# From Amino Acids to Fused Chiral Pyrrolidines and Piperidines via the INOC Route

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**Keywords:** INOC / Pyrrolidines / Piperidines / Stereoselective synthesis

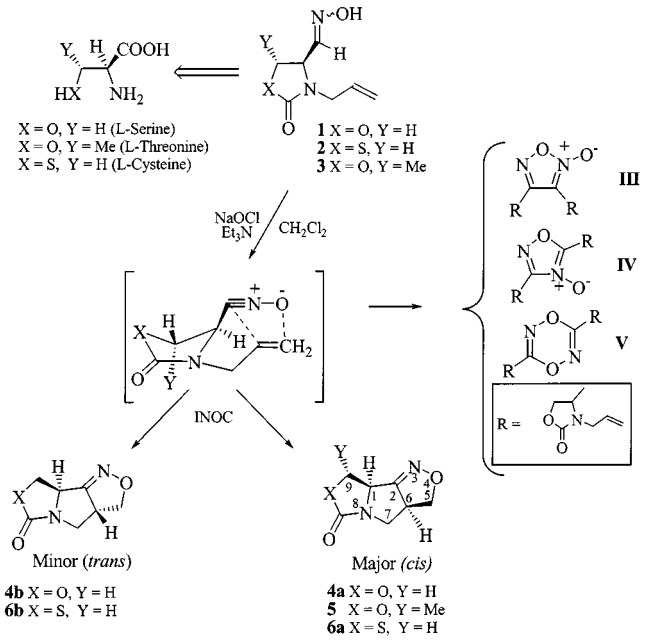
**I**ntramolecular **n**itrile oxide **o**lefin **c**ycloaddition (INOC) reactions of oximes **1–3** and of **24–27** derived from L-amino acids have been found to proceed stereoselectively, yielding tricyclic fused pyrrolidines and piperidines. Further manipulation led to chiral hydroxymethyl-substituted fused piperidines **33–35** and to 3-amino-4-(1-hydroxypropyl)-2-mercaptomethyl-*N*-methylpiperidine (**36**). The structures and stereochemistries of the fused systems, as well as those of the piperidines, have been established by NMR.

## Introduction

The **i**ntramolecular **n**itrile oxide **o**lefin **c**ycloaddition (INOC)[1] and **i**ntramolecular **o**xime **o**lefin **c**ycloaddition (IOOC)[2] reactions have proven to be useful stereoselective tools for the construction of fused isoxazole derivatives as well as of amino alcohol derivatives, keto alcohols, and other polyfunctionalized molecules. Polyfunctional pyrrolidines and piperidines possess antiviral and other pharmacological properties.[3] Based on an IOOC approach, we recently reported the synthesis of chiral, branched-chain 5-membered ring aza sugar analogs possessing glycosidase inhibition properties, starting from naturally occurring amino acids and their enantiomers.[4]

## Results and Discussion

We now report on our investigations into the use of the INOC reaction for the synthesis of chiral, tricyclic fused pyrrolidines **4–6** and piperidines **29–32**. Subsequent manipulation of the tricyclic intermediates led to the bicyclic fused piperidines **33–35** as well as to the piperidine **36**, trisubstituted with OH, $NH_2$, and SH groups. The INOC pathway, starting from L-serine, L-threonine, and L-cysteine, proved to be somewhat less stereoselective than the IOOC reaction and led to tricyclic fused pyrrolidines **4–6** with only moderate stereochemical control (Scheme 1). NMR analysis indicated formation of **4a**, **5**, and **6a**, possessing *cis* stereochemistry, as the major cycloadducts, with the *trans* isomers **4b** and **6b** being present in minor amounts. This is in contrast to the IOOC reaction of oximes **1–3**, which led exclusively to *trans* isomers.[4] Furthermore, dimerization of the intermediate nitrile oxides gave a mixture (as indicated by NMR) of furoxans **III** and **IV** and dioxadiazine **V**,[5] which partly accounted for the low overall yields of the cycloadducts **4–6** (Scheme 1).




Scheme 1. The INOC route to fused pyrrolidines

The structure and stereochemistry of the major *cis*-isoxazoline **4a** was established by $^1$H-NMR analysis in [$D_6$]acetone solution; in this medium good signal separation was observed, which allowed a full assignment by means of a COSY experiment (see Table 1 and Figure 1). The coupling pattern, however, did not shed much light on the stereochemistry. For instance, a coupling of $^4J_{HH}$ = 1.5 Hz was observed between the two bridgehead H atoms at δ = 4.84 and 4.25. This relatively large coupling constant reflects the fact that these two CH moieties are bonded to the same $sp^2$ carbon atom, and we have often seen such measurable *J*'s between H atoms of an α,α'-allylic arrangement.[6] Unfortunately, however, this type of coupling is rather insensitive to stereochemistry and thus its presence is not diagnostic. Similarly, $^{13}$C chemical shifts did not provide much insight

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  1434–193X/00/0204–0645 $ 17.50+.50/0 

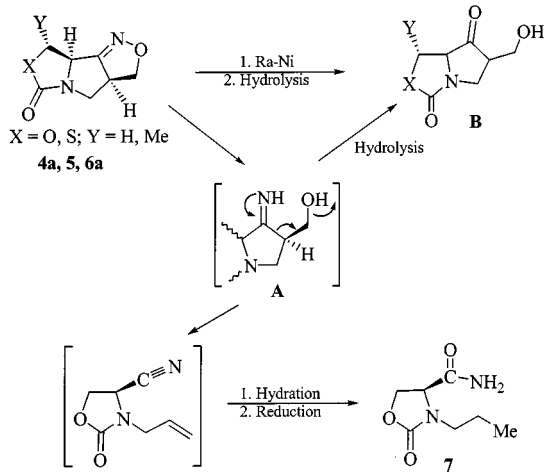
Table 1. $^1$H-chemical shifts and coupling constants for the **4**, **5**, and **6** isomers

| | *cis* | | | *trans* | |
|---|---|---|---|---|---|
| δ[a] | **4a** | **5** | **6a** | **4b** | **6b** |
| 1 | 4.84 | 4.34 | 5.01 | 4.87 | 5.01 |
| 5α | 4.56 | 4.56 | 4.58 | 3.91 | 4.03 |
| 5β | 3.98 | 3.98 | 3.98 | 4.72 | 4.75 |
| 6 | 4.25 | 4.28 | 4.41 | 4.36 | 4.28 |
| 7α | 4.04 | 4.03 | 4.16 | 3.68 | 3.71 |
| 7β | 3.21 | 3.18 | 3.13 | 3.50 | 3.53 |
| 9α | 4.77 | 1.55 (Me) | 3.61 | 4.56 | 3.75 |
| 9β | 4.37 | 4.69 | 3.68 | 4.69 | 3.58 |
| *J* | | | | | |
| 1,6 | 1.5 | 1.5 | 1.5 | 1 | 1 |
| 1,7α | 0.6 | 0.5 | 0.5 | – | – |
| 1,9α | 9.4 | – | 11 | 8 | 9 |
| 1,9β | 5.5 | 6 | 7.5 | 3 | 7.5 |
| 5α,5β | 8.7 | 8 | 8 | 8.5 | 8.5 |
| 5α,6 | 9.5 | 9.5 | 8 | 12.5 | 12.5 |
| 5β,6 | 12.7 | 12 | 12.5 | 10 | 10 |
| 6,7α | 8.0 | 8 | 8 | 9 | 9.5 |
| 6,7β | 10.1 | 10 | 9.5 | 5.5 | 6.5 |
| 7α,7β | 11.5 | 11.5 | 11.5 | 11.5 | 11.5 |
| 9α,9β | 8.1 | 6 (Me) | 10.5 | 9 | 11 |

[a] In [$D_6$]acetone.

into this issue. The *cis* relationship between the two bridgehead H atoms was established by NOE experiments, where a 3% enhancement in the 1-H signal was seen upon irradiation of 6-H (see Figure 1). The minor *trans* isoxazolines **4b** and **6b** displayed coupling patterns similar to those of their *cis* isomers, including the characteristic $^4J_{H1–H6}$ = 1–1.5 Hz, but the long-range $^4J_{H1–H7'}$ (0.6 Hz in **4a**) was missing. The main difference between the two isomers of **4** and **6** is seen in the chemical shifts of the 7-methylene protons and their coupling constants with 6-H (see Table 1).

Reductive cleavage (Raney Ni)[7] of the tricyclic products **4a**, **5**, and **6a** followed by hydrolysis gave inseparable mixtures of bicyclic fused pyrrolidines bearing hydroxy and keto substituents, which were tentatively assigned the structure **B** on the basis of MS data. In the case of **4a**, a side




Scheme 2. Cleavage of 2-isoxazolines

product identified as the oxazolidinone **7** was also isolated, which was most probably formed via intermediate A (Scheme 2).

In view of the difficulties encountered in the stereoselective conversion of **4a**, **5**, and **6a** into substituted pyrrolidines, attention was turned to the synthesis of substituted piperidines. Here, the unmasking operation of the 6-membered rings having rigid chair conformations was expected to proceed with greater stereoselectivity, due to the clear distinction between axial and equatorial substituents. Such a distinction is lacking in non-rigid five-membered rings.

