl Carbamate (14b): Treatment of alcohol 13b (1.26 g, 3.92 mmol) with trichloroacetyl isocyanate (0.49 mL, 4.12 mmol) according to GP1 and purification by chromatography (EtOAc/iPrOH, 4:1) gave carbamate 14b (1.29 g, 90%) as a colorless solid, together with the corresponding N-trichloroacetyl carbamate (190 mg, 10%). M.p. 53-55 °C, $[\alpha]_D$ = $-210.0 (c = 0.20, CH_2Cl_2)$. ¹H NMR (300 MHz, CDCl₃): $\delta = 0.85$ (d, J = 6.8 Hz, 3 H, iPr), 0.91 (d, J = 6.8 Hz, 3 H, iPr), 0.90-0.95(m, 1 H), 1.10-1.40 (m, 3 H), 1.80-2.00 (m, 4 H), 2.50-2.60 (m, 4 H), 3.60 (dd, J = 10.5, J = 2.4 Hz, 1 H, CHC=C), 4.95 (dd, J = 10.5, J = 2.2 Hz, 1 H, CHO), 5.00 (br. s, 2 H, NH₂), 6.30 (d, J =1.4 Hz, 1 H, C=CH), 7.45-7.55 (m, 3 H, Ph), 7.80-7.85 (m, 2 H, Ph) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 14.70$ (d), 20.15 (d), 20.33 (d), 20.46 (u), 27.76 (u), 28.60 (d), 29.33 (d), 33.61 (u), 38.35 (d), 75.47 (d), 126.73 (d), 129.10 (d), 129.26 (d) 132.37 (d), 141.32 (u), 157.83 (u), 159.84 (u) ppm. IR (KBr): $\tilde{v} = 3431$ (s), 3356 (s), 3177 (m), 1723 (vs), 1654 (s), 1446 (s), 1240 (vs), 1148 (s) 1070 (s) cm⁻¹. MS (EI): m/z (relative intensity, %) = 365 [M⁺ + 1] (3), 364 $[M^+]$ (3), 304 (10), 116 (16), 156 (100), 149 (55), 148 (28), 133 (40), 125 (63), 123 (59), 105 (27), 91 (18). C₁₉H₂₈N₂O₃S (364.50): calcd. C 62.61, H 7.69, N 7.69; found C 62.27, H 7.88, N 7.52.

N-Trichloroacetyl Carbamate: ¹H NMR (300 MHz, CDCl₃): $\delta = 0.97$ (d, J = 6.9 Hz, 3 H, *i*Pr), 1.01 (d, J = 6.7 Hz, 3 H, *i*Pr), 1.21–1.54 (m, 4 H, CH₂), 1.60–1.71 (m, 2 H, CH₂), 2.02–2.07 (m, 4 H, *i*Pr, CH₂), 2.41–2.47 (m, 1 H, CH₂), 2.67 (s, 3 H, NMe), 3.95–4.05 (m, 1 H, CHC=CH), 5.10 (dd, J = 11.0, J = 2.1 Hz, 1 H, CHO), 6.26 (d, J = 1.7 Hz, 1 H, C=CH), 7.52–7.62 (m, 3 H, Ph), 7.88–7.94 (m, 2 H, Ph), 8.70 (br. s, 1 H, NH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 14.51$ (d), 20.11 (d), 20.30 (u), 27.33 (u), 27.89 (u), 28.49 (d), 29.05 (d), 33.20 (u), 37.38 (d), 77.47 (d), 126.23 (d), 128.70 (d), 129.10 (d), 132.35 (d), 139.83 (u), 153.74 (u), 154.42 (u), 157.65 (u) ppm, signal of CCl₃ was not observed.

(+)-(4S,4aR,7aS)-Hexahydro-4-(1-methylethyl)-7a-{[(S)-N-methyl-S-phenylsulfonimidoyl]methyl}cyclopenta[d][1,3]oxazin-2(1H)-one (15a): Treatment of carbamate 14a (2.35 g, 6.71 mmol) with nBuLi (4.39 mL of 1.6 M in hexane, 7.02 mmol) according to GP2 and purification by crystallization (Et₂O) and chromatography (EtOAc/ iPrOH, 8:1) of the mother liquor gave oxazinone 15a as a light yellow solid (1.88 g, 80%), together with sulfoximine 12a (93 mg, 6%). M.p. 147 °C. $[\alpha]_D = +84.5$ (c = 0.40, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): $\delta = 0.89$ (d, J = 7.0 Hz, 3 H, *i*Pr), 1.05 (d, J = 7.0 Hz, 3 H, *i*Pr), 1.46–1.54 (m, 1 H, CH₂), 1.61–1.71 (m, 1 H, CH₂), 1.76-2.00 (m, 5 H, CH₂, *i*Pr), 2.62-2.69 (m, 1 H, CHCNH), 2.67 (s, 3 H, NMe), 3.26 (dd, J = 14.3, J = 0.8 Hz, 1 H, CH₂S), 3.55 (d, J = 14.3 Hz, 1 H, CH₂S), 3.72 (dd, J = 9.9, J = 3.0 Hz, 1 H, CHO), 6.82 (s, 1 H, NH), 7.56-7.66 (m, 3 H, Ph), 7.84–7.88 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 15.10$ (d), 19.82 (d), 22.93 (u), 27.16 (u), 28.90 (d), 29.67 (d), 38.52 (u), 44.78 (d), 63.28 (u), 65.64 (u), 82.80 (d), 128.47 (d), 129.57 (d), 133.00 (d), 139.59 (u), 154.83 (u) ppm. IR (KBr): $\tilde{v} =$ 3404 (w), 3309 (m), 2968 (s), 2918 (m), 2888 (m), 2805 (m), 1707 (s), 1579 (w), 1447 (m), 1432 (m), 1415 (m), 1396 (m), 1372 (m), 1330 (m), 1295 (m), 1237 (s), 1196 (w), 1141 (s), 1103 (m), 1074 (m), 1015 (s) cm⁻¹. MS (CI): m/z (relative intensity, %) = 351 [M⁺ + 1] (16), 199 (17), 198 (100), 196 (26), 156 (67). $C_{18}H_{26}N_2O_3S$ (350.48): calcd. C 61.69, H 7.48, N 7.99; found C 61.64, H 7.45, N 7.75.

 $(+)-(4S,4aR,8aS)-Octahydro-4-(1-methylethyl)-8a-{[(S)-$ N-methyl-S-phenylsulfonimidoyl|methyl}-2H-3,1-benzoxazin-2-one (15b): Treatment of carbamate 14b (1.15 g, 3.15 mmol) with *n*BuLi (2.1 mL of 1.60 м in hexane, 3.32 mmol) according to GP2 and purification by crystallization (EtOAc) gave oxazinone **15b** (965 mg, 84%) as a light yellow solid. M.p. 206–207 °C, $[\alpha]_{D} =$ +89.3 (c = 0.70, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): $\delta = 0.80$ (d, J = 6.7 Hz, 3 H, iPr), 1.10 (d, J = 6.7 Hz, 3 H, iPr), 1.15-1.80(m, 8 H, CH₂), 1.95 (septd, J = 7.0, J = 2.0 Hz, 1 H, *i*Pr), 2.55-2.60 (m, 1 H, CHCNH), 2.70 (s, 3 H, NMe), 3.10 (dd, J =14.4, J = 1.6 Hz, 1 H, CH₂S), 3.90 (dd, J = 14.4, J = 2.2 Hz, 1 H, CH₂S), 4.30 (dd, J = 10.4, J = 2.0 Hz, 1 H, CHO), 7.50 (s, 1 H, NH), 7.55-7.65 (m, 3 H, Ph), 7.80-7.85 (m, 2 H, Ph) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 13.44$ (d), 19.84 (d), 20.05 (u), 22.31 (u), 28.01 (d), 29.67 (d), 33.55 (u), 39.00 (d), 55.88 (u), 62.66 (u), 78.39 (d) 128.81 (d), 128.95 (d), 129.76 (d), 133.31 (d), 140.06 (u), 153.18 (u) ppm. IR (KBr): $\tilde{v} = 3390(s)$, 2967 (s), 2934 (s), 2884 (m), 1699 (vs), 1580 (w), 1441 (s), 1373 (m), 1277 (s), 1169 (s) cm⁻¹. MS (EI): m/z (relative intensity, %) = 365 [M⁺ + 1] (1), 364 [M⁺] (1), 336 (28), 321 (14), 210 (45), 170 (34), 167 (16), 166 (37), 156 (17), 150 (57), 140 (100), 138 (28), 125 (50), 95 (39). C₁₉H₂₈N₂O₃S (364.50): calcd. C 62.61, H 7.69, N 7.69; found C 62.30, H 7.91, N 7.55.

(+)-(4*S*,5*R*,6*S*)-Tetrahydro-6-ethyl-5-methyl-4-{(1*R*)-1-[(*S*)-*N*-methyl-*S*-phenylsulfonimidoyl]ethyl}-2*H*-1,3-oxazin-2-one (16a): Successive treatment of sulfoximine 5a (216 mg, 0.70 mmol)

with nBuLi (1.09 mL of 1.60 M in hexane, 1.74 mmol) and MeI (0.50 mL, 8.03 mmol) according to GP3 gave a mixture of sulfoximines 16a, epi-16a, and 5a in a ratio of 18:2:1. Purification by chromatography (EtOAc/cyclohexane, 4:1) and crystallization (Et₂O) afforded sulfoximine 16a (154 mg, 68%) as a colorless solid. M.p. 147 °C. $[\alpha]_{D} = +134.0$ (c = 0.70, CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃): $\delta = 0.68$ (d, J = 6.5 Hz, 3 H, CHMe), 1.00 (t, J = 7.3 Hz, 3 H, Et), 1.38 (d, J = 7.0 Hz, 3 H, CH(Me)S], 1.51 (dquin, J =14.8, J = 7.3 Hz, 1 H, Et), 1.57 (tq, J = 10.0, J = 6.5 Hz, 1 H, CHMe), 1.78 (dqd, J = 14.8, J = 7.3, J = 3.0 Hz, 1 H, Et), 2.71 (s, 3 H, NMe), 3.07 (brq, J = 7.0 Hz, 1 H, CHS), 3.50 (dd, J =10.0, J = 1.0 Hz, 1 H, CHNH), 3.81 (ddd, J = 10.0, J = 7.3, J =3.0 Hz, 1 H, CHO), 7.12 (s, 1 H, NH), 7.62 (m, 2 H, Ph), 7.68 (m, 1 H, Ph), 7.82 (m, 2 H, Ph) ppm. ¹³C NMR (125 MHz, CDCl₃): $\delta = 5.82$ (d), 8.32 (d), 12.44 (d), 24.89 (u), 29.06 (d), 32.58 (d), 55.09 (d), 59.94 (d), 80.91 (d), 129.71 (d), 133.52 (d), 136.07 (u), 154.17 (u) ppm. IR (KBr): $\tilde{v} = 3397$ (m), 3226 (vs), 3089 (m), 3066 (m), 2974 (vs), 2944 (s), 2921 (s), 2880 (s), 2805 (m), 1708 (vs), 1582 (w), 1529 (w), 1463 (s), 1448 (s), 1417 (s), 1405 (s), 1387 (m), 1377 (m), 1358 (s), 1332 (m), 1304 (s), 1268 (s), 1237 (vs), 1227 (vs), 1174 (m), 1148 (s), 1133 (vs), 1107 (s), 1078 (s), 1060 (m), 1028 (s) cm^{-1} . MS (EI): m/z (relative intensity, %) = 325 [M⁺ + 1] (5), 183 (20), 170 (22), 169 (76), 156 (39), 154 (20), 126 (44), 125 (100), 110 (90), 107 (17), 106 (18), 105 (31), 97 (18), 96 (44). C₁₆H₂₄N₂O₃S (324.44): calcd. C 59.23, H 7.46, N 8.63; found C 58.99, H 7.40, N 8.59.

(4S,5R,6S)-Tetrahydro-6-methyl-5-(1-methylethyl)-4-{[(S)-N-methyl-S-phenylsulfonimidoyl)deuteriomethyl}-2H-1,3-oxazin-2-one (16b and epi-16b): Successive treatment of sulfoximine 5b (46 mg, 0.14 mmol) with *n*BuLi (0.27 mL of 1.60 м in hexane, 0.43 mmol) and CD₃OD (0.5 mL) according to GP3 gave a mixture of sulfoximines 16b and epi-16b in a ratio of 3:1 (46 mg, 99%) as a yellow oil. ¹H NMR (300 MHz, CDCl₃): $\delta = 0.66$ (d, J = 7.1 Hz, 3 H, *i*Pr), 0.79 (d, J = 7.1 Hz, 3 H, *i*Pr), 1.32 (td, J = 9.2, J =2.5 Hz, 1 H, CHiPr), 1.35 (d, J = 6.2 Hz, 3 H, Me), 1.63 (septd, J = 7.1, J = 2.5 Hz, 1 H, *i*Pr), 2.73 (s, 3 H, NMe), 3.18 (br. d, J = 10.2 Hz, 0.25 H, CH₂S), 3.24 (br. s, 0.75 H, CH₂S), 3.58 (br. d, J =9.0 Hz, 1 H, CHNH), 4.15 (dq, J = 9.2, J = 6.2 Hz, 1 H, CHO), 7.22 (s, 1 H, NH), 7.60-7.73 (m, 3 H, Ph), 7.87 (m, 2 H, Ph) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 18.80 (d), 18.98 (d), 20.02 (d), 27.29 (d), 29.20 (d), 47.42 (d), 48.16 (d), 62.21 (u), 74.30 (d), 129.35 (d), 129.90 (d), 133.69 (d), 137.13 (u), 154.03 (u) ppm.

(+)-(4*S*,5*R*,6*S*)-Tetrahydro-6-methyl-5-(1-methylethyl)-4-{(1*R*)-1-[(*S*)-*N*-methyl-*S*-phenylsulfonimidoyl]ethyl}-2*H*-1,3-oxazin-2-one (16c): Successive treatment of sulfoximine 5b (162 mg, 0.50 mmol) with *n*BuLi (0.80 mL of 1.60 M in hexane, 1.28 mmol) and MeI (0.40 mL, 6.43 mmol) according to *GP3* gave a mixture of sulfoximines 16c, *epi*-16c, and 5b in a ratio of 10:2:1. Purification by chromatography (EtOAc/cyclohexane, 4:1) afforded sulfoximine 16c (127 mg, 75%) and a mixture of *epi*-16c and 5b (16 mg) in a ratio of 5:1 as colorless solids.