Alkylation of thiazolidinone **8** and of oxazolidinones **9** and **10**[8] using homoallyl bromide[9] was expected to be the simplest means of attaching a homoallyl chain to these systems. However, in contrast to facile allylation, homoallylation of **8–10** using the DMF/NaH procedure was found to be problematic.[10] The maximum isolated yield for *N*-homoallylation to give **11–13** was 36% with thiazolidinone **8** and was considerably lower with **9** and **10**. Alkylations with homoallyl iodide, prepared from the commercial

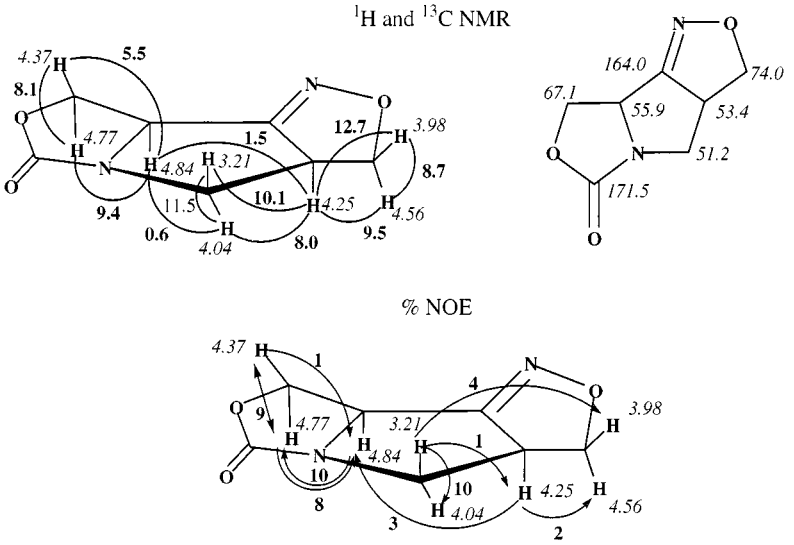
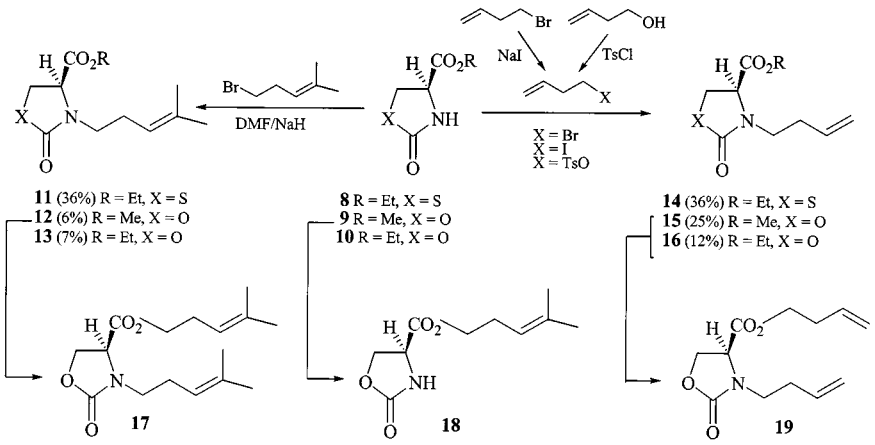


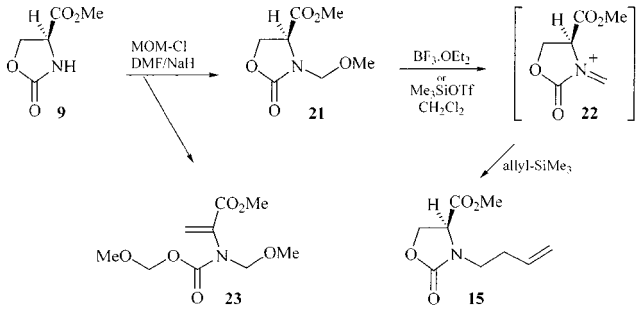

Figure 1. $^1$H, $^{13}$C NMR and % NOE assignments of **4a**

bromide, or with the corresponding tosylate, prepared from 3-butenol, did not give appreciably higher yields. As in the *N*-allylation of oxazolidinone, homoallylation of **9** and **10** also gave transesterification products **17–19** (Scheme 3).

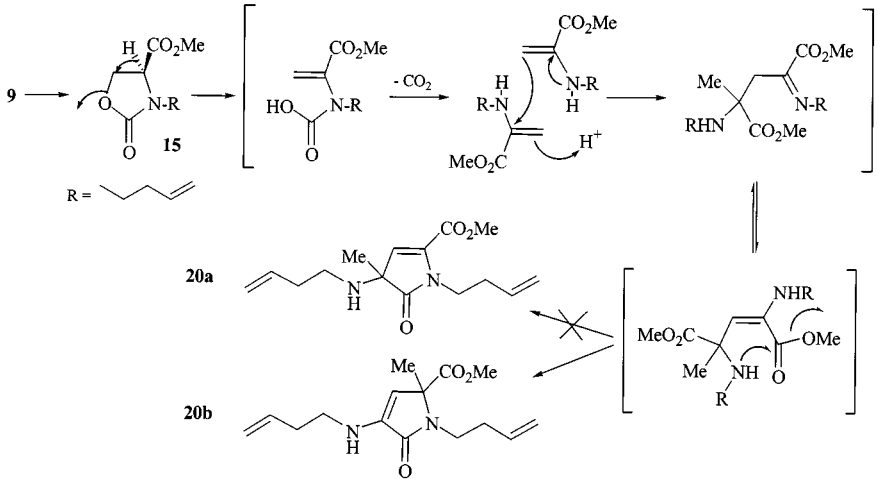



Scheme 3. Products of homoallylation of thiazolidinone **8** and oxazolidinones **9** and **10**

In addition, a new compound that lacked an oxazolidinone ring system was isolated. Its $^1$H-NMR spectrum indicated the presence of a homoallylic group, a vinylic H, a Me group, and a Me ester moiety. Its structure was assigned ($^1$H- and $^{13}$C-NMR) as that of pyrrolinone **20b**, formation of which may be rationalized in terms of the familiar serine[4,11] and cysteine[12] β-elimination and dimerization reaction. The intermediate enamine obtained upon decarboxylation evidently underwent dimerization and cyclization to **20b** but not to **20a**. This was clear from the NMR data, which revealed that the NH-bound homoallylic chain resides in a non-chiral environment, and that the NH and its adjacent $CH_2$ show long-range couplings with the vinylic CH (Scheme 4).




Scheme 5. Homoallylation of oxazolidinone **9**




Scheme 4. β-Elimination and dimerization of a serine derivative

Homoallylation of the L-serine derivative **9** to give **15** by a Mannich-type reaction was accomplished using allylsilane, the reaction proceeding via the *N*-acyliminium ion **22**[13] (Scheme 5). Following the *N*-alkylation of **9** with MOMCl, besides the desired oxazolidinone **21**, the dialkylated product **23**, resulting from a β-elimination reaction, was also isolated albeit only in low yield (9%). This phenomenon of C–O and C–S bond cleavage is known to occur in serine and cysteine derivatives.[4,11,12] Whereas in open-chain systems such β-eliminations are prevalent, they are

suppressed to a large extent in cyclic derivatives. Evidently, conversion of cysteine and serine into their respective cyclic derivatives **8** and **9** strongly retards the β-elimination reaction on stereoelectronic grounds. According to Baldwin's rule,[14] this β-elimination in oxazolidinone systems would be a retrograde 5-*endo-trig* process and is therefore disfavored. Nevertheless, a small amount of elimination product **23** was still detected. Treatment of **21** with allyltrimethylsilane in the presence of one equivalent of $BF_3Et_2O$[15] gave *N*-homoallyloxazolidinone **15**. Under optimized conditions at 0 °C, catalytic amounts of TMS–OTf promoted the formation of intermediate **22**, further allylation of which provided **15** almost quantitatively (Scheme 5).

With homoallylation products **14–17** and **19** in hand, the synthetic methodology could now be extended from 5- to 6-membered *N*-containing rings. Ester reduction and oximation provided the oxime-olefin intermediates **24–27**, which were accompanied by some thiazolidine **28** as a by-product (5%, Scheme 6).

in a fused tricyclic system, it has essentially a chair conformation, as indicated by the strong diaxial *anti* couplings ($J$ = 12–12.5 Hz) observed between the vicinal H atoms (δ = 3.43, 1.63, and 3.06) of the ring, together with smaller *gauche* couplings (3–6 Hz). This suggests that the bridgehead H atoms assume a pseudoaxial orientation (see Figure 2).

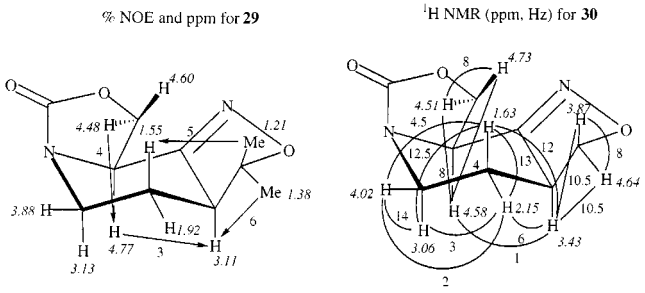
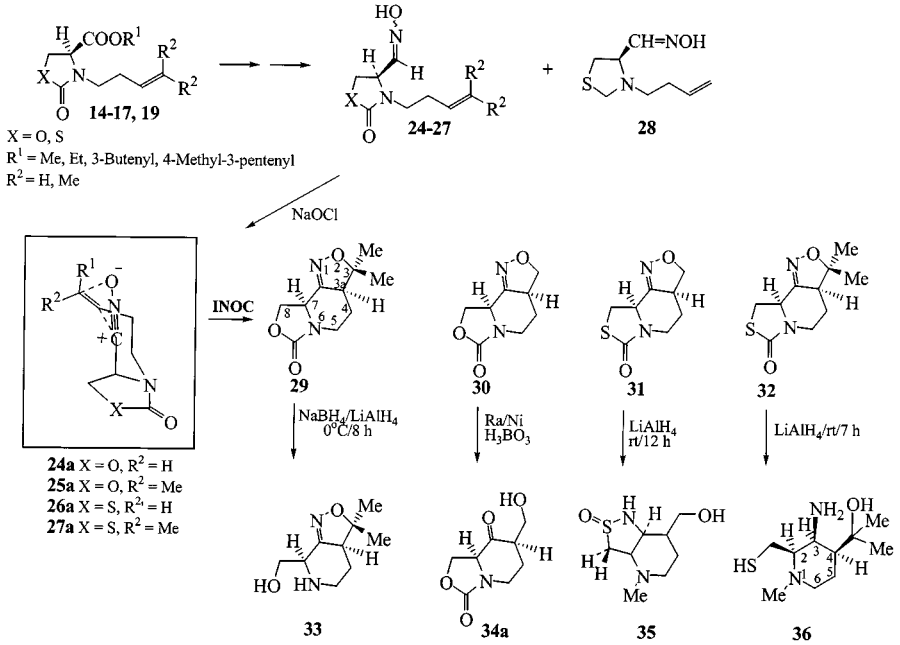



Figure 2. NMR data of fused piperidines




Scheme 6. INOC reaction leading to substituted piperidines

Oximes **24–27** were oxidized with commercial bleach (NaOCl)[16] under $Et_3N$ catalysis to give the intermediate nitrile oxides **24a–27a**. INOC reactions of the latter furnished the tricyclic piperidines **29–32**. In contrast to the low degree of stereoselectivity seen in the cycloadditions to the allylic double bond leading to fused pyrrolidines **4–6** (Scheme 1), here (Scheme 6) the nitrile oxides underwent cycloaddition to the homoallylic double bond in good yield and with excellent stereoselectivity. While in the previous cases of **1–3**, the transition state is flexible (Scheme 1), the transient nitrile oxides **24a**–**27a** leading to the fused 6-membered rings **29–32** can easily adopt a chair transition state resulting in the exclusive formation of *cis* products, as has been shown in related cases.[17] The *cis* assignment of the two bridgehead H atoms (δ = 3.43 and 4.58 in **30**) is based on NOE data. Furthermore, although the piperidine ring is

The marked contrast between the 5- and 6-membered rings in terms of stereochemical assignments is also reflected in the $^1$H-NMR spectrum of **30**. The bridgehead H at δ = 3.43, which shows very different couplings with its vicinal H atoms in the piperidine part of the molecule, shows two identical couplings (10.5 Hz) with the *cis* and *trans* vicinal H atoms of the isoxazoline methylene unit. The stereochemical assignments for each of these (α-H at δ = 4.64; β-H at δ = 3.87) could be made solely on the basis of their NOE's. From analogous analysis of NMR data, the structures and stereochemistries of compounds **29**, **31**, and **32** could be deduced (Figure 2 and Table 2–4).

In contrast to the case of the pyrrolidine–isoxazoline fused systems **4–6**, N–O reductive cleavage of the piperidine analog **30** with Raney Ni followed by hydrolysis with

Table 2. $^1$H-chemical shifts and coupling constants for **29**–**32**

| δ[a] | **29**[a] | **30**[a] | **31**[a] | **32**[b] |
|---|---|---|---|---|
| 3α[c] | 1.38 | 4.64 | 4.63 | 1.48 |
| 3β[c] | 1.21 | 3.87 | 3.83 | 1.23 |
| 3a | 3.11 | 3.43 | 3.61 | 2.97 |
| 4α | 1.92 | 2.15 | 2.23 | 1.89 |
| 4β | 1.55 | 1.63 | 1.50 | 1.59 |
| 5α | 3.13 | 3.06 | 3.05 | 2.86 |
| 5β | 3.88 | 4.02 | 4.09 | 4.27 |
| 7 | 4.77 | 4.58 | 4.75 | 4.52 |
| 8α | 4.48 | 4.51 | 3.63 | 3.54 |
| 8β | 4.60 | 4.73 | 3.63 | 3.70 |
| *J* | | | | |
| 3a,3α | – | 10.5 | 10.5 | – |
| 3a,3β | – | 10.5 | 11 | – |
| 3α,3β | – | 8 | 8 | – |
| 3a,4α | 5.5 | 6 | 6 | 6 |
| 3a,4β | 12.5 | 12 | 11.5 | 12.5 |
| 3a,7 | 1.5 | 1 | 1 | 1 |
| 4α,4β | 13 | 13 | 13 | 12.5 |
| 4α,5α | 2.5 | 3 | 3 | 2.5 |
| 4α,5β | 2 | 2 | 2 | 2.5 |
| 4β,5α | 12 | 12.5 | 12.5 | 12.5 |
| 4β,5β | 4.5 | 4.5 | 4.5 | 4 |
| 5α,5β | 13.5 | 14 | 13.5 | 13.5 |
| 7,8α | 8 | 8 | 7.5 (av.) | 7.5 |
| 7,8β | 4 | 4 | 7.5 (av.) | 8 |
| 8α,8β | 8.5 | 8 | unknown | 11.5 |

[a] In [D$_6$]acetone. – [b] In $CDCl_3$. – [c] For **29** and **32**, methyl groups.

Table 3. NOE enhancements (in % of the original signal integrals; when two values are given, the enhancements were measured in both directions, this should not necessarily give the same result) for **29** and **30** (in [D$_6$]acetone)

| Protons | **29** | **30** | Protons | **29** | **30** |
|---|---|---|---|---|---|
| 3a,3α[a] | 6 | | 4α,4β | 11–16 | 16–19 |
| 3a,3β | | 1 | 4α,5α | 3 | 2–3 |
| 3a,4α | 3 | 4–4 | 4α,5β | | 2–3 |
| 3a,5α | | 4 | 4β,5β | 2–7 | 3–6 |
| 3a,7 | 3 | | 5α,5β | 16 | 18–20 |
| 3α,3β | | 14 | 7,8α | 4 | |
| 3β,4β | 5 | 4–6 | 8α,8β | 9–11 | |

[a] For **29**, methyl groups.

Table 4. $^{13}$C-chemical shifts for **29**–**32**

| | **29**[a] | **30**[a] | **31**[a] | **32**[b] |
|---|---|---|---|---|
| 3 | 86.09 | 73.86 | 74.41 | 86.19 |
| 3α-Me | 28.27 | – | – | 27.78 |
| 3β-Me | 22.26 | – | – | 22.22 |
| 3a | 54.67 | 46.37 | 47.77 | 54.86 |
| 4 | 26.97 | 30.74 | 31.07 | 24.95 |
| 5 | 40.85 | 39.98 | 41.96 | 41.27 |
| 6a | 155.28 | 154.04 | 170.80 | 171.07 |
| 7 | 53.69 | 52.61 | 56.86 | 56.53 |
| 7a | 157.28 | 156.48 | 156.68 | 155.15 |
| 8 | 63.89 | 63.63 | 27.47 | 27.25 |

[a] in [D$_6$]acetone. – [b] in $CDCl_3$.

$B(OH)_3$ (5 equiv.)[18] gave the β-hydroxy ketone **34a**,**b** in a more stereoselective fashion as a 5:1 mixture of inseparable isomers. The $^1$H-NMR spectrum revealed that the stereochemistry present in **30** was maintained in **34a**, with the $CH_2OH$ substituent being in an equatorial position in the major isomer (Figure 3). This assignment was based on the chemical shift and coupling pattern of the H at δ = 2.75 (the former bridgehead proton 3a at δ = 3.43 in **30**), which gave rise to a dq with one diaxial (13.0 Hz) and three *gauche* (av. 5 Hz) couplings. In contrast, the equivalent proton in **34b** shows four similar *gauche* couplings (av. 5.5 Hz). Moreover, the piperidine and oxazolidinone parts of the molecule exhibit similar coupling patterns and chemical shifts as in **30**. It is not surprising that the isoxazoline unmasking operation, which proved very problematic for the fused pyrrolidines, was diastereoselective in the case of the piperidine analog. While in the 5-membered rings the thermodynamic stabilities of the α and β substituents are almost equal, in the case of 6-membered rings possessing rigid chair conformations, there is a marked stability difference between the axial and equatorial substituents. The $CH_2OH$ group in **34a** prefers to be equatorial, where it encounters less severe 1,3-steric interactions than it would if it were to adopt an axial orientation.

Isoxazolines **29–32** may also be viewed as masked amino alcohols. Metal hydride reduction of the C=N–O bonds yields the γ-amino alcohol unit with concomitant creation of a new asymmetric center. Initial attempts to reduce this group in **29** were made using $NaBH_4$. Since no reduction took place, $LiAlH_4/Et_2O$[19] was added until TLC indicated complete consumption of the starting material. Surprisingly, the product isolated was **33**, generated by reduction of the cyclic carbamate rather than of the isoxazoline (Scheme 6). Exposure of isoxazoline **31** to $LiAlH_4$/DME led to the hydroxymethyl-substituted piperidine **35**, bearing a unique sulfinamide functionality. The $^1$H-NMR signals due to the piperidine and $CH_2OH$ parts of the molecule were fairly similar to those seen in the spectra of the other piperidine derivatives **29–34**. However, the $CH_2$ unit of the cyclic sulfinamide moiety exhibited a large chemical anisotropy shift ($\Delta\delta > 1$ ppm) attributable to S=O deshielding of one H as opposed to shielding of its geminal H by the nonbonded S lone electron pair. The particular arrangement of these two H atoms is also reflected in their markedly different vicinal couplings ($J$ = 5 vs. 0.5 Hz) with the bridgehead H. It is assumed that oxidation of the S to S=O occurred during the course of the isolation and purification steps. Finally, $LiAlH_4$ reduction of isoxazoline **32** in $Et_2O$ solution gave the substituted *N*-Me piperidine **36**, where the isoxazoline reduction took place stereospecifically from the less hindered side of the molecule (Figure 3).In contrast to the $^1$H-NMR spectra of pyrrolidines, where coupling constants are almost meaningless in terms of stereochemistry, in the piperidine system they are very informative. Thus, in **36**, 4-H must be axial since it shows a 13.0 Hz *anti* coupling with the axial H on the adjacent (C-5) methylene (δ = 1.64), and since $J_{3,4}$ only measures 3.0 Hz, 3-H must be equatorial. This is supported by the observation of a 1.0 Hz "*w*" coupling with the equatorial H at C-5 (δ = 1.78). The chemical shift of 2-H (δ = 2.34) is similar to that of the axial H at C-6 (δ = 2.22) as both are shielded by being antiperiplanar to the axial N lone pair[20] (the equatorial H at C-6 appears at