Compound 16c: M.p. 134 °C, $[\alpha]_D = +140.4$ (c = 0.29, CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃): $\delta = 0.55$ (d, J = 7.1 Hz, 3 H, *i*Pr), 0.73 (d, J = 7.1 Hz, 3 H, *i*Pr), 1.34 (d, J = 6.4 Hz, 3 H, CH*Me*), 1.33–1.58 (m, C*Hi*Pr), 1.40 (d, J = 7.0 Hz, 3 H, *i*Pr), 1.40 [d, J =7.0 Hz, 3 H, CH(*Me*)S], 1.58 (m, 1 H, *i*Pr), 2.73 (s, 3 H, NMe), 3.03 (m, 1 H, CHS), 3.76 (br. d, J = 9.0 Hz, 1 H, C*H*NH), 4.08 (dq, J = 10.4, J = 6.1 Hz, 1 H, CHO), 6.98 (s, 1 H, NH), 7.62 (m, 2 H, Ph), 7.68 (m, 1 H, Ph), 7.84 (m, 2 H, Ph) ppm. ¹³C NMR (125 MHz, CDCl₃): $\delta = 5.82$ (d), 18.46 (d), 18.66 (d), 19.76 (d), 27.03 (d), 28.95 (d), 45.84 (d), 50.34 (d), 62.76 (d), 74.19 (d), 129.74 (d), 129.84 (d), 133.52 (d), 136.52 (u), 155.65 (u) ppm. IR (KBr): $\tilde{\nu} = 3854$ (m), 3399 (w), 3231 (s), 3089 (m), 3061 (m), 2995 (s), 2975 (vs), 2938 (s), 2901 (s), 2878 (s), 2813 (m), 1718 (vs), 1713 (vs), 1581 (w), 1531 (w), 1466 (s), 1445 (s), 1423 (m), 1403 (m), 1392 (s), 1375 (s), 1364 (m), 1350 (m), 1330 (w), 1307 (s), 1284 (m), 1268 (m), 1244 (vs), 1233 (vs), 1188 (m), 1150 (s), 1129 (s), 1112 (s), 1078 (s), 1051 (s), 1018 (s) cm⁻¹. MS (EI): *m/z* (relative intensity, %) = 339 [M⁺ + 1] (1), 184 (18), 183 (70), 156 (34), 154 (24), 141 (100), 138 (11), 126 (66), 125 (65), 124 (30), 112 (11), 110 (17), 109 (10), 107 (23), 106 (18), 105 (30), 98 (10), 97 (23), 96 (22), 83 (13), 82 (17), 81 (15). C₁₇H₂₆N₂O₃S (338.5): calcd. C 60.33, H 7.74, N 8.28; found C 60.08, H 7.71, N 8.18.

Compound *epi*-16c: ¹H NMR (500 MHz, CDCl₃): $\delta = 0.84$ (d, J = 6.7 Hz, 3 H, *i*Pr), 0.88 (d, J = 6.5 Hz, 3 H, *i*Pr), 1.21 [d, J = 7.2 Hz, 3 H, CH(*Me*)S], 1.41 (d, J = 6.7 Hz, 3 H, CH*Me*), 1.52 (m, 1 H, C*Hi*Pr), 1.68 (m, 1 H, *i*Pr), 2.73 (s, 3 H, NMe), 3.33 (dq, J = 8.7, J = 7.2 Hz, 1 H, CHS), 3.63 (m, 1 H, C*H*NH), 4.40 (qd, J = 6.7, J = 3.7 Hz, 1 H, CHO), 7.45 (s, 1 H, NH), 7.58–7.72 (m, 3 H, Ph), 7.81 (m, 2 H, Ph) ppm. ¹³C NMR (125 MHz, CDCl₃): $\delta = 12.85$ (d), 19.40 (d), 20.44 (d), 20.69 (d), 29.45 (d), 30.86 (d), 43.48 (d), 52.49 (d), 66.02 (d), 73.58 (d), 129.60 (d), 130.66 (d), 133.59 (d), 137.36 (u), 153.27 (u) ppm.

(+)-(4S,5R,6S)-Tetrahydro-6-methyl-5-(1-methylethyl)-4-[(1S)-1-[(S)-N-methyl-S-phenylsulfonimidoyl)-2-(phenylmethoxy)ethyl]-2H-1,3-oxazin-2-one (16d): Successive treatment of sulfoximine 5b (207 mg, 0.64 mmol) with *n*BuLi (1.21 mL of 1.60 м in hexane, 1.93 mmol) and PhCH₂OCH₂Cl (0.67 mL, 4.79 mmol) according to GP3 and purification by chromatography (EtOAc/cyclohexane, 4:1) afforded sulfoximine 16d (198 mg, 70%) as a slightly yellow oil. $[\alpha]_D = +81.2 (c = 1.05, CH_2Cl_2)$. ¹H NMR (300 MHz, CDCl₃): $\delta = 0.50$ (d, J = 7.1 Hz, 3 H, *i*Pr), 0.70 (d, J = 7.1 Hz, 3 H, *i*Pr), 1.27 (d, J = 6.1 Hz, 3 H, Me), 1.50 (septd, J = 7.1, J = 7.12.0 Hz, 1 H, *i*Pr), 1.83 (td, J = 9.9, J = 2.0 Hz, 1 H, CH*i*Pr), 2.70 (s, 3 H, NMe), 3.29 (dd, J = 6.4, J = 3.7 Hz, 1 H, CHS), 3.73 (d, J = 9.5 Hz, 1 H, CHNH), 3.96 (dd, J = 10.4, J = 6.4 Hz, 1 H, CH₂O), 4.03 (dq, J = 10.2, J = 6.1 Hz, 1 H, CHO), 4.23 (dd, J = $10.4, J = 3.7 \text{ Hz}, 1 \text{ H}, \text{CH}_2\text{O}), 4.40 \text{ (symm m, 2 H, PhC}H_2\text{O}), 7.00$ (s, 1 H, NH), 7.23-7.36 (m, 5 H, Ph), 7.57-7.70 (m, 3 H, Ph), 7.84 (m, 2 H, Ph) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 18.03 (d), 18.99 (d), 19.93 (d), 26.81 (d), 29.14 (d), 44.73 (d), 50.61 (d), 63.10 (u), 73.71 (u), 66.65 (d), 74.52 (d), 127.94 (d), 128.05 (d), 128.44 (d), 129.83 (d), 130.00 (d), 133.73 (d), 136.42 (u), 137.27 (u), 155.41 (u) ppm. IR (neat): $\tilde{v} = 3381$ (w), 3290 (m), 3062 (m), 3031 (w), 2964 (s), 2937 (s), 2878 (s), 2809 (w), 2337 (w), 1724 (vs), 1582 (w), 1496 (w), 1447 (s), 1422 (s), 1373 (s), 1303 (s), 1246 (s), 1146 (s), 1109 (s), 1077 (s), 1047 (s), 1025 (m) cm⁻¹. MS (EI): m/z (relative intensity, %) = 445 [M⁺] (1), 290 (4), 289 (4), 288 (4), 198 (16), 183 (10), 182 (11), 156 (13), 155 (14), 141 (14), 125 (21), 124 (22), 107 (27), 91 (100). C₂₄H₃₂N₂O₄S (444.59): calcd. C 64.84, H 7.25, N 6.30; found C 64.95, H 7.34, N 6.54.

(4*S*,5*R*,6*S*)-Tetrahydro-4-{(1*S*,2*S*)-2-hydroxy-1-[(*S*)-*N*-methyl-*S*-phenylsulfonimidoyl]propyl}-6-methyl-5-(1-methylethyl)-2*H*-1,3-oxazin-2-one (16e) and (4*S*,5*R*,6*S*)-Tetrahydro-4-{(1*S*,2*R*)-2hydroxy-1-[(*S*)-*N*-methyl-*S*-phenylsulfonimidoyl]propyl}-6-methyl-5-(1-methylethyl)-2*H*-1,3-oxazin-2-one (*epi*-16e): Successive treatment of sulfoximine **5b** (78 mg, 0.24 mmol) with *n*BuLi (0.45 mL of 1.60 M in hexane, 0.72 mmol) and ethanal (0.3 mL, 5.3 mmol) according to *GP3* and purification by chromatography (EtOAc/cyclohexane, 4:1) gave a mixture of sulfoximines **16e**, *epi*-**16e**, and **5b** (78 mg) in a ratio of 1.7:1:1 as a colorless solid.

Compound 16e: ¹H NMR (300 MHz, CDCl₃): $\delta = 0.47$ (d, J = 7.1 Hz, 3 H, *i*Pr), 0.78 (d, J = 7.1 Hz, 3 H, *i*Pr), 1.35 (d, J = 6.0 Hz, 3 H, CH*Me*), 1.30–1.38 (m, 1 H, *i*Pr), 1.48 [d, J = 6.5 Hz, 3 H, CH(OH)*Me*], 1.71 (td, J = 10.1, J = 1.7 Hz, 1 H, C*Hi*Pr),

2.79 (s, 3 H, NMe), 3.04 (br. d, J = 5.6 Hz, 1 H, CHS), 3.69 (br. d, J = 10.1 Hz, 1 H, CHNH), 4.04 (m, 1 H, CHO), 4.64 (quin, J = 6.3 Hz, 1 H, CHOH), 6.55 (s, 1 H, NH), 7.60–7.76 (m, 3 H, Ph), 7.85–7.92 (m, 2 H, Ph) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 17.03$ (d), 19.92 (d), 20.22 (d), 23.14 (d), 26.68 (d), 29.06 (d), 45.47 (d), 51.33 (d), 65.84 (d), 70.50 (d), 74.58 (d), 129.92 (d), 130.10 (d), 134.15 (d), 137.12 (u), 154.53 (u).

Compound *epi*-16e: ¹H NMR (300 MHz, CDCl₃) signals for *epi*-16 are partially superposed by those for 16; only those signals that could be unequivocally assigned are listed: $\delta = 0.37$ (d, J = 7.1 Hz, 3 H, *i*Pr), 0.67 (d, J = 7.1 Hz, 3 H, *i*Pr), 1.33 (d, J = 6.0 Hz, 3 H, CH*Me*), 1.76 [d, J = 6.5 Hz, 3 H, CH(OH)*Me*], 1.83 (td, J = 9.5, J = 2.0 Hz, 1 H, C*Hi*Pr), 2.77 (s, 3 H, NMe), 3.14 (bdd, J = 3.7, J = 1.0 Hz, 1 H, CHS), 3.62 (br. d, J = 9.5 Hz, 1 H, C*H*NH), 4.04 (m, 1 H, CHO), 4.53 (m, 1 H, C*H*OH), 7.17 (s, 1 H, NH), 7.60–7.76 (m, 3 H, Ph), 7.85–7.92 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃) only those signals are listed, which could be unequivocally assigned: $\delta = 17.85$ (d), 23.20 (d), 27.00 (d), 45.38 (d), 50.75 (d), 65.29 (d), 71.07 (d), 74.42 (d), 136.19 (u), 155.33 (u) ppm.

(+)-(4S,5R,6S)-Tetrahydro-4-methyl-6-(1-methylethyl)-4-{[(S)-*N*-methyl-*S*-phenylsulfonimidoyl]deuteriomethyl}-5-phenyl-2*H*-1,3-oxazin-2-one (9-D and epi-9-D): Successive treatment of sulfoximine 9 (85 mg, 0.21 mmol) with nBuLi (0.29 mL of 1.60 M in hexane, 0.46 mmol) and CD₃OD (0.75 mL) according to GP3 gave a mixture of sulfoximines 9-D and epi-9-D in a ratio of 1.1:1 (84 mg, 99%) as a light yellow oil. ¹H NMR (400 MHz, CDCl₃): $\delta = 0.75$ (d, J = 6.9 Hz, 3 H, iPr), 1.05 (d, J = 6.9 Hz, 3 H, iPr), 1.52-1.59(m, 1 H, *i*Pr), 1.53 (s, 3 H, Me), 2.64 (s, 3 H, NMe), 3.03 (d, J =11.3 Hz, 1 H, CHPh), 3.18 (s, 0.5 H, CHD), 3.23 (s, 0.5 H, CHD), 4.65 (dd, J = 11.3, J = 1.9 Hz, 1 H, CHO), 7.10–7.13 (m, 2 H, Ph), 7.30-7.37 (m, 3 H, Ph), 7.54-7.65 (m, 3 H, Ph), 7.70 (br. s, 1 H, NH), 7.78-7.82 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, $CDCl_3$): $\delta = 14.44$ (d), 19.79 (d), 23.90 (d), 28.81 (d), 28.58 (d), 50.87 (d), 56.47 (u), 64.50 (d), 79.44 (d), 128.15 (d), 128.56 (d), 128.78 (d), 129.54 (d), 133.12 (d), 133.79 (u), 139.46 (u), 152.54 (u) ppm.

(-)-(4R,5R,6S)-Tetrahydro-4,6-dimethyl-5-(1-methylethyl)-2H-1,3-oxazin-2-one (17a): Treatment of sulfoximine 5b (230 mg, 0.71 mmol) with Raney nickel, prepared from 2.5 g Ni/ Al, for 5.5 h according to GP4 and purification by chromatography (EtOAc/cyclohexane, 4:1) afforded oxazinone 17a (107 mg, 88%) as a colorless solid. M.p. 54 °C. $[\alpha]_D = -44.7 (c = 0.55, CH_2Cl_2)$. ¹H NMR (300 MHz, CDCl₃): $\delta = 0.97$ (d, J = 7.1 Hz, 3 H, *i*Pr), 1.01 (d, J = 7.1 Hz, 3 H, iPr), 1.26 [d, J = 6.1 Hz, 3 H, CH(N)Me], 1.31 (td, J = 9.3, J = 2.2 Hz, 1 H, CHiPr), 1.40 [d, J = 6.1 Hz, 3 H, CH(O)Me], 1.92 (septd, J = 7.1, J = 2.2 Hz, 1 H, *i*Pr), 3.37 (dq, J = 8.8, J = 6.1 Hz, 1 H, CHN), 4.23 (dq, J = 9.5, J =6.1 Hz, 1 H, CHO), 6.48 (br. s, 1 H, NH) ppm. ¹³C NMR (75 MHz, $CDCl_3$): $\delta = 19.11$ (d), 19.78 (d), 20.46 (d), 23.18 (d), 27.13 (d), 48.43 (d), 49.96 (d), 75.76 (d), 155.68 (u) ppm. IR (KBr): $\tilde{v} = 3383$ (m), 3245 (m), 3136 (m), 2963 (s), 2904 (m), 1708 (vs), 1489 (m), 1458 (s), 1416 (s), 1390 (s), 1372 (s), 1343 (m), 1305 (s), 1245 (m), 1197 (s), 1151 (m), 1110 (m), 1054 (s) cm⁻¹. MS (EI): m/z (relative intensity, %) = $172 [M^+ + 1] (1)$, $171 [M^+] (2)$, 112 (13), 84 (51). C₉H₁₇NO₂ (171.24): calcd. C 63.13. H 10.01. N 8.18; found C 62.87, H 10.09, N 8.10.

(-)-(4*R*,5*R*,6*S*)-Tetrahydro-4-ethyl-6-methyl-5-(1-methylethyl)-2*H*-1,3-oxazin-2-one (17b): Treatment of sulfoximine 16c (94 mg, 0.28 mmol) with Raney nickel, prepared from 1.6 g Ni/Al, for 18 h according to *GP4* and purification by chromatography (EtOAc/cyclohexane, 4:1) afforded oxazinone 17b (45 mg, 88%) as a colorless oil. $[\alpha]_D = -28.0$ (c = 0.69, CH₂Cl₂). ¹H NMR $(300 \text{ MHz}, \text{CDCl}_3)$: $\delta = 0.97 \text{ (d, } J = 7.0 \text{ Hz}, 3 \text{ H}, i\text{Pr}), 0.97 \text{ (t, } J = 7.0 \text{ Hz}, 3 \text{ H}, i\text{Pr})$ 7.4 Hz, 3 H, Et), 1.00 (d, J = 7.0 Hz, 3 H, *i*Pr), 1.41 (d, J = 6.3 Hz, 3 H, Me), 1.44 (ddd, J = 8.8, J = 7.7, J = 2.7 Hz, 1 H, CHiPr), 1.53 (sept, J = 7.2 Hz, 1 H, Et), 1.68 (dqd, J = 14.4, J = 7.4, J = 73.9 Hz, 1 H, Et), 1.87 (septd, J = 7.0, J = 2.7 Hz, 1 H, *i*Pr), 3.19 (ddd, J = 7.7, J = 7.2, J = 3.9 Hz, 1 H, CHNH), 4.23 (dq, J = 8.8, J = 6.3 Hz 1 H, CHO), 5.76 (br. s, 1 H, NH) ppm. ¹³C NMR $(75 \text{ MHz}, \text{ CDCl}_3)$: $\delta = 9.05 \text{ (d)}, 18.92 \text{ (d)}, 19.82 \text{ (d)}, 20.57 \text{ (d)},$ 27.84 (d), 29.31 (u), 46.84 (d), 53.48 (d), 75.35 (d), 156.42 (u) ppm. IR (neat): $\tilde{v} = 3256$ (m), 3136 (w), 2965 (s), 2938 (m), 2879 (m), 2240 (w), 1713 (s), 1462 (m), 1417 (m), 1392 (m), 1381 (m), 1353 (w), 1301 (m), 1268 (w), 1185 (w), 1143 (w), 1098 (w), 1068 (m), 1031 (w), 1010 (w) cm⁻¹. GC-MS: m/z (relative intensity, %) = 187 $[M^+ + 2]$ (4), 186 $[M^+ + 1]$ (26), 156 (10), 112 (40), 102 (9), 89 (12). C₁₀H₁₉NO₂ (185.26): calcd. C 64.83, H 10.34, N 7.56; found C 64.74, H 10.47, N 7.85.

(-)-(4S,4aR,8aS)-Octahydro-4-(1-methylethyl)-8a-methyl-**2H-3,1-benzoxazin-2-one** (18): Treatment of 15b (320 mg, 0.88 mmol) with Raney nickel, prepared from 2.6 g Ni/Al, for 6 h according to GP4 and purification by chromatography (EtOAc/ cyclohexane, 1:1) afforded 18 (160 mg, 86%) as a colorless solid. M.p. 190 °C, $[\alpha]_D = -37.3$ (c = 0.23, CH₂Cl₂). ¹H NMR $(300 \text{ MHz}, \text{ CDCl}_3)$: $\delta = 0.80 \text{ (d, } J = 6.7 \text{ Hz}, 3 \text{ H}, i\text{Pr}), 1.10 \text{ (d,}$ J = 6.7 Hz, 3 H, *i*Pr), 1.07–1.80 (m, 12 H, CH₂), 1.95 (septd, J =6.8, J = 2.3 Hz, 1 H, iPr, 4.30 (dd, J = 10.08, J = 2.02 Hz, 1 H,CHNH), 6.30 (br. s, 1 H, NH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 13.68$ (d), 20.02 (d), 20.55 (u), 22.75 (u), 22.92 (u), 26.85 (d), 28.14 (d), 36.92 (u), 39.02 (d), 52.83 (u), 79.99 (d), 155.02 (u) ppm. IR (KBr): $\tilde{v} = 3242$ (w), 2945 (s), 2870 (m), 1700 (s), 1446 (s), 1371 (m) 1141 (m), 1070 (m) cm⁻¹. MS (EI): m/z (relative intensity, %) = 211 [M⁺] (12), 169 (10), 168 (100). C₁₂H₂₁NO₂ (211.30): calcd. C 68.21, H 10.02, N 6.63; found C 68.08, H 10.14, N 6.59.

(4R,5R,6S)-Tetrahydro-6-methyl-5-(1-methylethyl)-4-[(1E)-propenyl]-2H-1,3-oxazin-2-one [(E)-19] and (4R,5R,6S)-Tetrahydro-6-methyl-5-(1-methylethyl)-4-[(1Z)-propenyl]-2H-1,3-oxazin-2-one [(Z)-19]: Amalgamated aluminium was prepared as follows: aluminium powder (1.5 g) was treated with a solution of $HgCl_2$ in water (2%, 50 mL) for 2 min. The aqueous phase was decanted and the residue was washed with water (2 \times 25 mL). A suspension of the obtained amalgamated aluminium in THF/H₂O/HOAc (2:1:1, 40 mL) was added at room temperature to a rapidly stirred solution of a mixture of 16e, epi-16e, and 5b (190 mg, in a ratio of 1.8:1:1) in THF (20 mL). After the mixture had been stirred for 2 h, it was filtered through a pad of Celite. The residue was washed with CH_2Cl_2 (4 × 25 mL). The combined organic phases were washed with water $(2 \times 25 \text{ mL})$ and aqueous NaOH (10%, $2 \times 25 \text{ mL})$, dried (MgSO₄), and concentrated in vacuo. Purification by chromatography (EtOAc/cyclohexane, 4:1) gave a mixture of alkenes (E)-19 and (Z)-19 (66 mg, 85%) in a ratio of 1:1, together with oxazinone 17a (11 mg, 46%) as colorless solids.

Compounds (E)-19/(Z)-19: ¹H NMR (300 MHz, CDCl₃): $\delta = 0.94$ (d, J = 7.1 Hz, 3 H, Me), 0.95 (d, J = 7.1 Hz, 3 H, Me), 0.99 (br. d, J = 7.1 Hz, 6 H, $2 \times$ Me), 1.40 [d, J = 6.1 Hz, 3 H, CH(O)*Me*], 1.41 [d, J = 6.2 Hz, 3 H, CH(O)*Me*], 1.44 (m, 2 H, $2 \times$ C*Hi*Pr), 1.71 (m, 6 H, $2 \times$ CH=CH*Me*), 1.93 (m, 2 H, $2 \times$ *i*Pr), 3.71 (t, J = 9.1 Hz, 1 H, C*H*NH), 4.14 (t, J = 9.6 Hz, 1 H, C*H*NH), 4.23 (dq, J = 9.7, J = 6.2 Hz, 1 H, CHO), 4.27 (dq, J = 9.9, J = 6.1 Hz 1 H, CHO), 5.27 (m, 1 H, C*H*=CHMe), 5.33 (dq, J = 8.6, J =1.7 Hz, 1 H, C*H*=CHMe), 5.62–5.76 (m, 4 H, $2 \times$ CH=C*H*Me, $2 \times$ NH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 13.16$ (d), 17.63 (d), 18.72 (d), 18.84 (d), 19.95 (d), 20.09 (d), 20.24 (d), 26.53 (d), 26.66 (d), 47.88 (d), 48.03 (d), 49.57 (d), 56.03 (d), 75.63 (d), 75.75 (d), 128.73 (d), 130.17 (d), 131.08 (d), 131.98 (d), 154.58 (u) ppm. IR (neat): $\tilde{v} = 3251$ (m), 3127 (m), 2962 (s), 2937 (s), 2878 (m), 1713 (vs), 1456 (m), 1407 (s), 1378 (s), 1351 (m), 1330 (m), 1307 (m), 1294 (m), 1264 (m), 1223 (w), 1187 (w), 1165 (m), 1135 (m), 1048 (m), 1019 (w) cm⁻¹. GC-MS: *m*/*z* (relative intensity, %) = 199 [M⁺ + 2] (10), 198 [M⁺ + 1] (100), 114 (24), 110 (13). C₁₁H₁₉NO₂ (197.27): calcd. C 66.97, H 9.71, N 7.10; found C 66.41, H 9.22, N 6.98. C₁₁H₁₉NO₂: calcd. 197.14158; found (HRMS, EI) 197.14154.

Methyl ($\alpha S, 4S, 5R, 6S$)- and ($\alpha R, 4S, 5R, 6S$)-[Tetrahydro-6-methyl-5-(1-methylethyl)-2-oxo-2*H*-1,3-oxazin-4-yl][(*S*)-*N*-methyl-*S*-phenyl sulfonimidoyl]acetate (20 and *epi*-20): Successive treatment of sulfoximine **5b** (220 mg, 0.68 mmol) with *n*BuLi (1.06 mL of 1.60 M in hexane, 1.70 mmol) and ClCO₂Me (0.13 mL, 1.69 mmol) according to *GP3* and purification by chromatography (EtOAc/cyclohexane, 1:1) gave a mixture of esters **20** and *epi*-**20** (165 mg, 64%) in a ratio of 5.2:1 as a colorless solid.

Compound 20: ¹H NMR (400 MHz, CDCl₃): $\delta = 0.91$ (d, J = 7.1 Hz, 3 H, *i*Pr), 0.96 (d, J = 7.1 Hz, 3 H, *i*Pr), 1.45 (d, J = 6.3 Hz, 3 H, Me), 1.64–1.78 (m, 2 H, CH*i*Pr, *i*Pr), 2.61 (s, 3 H, NMe), 3.78 (s, 3 H, CO₂Me), 4.04–4.16 (m, 3 H, CHN, CHS, CHO), 6.60 (br. s, 1 H, NH), 7.60–7.70 (m, 3 H, Ph), 7.85–7.90 (m, 2 H, Ph) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 18.71$ (d), 19.29 (d), 20.12 (d), 27.89 (d), 29.86 (d), 46.25 (d), 50.82 (d), 53.64 (d), 73.02 (d), 74.02 (d), 129.86 (d), 130.05 (d), 134.10 (d), 137.23 (u), 155.25 (u), 163.89 (u) ppm.

Compound *epi-20*: ¹H NMR (400 MHz, CDCl₃): $\delta = 0.78$ (d, J = 7.1 Hz, 3 H, *i*Pr), 0.90 (d, J = 7.0 Hz, 3 H, *i*Pr), 1.38 (d, J = 6.4 Hz, 3 H, Me), 2.75 (s, 3 H, NMe), 3.65 (s, 3 H, CO₂Me), 4.38 (m, 1 H), 4.42 (d, J = 10.0 Hz, 1 H), 6.25 (br. s, 1 H, NH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 20.00$ (d), 20.43 (d), 21.99 (d), 31.09 (d), 51.64 (d), 53.33 (d), 75.61 (d) ppm. IR (KBr): $\tilde{v} = 3303$ (s), 2960 (m), 1754 (vs), 1725 (s), 1447 (m), 1338 (w), 1260 (s), 1163 (m), 1018 (m) cm⁻¹. MS (EI): *m/z*, relative intensity, %) = 354 (2), 228 (89), 227 (40), 198 (27), 196 (38), 185 (21), 170 (18), 154 (59), 146 (21), 125 (100), 107 (57). C₁₈H₂₆N₂O₅S (382.48): calcd. C 56.52, H 6.85, N 7.32; found C 56.35, H 7.01, N 7.24.

Methyl (+)-(4R,5R,6S)-[Tetrahydro-6-methyl-5-(1-methylethyl)-2oxo-2H-1,3-oxazin-4-yl]acetate (21): Treatment of sulfoximines 20 and epi-20 (230 mg, 0.60 mmol) with Raney nickel, prepared from 1.8 g Ni/Al, for 8 h according to GP4 and purification by chromatography (EtOAc/cyclohexane, 1:1) afforded 21 (120 mg, 87%) as a viscous liquid. $[\alpha]_D = +51.42$ (c = 0.70, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): $\delta = 0.85$ (d, J = 7.1 Hz, 3 H, *i*Pr), 0.95 (d, J = 7.1 Hz, 3 H, *i*Pr), 1.40 (d, J = 6.5 Hz, 3 H, Me), 1.40 (symm. m, 1 H, CHiPr), 1.80-1.85 (m, 1 H, iPr), 2.50 (dd, J = 17.1, J =10.1 Hz, 1 H, CH₂), 2.65 (dd, J = 17.1, J = 2.7 Hz, 1 H, CH₂), 3.60 (m, 1 H, CHNH), 3.70 (s, 3 H, CO_2Me), 4.20 (dq, J = 9.3, J = 6.5 Hz, 1 H, CHO), 5.80 (br. s, 1 H, NH) ppm. ¹³C NMR $(75 \text{ MHz}, \text{ CDCl}_3)$: $\delta = 19.53 \text{ (d)}, 19.61 \text{ (d)}, 20.55 \text{ (d)}, 28.34 \text{ (d)},$ 42.12 (u), 48.36 (d), 49.12 (d), 52.42 (d), 75.17 (d), 155.17 (u), 171.94 (u) ppm. IR (CHCl₃): $\tilde{v} = 3261$ (m), 3141 (w), 2961(s), 1714 (vs), 1439 (s), 1373 (m), 1047 (m) cm⁻¹. MS (EI): m/z (relative intensity, %) = 229 [M⁺] (8), 198 (8), 186 (18), 170 (11), 156 (28), 142 (100), 112 (32), 84 (17). C₁₁H₁₉NO₄ (229.27): calcd. C 57.62, H 8.35, N 6.11; found C 57.08, H 8.30, N 6.34.