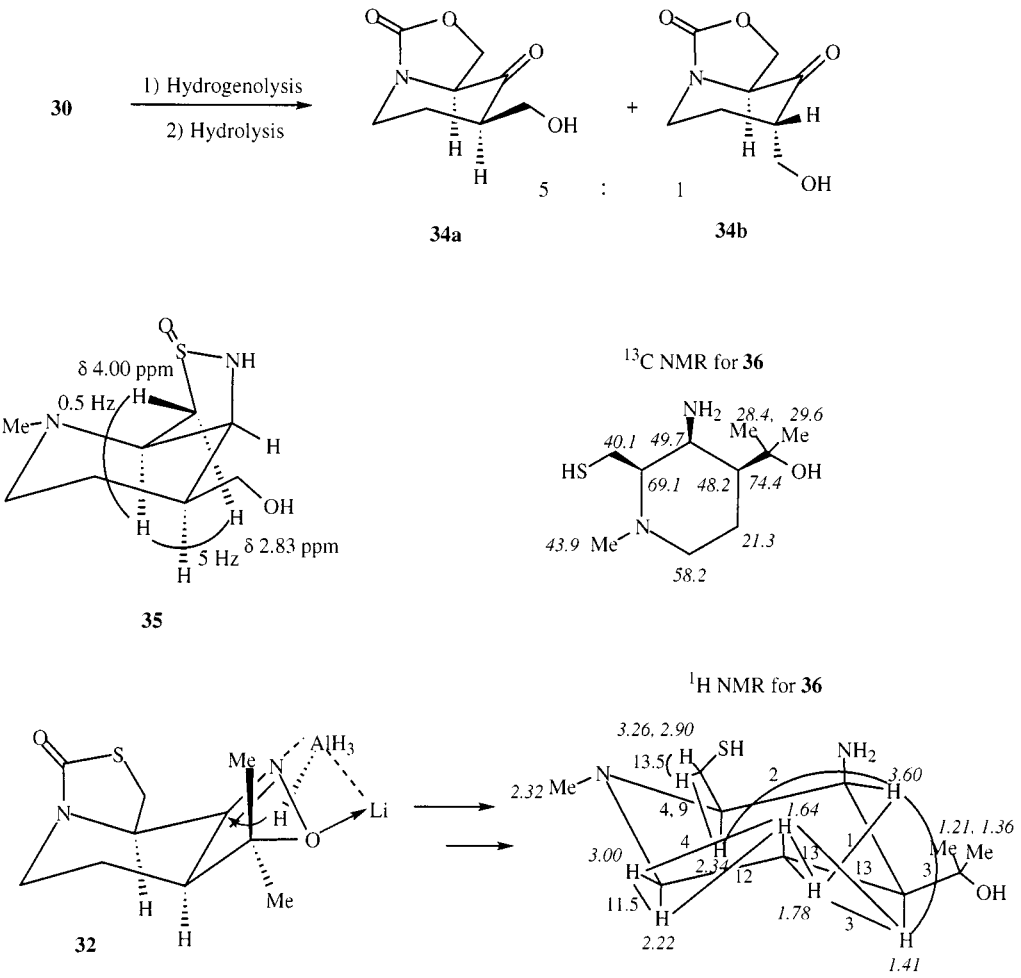



Figure 3. NMR and structural assignments of compounds **32**, **34a,b**, **35** and **36**

δ = 3.00). Therefore, 2-H must also be axial, indicating an all-*cis* stereochemistry for **36**. The broad-band decoupled $^{13}$C-NMR spectrum was again indicative of the absence of the other diastereomer (Figure 3).

## Experimental Section

**General:** $^1$H- and $^{13}$C-NMR spectra were recorded on Bruker AM-300 and AC-200 spectrometers; NOE and NOESY experiments were carried out at 600 MHz. For chloroform solutions, chemical shifts are expressed in ppm downfield from MeSi used as an internal standard; for $D_2O$ solutions, the HOD peak was taken as δ = 4.80 ($^1$H spectra) or the peak due to a small amount of added MeOH was taken as δ = 49.50 ($^{13}$C). Multiplicities in the $^{13}$C-NMR spectra were determined by off-resonance decoupling. – Mass spectra were obtained on a Finnigan 4021 spectrometer operating in CI (chemical ionization), DCI (desorption chemical ionization), EI (electron impact), or HRMS (high-resolution) modes. – The progress of the reactions was monitored by TLC on Merck silica gel 60 (0.040–0.063 mm) or Fluka neutral alumina type 507 C. – Flash chromatography was carried out on silica gel (Riedel-de-Haen, 32–63 μm). – Melting points were determined on a Fisher-Johns apparatus.

**Isoxazoline 4a:** To a stirred solution of **1**[4] (85 mg, 0.50 mmol) and $Et_3N$ (6.66 μL) in $CH_2Cl_2$ (8 mL) at 0 °C, aqueous NaOCl solution (10%, 1.8 mL, 2.4 mmol) was added dropwise. After 2 h at 0 °C, the mixture was allowed to warm to room temp. over a period of 1 h and then stirred for a further 12 h (until TLC indicated complete consumption of the starting material). The organic and aqueous layers were then separated and the solvents were evaporated. The residue from the aqueous layer was extracted with $CH_2Cl_2$ (2 × 10 mL) and the combined organic layers were dried ($MgSO_4$) and concentrated to give a white oil (63 mg). Flash chromatography (hexane/EtOAc, 1:4) gave **4a** as a white solid (25 mg, 30%); m.p. 163–165 °C. – $[\alpha]_D^{20}$ = –99.33 (*c* = 0.0151, acetone). – $^1$H NMR: See Table 1. – $^{13}$C NMR ([D$_6$]acetone): δ = 51.2 (t, CON*C*H$_2$), 53.4 (d, CH$_2$*C*HCH$_2$), 55.9 (d, CON*C*H), 67.1 (t, CO$_2$*C*H$_2$), 74.0 (t, OCH$_2$), 164.0 (s, C=N), 171.5 (s, OCON). – MS (CI, $NH_4$): *m*/*z* = 186 [MNH$_4^+$] (100). – HRMS (CI, $CH_4$): exact mass calcd. for $C_7H_8N_2O_3$ + H 169.0613; found 169.0592.

**Isoxazoline 4b:** Chromatography (hexane/EtOAc, 1:4) of the crude oily residue of **4a** gave diastereomer **4b** as a white solid (10 mg, 12%). – $^1$H NMR: See Table 1.

**Isoxazoline 5:** Obtained in 24% yield as described for **4a**. – $^1$H NMR: See Table 1.

**Isoxazoline 6a:** Obtained in 32% yield as described for **4a**; m.p. > 150 °C (dec). – $[\alpha]_D^{20}$ = –260.28 (*c* = 0.0214, $CHCl_3$). – $^1$H NMR: See Table 1. – $^{13}$C NMR ([D$_6$]acetone): δ = 33.1 (t, SCH$_2$), 49.2 (t,

CON*C*H$_2$), 55.0 (d, CH$_2$*C*HCH$_2$), 56.8 (d, CON*C*H), 73.9 (t, OCH$_2$), 168.3 (s, C=N), 171.6 (s, SCON). – HRMS (DCI, CH$_4$): exact mass calcd. for $C_7H_8N_2O_2S$ + H 185.0384; found 185.0350.

**Isoxazoline 6b:** Chromatography (hexane/EtOAc, 1:4) of the crude oily residue of **6a** gave diastereomer **6b** as a white solid (10 mg, 7%). – $^1$H NMR: See Table 1. – $^{13}$C NMR (CDCl$_3$): δ = 29.7 (t, SCH$_2$), 41.3 (t, CON*C*H$_2$), 46.9 (t, OCH$_2$), 54.1 (d, CH$_2$*C*HCH$_2$), 56.6 (d, CON*C*H), 162.5 (s, C=N), 171.1 (s, SCON).

C**arboxamide 7:** A solution of **4a** (35 mg, 0.2 mmol) and B(OH)$_3$ (99 mg, 1.6 mmol) in water/dioxane/MeOH (1:1:3, 2.5 mL) was hydrogenated at 1 atm. over Raney Ni for 4 h. The catalyst was then filtered off, the filtrate was concentrated, and the white residue obtained was treated with acetone, subsequent evaporation of which left an oil. Flash chromatography (hexane/EtOAc, 1:4, EtOAc/EtOH, 4:1) gave **7** as a colorless oil (10 mg, 29%). – $^1$H NMR ([D$_6$]acetone): δ = 0.89 (t, 3 H, *J* = 7.0 Hz, Me), 1.45–1.70 (m, 2 H, NCH$_2$C*H*$_2$), 3.01 (ddd, 1 H, *J* = 14.0, 8.0, 5.0 Hz, NCH$_2$), 3.38 (ddd, 1 H, *J* = 14.0, 8.0, 7.0 Hz, NCH$_2$), 4.18 (dd, 1 H, *J* = 7.0, 3.0 Hz, OCNCH), 4.42 (dd, 1 H, *J* = 9.0, 3.0 Hz, OCH$_2$), 4.47 (dd, 1 H, *J* = 9.0, 7.0 Hz, OCH$_2$), 6.75 and 7.30 (br. s, 2 H, CONH$_2$). – $^{13}$C NMR ([D$_6$]acetone): δ = 11.4 (Me), 21.2 (NCH$_2$*C*H$_2$), 45.6 (NCH$_2$), 58.6 (OCN*C*H), 66.7 (OCH$_2$), 158.7 (OCON), 172.1 (CONH$_2$). – MS (CI, CH$_4$): *m*/*z* = 190 [MNH$_4^+$] (100), 173 [MH$^+$] (80).