Methyl (-)-(4*R*,5*R*,6*S*)-[Tetrahydro-4-methyl-6-[(1-methylethyl)-2oxo-5-phenyl-2*H*-1,3-oxazin-4-yl]acetate (23a): Successive treatment of sulfoximine 9 (223 mg, 0.56 mmol) with *n*BuLi (0.77 mL of 1.60 M in hexane, 1.23 mmol) and ClCO₂Me (0.09 mL, 1.23 mmol) and reduction of the functionalized sulfoximine 22a with Raney nickel, prepared from 3.5 g Ni/Al, according to GP5 and purification by chromatography afforded ester 23a (82 mg, 48%) as a colorless solid, together with sulfoximine 9 (16 mg, 7%). M.p. 104 °C. [α]_D = $-53.0 (c = 0.77, CH_2Cl_2)$. ¹H NMR (400 MHz, CDCl₃): $\delta = 0.78$ (d, J = 7.0 Hz, 3 H, iPr), 1.06 (d, J = 7.0 Hz, 3 H, iPr), 1.29 (s, 3 H)H, Me), 1.62 (septd, J = 6.9, J = 1.9 Hz, 1 H, *i*Pr), 2.37 (d, J =15.7 Hz, 1 H, CH₂), 2.48 (d, J = 15.7 Hz, 1 H, CH₂), 2.98 (d, J =11.4 Hz, 1 H, CHPh), 3.67 (s, 1 H, OMe), 4.66 (dd, J = 11.4, J =1.9 Hz, 1 H, CHO), 6.48 (br. s, 1 H, NH), 7.06-7.12 (m, 2 H, Ph), 7.23–7.33 (m, 3 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 13.79 (d), 20.23 (d), 23.56 (d), 29.08 (d), 44.87 (u), 51.04 (d), 52.32 (d), 55.05 (u), 80.17 (d), 128.32 (d), 128.96 (d), 134.70 (u), 153.48 (u), 171.22 (u) ppm. IR (KBr): $\tilde{v} = 3375$ (m), 3253 (w), 3088 (w), 3033 (w), 2966 (m), 2920 (m), 2877 (w), 1715 (s), 1499 (w), 1439 (s), 1422 (m), 1389 (m), 1370 (m), 1355 (m), 1332 (w), 1300 (m), 1266 (w), 1243 (m), 1227 (m), 1204 (w), 1178 (m), 1159 (w), 1114 (m), 1096 (m), 1055 (s), 1004 (w) cm⁻¹. MS (CI): m/z (relative intensity, %) = 306 [M⁺ + 1] (100), 248 (14). $C_{17}H_{23}NO_4$ (305.37): calcd. C 66.86, H 7.59, N 4.59; found C 66.88, H 7.48, N 4.59.

Isopropyl (-)-(4R,5R,6S)-[Tetrahydro-4-methyl-6-(1-methylethyl)-2oxo-5-phenyl-2H-1,3-oxazin-4-yl]acetate (23b): Successive treatment of sulfoximine 9 (114 mg, 0.28 mmol) with nBuLi (0.39 mL of 1.60 м in hexane, 0.63 mmol) and ClCO₂iPr (0.63 mL of 1.0 м in toluene, 0.63 mmol), reduction of the functionalized sulfoximine 22b with Raney nickel, prepared from 1.7 g Al-Ni, according to GP5, and purification by chromatography afforded ester 23b (56 mg, 59%) as a colorless solid, together with sulfoximine 9 (21 mg, 18%). M.p. 151 °C. $[\alpha]_D = -42.7$ (c = 0.95, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): $\delta = 0.73$ (d, J = 6.6 Hz, 3 H, *i*Pr), 1.01 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.15 (d, J = 6.0 Hz, 3 H, *i*Pr), 1.17 (d, J =5.8 Hz, 3 H, *i*Pr), 1.31 (s, 3 H, Me), 1.56 (septd, J = 7.0, J =1.8 Hz, 1 H, *i*Pr), 2.28 (d, J = 15.4 Hz, 1 H, CH₂), 2.40 (d, J =15.4 Hz, 1 H, CH₂), 2.96 (d, J = 11.5 Hz, 1 H, CHPh), 4.61 (dd, J = 11.4, J = 1.8 Hz, 1 H, CHO), 4.98 (sept, J = 6.3 Hz, 1 H, OiPr), 6.58 (s, 1 H, NH), 7.10-7.16 (m, 2 H, Ph), 7.26-7.34 (m, 3 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 13.41$ (d), 19.88 (d), 21.70 (d), 21.78 (d), 23.34 (d), 28.71 (d), 44.90 (u), 50.54 (d), 54.85 (u), 68.78 (d), 79.88 (d), 128.05 (d), 128.74 (d), 134.66 (u), 153.36 (u), 170.21 (u) ppm. IR (KBr): $\tilde{v} = 3415$ (s), 3029 (m), 2975 (m), 2934 (m), 2879 (m), 1721 (s), 1497 (m), 1442 (m), 1388 (m), 1369 (m), 1334 (m), 1226 (m), 1179 (m), 1149 (m), 1105 (m), 1059 (m) cm⁻¹. MS (CI): m/z (relative intensity, %) = 334 [M⁺ + 1] (100). C₁₉H₂₇NO₄ (333.42): calcd. C 68.44. H 8.16. N 4.20; found C 68.35, H 8.04, N 4.04.

Isobutyl (-)-(4R,5R,6S)-[Tetrahydro-4-methyl-6-(1-methylethyl)-2oxo-5-phenyl-2H-1,3-oxazin-4-yl]acetate (23c): Successive treatment of sulfoximine 9 (1.18 g, 2.94 mmol) with nBuLi (3.86 mL of 1.60 м in hexane, 6.18 mmol) and ClCO₂iBu (0.81 mL, 2.95 mmol), reduction of the functionalized sulfoximine 22c with Raney nickel, prepared from 1.8 g Ni/Al, according to GP5, and purification by chromatography furnished ester 23c (754 mg, 74%) as a colorless solid, together with sulfoximine 9 (141 mg, 12%). M.p. 119 °C. $[\alpha]_{\rm D} = +34.0 \ (c = 1.21, \ {\rm CH}_2{\rm Cl}_2).$ ¹H NMR (400 MHz, CDCl₃): $\delta = 0.79$ (d, J = 6.9 Hz, 3 H, *i*Pr), 0.91 (dd, J = 6.6, J = 3.1 Hz, 6 H, *i*Pr), 1.07 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.32 (s, 3 H, Me), 1.63 (septd, J = 6.9, J = 1.9 Hz, 1 H, *i*Pr), 1.83–1.96 (m, 1 H, *i*Pr), 2.36 (d, J = 15.7 Hz, 1 H, CH₂), 2.50 (d, J = 15.7 Hz, 1 H, CH₂), 3.01 (d, J = 11.4 Hz, 1 H, CHPh), 3.86 (dd, J = 12.2, J = 6.7 Hz, 1 H, OCH₂), 3.88 (dd, J = 12.2, J = 6.7 Hz, 1 H, OCH₂), 4.67 (dd, J = 11.4, J = 1.7 Hz, 1 H, CHO), 6.60 (br. s, 1 H, NH),7.16-7.18 (m, 2 H, Ph), 7.32-7.40 (m, 3 H, Ph) ppm. ¹³C NMR $(100 \text{ MHz}, \text{CDCl}_3)$: $\delta = 13.42 \text{ (d)}, 19.04 \text{ (d)}, 19.85 \text{ (d)}, 23.23 \text{ (d)},$ 27.55 (d), 28.70 (d), 44.59 (u), 50.70 (d), 54.68 (u), 71.09 (u), 79.80

Eur. J. Org. Chem. 2003, 1500-1526

(d), 127.90 (d), 128.57 (d), 134.43 (u), 153.06 (u), 170.52 (u) ppm. IR (KBr): $\tilde{v} = 3413$ (s), 3085 (w), 3063 (w), 3030 (w), 2968 (s), 2896 (m), 1712 (s), 1604 (w), 1497 (w), 1471 (m), 1438 (s), 1394 (m), 1372 (m), 1346 (m), 1222 (s), 1179 (m), 1146 (s), 1120 (m), 1103 (m), 1056 (m) cm⁻¹. MS (EI): *m/z* (relative intensity, %) = 348 [M⁺ + 1] (100). C₂₀H₂₉NO₄ (347.45): calcd. C 69.14, H 8.41, N 4.03; found C 68.96, H 8.21, N 4.00.

Neopentyl (-)-(4R,5R,6S)-[Tetrahydro-4-methyl-6-(1-methylethyl)-2-oxo-5-phenyl-1,3-oxazine-4-ylacetate (23d): Successive treatment of sulfoximine 9 (226 mg, 0.56 mmol) with nBuLi (0.77 mL of 1.60 м in hexane, 1.23 mmol) and ClCO₂CH₂tBu (0.18 mL, 1.23 mmol), reduction of the functionalized sulfoximine 22d with Raney nickel, prepared from 3.3 g of Ni/Al, according to GP5, and purification by chromatography afforded ester 23d (104 mg, 51%) as a colorless solid, together with sulfoximine 9 (38 mg, 17%). M.p. 133 °C. $[\alpha]_{\rm D} = -3.7 \ (c = 0.83, \text{CH}_2\text{Cl}_2).$ ¹H NMR (400 MHz, CDCl₃): $\delta =$ 0.79 (d, J = 6.9 Hz, 3 H, *i*Pr), 0.91 (s, 9 H, *t*Bu), 1.07 (d, J =7.1 Hz, 3 H, *i*Pr), 1.33 (s, 3 H, Me), 1.63 (septd, J = 6.9, J =1.8 Hz, 1 H, *i*Pr), 2.37 (d, J = 15.7 Hz, 1 H, CH₂), 2.52 (d, J =15.7 Hz, 1 H, CH₂), 3.03 (d, J = 11.5 Hz, 1 H, CHPh), 3.79 (symm m, 2 H, OCH₂), 4.68 (dd, J = 11.4, J = 1.8 Hz, 1 H, CHO), 6.60 (br. s, 1 H, NH), 7.16-7.21 (m, 2 H, Ph), 7.32-7.41 (m, 3 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 13.40$ (d), 19.85 (d), 23.28 (d), 26.37 (d), 28.66 (d), 31.16 (u), 44.51 (u), 50.62 (d), 54.65 (u), 74.25 (u), 79.75 (d), 127.88 (d), 128.56 (d), 134.41 (u), 153.07 (u), 170.59 (u) ppm. IR (KBr): $\tilde{v} = 3368$ (m), 3035 (w), 2959 (m), 2920 (m), 2876 (m), 1711 (s), 1499 (m), 1467 (m), 1439 (m), 1411 (m), 1383 (m), 1368 (m), 1352 (m), 1339 (w), 1299 (w), 1268 (w), 1241 (m), 1228 (m), 1178 (m), 1110 (m), 1095 (m), 1057 (m) cm⁻¹. MS (CI): m/z (relative intensity, %) = 362 [M⁺ + 1] (100). C₂₁H₃₁NO₄ (361.48): calcd. C 69.78, H 8.64, N 3.87; found C 69.26, H 8.71, N 3.74.

Methyl (+)-(αR ,4S,4aR,8aS)-{Octahydro-4-(1-methylethyl)-2-oxo-8aH-3,1-benzoxazin-8a-yl}-α-[(S)-N-methyl-S-phenylsulfonimidoyl]acetate (24): Successive treatment of sulfoximine 15b (538 mg, 1.48 mmol) with nBuLi (2.31 mL of 1.60 м in hexane, 3.70 mmol) and ClCO₂Me (0.28 mL, 3.70 mmol) according to GP3 and purification by chromatography (EtOAc/cyclohexane, 2:1) gave ester 24 (437 mg, 70%) as a colorless solid. M.p. 64–65 °C, $[\alpha]_D = +49.3$ $(c = 0.15, CH_2Cl_2)$. ¹H NMR (400 MHz, CDCl₃): $\delta = 0.90$ (d, J =6.8 Hz, 3 H, *i*Pr), 1.05 (d, J = 6.8 Hz, 3 H, *i*Pr), 1.10–1.80 (m, 8 H, CH₂), 1.90 (septd, J = 6.8, J = 2.2 Hz, 1 H, *i*Pr), 2.75 (s, 3 H, NMe), 2.95 (m, 1 H), 3.70 (s, 3 H, CO_2Me), 4.20 (dd, J = 10.9, J = 2.2 Hz, 1 H, CHO), 4.70 (s, 1 H, CHS), 6.09 (s, 1 H, NH), 7.50-7.70 (m, 3 H, Ph), 7.75-7.80 (m, 2 H, Ph) ppm. ¹³C NMR $(75 \text{ MHz}, \text{ CDCl}_3)$: $\delta = 13.62 \text{ (d)}, 19.84 \text{ (u)}, 20.08 \text{ (u)}, 22.47 \text{ (u)},$ 28.20 (d), 29.86 (d), 32.60 (d), 37.31 (u), 53.36 (d), 56.98 (u), 70.28 (d), 70.66 (d), 129.57 (d), 129.76 (d), 133.72 (d), 138.04 (u), 152.94 (u), 166.96 (u) ppm. IR (KBr): $\tilde{v} = 3394$ (s), 2943 (s), 2876 (m), 1711 (s), 1446 (s), 1379 (m), 1263 (s), 1073 (m) cm^{-1} . MS (EI): m/z (relative intensity, %) = 394 (1), 278 (3), 228 (6), 227 (8), 198 (9), 195 (21), 156 (10), 154 (100), 150 (11), 136 (21), 125 (46), 108 (32). C₂₁H₃₀N₂O₅S (422.54): calcd. C 59.69, H 7.16, N 6.63; found C 59.18, H 7.09, N 6.33.

Methyl (+)-(4*S*,4*aR*,8*aR*)-{Octahydro-4-(1-methylethyl)-2-oxo-8*aH*-[3,1]benzoxazin-8*a*-yl}acetate (25): Treatment of sulfoximine 24 (160 mg, 0.38 mmol) with Raney nickel, prepared from 1.6 g Ni/ Al, according to *GP4* and purification by chromatography (EtOAc/ cyclohexane, 1:1) afforded 20 (80 mg, 78%) as a colorless solid. M.p. 132 °C, $[\alpha]_D = +23.33$ (c = 0.24, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): $\delta = 0.90$ (d, J = 6.7 Hz, 3 H, *i*Pr), 1.05 (d, J = 6.7 Hz, 3 H, *i*Pr), 1.10–1.30 (m, 4 H), 1.50–1.85 (m, 9 H),

1.95 (septd, J = 7.0, J = 2.1 Hz, 1 H, *i*Pr), 2.40 (dd, J = 15.5, J = 1.5 Hz, 1 H, CH₂CO), 3.02 (d, J = 15.5 Hz, 1 H, CH₂CO), 3.70 (s, 3 H, CO₂Me), 4.30 (dd, J = 10.6, J = 2.1 Hz, 1 H, CHO), 6.35 (br. s, 1 H, NH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 13.54$ (d), 19.93 (d), 20.43 (u), 22.43 (u), 22.66 (u), 28.12 (d), 33.98 (u), 38.55 (d), 41.66 (u), 52.12 (d), 53.90 (u), 79.06 (d), 153.76 (u), 171.28 (u) ppm. IR (KBr): $\tilde{v} = 3372$ (s), 3000 (w), 2961 (s), 2930 (s), 1697 (vs), 1525 (w), 1464 (s), 1379 (m), 1207 (s) cm⁻¹. MS (EI): *m/z* (relative intensity, %) = 269 [M⁺] (2), 238 (2), 227 (13), 226 (100), 213 (35), 196 (25), 194 (19), 170 (63), 152 (15). C₁₄H₂₃NO₄ (269.34): calcd. C 62.43, H 8.61, N 5.20; found C 62.25, H 8.56, N 4.90.

(-)-(4S,5R,6S)-4-(Chloromethyl)-tertahydro-6-ethyl-5methyl-2H-1,3-oxazin-2-one (27a): Treatment of sulfoximine 5a (77 mg, 0.25 mmol) with ClCO₂Me (0.28 mL, 3.7 mmol) at room temperature for 3 days (95% conversion) according to GP6 and purification by chromatography (EtOAc) afforded chloride 27a (40 mg, 84%) as a colorless solid. M.p. 138 °C. $[\alpha]_{\rm D} = -1.0$ (c = 0.67, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): $\delta = 1.01$ (d, J =6.7 Hz, 3 H, CHMe), 1.04 (t, J = 7.4 Hz, 3 H, Et), 1.59 (dquin, J = 14.4, J = 7.4 Hz, 1 H, Et), 1.75 (tq, J = 10.0, J = 6.7 Hz, 1 H, CHMe), 1.86 (dqd, J = 14.4, J = 7.4, J = 3.0 Hz, 1 H, Et), 3.33 (ddd, J = 9.7, J = 7.1, J = 2.7 Hz, 1 H, CHNH), 3.48 (dd, J = 11.4, J = 7.1 Hz, 1 H, CH₂Cl), 3.78 (dd, J = 11.4, J = 2.7 Hz, 1 H, CH₂Cl), 3.93 (ddd, *J* = 10.1, *J* = 7.4, *J* = 3.0 Hz, 1 H, CHO), 6.29 (s, 1 H, NH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 8.27$ (d), 13.02 (d), 24.74 (u), 33.16 (d), 46.76 (u), 57.58 (d), 81.51 (d), 154.59 (u) ppm. IR (KBr): $\tilde{v} = 3310$ (s), 3172 (m), 2980 (s), 2930 (s), 2883(s), 1712 (vs, br), 1664 (s), 1531 (m), 1478 (s), 1435 (s), 1411 (s), 1386 (s), 1358 (s), 1327 (s), 1304 (s), 1269 (s), 1244 (s), 1216 (s), 1140 (s), 1117 (s), 1075 (s), 1045 (m), 1023 (s) cm⁻¹. MS (EI): m/z(relative intensity, %) = 192 [M⁺ + 1] (3), 162 (2), 143 (5), 142 (61), 117 (3), 99 (7), 98 (100), 81 (36). C₈H₁₄ClNO₂ (191.66): calcd. C 50.13, H 7.36, N 7.31; found C 50.15, H 7.28, N 7.06.

(+)-(4S,5R,6S)-4-(Chloromethyl)-tertahydro-6-methyl-5-(1-methylethyl)-2H-1,3-oxazin-2-one (27b): Treatment of sulfoximine **5b** (280 mg, 0.86 mmol) with ClCO₂Me (0.33 mL, 4.32 mmol) for 3 days (95% conversion) according to GP6 and purification by chromatography (EtOAc/pentane, 1:1) afforded chloride 27b (151 mg, 85%) as a low-melting, colorless solid. $[\alpha)^d = +4.0$ (c = 0.30, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): $\delta = 0.90$ (d, J =1.4 Hz, 3 H, *i*Pr), 0.95 (d, *J* = 1.6 Hz, 3 H, *i*Pr), 1.35 (d, *J* = 6.3 Hz, 3 H, CHMe), 1.55 (ddd, J = 9.0, J = 6.7, J = 3.0 Hz, 1 H, CHMe), 1.85 (septd, J = 7.1, J = 3.0 Hz, 1 H, *i*Pr), 3.45 (dd, J = 14.1, J =7.6 Hz, 1 H, CH₂Cl), 3.60 (dd, J = 14.8, J = 7.1 Hz, 1 H, CH₂Cl), 4.15 (dq, J = 9.0, J = 2.7 Hz, 1 H, CHO), 6.30 (br. s, 1 H, NH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 19.15$ (d), 19.89 (d), 20.46 (d), 28.23 (d), 46.13 (d), 49.39 (u), 53.55 (d), 75.20 (d), 155.94 (u) ppm. IR (KBr): $\tilde{v} = 3253$ (m), 2879 (s), 1709 (vs), 1412 (s), 1301 (s), 1116 (m), 1039 (m) cm⁻¹. MS (EI): m/z (relative intensity, %) = 205 [M⁺] (1), 157 (6), 155 (90), 112 (100), 95 (10). C₉H₁₆ClNO₂ (205.68): calcd. C 52.56, H 7.84, N 6.81; found C 52.56, H 7.86, N 6.85.

(+)-(4*S*,5*R*,6*S*)-4-(Chloromethyl)tetrahydro-6-(1-methylethyl)-5-phenyl-2*H*-1,3-oxazin-2-one (27c) and Methyl (*S*)-*N*-Phenylsulfinylcarbamate (26): Treatment of sulfoximine 5c (1.30 g, 3.36 mmol) with ClCO₂Me (2.60 mL, 33.50 mmol) according to *GP6* and purification by HPLC (EtOAc) gave chloride 27c (730 mg, 81%) as a colorless solid, carbamic acid ester 26 (540 mg, 75%) as a colorless oil, and oxazinone 5c (190 mg, 15%). 27c: M.p. 154 °C. $[\alpha]_D = +1.4 (c = 1.05, CH_2Cl_2)$. ¹H NMR (400 MHz, CDCl₃): $\delta =$ 0.87 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.02 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.53 (septd, J = 7.1, J = 1.9 Hz, 1 H, *i*Pr), 2.95 (t, J = 10.7 Hz, 1 H, CHPh), 3.28 (dd, J = 11.6, J = 6.0 Hz, 1 H, CH₂), 3.52 (dd, J = 11.6, J = 2.7 Hz, 1 H, CH₂), 3.86 (ddd, J = 10.6, J = 6.0, J = 2.7 Hz, 1 H, CHN), 4.67 (dd, J = 10.7, J = 1.9 Hz, 1 H, CHO), 6.75 (br. s, 1 H, NH), 7.17–7.21 (m, 2 H, Ph), 7.31–7.42 (m, 3 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 13.66$ (d), 19.66 (d), 28.43 (d), 44.05 (d), 46.04 (u), 57.60 (d), 83.50 (d), 127.98 (d), 128.07 (d), 129.23 (d), 135.46 (u), 154.62 (u) ppm. IR (KBr): $\tilde{v} = 3362$ (w), 3231 (s), 3138 (m), 3029 (m), 2972 (s), 2935 (m), 2877 (m), 1697 (s), 1605 (m), 1496 (m), 1473 (s), 1435 (s), 1387 (m), 1369 (m), 1338 (m), 1313 (m), 1289 (s), 1251 (w), 1210 (m), 1130 (s), 1087 (w), 1062 (m), 1036 (s) cm⁻¹. MS (CI): *m*/*z* (relative intensity, %) = 268 [M⁺ + 1] (100), 234 (16), 232 (12). C₁₄H₁₈CINO₂ (267.75): calcd. C 62.80, H 6.78, N 5.23; found C 62.73, H 6.85, N 5.13.

(+)-(4R,5R,6S)-4-(Cyanomethyl)-tertahydro-6-(1-methylethyl)-5-phenyl-2H-1,3-oxazin-2-one (28): Treatment of chloride 27c (440 mg, 1.64 mmol) with NaCN (160 mg, 3.27 mmol) according to GP7 gave nitrile 28 (370 mg, 87%) as a colorless solid. Nitrile 28 was isolated by filtration of the reaction mixture after addition of water. M.p. 244–246 °C (decomposition). $[\alpha]_D = +30.6$ (c =0.31, DMSO). ¹H NMR (400 MHz, [D₆]DMSO): $\delta = 0.74$ (d, J =6.9 Hz, 3 H, *i*Pr), 0.86 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.30 (septd, J =6.9, J = 1.8 Hz, 1 H, *i*Pr), 2.11 (dd, J = 17.2, J = 3.1 Hz, 1 H, CH₂), 2.65 (dd, J = 17.2, J = 4.3 Hz, 1 H, CH₂), 2.70 (t, J =10.4 Hz, 1 H, CHPh), 3.86 (ddd, J = 10.6, J = 4.3, J = 3.1 Hz, 1 H, CHN), 4.52 (dd, J = 10.5, J = 1.8 Hz, 1 H, CHO), 7.27–7.39 (m, 5 H, Ph), 7.71 (s, 1 H, NH) ppm. ¹³C NMR (100 MHz, $[D_6]DMSO$: $\delta = 14.38$ (d), 20.29 (d), 22.41 (u), 28.85 (d), 46.18 (d), 52.54 (d), 80.60 (d), 117.72 (u), 128.64 (d), 129.03 (d), 129.85 (d), 136.49 (u), 153.48 (u) ppm. IR (KBr): $\tilde{v} = 3220$ (m), 3123 (m), 2969 (m), 2929 (m), 2879 (m), 2245 (w), 1693 (s), 1500 (w), 1473 (w), 1428 (m), 1386 (w), 1369 (w), 1351 (w), 1327 (w), 1290 (m), 1260 (w), 1220 (m), 1187 (w), 1151 (m), 1132 (w), 1107 (w), 1089 (w), 1065 (w), 1034 (s) cm⁻¹. MS (CI): m/z (relative intensity, %) = 259 $[M^+ + 1]$ (100). $C_{15}H_{18}N_2O_2$ (258.32): calcd. C 69.74, H 7.02, N 10.84; found C 69.53, H 7.02, N 10.83.

(−)-(4*S*,5*R*,6*S*)-4-(Chloromethyl)-tertahydro-4-methyl-6-(1-methylethyl)-5-phenyl-2*H*-1,3-oxazin-2-one (29) and Methyl (*S*)-*N*-Phenylsulfinylcarbamate (26): Treatment of sulfoximine 9 (204 mg, 0.51 mmol) with ClCO₂Me (0.39 mL, 5.10 mmol) according to *GP5* and purification by chromatography (EtOAc) gave chloride 29 (116 mg, 81%) as a colorless solid, carbamic acid ester 26 (79 mg, 73%) of ≥99% *ee* (GC, permethyl-β-cyclodextrin, chemically bound, $t_R(R) = 24.61 \min, t_R(S) = 24.71 \min)$ as a colorless oil, and oxazinone 9 (28 mg, 14%).

Compound 29: M.p. 161 °C. $[\alpha]_D = -57.2$ (c = 1.25, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): $\delta = 0.81$ (d, J = 6.6 Hz, 3 H, *i*Pr), 1.09 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.26 (s, 3 H, Me), 1.72 (septd, J = 6.9, J = 1.8 Hz, 1 H, *i*Pr), 3.33 (d, J = 11.4 Hz, 1 H, CHPh), 3.41 (symm. m, 2 H, CH₂), 4.67 (dd, J = 11.4, J = 1.8 Hz, 1 H, CHO), 6.95 (br. s, 1 H, NH), 7.17-7.22 (m, 2 H, Ph), 7.30-7.39 (m, 3 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 13.44$ (d), 19.88 (d), 23.18 (d), 28.60 (d), 46.05 (d), 51.79 (u), 56.73 (u), 79.96 (d), 127.90 (d), 128.59 (d), 134.14 (u), 154.73 (u) ppm. IR (KBr): $\tilde{v} = 3239$ (m), 3111 (w), 2971 (m), 2932 (m), 2876 (w), 1702 (s), 1604 (w), 1583 (w), 1497 (w), 1469 (m), 1456 (m), 1430 (s), 1413 (s), 1386 (m), 1368 (m), 1352 (m), 1335 (m), 1312 (m), 1300 (s), 1267 (w), 1251 (m), 1193 (m), 1146 (m), 1115 (m), 1092 (m), 1071 (w), 1048 (s) cm⁻¹. MS (CI): m/z (relative intensity, %) = 282 [M⁺ + 1] (100). C15H20CINO2 (281.78): calcd. C 63.94, H 7.15, N 4.97; found C 63.68, H 7.00, N 4.82.

Compound 26: $[\alpha]_D = -78.1 (c = 0.78, Et_2O)$. ¹H NMR (400 MHz, CDCl₃): $\delta = 2.69$ (s, 3 H, Me), 3.30 (s, 3 H, OMe), 7.52–7.57 (m, 3 H, Ph), 7.61–7.67 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 25.67$ (d), 54.01 (d), 125.15 (d), 129.33 (d), 131.85 (d), 142.31 (u), 155.55 (u) ppm. IR (neat): $\tilde{v} = 3058$ (w), 3001 (w), 2955 (m), 2844 (w), 1725 (s), 1582 (w), 1444 (s), 1414 (m), 1313 (s), 1201 (m), 1145 (s), 1108 (s), 1078 (m), 1066 (m), 1023 (w) cm⁻¹. MS (CI): *m/z* (relative intensity, %) = 214 [M⁺ + 1] (7), 125 (100), 97 (24). C₉H₁₁NOS (213.25): calcd. C 50.69, H 5.20, N 6.57; found C 50.69, H 5.41, N 6.89.

(-)-(4R,5R,6S)-4-(Cyanomethyl)-tertahydro-4-methyl-6-(1-methylethyl)-5-phenyl-2H-1,3-oxazin-2-one (30): Treatment of chloride 29 (1.14 g, 4.05 mmol) with NaCN (40 mg, 0.82 mmol) according to GP6 and purification by chromatography (EtOAc) gave nitrile **30** (960 mg, 87%) as a colorless solid. M.p. 164 °C. $[\alpha]_D$ = $-28.7 (c = 0.55, CH_2Cl_2)$. ¹H NMR (400 MHz, CDCl₃): $\delta = 0.84$ (d, J = 6.9 Hz, 3 H, *i*Pr), 1.09 (d, J = 7.1 Hz, 3 H, *i*Pr), 1.34 (s, 3 H, Me), 1.70 (septd, J = 6.9, J = 1.7 Hz, 1 H, *i*Pr), 2.38 (d, J =17.0 Hz, 1 H, CH₂), 2.61 (d, J = 17.0 Hz, 1 H, CH₂), 3.30 (d, J =11.4 Hz, 1 H, CHPh), 4.69 (dd, J = 11.4, J = 1.9 Hz, 1 H, CHO), 7.24-7.27 (m, 2 H, Ph), 7.34-7.42 (m, 3 H, Ph), 7.73 (s, 1 H, NH) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 13.51$ (d), 19.88 (d), 24.81 (d), 28.77 (d), 30.30 (u), 48.40 (d), 55.08 (u), 80.52 (d), 116.08 (u), 128.51 (d), 129.07 (d), 133.73 (u), 154.92 (u) ppm. IR (KBr): $\tilde{v} =$ 3455 (w), 3219 (w), 3108 (w), 2961 (m), 2931 (w), 2876 (w), 2257 (w), 1700 (s), 1451 (w), 1418 (s), 1389 (w), 1371 (m), 1350 (m), 1338 (m), 1315 (m), 1268 (w), 1189 (w), 1167 (w), 1101 (w), 1056 (m) cm⁻¹. MS (CI): m/z (relative intensity, %) = 273 [M⁺ + 1] (100). C16H20N2O2 (272.34): calcd. C 70.56, H 7.40, N 10.29; found C 70.30, H 7.49, N 10.04.