**4-Iodobut-1-ene:** To a solution of NaI (1.62 g, 10.8 mmol) in dry acetone (10 mL) was added 4-bromobut-1-ene (1.0 mL, 9.85 mmol) and the mixture was stirred at room temp. for ca. 12 h. The white precipitate formed was filtered off, the filtrate was concentrated, and the residue was extracted with CH$_2$Cl$_2$. Evaporation of the solvents from the organic phase gave the product as a dark oil (0.42 g, 23%). – $^1$H NMR (CDCl$_3$): δ = 2.65 (qt, 2 H, *J* = 7.0, 1.0 Hz, =CHC*H*$_2$CH$_2$), 3.20 (t, 2 H, *J* = 7.0 Hz, CH$_2$I), 5.06 (dq, 1 H, *J* = 17.0, 1.0 Hz, CH=C*H*$_2$), 5.07 (dq, 1 H, *J* = 10.0, 1.0 Hz, CH=C*H*$_2$), 5.77 (ddt, 1 H, *J* = 17.0, 10.0, 7.0 Hz, CH=C*H*$_2$).

**But-3-enyl Toluene-4-sulfonate:** To a solution of 3-buten-1-ol (1.0 mL, 11.6 mmol) in CHCl$_3$ (11 mL) at 0 °C were added pyridine (2.0 mL, 24 mmol), *p*-TsCl (3.3 g, 17.4 mmol), and DMAP (100 mg). After stirring at room temp. for 24 h, the mixture was poured into Et$_2$O (30 mL) and water (10 mL). The organic layer was separated, washed sequentially with HCl (2 N, 10 mL), NaHCO$_3$ solution (5%, 10 mL), and water (10 mL), and dried over MgSO$_4$. Evaporation of the solvent left a colorless liquid, which was chromatographed (petroleum ether/Et$_2$O, 6.75:1) to give the tosylate as a colorless oil, (1.85 g, 71%). – $^1$H NMR (CDCl$_3$): δ = 2.40 (qt, 2 H, *J* = 6.0, 1.0 Hz, =CHC*H*$_2$), 2.46 (s, 3 H, Me), 4.06 (t, 2 H, *J* = 6.0 Hz, C*H*$_2$OTs), 5.06 (dq, 1 H, *J* = 16.0, 1.0 Hz, CH=C*H*$_2$), 5.09 (dq, 1 H, *J* = 8.0, 1.0 Hz, CH=C*H*$_2$), 5.67 (ddt, 1 H, *J* = 16.0, 8.0, 6.0 Hz, C*H*=CH$_2$), 7.35 (d, 2 H, *J* = 8.0 Hz, 3,3'-Ar), 7.79 (d, 2 H, *J* = 8.0 Hz, 2,2'-Ar). – $^{13}$C NMR (CDCl$_3$): δ = 21.6 (q, Me), 33.1 (t, =CH*C*H$_2$), 69.4 (t, *C*H$_2$OTs), 118.1 (t, CH=*C*H$_2$), 127.8 (d, 3,3'-Ar), 129.7 (d, 2,2'-Ar), 132.3 (d, *C*H=CH$_2$), 133.1 (s, 4-Ar), 144.7 (s, 1-Ar). – MS (CI, *i*Bu): *m*/*z* = 227 [MH$^+$] (100).

**Ethyl (4*S*)-3-(4-Methylpent-3-enyl)-2-oxothiazolidine-4-carboxylate (11):** Obtained from **8**[8] as an oil in 36% yield as described for **14**. – $^1$H NMR (CDCl$_3$): δ = 1.32 (t, 1 H, *J* = 7.0 Hz, CH$_2$*Me*), 1.62 (s, 3 H, Me), 1.70 (s, 3 H, Me), 2.22 (dq, 1 H, *J* = 14.0, 7.0 Hz, C*H*$_2$CH), 2.30 (dq, 1 H, *J* = 14.0, 7.0 Hz, C*H*$_2$CH), 2.96 (ddd, 1 H, *J* = 14.0, 8.0, 6.0 Hz, NCH$_2$), 3.37 (dd, 1 H, *J* = 11.0, 3.0 Hz, SCH$_2$), 3.56 (dd, 1 H, *J* = 11.0, 8.0 Hz, SCH$_2$), 3.80 (ddd, 1 H, *J* = 14.0, 8.0, 6.0 Hz, NCH$_2$), 4.27 (ABq of q $J_{gem}$ = 14.0 Hz, $J_{vic}$ = 6.0 Hz, 2 H, CH$_2$Me), 4.40 (dd, 1 H, *J* = 8.0, 3.0 Hz, CH), 5.06 (t sept., 1 H, *J* = 7.0, 1.0 Hz, CH$_2$C*H*). – $^{13}$C NMR (CDCl$_3$): δ = 14.00 (q, CH$_2$*Me*), 17.63 (q, *cis*-Me), 25.55 (q, *trans*-Me), 26.40 (t, *C*H$_2$CH), 29.14 (t, SCH$_2$), 44.16 (dd, NCH$_2$), 60.66 (d, CH), 62.00 (t, *C*H$_2$Me), 119.97 (d, CH$_2$*C*H), 134.45 (s, CH=*C*Me$_2$), 169.90 (s, SCON), 171.14 (s, *C*O$_2$Et). – MS (CI, CH$_4$): *m*/*z* = 275 [M$^+$] (5), 258 [MH$^+$] (100).

**Methyl (4*S*)-3-(4-Methylpent-3-enyl)-2-oxooxazolidine-4-carboxylate (12):** Obtained as an oil in 6% yield as described for **14**. – $^1$H NMR (CDCl$_3$): δ = 1.63 (s, 3 H, Me), 1.70 (s, 3 H, Me), 2.26 (m, 2 H, C*H*$_2$CH=), 3.11 (dt, 1 H, *J* = 14.0, 6.0 Hz, NCH$_2$), 3.61 (ddd, 1 H, *J* = 14.0, 8.0, 7.0 Hz, NCH$_2$), 3.82 (s, 3 H, OMe), 4.33 (dd, 1 H, *J* = 8.0, 4.0 Hz, OCH$_2$), 4.39 (dd, 1 H, *J* = 8.0, 6.0 Hz, OCH$_2$), 4.45 (dd, 1 H, *J* = 6.0, 4.0 Hz, CH), 5.06 (t sept., 1 H, *J* = 6.0, 1.0 Hz, CH$_2$C*H*=). – $^{13}$C NMR (CDCl$_3$): δ = 17.64 (q, *cis*-Me), 25.54 (q, *trans*-Me), 26.04 (t, *C*H$_2$CH=), 43.03 (dd, NCH$_2$), 52.72 (q, OMe), 56.92 (d, CH), 64.21 (t, OCH$_2$), 119.81 (d, CH$_2$*C*H=), 134.54 (s, CH=*C*Me$_2$), 157.41 (s, OCON), 170.05 (s, *C*O$_2$Me). – MS (CI, NH$_3$): *m*/*z* = 245 [MNH$_4^+$] (10), 228 [MH$^+$] (30).

**Ethyl (4*S*)-3-(4-Methylpent-3-enyl)-2-oxooxazolidine-4-carboxylate (13):** Obtained as an oil in 7% yield as described for **14**. – $[\alpha]_D^{20}$ = –11.26 (*c* = 0.071, CHCl$_3$). – $^1$H NMR (CDCl$_3$): δ = 1.32 (t, 1 H, *J* = 7.0 Hz, CH$_2$*Me*) 1.63 (s, 3 H, Me), 1.70 (s, 3 H, Me), 2.22 (dq, 1 H, *J* = 14.0, 7.0 Hz, C*H*$_2$CH=), 2.31 (dq, 1 H, *J* = 14.0, 7.0 Hz, C*H*$_2$CH=), 3.12 (ddd, 1 H, *J* = 14.0, 8.0, 6.0 Hz, NCH$_2$), 3.59 (dt, 1 H, *J* = 14.0, 7.0 Hz, NCH$_2$), 4.26 and 4.28 (ABq of q, $J_{gem}$ = 11.0 Hz, $J_{vic}$ = 7.0 Hz, 2 H, C*H*$_2$Me), 4.32 (dd, 1 H, *J* = 8.0, 4.0 Hz, NCOCH$_2$), 4.36 (dd, 1 H, *J* = 9.0, 4.0 Hz, NCOCH$_2$), 4.44 (t, 1 H, *J* = 8.5 Hz, CH), 5.07 (t sept., 1 H, *J* = 7.0, 1.0 Hz, CH$_2$C*H*=). – $^{13}$C NMR (CDCl$_3$): δ = 13.88 (q, CH$_2$*Me*), 17.56 (q, *cis*-Me), 25.47 (q, *trans*-Me), 25.95 (t, *C*H$_2$CH=), 42.91 (t, N*C*H$_2$), 56.90 (d, CH), 61.94 (t, *C*H$_2$Me), 64.20 (t, OCH$_2$), 119.80 (d, CH$_2$*C*H=), 134.45 (s, CH=*C*Me$_2$), 157.45 (s, OCON), 169.56 (s, *C*O$_2$Et). – HRMS (CI, CH$_4$): exact mass calcd. for $C_{12}H_{19}NO_4$ + H 242.1392; found 242.1350.