(-)-(4R,5R,6S)-{Tetrahydro-4-methyl-6-(1-methylethyl)-2-oxo-5-phenyl-2*H*-[1,3]-oxazin-4-yl}acetic Acid (31). From Nitrile 30: Treatment of 30 (170 mg, 0.62 mmol) with NaOH (2 N, 5 mL) according to *GP8* and purification by recrystallization (CHCl₃/hexane, 5:1) afforded amino acid 31 (130 mg, 72%) as fine, colorless needles.

From Ester 23b: Aqueous NaOH (2 N, 2 mL) was added to a solution of the amino ester **23b** (101 mg, 0.29 mmol) in EtOH (6 mL) and the mixture was heated at 55 °C for 3 h. After the mixture had cooled to room temperature, EtOH was removed in vacuo and the solution was acidified with aqueous 3 N HCl until a colorless solid precipitated. The mixture was then extracted with CHCl₃, where-upon the solid dissolved, and the combined organic phases were concentrated in vacuo. Purification by recrystallization (CHCl₃/ hexane, 5:1) afforded the amino acid **31** (70 mg, 82%) as fine, colorless needles.

Compound 31: M.p. 185 °C (dec.). $[\alpha]_D = -26.7$ (c = 0.45, MeOH). ¹H NMR (400 MHz, CD₃OD): $\delta = 0.82$ (d, J = 6.9 Hz, 3 H, *i*Pr), 1.10 (d, J = 7.1 Hz, 3 H, *i*Pr), 1.30 (s, 3 H, Me), 1.70 (septd, J = 6.9, J = 1.7 Hz, 1 H, *i*Pr), 2.37 (d, J = 15.7 Hz, 1 H, CH₂), 2.53 (d, J = 15.7 Hz, 1 H, CH₂), 3.44 (d, J = 11.5 Hz, 1 H, CH₂), 2.53 (d, J = 15.7 Hz, 1 H, CH₂), 3.44 (d, J = 11.5 Hz, 1 H, CHPh), 4.88 (dd, J = 11.5, J = 1.9 Hz, 1 H, HCO), 7.33–7.45 (m, 5 H, Ph) ppm. ¹³C NMR (100 MHz, CD₃OD): $\delta = 12.76$ (d), 19.04 (d), 23.46 (d), 28.79 (d), 43.21 (u), 48.52 (d), 54.89 (u), 80.35 (d), 127.82 (d), 128.43 (d), 135.01 (u), 155.38 (u), 172.75 (u) ppm. IR (KBr): $\tilde{v} = 3372$ (m), 3266 (m), 3068 (m), 2974 (m), 2935 (m), 2881 (m), 2734 (w), 2557 (w), 1730 (s), 1717 (s), 1667 (s), 1500 (w), 1469 (m), 1432 (s), 1389 (m), 1377 (m), 1346 (m), 1317 (m), 1288 (w), 1237 (m), 1206 (m), 1192 (m), 1154 (w), 1113 (w), 1101 (w), 1062 (m) cm⁻¹. MS (CI): *m/z* (relative intensity, %) = 292 [M⁺ + 1] (100), 267 (34), 248 (18), 183 (16), 165 (33), 141 (31), 123 (10), 99 (11). (-)-(4S,4aR,7aS)-7a-(Chloromethyl)-hexahydro-4-(1-methylethyl)-cyclopenta[d][1,3]oxazin-2(1H)-one (32a) and Methyl (S)-N-Phenylsulfinylcarbamate (26): Treatment of sulfoximine 15a (1.02 g, 2.91 mmol) with ClCO₂Me (3.5 mL, 45.45 mmol) according to GP5 and purification by double chromatography (EtOAc/cyclohexane, 4:1; aluminium oxide, EtOAc/MeOH, 10:1) gave chloride 32a (560 mg, 83%) as a white solid and carbamic acid ester 26 (420 mg, 68%) as a colorless oil. **32a:** M.p. 96 °C. $[\alpha]_{D} = -9.8$ (c = 1.20, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): $\delta = 1.01$ (d, J = 6.9 Hz, 3 H, *i*Pr), 1.10 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.49–1.68 (m, 2 H, CH₂), 1.74-2.06 (m, 5 H, CH₂, *i*Pr), 2.28 (ddd, J = 10.2, J = 8.5, J =4.1 Hz, 1 H, CHCN), 3.54 (symm. m, 2 H, CH₂Cl), 3.74 (dd, J = 10.2, J = 3.0 Hz, 1 H, CHO), 6.84 (s, 1 H, NH) ppm. ¹³C NMR $(100 \text{ MHz}, \text{CDCl}_3)$: $\delta = 15.16 \text{ (d)}, 19.91 \text{ (d)}, 23.29 \text{ (u)}, 28.77 \text{ (u)},$ 29.31 (d), 38.11 (u), 41.28 (d), 52.72 (u), 64.79 (u), 83.77 (d), 157.25 (u) ppm. IR (KBr): $\tilde{v} = 3249$ (w), 3128 (w), 2964 (s), 2878 (m), 1713 (s), 1469 (w), 1407 (m), 1371 (w), 1333 (m), 1303 (w), 1144 (w), 1085 (w), 1038 (w), 1021 (w) cm⁻¹. MS (CI): m/z (relative intensity, %) = 332 [M⁺ + 1] (100). $C_{11}H_{18}CINO_2$ (231.72): calcd. C 57.02, H 7.83, N 6.04; found C 57.08, H 7.48, N 5.83.

(+)-(4S,4aR,8aS)-8a-(Chloromethyl)-octahydro-4-(1-methylethyl)-2H-3,1-benzoxazin-2-one (32b): Treatment of sulfoximine 15b (392 mg, 1.08 mmol) with ClCO₂Me (1.25 mL, 16.2 mmol) for 3 days according to GP5 and purification by chromatography (EtOAc/pentane, 1:1) afforded chloride 32b (227 mg, 86%) as a colorless solid and carbamic acid ester 26 (152 mg, 66%). M.p. 145–146 °C, $[\alpha]_{\rm D}$ = +4.8 (*c* = 0.25, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): $\delta = 0.85$ (d, J = 6.8 Hz, 3 H, *i*Pr), 1.00 (d, J = 6.8 Hz, 3 H, *i*Pr), 1.10-1.80 (m, 8 H), 1.92 (septd, J = 6.8, J = 2.2 Hz, 1 H, *i*Pr), 2.00-2.05 (m, 1 H), 3.45 (dd, J = 11.3, J = 1 Hz, 1 H, CH₂Cl), 3.85 (d, J = 11.3 Hz, 1 H, CH₂Cl), 4.25 (dd, J = 10.4, J = 2.2 Hz, 1 H, CHO), 5.65 (br. s, 1 H, NH) ppm. ¹³C NMR $(75 \text{ MHz}, \text{ CDCl}_3)$: $\delta = 14.05 \text{ (d)}, 20.21 \text{ (d)}, 20.76 \text{ (u)}, 22.57 \text{ (u)},$ 22.99 (u), 28.44 (d), 33.10 (u), 36.20 (d), 51.05 (u), 55.59 (u), 80.01 (d), 154.59 (u) ppm. IR (KBr): $\tilde{v} = 3351$ (m), 2935 (s), 1725 (s), 1678 (s), 1433 (m), 1332 (m), 1031 (s) cm⁻¹. MS (EI): m/z (relative intensity, %) = 205 (1), 204 (9), 202 (33), 196 (100), 152 (88), 145 (14), 95 (25), 80 (14). C₁₂H₂₀ClNO₂ (245.75): calcd. C 58.65, H 8.20, N 5.70; found C 58.46, H 8.00, N 5.67.

(-)-(4R,4aR,7aS)-7a-(Cyanomethyl)-hexahydro-4-(1-methylethyl)-2H-3,1-cyclopenta[d][1,3]oxazin-2(1H)-one (33a): Treatment of chloride 32a (348 mg, 1.50 mmol) with NaCN (147 mg, 3.00 mmol) according to GP6 and purification by chromatography (EtOAc) gave nitrile 33a (308 mg, 92%) as a colorless solid. M.p. 132 °C. $[\alpha]_D = -34.8$ (c = 1.63, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): $\delta = 0.96$ (d, J = 6.9 Hz, 3 H, *i*Pr), 1.05 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.47 - 1.69 (m, 2 H), 1.73 - 2.03 (m, 5 H), 2.28 (td, J = 0.9, J = 9.8, J = 4.1 Hz, 1 H, CHCN), 2.59 (d, J = 16.7 Hz, 1 H, CH₂CN), 2.66 (d, J = 16.8 Hz, 1 H, CH₂CN), 3.69 (dd, J = 10.0, J = 3.4 Hz, 1 H, CHO), 7.53 (s, 1 H, NH) ppm. ¹³C NMR $(100 \text{ MHz}, \text{CDCl}_3)$: $\delta = 15.76 \text{ (d)}, 20.15 \text{ (d)}, 23.60 \text{ (u)}, 29.12 \text{ (u)},$ 29.79 (d), 31.27 (u), 40.43 (u), 43.04 (d), 62.41 (u), 84.51 (d), 117.12 (u), 157.48 (u) ppm. IR (KBr): $\tilde{v} = 3326$ (s), 2971 (m), 2937 (m), 2880 (m), 2256 (m), 1716 (s), 1456 (w), 1412 (m), 1386 (m), 1334 (m), 1301 (m), 1272 (w), 1254 (w), 1192 (w), 1158 (w), 1126 (w), 1055 (w), 1036 (m), 1018 (m) cm⁻¹. MS (EI): *m/z* (relative intensity, %) = 223 $[M^+ + 1]$ (1), 182 (84), 180 (12), 179 (21), 139 (10), 138 (100), 137 (23), 136 (51), 135 (12), 122 (12), 121 (69), 110 (21), 109 (10), 108 (60), 107 (21), 96 (16), 95 (22), 94 (13), 93 (54), 82 (54), 81 (50), 80 (19). C₁₂H₁₈N₂O₂ (222.28): calcd. C 64.84, H 8.16, N 12.60; found C 64.83, H 8.33, N 12.64.

(+)-(4R,4aR,8aS)-8a-(Cyanomethyl)-octahydro-4-(1-methylethyl)-2H-3,1-benzoxazin-2-one (33b): Treatment of chloride 32b (186 mg, 0.76 mmol) with NaCN (74 mg, 1.51 mmol) according to GP6 and purification by chromatography (EtOAc) afforded nitrile **33b** (170 mg, 95%) as a colorless solid. M.p. 48–50 °C. $[\alpha]_D$ = +2.86 (c = 0.21, CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃): $\delta = 0.97$ (d, J = 6.7 Hz, 3 H, *i*Pr), 1.13 (d, J = 6.7 Hz, 3 H, *i*Pr), 1.19–1.35 (m, 2 H), 1.51-1.61 (m, 2 H), 1.69-1.76 (m, 1 H), 1.80-1.90 (m, 3 H), 2.00 (septd, J = 6.9, J = 3.0 Hz, 1 H, *i*Pr), 2.08 (dt, J = 9.8, J = 2.2, J = 2.2 Hz, 1 H, CHCN), 2.74 (d, J = 17.1 Hz, 1 H, CH_2CN , 2.86 (d, J = 17.1 Hz, 1 H, CH_2CN), 4.28 (dd, J = 9.8, J = 3.0 Hz, 1 H, CHO), 7.42 (s, 1 H, NH) ppm. ¹³C NMR $(125 \text{ MHz}, \text{CDCl}_3): \delta = 14.13 \text{ (d)}, 19.76 \text{ (d)}, 20.40 \text{ (u)}, 22.29 \text{ (u)},$ 22.98 (u), 28.10 (u), 28.52 (d), 35.54 (u), 36.23 (d), 53.83 (u), 80.59 (d), 116.26 (u), 155.42 (u) ppm. IR (KBr): $\tilde{v} = 3677$ (w), 3652 (w), 3340 (m), 3123 (w), 2939 (s), 2875 (m), 2247 (w), 1707 (s), 1468 (m), 1421 (m), 1383 (m), 1334 (m), 1276 (w), 1244 (w), 1192 (w), 1166 (w), 1142 (w), 1102 (w), 1077 (w), 1034 (m) cm⁻¹. MS (CI): m/z (relative intensity, %) = 237 [M⁺ + 1] (100). C₁₃H₂₀N₂O₂ -CH₂CN: calcd. 196.1338; found (HRMS, EI) 196.1337.

(-)-(4R,4aR,7aS)-[Hexahydro-4-(1-methylethyl)-2-oxocyclopenta[d][1,3]oxazin-7a(4H)-yl]acetic Acid (34a): Treatment of nitrile 33a (107 mg, 0.48 mmol) with aqueous NaOH (2 N, 1 mL) according to GP8 and purification by chromatography (EtOAc/AcOH, 95:5) afforded amino acid 33a (81 mg, 70%) as a colorless oil. $[\alpha]_{\rm D} = -4.4 \ (c = 1.45, \text{ MeOH}).$ ¹H NMR (400 MHz, CDCl₃): $\delta =$ 0.95 (d, J = 6.6 Hz, 3 H, *i*Pr), 1.09 (d, J = 6.9 Hz, 3 H, *i*Pr), 1.45–1.69 (m, 2 H, CH₂), 1.73–2.02 (m, 5 H, CH₂, *i*Pr, CHCN), 2.25-2.35 (m, 1 H, CH₂), 2.59 (d, J = 17 Hz, 1 H, CH₂CO), 2.65 $(d, J = 17 \text{ Hz}, 1 \text{ H}, \text{CH}_2\text{CO}), 3.69 (dd, J = 10.2, J = 2.8 \text{ Hz}, 1 \text{ H},$ CHO), 7.72 (s, 1 H, NH), 10.6 (br. s, 1 H, CO₂H) ppm. ¹³C NMR $(100 \text{ MHz}, \text{CDCl}_3)$: $\delta = 14.91 \text{ (d)}, 19.90 \text{ (d)}, 22.58 \text{ (u)}, 26.95 \text{ (u)},$ 28.71 (d), 38.55 (u), 43.95 (d), 44.94 (u), 61.83 (u), 83.39 (d), 157.97 (u), 173.85 (u) ppm. IR (KBr): $\tilde{v} = 3376$ (m), 2970 (s), 2879 (m), 2727 (w), 2627 (w), 1718 (s), 1640 (s), 1545 (w), 1440 (s), 1417 (m), 1394 (w), 1372 (w), 1333 (w), 1287 (w), 1239 (m), 1217 (s), 1182 (m), 1138 (w), 1106 (w), 1070 (m), 1050 (w) cm⁻¹. MS (EI): m/z(relative intensity, %) = $242 [M^+ + 1] (1)$, 199 (28), 198 (13), 182 (11), 156 (100), 155 (11), 138 (22), 137 (22), 101 (23), 93 (10), 82 (10), 81 (17).

(-)-(4R,4aR,8aS)-Octahydro-4-(1-methylethyl)-2-oxo-8aH-3,1-benzoxazin-8a-yl)acetic Acid (34b): Treatment of nitrile 33b (78 mg, 0.33 mmol) with aqueous NaOH (2 N, 2 mL) according to GP8 and purification by chromatography (EtOAc/AcOH, 95:5) afforded the amino acid 34b (58 mg, 69%) as a colorless solid. M.p. 215 °C (dec.). $[\alpha]_D = -2.6$ (*c* = 1.25, MeOH). ¹H NMR (300 MHz, CDCl₃): $\delta = 0.90$ (d, J = 6.6 Hz, 3 H, *i*Pr), 1.13 (d, J = 6.9 Hz, 3 H, iPr), 1.18-1.42 (m, 2 H, CH2, CHCN), 1.49-1.84 (m, 6 H, CH₂), 1.98 (septd, J = 6.9, J = 1.9 Hz, 1 H, *i*Pr), 2.30–2.43 (m, 2 H, CH₂CO, CHCNH), 3.10 (d, J = 16.8 Hz, 1 H, CH₂CO), 4.39 (dd, J = 10.5, J = 1.9 Hz, 1 H, CHO), 7.67 (s, 1 H, NH), 8.3 (br. s, 1 H, CO₂H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 13.41 (d), 19.79 (d), 20.39 (u), 22.20 (u), 22.50 (u), 27.64 (d), 33.03 (u), 39.17 (d), 40.86 (u), 53.77 (u), 79.27 (d), 156.07 (u), 173.93 (u) ppm. IR (KBr): $\tilde{v} = 3360$ (m), 2985 (m), 2944 (m), 2882 (w), 2515 (w), 1716 (s), 1646 (s), 1442 (s), 1386 (w), 1340 (w), 1307 (w), 1263 (m), 1209 (m), 1169 (w), 1140 (w), 1123 (w), 1101 (w), 1044 (m) cm⁻¹. MS (CI): m/z (relative intensity, %) = 256 [M⁺ + 1] (100).

(-)-(S)-(Methylsulfinyl)benzene (36): MeMgCl (0.9 mL, 22 wt% in THF, 2.66 mmol) was added at -78 °C to a solution of sulfinamide 26 (284 mg, 1.33 mmol) in THF (6 mL). After the mixture had been stirred at this temperature for 45 min, saturated aqueous NH₄Cl

was added and the aqueous phase was extracted with EtOAc. The combined organic phases were dried (MgSO₄) and concentrated in vacuo. Chromatography (EtOAc/*i*PrOH, 8:1) afforded sulfoxide **36** (131 mg, 70%) of 97% *ee* [GC, octakis(2,6-di-O-pentyl-3-O-butyryl)- γ -cyclodextrin, $t_{\rm R}$ (**36**) = 25.10, $t_{\rm R}$ (*ent*-**36**) = 21.40 min] as a colorless oil. [a]_D = -140.2 (c = 2.05, acetone). ¹H NMR (400 MHz, CDCl₃): δ = 2.73 (s, 3 H, CH₃), 7.47–7.56 (m, 3 H, Ph), 7.63–7.67 (m, 2 H, Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 43.89 (d), 123.28 (d), 129.15 (d), 130.82 (d), 145.47 (u) ppm.

(4R, 5R, 6S)-Tetrahydro-4-ethenyl-6-ethyl-5-methyl-2*H*-1,3-oxazin-2-one (39): ClCO₂CH(Cl)Me (0.13 mL, 1.20 mmol) and four drops of pyridine were added at room temperature to a solution of 16a (40 mg, 0.12 mmol) in CH₂Cl₂ (2 mL). The yellow mixture was stirred at room temperature for 1 h and then concentrated in vacuo. Purification by chromatography (EtOAc) gave a mixture of 39 and 40 in a ratio of 8:1 (119 mg) as a colorless solid.

Compound 39: ¹H NMR (400 MHz, CDCl₃): $\delta = 0.92$ (d, J = 6.7 Hz, 3 H, CH*Me*), 1.03 (t, J = 7.4 Hz, 3 H, Et), 1.61 (tq, J = 10.0, J = 6.7 Hz, 1 H, *CH*Me), 1.58 (dquin, J = 14.8, J = 7.4 Hz, 1 H, Et), 1.85 (dqd, J = 14.8, J = 7.4, J = 3.0 Hz, 1 H, Et), 3.46 (dd, J = 10.0, J = 8.3 Hz, 1 H, CHN), 3.93 (ddd, J = 10.0, J = 7.4, J = 3.0 Hz, 1 H, CHO), 5.28 (br. d, J = 9.9 Hz, 1 H, CH= *CH*₂), 5.29 (br. d, J = 17.1 Hz, 1 H, CH=*CH*₂), 5.38 (s, 1 H, NH), 5.65 (ddd, J = 17.1, J = 9.9, J = 8.3 Hz, 1 H, *CH*=*CH*₂) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 8.25$ (d), 12.54 (d), 24.94 (u), 35.16 (d), 61.02 (d), 82.19 (d), 119.75 (u), 136.84 (d), 154.18 (u) ppm. GC-MS: *m/z* (relative intensity, %) = 170 [M⁺ + 1] (99), 109 (13), 100 (21), 96 (22), 86 (10), 84 (18), 82 (14).

Compound 40: ¹H NMR (400 MHz, CDCl₃) (signals for **40** are partially superposed by those for **39**, so only those signals that could be unequivocally assigned are listed): $\delta = 1.00$ (d, J = 6.7 Hz, 3 H, Me), 1.04 (t, J = 7.4 Hz, 3 H, Et), 3.13 (dd, J = 9.3, J = 1.7 Hz, 1 H, *CH*NH), 3.90 (m, 1 H, *CHO*), 4.20 (qd, J = 7.0, J = 1.7 Hz, 1 H, *CHCl*) ppm. ¹³C NMR (100 MHz, CDCl₃) (only those signals are listed, which could be unequivocally assigned): $\delta = 8.37$, 13.40, 21.89, 24.88, 33.09, 56.85, 61.99, 81.42 ppm.

Acknowledgments

Financial support of this work by the Deutsche Forschungsgemeinschaft (SFB, 380, "Asymmetric Synthesis with Chemical and Biological Methods" and GKR 440 "Methods in Asymmetric Synthesis") and Grünenthal GmbH, Aachen, is gratefully acknowledged. We thank Dr. J. Runsink for NOE experiments and a reviewer for helpful suggestions.

^[1] For reviews, see: ^[1a] C. N. C. Drey, In *Chemistry and Biochemistry of Amino Acids. Peptides and Proteins*; Marcel Dekker, New York, **1972**; vol. 4, p. 242. ^[1b] A. F. Spatola, In *Chemistry and Biochemistry of Amino Acids* (Ed.: B. Weinstein), Marcel Dekker, New York, **1983**. ^[1c] C. N. C. Drey, In *Chemistry and Biochemistry of Amino Acids* (Ed.: G. C. Barret), Chapman and Hall, London, **1985**, p 25. ^[1d]D. C. Cole, *Tetrahedron* **1994**, *50*, 9517. ^[1e] M. B. Smith, *Methods of Non-α-Amino Acid Synthesis*; Marcel Dekker, New York, **1996**, *25*, 117. ^[1g] *Enantioselective Synthesis of β-Amino Acids* (Ed.: E. Juaristi), John Wiley & Sons, New York, **1997**. ^[1h]E. Juaristi, H. Lopéz-Ruiz, *Cur. Med. Chem.* **1999**, *6*, 983. ^[1i] S. Abele, D. Seebach, *Eur. J. Org. Chem.* **2000**, 1.

 ^[2] ^[2a] A. H. Berks, *Tetrahedron* 1996, 52, 331. ^[2b] R. Southgate, C. Branch, S. Coulton, E. Hunt, In *Recent Progress in the Chemical Synthesis of Antibiotics and Related Microbial Products* (Ed.: G. Lukacs), Springer Verlag, Berlin, 1993, vol. 2, p. 621.

- ^[3] ^[3a] D. Seebach, J. L. Matthews, Chem. Commun. 1997, 2015. ^[3b] D. Seebach, S. Abele, T. Sifferlen, M. Hänggi, S. Grüner, P. Seiler, Helv. Chim. Acta 1998, 81, 2218. [3c] C. Palomo, M. Oiarbide, S. Bindi, J. Org. Chem. 1998, 63, 2469. [3d] K. Gademann, T. Hintermann, J. V. Schreiber, Curr. Med. Chem. 1999, 6, 905. [3e] A. Gaucher, M. Wakselman, J.-P. Mazaleyrat, M. Crisma, F. Formaggio, C. Toniolo, Tetrahedron 2000, 56, 1715. ^[3f] J. Cheng, T. J. Deming, J. Am. Chem. Soc. 2001, 123, 9457. ^[3g] N. Umezawa, M. A. Gelman, M. C. Haigis, R. T. Raines, S. H. Gellman, J. Am. Chem. Soc. 2002, 124, 368. [3h] R. P. Cheng, S. H. Gellman, W. F. DeGrado, Chem. Rev. 2001, 101, 3219. [3i] M. Werder, H. Hauser, S. Abele, D. Seebach, Helv. Chim. Acta 1999, 82, 1774. [3] Y. Hamura, J. P. Schneider, W. F. DeGrado, J. Am. Chem. Soc. 1999, 121, 12200. [3k] E. A. Poerter, X. Wang, H.-S. Lee, B. Weisblum, S. H. Gellman, Nature 2000, 404, 565. [31] D. Liu, W. F. DeGrado, J. Am. Chem. Soc. 2001, 123, 7553. [3m] K. Gademann, T. Kimmerlin, D. Hoyer, D. Seebach, J. Med. Chem. 2001, 44, 2460.
- ^[4] For selected examples, see: ^[4a] R. Caputo, E. Cassano, L. Longobardo, G. Palumbo, Tetrahedron 1995, 51, 12337. [4b] D. Seebach, M. Overhand, F. N. M. Kühnle, B. Martioni, L. Oberer, U. Homml, H. Widmer, Helv. Chim. Acta 1996, 79, 913. [4c] J. K. Myers, E. N. Jacobsen, J. Am. Chem. Soc. 1999, 121, 8959. ^[4d] D. A. Evans, L. D. Wu, J. J. M. Wiener, J. S. Johnson, D. H. B. Ripin, J. S. Tedrow, J. Org. Chem. 1999, 64, 6411. [4e] H. Miyabe, K. Fujii, T. Naito, Org. Lett. 1999, 7, 569. [4f] H. Ohtake, Y. Imada, S.-I. Murahashi, J. Org. Chem. 1999, 64, 3790. [4g] S. Fustero, B. Pina, M. G. de la Torre, A. Navarro, C. Ramírez de Arellano, A. Simón, Org. Lett. 1999, 7, 977. [4h] M. Seki, T. Shimizu, K. Matsumoto, J. Org. Chem. 2000, 65, 1298. [4i] W. Zhuang, R. G. Hazell, K. A. Jørgensen, Chem. Commun. 2001, 1240.^[4j] C. Bolm, I. Schiffers, C. L. Dinter, L. Defrere, A. Gerlach, G. Raabe, Synthesis 2001, 1719. ^[4k] T. Yokomatsu, K. Takada, A. Yasumoto, Y. Yuasa, S. Shibuya, Hetereocycles 2002, 56, 545. [41] Z. Ma, Y. Zhao, N. Jiang, X. Jin, J. Wang, Tetrahedron Lett. 2002, 43, 3209. [4m] S. Murahashi, Y. Imada, T. Kawakami, K. Harada, Y. Yonemushi, N. Tomita, J. Am. Chem. Soc. 2002, 124, 2888. [4n] A. Córdova, S. Watanabe, F. Tanaka; W. Notz, C. F. Barbas, III, J. Am. Chem. Soc. 2002, 124, 1866. ^[40] H. M. L. Davies, C. Venkataramani, Angew. Chem. 2002, 114, 2301; Angew. Chem. Int. Ed. 2002, 41, 2197.
- ^[5] [^{5a]} D. H. Hua, S. W. Miao, J. S. Chen, S. Iguchi, J. Org. Chem. 1991, 56, 4. [^{5b]} F. A. Davis, R. T. Reddy, R. E. Reddy, J. Org. Chem. 1992, 57, 6387. [^{5c]} T. P. Tang, J. A. Ellman, J. Org. Chem. 2002, 67, 7819. [^{5d]} F. A. Davies, J. Deng, Y. Zhang, R. C. Haltiwanger, Tetrahedron 2002, 58, 7135. [^{5e]} E. Juaristi, M. Balderas, H. López-Ruiz, V. M. Jiménez-Pérez, M. L. Kaiser-Carril, Y. Ramírez-Quirós, Tetrahedron: Asymmetry 1999, 10, 3493.
- [6] [6a] M. Hirama, T. Shigemoto, T. Yamazaki, S. Itô, J. Am. Chem. Soc. 1985, 107, 1797. [6b] M. Hirama, S. Itô, Heterocycles 1989, 28, 1229. [6c] T. Kitazume, T. Kobayashi, T. Yamamoto, T. Yamazaki, J. Org. Chem. 1987, 52, 3218. [6d] U. Schmidt, F. Stäbler, A. Lieberknecht, Synthesis 1992, 462. [6e] J. de Blas, J. C. Carretero, E. Domínguez, Tetrahedron Lett. 1994, 35, 4603. [6f] N. Asao, T. Shimada, T. Sudo, N. Tsukada, K. Yazawa, Y. S. Gyoung, T. Uyehara, Y. Yamamoto, J. Org. Chem. 1997, 62, 6274. [6g] S. G. Davies, O. Ichihara, Tetrahedron Lett. 1999, 40, 9313. [6h] G. Delle Monache, D. Misiti, P. Salvatore, G. Zappia, Tetrahedron: Asymmetry 2000, 11, 1137.^[61] G. Guanti, A. Moro, E. Narisano, Tetrahedron Lett. 2000, 41, 3203. [6] D. Seebach, A. Jacobi, M. Rueping, K. Gademann, M. Ernst, B. Jaun, Helv. Chim. Acta 2000, 83, 2115. [6k] F. Schweizer, A. Lohse, A. Otter, O. Hindsgaul, Synlett 2001, 9, 1434. [61] G. V. M. Sharma, V. G. Reddy, A. S. Chander, K. R. Reddy, Tetrahedron: Asymmetry 2002, 13, 21. [6m] C. Palomo, M. Oiarbide, A. Landa, M. C. González-Rego, J. M. Garcia, A. González, J. M. Odriozola, M. Martín-Pastor, A. Linden, J. Am. Chem. Soc. 2002, 124, 8637.