**Ethyl (4*R*)-3-But-3-enyl-2-oxothiazolidine-4-carboxylate (14). – Procedure I:** To a stirred solution of **8**[8] (1.53 g, 8.74 mmol) in dry DMF (60 mL) at 0 °C was added NaH (60%, 10.2 mmol). After the evolution of H$_2$ had ceased, 4-bromobut-1-ene (1.1 mL, 10.8 mmol) was added. The reaction mixture was stirred at room temp. for 24 h and then partitioned between EtOAc (200 mL) and aqueous Na$_2$S$_2$O$_3$ solution (150 mL). The organic layer was separated and the aqueous phase again extracted with EtOAc (200 mL). The combined organic layers were dried (MgSO$_4$) and concentrated, and the residue was chromatographed (hexane/EtOAc mixtures) to give, after vacuum chromatography (hexane/EtOAc, 10–50%), **14** as a yellow oily liquid (0.72 g, 36%). – $[\alpha]_D^{20}$ = –47.14 (*c* = 0.035, CHCl$_3$). – $^1$H NMR (CDCl$_3$): δ = 1.32 (t, 1 H, *J* = 7.0 Hz, CH$_2$*Me*), 2.32 (ABq of q of t, 2 H, $J_{gem}$ = 14.0, $J_{vic}$ = 7.0, 1.0 Hz, C*H*$_2$CH=), 3.05 (ddd, 1 H, *J* = 14.0, 7.0, 6.0 Hz, NCH$_2$), 3.38 (dd, 1 H, *J* = 11.0, 2.5 Hz, SCH$_2$), 3.59 (dd, 1 H, *J* = 11.0, 8.0 Hz, SCH$_2$), 3.89 (dt, 1 H, *J* = 14.0, 7.0 Hz, NCH$_2$), 4.28 (ABq of q, $J_{gem}$ = 6.0, $J_{vic}$ = 7.0 Hz, C*H*$_2$Me), 4.41 (dd, 1 H, *J* = 8.0, 2.5 Hz, CH), 5.07 (dq, 1 H, *J* = 10.0, 1.0 Hz, CH=C*H*$_2$), 5.11 (dq, 1 H, *J* = 17.0, 1.0 Hz, CH=C*H*$_2$), 5.76 (ddt, 1 H, *J* = 17.0, 10.0, 7.0 Hz, C*H*=CH$_2$). – $^{13}$C NMR (CDCl$_3$): δ = 14.0 (q, CH$_2$*Me*), 29.1 (t, *C*H$_2$CH=), 31.9 (t, SCH$_2$), 43.5 (dd, NCH$_2$), 60.4 (d, CH), 62.0 (t, CO$_2$CH$_2$), 117.1 (t, CH=*C*H$_2$), 134.5 (d, *C*H=CH$_2$), 169.8 (s, SCON), 171.2 (s, *C*O$_2$Et). – MS (CI, CH$_4$): *m*/*z* = 247 [MNH$_4^+$] (40), 230 [MH$^+$] (100). – HRMS (CI, CH$_4$): exact mass calcd. for $C_{10}H_{15}NO_3S$ + H 230.0850; found 230.0840.

**Methyl (4*S*)-3-But-3-enyl-2-oxooxazolidine-4-carboxylate (15):** Obtained as a pale-yellow oil in 25% yield as described for **14**.

**Procedure II:** To a stirred solution of **21**[8a] (0.75 g, 3.92 mmol) and allyltrimethylsilane (0.86 mL, 5.41 mmol) in $CH_2Cl_2$ at 0 °C was added $Me_3SiOTf$ (0.1 mL, 0.51 mmol). After 3 h, when TLC indicated complete consumption of the starting material, the mixture was concentrated to give a dark oil (0.72 g, 92%), vacuum chromatography (hexane/EtOAc) of which gave **15** as a colorless oil (90%). – $[\alpha]_D^{20}$ = –23.52 (*c* = 0.017, $CH_2Cl_2$). – $^1$H NMR ($CDCl_3$): δ = 2.34 (ABq of q of t, 2 H, $J_{gem}$ = 14.0, $J_{vic}$ = 7.0, 1.5 Hz, C*H*$_2$CH=), 3.21 (ddd, 1 H, *J* = 14.0, 7.0, 6.0 Hz, $NCH_2$), 3.70 (dt, 1 H, *J* = 14.0, 7.0 Hz, $NCH_2$), 3.82 (s, 3 H, OMe), 4.34 (dd, 1 H, *J* = 6.5, 3.5 Hz, CH), 4.38 (dd, 1 H, *J* = 8.0, 3.5 Hz, $OCH_2$), 4.45 (dd, 1 H, *J* = 8.0, 6.5 Hz, $OCH_2$), 5.08 (dq, 1 H, *J* = 10.0, 1.5 Hz, CH=C*H*$_2$), 5.13 (dq, 1 H, *J* = 17.0, 1.5 Hz, CH=C*H*$_2$), 5.77 (ddt, 1 H, *J* = 17.0, 10.0, 6.5 Hz, C*H*=CH$_2$). – $^{13}$C NMR ($CDCl_3$): δ = 31.6 (t, *C*H$_2$CH=), 42.4 (t, $NCH_2$), 52.9 (q, OMe), 56.8 (d, NCH), 64.2 (t, $OCH_2$), 117.4 (t, CH=*C*H$_2$), 134.5 (d, *C*H=CH$_2$), 157.5 (s, OCON), 170.1 (s, *C*O$_2$Me). – MS (CI, *i*Bu): *m*/*z* = 200 [$MH^+$] (100). – HRMS (CI, $CH_4$): exact mass calcd. for $C_9H_{13}NO_4$ + H 200.0922; found 200.0970.

**Ethyl (4*S*)-3-But-3-enyl-2-oxooxazolidine-4-carboxylate (16):** Obtained from **10**[8] as a yellow oily liquid in 12% yield as described for **14**. – $[\alpha]_D^{20}$ = –20.0 (*c* = 0.032, $CDCl_3$). – $^1$H NMR ($CDCl_3$): δ = 1.32 (t, 1 H, *J* = 7.0 Hz, CH$_2$*Me*), 2.34 (ABq of q of t, 2 H, $J_{gem}$ = 14.0, $J_{vic}$ = 7.0, 1.5 Hz, C*H*$_2$CH=), 3.22 (ddd, 1 H, *J* = 14.0, 7.5, 6.0 Hz, $NCH_2$), 3.68 (dt, 1 H, *J* = 14.0, 7.5 Hz, $NCH_2$), 4.27 (ABq of q, $J_{gem}$ = 6.0, $J_{vic}$ = 7.0 Hz, CH$_2$*Me*), 4.33 (dd, 1 H, *J* = 7.0, 3.5 Hz, CH), 4.38 (dd, 1 H, *J* = 8.5, 3.5 Hz, $OCH_2$), 4.46 (dd, 1 H, *J* = 8.5, 7.0 Hz, $OCH_2$), 5.08 (dq, 1 H, *J* = 10.0, 1.5 Hz, CH=C*H*$_2$), 5.12 (dq, 1 H, *J* = 17.0, 1.5 Hz, CH=C*H*$_2$), 5.77 (ddt, 1 H, *J* = 17.0, 10.0, 6.5 Hz, C*H*=CH$_2$). – $^{13}$C NMR ($CDCl_3$): δ = 13.83 (q, CH$_2$*Me*), 31.39 (t, *C*H$_2$CH=), 42.29 (t, $NCH_2$), 56.71 (d, NCH), 61.87 (t, *C*H$_2$Me), 64.12 (t, $OCH_2$), 117.03 (t, CH=*C*H$_2$), 134.37 (d, *C*H=CH$_2$), 157.33 (s, OCON), 169.39 (s, *C*O$_2$Et). – HRMS (CI, $CH_4$): exact mass calcd. for $C_{10}H_{15}NO_4$ + H 214.1079; found 200.1110.

**4-Methyl-1-pent-3-enyl (4*S*)-3-(4-Methylpent-3-enyl)-2-oxooxazolidine-4-carboxylate (17):** Chromatography (hexane/EtOAc) of the crude residues of **12** or **13** gave **17** as a yellow oil (0.115 g, 6%). – $[\alpha]_D^{20}$ = –8.96 (*c* = 0.029, $CDCl_3$). – $^1$H NMR ($CDCl_3$): δ = 1.56 (s, 6 H, 2 × Me), 1.63 (s, 3 H, Me), 1.64 (s, 3 H, Me), 2.15 (dq, 1 H, *J* = 14.0, 7.0 Hz, $NCH_2$C*H*$_2$CH=), 2.22 (dq, 1 H, *J* = 14.0, 7.0 Hz, $NCH_2$C*H*$_2$CH=), 2.29 (q, 2 H, *J* = 6.5 Hz, $OCH_2$C*H*$_2$CH=), 3.03 (dt, 1 H, *J* = 14.0, 6.0 Hz, $NCH_2$), 3.53 (dt, 1 H, *J* = 14.0, 7.0 Hz, $NCH_2$), 4.11 (two ABq of t, 2 H, $J_{gem}$ = 9.0 Hz, $J_{vic}$ = 6.5 Hz, $CO_2CH_2$), 4.23 (dd, 1 H, *J* = 8.0, 4.0 Hz, $NCO_2CH_2$), 4.26 (dd, 1 H, *J* = 9.0, 4.0 Hz, $NCO_2CH_2$), 4.35 (t, 1 H, *J* = 8.0 Hz, CH), 4.99 (m, 2 H, 2 × $CH_2$C*H*=). – $^{13}$C NMR ($CDCl_3$) δ = 17.68 (q, 2 × *cis*-Me), 25.57 (q, *trans*-Me), 26.07 (q, *trans*-Me), 27.40 (t, 2 × *C*H$_2$CH=), 42.99 (dd, $NCH_2$), 57.03 (d, CH), 64.26 (t, $NCO_2CH_2$), 65.50 (t, $CO_2CH_2$), 118.42 (d, $OCH_2CH_2CH$=), 119.89 (d, $NCH_2CH_2CH$=), 134.52 (s, $NCH_2CH_2CH$=*C*Me$_2$), 135.19 (s, $OCH_2CH_2CH$=*C*Me$_2$), 157.43 (s, OCON), 169.64 (s, *C*O$_2$C$_6$H$_{11}$). – MS (CI, $NH_3$): *m*/*z* = 313 [$MNH_4^+$] (20), 296 [$MH^+$] (100). – HRMS (CI, $CH_4$): exact mass calcd. for $C_{16}H_{25}NO_4$ + H 296.1861; found 296.1840.