- ^[8] For the asymmetric synthesis of acyclic γ-unsubstituted δ-hydroxy-α,β-unsaturated esters through vinylogous aldol reaction, see for example: ^[8a] G. Casiraghim, F. Zanardi, G. Appendino, G. Rassu, *Chem. Rev.* 2000, 100, 1929. ^[8b] G. Bluet, B. Bazán-Tejeda, J.-M. Campagne, *Org. Lett.* 2001, *3*, 3807. ^[8c] G. Bluet, J.-M. Campagne, *J. Org. Chem.* 2001, *66*, 4293. ^[8d] D. A. Evans, E. Hu, J. D. Burch, G. Jaeschke, *J. Am. Chem. Soc.* 2002, *124*, 5654.
- [9] For the asymmetric synthesis of γ-substituted δ-hydroxy-α,βunsaturated esters through ring opening of diene expoxide esters, see for example: ^[9a] N. Abe, H. Hanawa, K. Maruoka, M. Sasaki, M. Miyashita, *Tetrahedron Lett.* **1999**, 40, 5369. ^[9b] Y. Noguchi, T. Yamada, H. Uchiro, S. Kobayashi, *Tetrahedron Lett.* **2000**, 41, 7493.
- [^{10]} For selected examples, see: [^{10a]} A. I. Meyers, R. F. Spohn, R. J. Linderman, J. Org. Chem. **1985**, 50, 3633. [^{10b]} D. E. Cane, R. H. Lambalot, P. C. Prabahkaran, W. R. Ott, J. Am. Chem. Soc. **1993**, 114, 522. [^{10c]} A. K. Gosh, W. Liu, J. Org. Chem. **1997**, 62, 7908. [^{10d]} T. K. Chakraborty, S. Jayaprakash, Tetrahedron Lett. **2001**, 42, 497.
- ^[11] ^[11a] S. Shibara, S. Kondo, K. Maeda, H. Umezawa, M. Ohno, J. Am. Chem. Soc. 1972, 94, 4353. [11b] V. Jäger, W. Schwab, V. Buss, Angew. Chem. 1981, 93, 573; Angew. Chem. Int. Ed. Engl. 1981, 20, 601. [11c] A. P. Kozikowski, Y.-Y. Chen, J. Org. Chem. 1981, 46, 5248. [11d] Y.-F. Wang, T. Izawa, S. Kobayashi, M. Ohno, J. Am. Chem. Soc. 1982, 104, 6465. [11e] W. A. König, H. Hahn, R. Rathmann, W. Hass, A. Keckeisen, H. Hagenmaier, C. Bormann, W. Dehler, R. Kurth, H. Zähner, Liebigs Ann. Chem. 1986, 407. [11f] S. Hashiguchi, A. Kawada, H. Natsugari, J. Chem. Soc., Perkin Trans. 1 1991, 2435. [11g] A. G. M. Barrett, S. A. Lebold, J. Org. Chem. 1991, 56, 4875. [11h] V. Jaeger, R. Mueller, T. Leibold, M. Hein, M. Schwarz, M. Fengler, L. Jaroskova, M. Paetzel, P.-Y. LeRoy, Bull. Soc. Chim. Belg. 1994, 103, 491. [11i] R. Sakai, H. Kamiya, M. Murata, K. Shimamoto, J. Am. Chem. Soc. 1997, 119, 4112. [11] D. L. Musso, N. B. Mehta, F. E. Soroko, Bioorg. Med. Chem. Lett. 1997, 7, 1. [11k] B. L. Chang, A. Ganesan, Bioorg. Med. Chem. Lett. 1997, 7, 1511. [111] P. R. Carlier, M. M.-C. Lo, P. C.-K. Lo, E. Richelson, M. Tatsumi, I. J. Reynolds, T. A. Sharma, Bioorg. Med. Chem. Lett. 1998, 8, 487. ^[11m] F. Benedetti, S. Norbedo, Chem. Commun 2001 203
- ^[12] ^[12a] A. Pohland, H. R. Sullivan, J. Am. Chem. Soc. 1953, 75, 4458.
 ^[12b] A. Pohland, H. R. Sullivan, J. Am. Chem. Soc. 1955, 77, 3400.
 ^[12c] B. Wünsch, G. Höfner, G. Bauschke, Arch. Pharm. 1993, 326, 101.
 ^[12d] P. R. Carlier, K. M. Lo, M. M. C. Lo, I. D. Williams, J. Org. Chem. 1995, 60, 7511.
 ^[12e] H.-J. Gais, C. Griebel, H. Buschmann, Tetrahedron: Asymmetry 2000, 11, 917.
 ^[12f] E. Friedrichs, T. Christoph, H. Buschmann, In Ullmann's Encyclopedia of Industrial Chemistry (Ed.: J. L. McGuire), Wiley-VCH, Weinheim, 2000.
- [13] [13a] B. T. Cho, N. Kim, *Tetrahedron Lett.* 1994, 35, 4115. ^[13b]
 S. Chicchi, S. Crea, A. Goti, A. Brandi, *Tetrahedron: Asymmetry* 1997, 8, 293. ^[13c] X. Li, C. Yeung, A. S. C. Chan, T.-K. Yang, *Tetrahedron: Asymmetry* 1999, 10, 759. ^[13d] M. J. Vilaplana, P. Molina, A. Arues, C. Andres, R. Pedrosa, *Tetrahedron: Asymmetry* 2002, 13, 5.
- [^{14]} For reviews, see: ^[14a] Stereoselective Synthesis; Houben-Weyl, Methods of Organic Chemistry (Eds.: G. Helmchen, R. W. Hoffmann, J. Mulzer, E. Schaumann), Thieme, Stuttgart, 1995, vol. E 21a. ^[14b]M. Frederickson, Tetrahedron 1997, 53, 403. ^[14c] D. Enders, U. Reinhold, Tetrahedron: Asymmetry 1997, 8, 1895. ^[14d] R. Bloch, Chem. Rev. 1998, 98, 1407. ^[14e] F. A. Davis, P. Zhou, B.-C. Chen, Chem. Soc. Rev. 1998, 27, 13. ^[14f] K. V. Gothelf, K. A. Jørgensen, Chem. Rev. 1998, 98, 863. ^[14g] S. Kobayashi, H. Ishitani, Chem. Rev. 1999, 99, 1069.

- ^[15] For selected recent examples, see: ^[15a] C. Lutz, V. Lutz, P. Knochel, *Tetrahedron* 1998, 54, 6385. ^[15b] B. F. Bonini, M. Comes-Franchini, M. Fochi, J. Gawronski, G. Mazzanti, A. Ricci, G. Varchi, *Eur. J. Org. Chem.* 1999, 437. ^[15c] J.-L. Toujas, L. Toupet, M. Vaultier, *Tetrahedron* 2000, 56, 2665. ^[15d] T. Kochi, T. P. Tang, J. A. Ellman, *J. Am. Chem. Soc.* 2002, 124, 6518. ^[15e] S. J. Veenstra, S. S. Kinderman, *Synlett* 2001, 1109. ^[15f] T. Dudding, A. M. Hafez, A. E. Taggi, T. R. Wagerle, T. Lectka, *Org. Lett.* 2002, 4, 387.
- ^[16] [^{16a]} J. Barluenga, A. L. Vadio, E. Aguilar, S. Fustero, B. Olano, J. Org. Chem. **1993**, 58, 5972. [^{16b]} J. Barluenga, F. Fernandez-Mari, A. L. Viado, E. Aquilar, B. Olano, J. Org. Chem. **1996**, 61, 5659. [^{16c]} X. Teng, A. Kasatkin, Y. Kawanaka, S. Okamoto, F. Sato, Tetrahedron Lett. **1997**, 38, 8977. [^{16d]} S. Kobayashi, M. Kawamura, J. Am. Chem. Soc. **1998**, 120, 5840. [^{16e]} M. Kossenjans, J. Martens, Tetrahedron: Asymmetry **1999**, 10, 3409. [^{16f]} H. Ohno, H. Hamaguchi, T. Tanaka, J. Org. Chem. **2001**, 66, 1867. [^{16g]} Y. Takemoto, M. Anzai, R. Yanada, N. Fujii, H. Ohno, T. Ibuka, Tetrahedron Lett. **2001**, 42, 1725.
- ^[17] [^{17a]} D. Enders, S. Oberbörsch, Synlett 2002, 471. [^{17b]} B. List,
 P. Pojarliev, W. T. Biller, H. Martin, J. Am. Chem. Soc. 2002,
 124, 827. [^{17c]} A. Cordova, W. Notz, G. Zhong, J. M. Betancort,
 C. F. Barbas, III, J. Am. Chem. Soc. 2002, 124, 1842. [^{17d]} S.
 Kobayashi, T. Hamada, K. Manabe, J. Am. Chem. Soc. 2002,
 124, 5640.
- ^[18] [18a] H.-J. Gais, H. Müller, J. Decker, R. Hainz, *Tetrahedron Lett.* 1995, 36, 7433. ^[18b] R. Hainz, H.-J. Gais, G. Raabe, *Tetrahedron: Asymmetry* 1996, 7, 2505. ^[18c] H.-J. Gais, R. Hainz, H. Müller, P. R. Bruns, N. Giesen, G. Raabe, J. Runsink, S. Nienstedt, J. Decker, M. Schleusner, J. Hachtel, R. Loo, C.-W. Woo, P. Das, *Eur. J. Org. Chem.* 2000, 3973.
- ^[19] See also: ^[19a] M. Reggelin, H. Weinberger, M. Gerlach, R. Welcker, J. Am. Chem. Soc. **1996**, 118, 4765. ^[19b] M. Reggelin, M. Gerlach, M. Vogt, Eur. J. Org. Chem. **1999**, 1011.
- ^[20] For a review, see: M. Reggelin, C. Zur, Synthesis 2000, 1.
- ^[21] L. R. Reddy, H.-J. Gais, C.-W. Woo, J. Am. Chem. Soc. 2002, 124, 10427.
- [22] [22a] R. Annunziata, M. Cinquini, J. Chem. Soc., Perkin Trans. 1 1979, 1684. [22b] S. G. Pyne, J. Chem. Soc., Chem. Commun. 1986, 1686. [22c] M. Reggelin, T. Heinrich, Angew. Chem. 1998, 110, 3005; Angew. Chem. Int. Ed. 1998, 37, 2883.
- ^[23] R. Loo, PhD Thesis, RWTH Aachen 1999.
- ^[24] R. Loo, H.-J. Gais, M. Günter, S. Babu, unpublished results.
- ^[25] For a previous short communication about parts of this work, see: H.-J. Gais, R. Loo, P. Das, G. Raabe, *Tetrahedron Lett.* 2000, 41, 2851.

- ^[26] M. Schleusner, H.-J. Gais, S. Koep, G. Raabe, J. Am. Chem. Soc. 2002, 124, 7784.
- ^[27] M. Scommoda, H.-J. Gais, S. Bosshammer, G. Raabe, J. Org. Chem. **1996**, 61, 4379.
- ^[28] S. Boßhammer, H.-J. Gais, Synlett 1998, 99.
- ^[29] J. Brandt, H.-J. Gais, *Tetrahedron: Asymmetry* 1997, 8, 909.
- ^[30] Cyclization of the trichloroacetyl carbamates in the presence of bases with formation of the corresponding *N*-trichloroacetyl oxazinones could not be achieved.
- ^[31] H.-J. Gais, H. Müller, J. Bund, M. Scommoda, J. Brandt, G. Raabe, J. Am. Chem. Soc. 1995, 117, 2453.
- ^[32] Occasionally the cyclization of the carbamates with *n*BuLi was accompanied to a minor extent by decomposition with formation of the corresponding allylic sulfoximine.
- ^[33] ^[33a] H.-J. Gais, I. Erdelmeier, H. J. Lindner, J. Vollhardt, Angew. Chem. 1986, 98, 914; Angew. Chem. Int. Ed. Engl. 1986, 25, 938. ^[33b] H.-J. Gais, U. Dingerdissen, C. Krüger, K. Angermund, J. Am. Chem. Soc. 1987, 109, 3775. ^[33c] H.-J. Gais, D. Lenz, G. Raabe, Tetrahedron Lett. 1995, 36, 7437.
- ^[34] J. F. K. Müller, M. Neuburger, M. Zehnder, *Helv. Chim. Acta* **1997**, *80*, 2182.
- ^[35] ^[35a] X.-M. Zhang, F. Bordwell, J. Org. Chem. 1994, 59, 6456.
 ^[35b] F. Bordwell, Acc. Chem. Res. 1988, 21, 456.
- ^[36] S. Boßhammer, H.-J. Gais, Synthesis 1998, 919.
- ^[37] C. R. Johnson, C. J. Stark, Jr, J. Org. Chem. 1982, 47, 1193.
- ^[38] C. R. Johnson, J. R. Shanklin, R. A. Kirchhoff, J. Am. Chem. Soc. 1973, 95, 6462.
- ^[39] J. Jacobus, K. Mislow, J. Am. Chem. Soc. 1967, 89, 5228.
- ^[40] T. Bach, C. Körber, Eur. J. Org. Chem. 1999, 1033.
- [41] For a potential one-step synthesis of 38 from 37, see: C. R. Johnson, R. A. Kirchhoff, H. G. Corkins, J. Org. Chem. 1974, 39, 2458.
- ^[42] C. R. Johnson, C. W. Schroeck, J. R. Shanklin, J. Am. Chem. Soc. 1973, 95, 7424.
- [43] Fusco, F. Tericoni, Chim. Ind. (Milan) 1965, 61.
- ^[44] C. R. Johnson, C. Schroeck, J. Am. Chem. Soc. 1973, 95, 7418.
- [45] (Eds.: S. R. Hall, D. J. du Boulay, R. Olthof-Hazekamp), XTAL 3.7 System, Universities of Western Australia and Maryland, Lamb, Perth, 2000.
- [^{46]} E. Keller, SCHAKAL 92, Universität Freiburg, Germany, 1992.
 [^{47]} CCDC 191348–191354 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB 2 1EZ (UK); Fax: (internat.) +44-1-223-336-033; or deposit@ccdc.cam.ac.uk).

Received November 4, 2002 [O02606]