**4-Methylpent-3-enyl (4*S*)-2-Oxooxazolidine-4-carboxylate (18):** Flash chromatography (hexane/EtOAc, 2:1 1:1) of the crude oily residue of **12** gave **18** as an oil (66 mg, 4%). – $^1$H NMR ($CDCl_3$): δ = 1.62 (s, 3 H, Me), 1.71 (s, 3 H, Me), 2.36 (q, 2 H, *J* = 7.0 Hz, C*H*$_2$CH=), 4.16 (dt, 2 H, *J* = 10.0, 7.0 Hz, $CO_2CH_2$), 4.43 (dd, 1 H, *J* = 9.0, 4.0 Hz, $NCOCH_2$), 4.48 (dd, 1 H, *J* = 9.0, 4.0 Hz, $NCOCH_2$), 4.61 (t, 1 H, *J* = 9.0 Hz, CH), 5.07 (t sept., 1 H, *J* = 7.0, 1.0 Hz, $CH_2$C*H*=), 6.78 (br. s, 1 H, NH). – $^{13}$C NMR ($CDCl_3$): δ = 17.62 (q, *cis*-Me), 25.50 (q, *trans*-Me), 27.34 (t, *C*H$_2$CH=), 53.77 (d, CH), 65.62 (t, $NCO_2CH_2$), 66.64 (t, $CO_2CH_2$), 118.31 (d, CH=), 135.14 (s, =*C*Me$_2$), 158.94 (s, OCON), 170.05 (s, *C*O$_2$C$_6$H$_{11}$). – MS (CI, $NH_3$): *m*/*z* = 231 [$MNH_4^+$] (100), 214 [$MH^+$] (5).

**But-3-enyl (4*S*)-3-But-3-enyl-2-oxooxazolidine-4-carboxylate (19):** Flash chromatography (hexane/EtOAc, 2:1) of the crude oily residues of **15** or **16** gave **19** as a yellow oil (5%). – $[\alpha]_D^{20}$ = –5.98 (*c* = 0.0167, $CHCl_3$). – $^1$H NMR ($CDCl_3$): δ = 2.35 (ABq of q of t, 2 H, $J_{gem}$ = 14.0, $J_{vic}$ = 7.0, 1.0 Hz, $NCH_2$C*H*$_2$CH), 2.45 (ABq of t, 2 H, *J* = 6.0, 1.0 Hz, $OCH_2$C*H*$_2$CH), 3.20 (ddd, 1 H, *J* = 14.0, 7.0, 6.0 Hz, $NCH_2$), 3.68 (t, 1 H, *J* = 6.5 Hz, $CHCO_2CH_2$), 3.70 (dt, 1 H, *J* = 14.0, 7.0 Hz, $NCH_2$), 4.27 (dd, 1 H, *J* = 6.0, 4.0 Hz, CH), 4.31 (t, 1 H, *J* = 6.5 Hz, $CHCO_2CH_2$), 4.36 (dd, 1 H, *J* = 10.0, 4.0 Hz, $OCH_2$), 4.43 (dd, 1 H, *J* = 10.0, 6.0 Hz, $OCH_2$), 5.05–5.20 (m, 4 H, 2 × CH=C*H*$_2$), 5.68–5.85 (m, 2 H, 2 × CH=C*H*$_2$). – $^{13}$C NMR ($CDCl_3$): δ = 31.55, 32.87 (2 t, 2 × *C*H$_2$CH=), 42.41 (t, $NCH_2$), 56.87 (d, NCH), 64.24 (t, $CO_2CH_2$), 64.76 (t, O*C*H$_2$CH), 116.96, 117.78 (2 t, 2 × CH=*C*H$_2$), 133.16, 134.48 (2 d, 2 × *C*H=CH$_2$), 157.44 (s, OCON), 169.50 (s, *C*O$_2$C$_4$H$_7$). – MS (CI, *i*Bu): *m*/*z* = 240 [$MH^+$] (100). – HRMS (CI, $CH_4$): exact mass calcd. for $C_{12}H_{17}NO_4$ + H 240.1235; found 240.1150.

**Methyl 1-(But-3-enyl)-4-(but-3-enylamino)-2-methyl-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxylate (20b):** Obtained from **9** (2.44 g, 16.8 mmol) and 4-bromobut-1-ene (2 mL, 20 mmol) as described for **14** to give, after flash chromatography (hexane/EtOAc, 2:1), **20b** as a yellow oil (0.15 g, 3%). – $^1$H NMR ($CDCl_3$): δ = 1.57 (s, 3 H, Me), 2.33 (qt, 2 H, *J* = 7.0, 1.0 Hz, $NHCH_2$C*H*$_2$CH), 2.42 (dddt, 2 H, *J* = 9.5, 7.0, 6.0, 1.0 Hz, $NCH_2$C*H*$_2$CH), 3.03 (dt, 2 H, *J* = 13.0, 7.0 Hz, NHC*H*$_2$), 3.17 (ddd, 1 H, *J* = 14.0, 9.5, 6.0 Hz, $CONCH_2$), 3.57 (ddd, 1 H, *J* = 14.0, 9.5, 6.0 Hz, $CONCH_2$), 3.68 (s, 3 H, $CO_2$Me), 4.21 (br. t, 1 H, *J* = 5.0 Hz, NH), 5.03 (dq, 1 H, *J* = 10.0, 1.0 Hz, CH=C*H*$_2$), 5.06 (s, 1 H, NHC=C*H*), 5.08 (dq, 1 H, *J* = 17.0, 1.0 Hz, CH=C*H*$_2$), 5.12 (dq, 1 H, *J* = 17.0, 1.0 Hz, CH=C*H*$_2$), 5.13 (dq, 1 H, *J* = 10.0, 1.0 Hz, CH=C*H*$_2$), 5.79 (ddt, 2 H, *J* = 17.0, 10.0, 7.0 Hz, C*H*=CH$_2$). – $^{13}$C NMR ($CDCl_3$): δ = 21.7 (q, Me), 32.7, 33.0 (2 t, 2 × *C*H$_2$CH=), 41.2 (t, $NHCH_2$), 43.2 (t, $CONCH_2$), 52.5 (q, $CO_2Me$), 67.4 (s, Me*C*CO$_2$Me), 102.3 (d, NHC=*C*H), 116.6, 117.1 (2 t, 2 × CH=*C*H$_2$), 135.1, 135.28 (2 d, 2 × *C*H=CH$_2$), 140.0 (s, NH*C*=CH), 167.8 (s, CON), 172.5 (s, *C*O$_2$Me). – HRMS (CI, $CH_4$): exact mass calcd. for $C_{15}H_{22}N_2O_3$ + H 279.1708; found 279.1650.

**Methyl (4*S*)-3-Methoxymethyl-2-oxooxazolidine-4-carboxylate (21):** To a stirred solution of **9**[8a] (1.67 g, 11.5 mmol) in dry DMF (20 mL) at 0 °C was added NaH (60%, 0.50 g, 12.5 mmol). After the evolution of $H_2$ had ceased, MOMCl (0.90 mL, 11.8 mmol) and $Bu_4NI$ (20 mg) were added. The resulting mixture was stirred at room temp. for ca. 12 h and then partitioned between EtOAc (20 mL) and aqueous $Na_2S_2O_3$ solution (10 mL). The organic layer was separated and the aqueous phase was further extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), and concentrated to give a yellow oil (1.47 g, 68%), vacuum chromatography (hexane/EtOAc) of which gave **21** (0.8 g, 37%) as a colorless oil. – $[\alpha]_D^{20}$ = –92.5 (*c* = 0.012, $CH_2Cl_2$). – $^1$H NMR ($CDCl_3$): δ = 3.34 (s, 3 H, $CH_2O$*Me*), 3.82 (s, 3 H, OMe), 4.40 (dd, 1 H, *J* = 8.0, 4.5 Hz, CH), 4.51 (dd, 1 H, *J* = 9.5, 4.5 Hz, $OCH_2$), 4.54 (dd, 1 H, *J* = 9.5, 8.0 Hz, $OCH_2$, ABX system), 4.76 (d, 1 H, *J* = 11.0 Hz, $NCH_2O$), 4.89 (d, 1 H, *J* = 11.0 Hz, $NCH_2O$). – $^{13}$C NMR ($CDCl_3$): δ = 53.0 (d, CH), 55.2, 56.4 (2 q, OMe), 64.6 (t, OCO*C*H$_2$), 75.6 (t, $NCH_2O$), 157.5 (s, OCON), 170.0 (s, *C*O$_2$Me). – HRMS (CI, $CH_4$): exact mass calcd. for $C_7H_{11}NO_5$ + H 190.0715; found 190.0710.

**Methyl 2-[(Methoxymethoxycarbonyl)(methoxymethyl)amino]acrylate (23):** Chromatography (hexane/EtOAc) of the crude oily residue of **21** gave **23** as a colorless oil (0.25 g, 9%). – $^1$H NMR ($CDCl_3$): δ = 3.42 (s, 3 H, $NCH_2O$*Me*), 3.44 (br. s, 3 H, $OCH_2O$*Me*), 3.80 (s, 3 H, $CO_2$Me), 4.91 (s, 2 H, $NCH_2O$), 5.25 (br. s, 2 H, $OCH_2O$), 5.79 (s, 1 H, =$CH_2$), 6.18 (s, 1 H, =$CH_2$). – $^{13}$C NMR ($CDCl_3$): δ = 52.4 (q, $CO_2$*Me*), 56.0 (q, $NCH_2O$*Me*), 57.5 (q, $OCH_2O$*Me*), 80.7 (t, N*C*$H_2$OMe), 91.9 (t, $OCH_2O$), 122.1 (t, =$CH_2$), 138.1 (s, =*C*$CO_2$Me), 154.4 (s, $NCO_2$), 164.4 (s, *C*$O_2$Me). – HRMS (CI, $CH_4$): exact mass calcd. for $C_9H_{15}NO_6$ + H 234.0977; found 234.0940.

**Reduction and Oximation of 14–17 and 19 To Give Aldoximes 24–27. – Procedure III:** To a solution of the appropriate ester **14–17** or **19** (4.3 mmol) in dry $CH_2Cl_2$ (13 mL) under $N_2$, a solution of DIBAL-H in hexane (1 M, 9.1 mL, 9.1 mmol) was added dropwise over a period of 30–60 min., while the temperature was kept below –75 °C. After 2 h, MeOH (1 mL) was added. The reaction mixture was then partitioned between EtOAc (25 mL) and saturated aqueous sodium potassium tartrate solution (15 mL) containing $NH_2OH$HCl (0.64 g, 9.2 mmol) and NaOH (0.4 g, 10 mmol) at pH 11–12. The biphasic mixture was stirred vigorously at room temperature for 12 h until all the solids had dissolved. The organic layer was then separated and the aqueous phase was further extracted with EtOAc (2 × 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. The residue was chromatographed on silica gel to give **24–27**.

**(4*S*)-3-(But-3-enyl)-2-oxooxazolidine-4-carbaldehyde Oxime (24):** Obtained as a white solid (0.46 g, 47%); m.p. 105–110 °C. – $[\alpha]_D^{20}$ = –11.17 (*c* = 0.017, $CHCl_3$). – $^1$H NMR ($CDCl_3$) for 3:1 mixture of *syn*/*anti* isomers: δ = 2.30–2.40 (m, 4 H, *syn*/*anti* $NCH_2CH_2CH$=), 3.16 (dt, 2 H, *J* = 14.0, 6.0 Hz, *syn*/*anti* $NCH_2$), 3.52 (dt, 1 H, *J* = 14.0, 7.5 Hz, *syn* $NCH_2$), 3.60 (dt, 1 H, *J* = 14.0, 8.0 Hz, *anti* $NCH_2$), 4.09 (dd, 1 H, *J* = 9.0, 6.0 Hz, *anti* $OCH_2$), 4.15 and 4.47 (m, 3 H, *syn* $OCH_2$ and *syn* CH), 4.56 (t, 1 H, *J* = 9.0 Hz, *anti* $OCH_2$), 5.07 (dq, 2 H, *J* = 10.0, 1.5 Hz, *syn*/*anti* $CH=CH_2$), 5.09 (dt, 1 H, *J* = 9.0, 6.0 Hz, *anti* CH), 5.13 and 5.14 (dq, 2 H, *J* = 17.0, 1.5 Hz, *syn*/*anti* $CH=CH_2$), 5.75 and 5.77 (ddt, 2 H, *J* = 17.0, 10.0, 7.0 Hz, *syn*/*anti* $CH=CH_2$), 6.89 (d, 1 H, *J* = 6.0 Hz, *anti* CH=NOH), 7.35 (d, 1 H, *J* = 7.5 Hz, *syn* CH=NOH), 8.39 (br. s, 1 H, *syn* NOH), 8.75 (br. s, 1 H, *anti* NOH). – $^{13}$C NMR ($CDCl_3$) for 3:1 mixture of *syn*/*anti* isomers: δ = 31.8 (t, *syn*/*anti* $CH_2CH$=), 41.8, 42.32 (2 t, *syn*/*anti* $NCH_2$), 50.3 (d, *anti* NCH), 55.2 (d, *syn* NCH), 64.92, 65.6 (2 t, *syn*/*anti* $OCH_2$), 117.6, 117.7 (t, *syn*/*anti* $CH=CH_2$), 134.3, 134.4 (d, *syn*/*anti* $CH=CH_2$), 147.5 (d, *syn* CH=NOH), 149.1 (d, *anti* CH=NOH), 157.9, 158.3 (2 s, *syn*/*anti* OCON). – MS (CI, *i*Bu): *m*/*z* = 185 [$MH^+$] (60), 184 [$M^+$] (100), 142 [M – CNO] (60). – HRMS (DCI, $CH_4$): exact mass calcd. for $C_8H_{12}N_2O_3$ + H 185.0926; found 185.0900.

**(4*S*)-3-(4-Methylpent-3-enyl)-2-oxooxazolidine-4-carbaldehyde Oxime (25):** Obtained according to Procedure III from a mixture of **12** and **17** (2.5–3.0 mmol) by reaction with DIBAL-H (1 M in hexane, 7 mL) for 4.5 h. Flash chromatography (EtOAc/hexane, 1:2 4:1) gave **25a** (73 mg, 14%). Analogous treatment of a mixture of **13** (0.29 g, 1.18 mmol) and **17** (90 mg, 0.30 mmol) according to Procedure III, followed by flash chromatography (EtOAc/hexane, 1:2 4:1) gave **25a** as a white solid (0.11 g, 35%); m.p. 75–80 °C. – $[\alpha]_D^{20}$ = –2.18 (*c* = 0.032, acetone). – $^1$H NMR ($CDCl_3$) for a 2:1 mixture of *syn*/*anti* isomers: δ = 1.61 (s, 3 H, Me), 1.62 (s, 3 H, Me), 1.70 (s, 6 H, Me), 2.26 (m, 4 H, *syn*/*anti* $NCH_2CH_2CH$=), 3.08 (ddd, 2 H, *J* = 14.0, 8.0, 6.0 Hz, *syn*/*anti* $NCH_2$), 3.39 (ddd, 1 H, *J* = 14.0, 8.5, 7.0 Hz, *syn* $NCH_2$), 3.49 (ddd, 1 H, *J* = 14.0, 8.0, 7.0 Hz, *anti* $NCH_2$), 4.10 (dd, 1 H, *J* = 9.0, 6.0 Hz, *anti* $OCH_2$), 4.16 and 4.48 (m, 3 H, *syn* $OCH_2$ and *syn* CH), 4.57 (t, 1 H, *J* = 9.0 Hz, *anti* $OCH_2$), 5.05 (t sept., 2 H, *J* = 8.0, 1.0 Hz, *syn*/*anti* $CH=CMe_2$), 5.09 (dt, 1 H, *J* = 9.0, 6.0 Hz, *anti* CH), 6.87 (d, 1 H, *J* = 5.5 Hz, *anti* CH=NOH), 7.34 (d, 1 H, *J* = 7.5 Hz, *syn* CH=NOH), 9.47 (br. s, 1 H, *syn* NOH), 9.82 (br. s, 1 H, *anti* NOH). – $^{13}$C NMR ($CDCl_3$) for 1:1 mixture of *syn*/*anti* isomers: δ = 17.68 (q, *syn*/*anti cis*-Me), 25.56 (q, *syn*/*anti trans*-Me), 26.2 (t, $CH_2CH$=), 42.4, 42.9 (2 t, *syn*/*anti* $NCH_2$), 50.5 (d, *anti* NCH), 55.4 (d, *syn* NCH), 65.0, 65.64 (2 t, *syn*/*anti* $OCH_2$), 119.7 (d, *syn*/*anti* $CH=CMe_2$), 134.7, 134.8 (s, *syn*/*anti* $CH=CMe_2$), 147.2 (d, *syn* CH=NOH), 148.7 (d, *anti* CH=NOH), 158.0, 158.4 (2 s, *syn*/*anti* OCON). – MS (CI, $NH_3$): *m*/*z* = 230 [$MNH_4^+$] (60), 213 [$MH^+$] (100). – HRMS (DCI, $CH_4$): exact mass calcd. for $C_{10}H_{16}N_2O_3$ + H 213.1239; found 213.1224.

**(4*R*)-3-(But-3-enyl)-2-oxothiazolidine-4-carbaldehyde Oxime (26):** Obtained according to Procedure III from **14** (0.76 g, 3.33 mmol). Purified by combined flash vacuum chromatography (EtOAc/hexane, 1:2) to give **26** as a white solid (0.34 g, 51%); m.p. 88–90 °C. – $[\alpha]_D^{20}$ = –15.23 (*c* = 0.021, $CHCl_3$). – $^1$H NMR ([$D_6$]acetone) for a 2.5:1 mixture of *syn*/*anti* isomers: δ = 2.20–2.40 (m, 4 H, *syn*/*anti* $NCH_2CH_2CH$=), 3.07 (dt, 2 H, *J* = 13.5, 7.5 Hz, *syn*/*anti* $NCH_2$), 3.20 (dd, 1 H, *J* = 11.0, 4.5 Hz, *anti* $SCH_2$), 3.28 (dd, 1 H, *J* = 11.0, 5.0 Hz, *syn* $SCH_2$), 3.59 (dd, 1 H, *J* = 11.0, 7.5 Hz, *syn* $SCH_2$), 3.60 (dt, 2 H, *J* = 13.5, 7.5 Hz, *syn*/*anti* $NCH_2$), 3.62 (dd, 1 H, *J* = 11.0, 8.0 Hz, *anti* $SCH_2$), 4.55 (ddd, 1 H, *J* = 7.5, 7.0, 5.0 Hz, *syn* CH), 5.03 (dq, 2 H, *J* = 10.0, 1.0 Hz, *syn*/*anti* $CH=CH_2$), 5.10 and 5.11 (dq, 2 H, *J* = 17.0, 1.0 Hz, *syn*/*anti* $CH=CH_2$), 5.25 (ddd, 1 H, *J* = 8.0, 6.5, 4.5 Hz, *anti* CH), 5.77 and 5.79 (ddt, 2 H, *J* = 17.0, 10.0, 7.0 Hz, *syn*/*anti* $CH=CH_2$), 6.95 (d, 1 H, *J* = 6.5 Hz, *anti* CH=NOH), 7.46 (d, 1 H, *J* = 7.0 Hz, *syn* CH=NOH), 10.41 (s, 1 H, *syn* NOH), 10.79 (s, 1 H, *anti* NOH). – $^{13}$C NMR ($CDCl_3$) for a 2.5:1 mixture of *syn*/*anti* isomers: δ = 29.7 ($CH_2CH$=), 32.5, 32.6 (t, *syn*/*anti* $SCH_2$), 43.3, 43.7 (2 t, *syn*/*anti* $NCH_2$), 53.7 (d, *anti* NCH), 59.1 (d, *syn* NCH), 64.9, 65.6 (2 t, *syn*/*anti* $OCH_2$), 117.1 (t, *syn*/*anti* $CH=CH_2$), 136.0 (d, *syn*/*anti* $CH=CH_2$), 147.6 (d, *syn* CH=NOH), 149.4 (d, *anti* CH=NOH), 171.3, 171.5 (2 s, *syn*/*anti* SCON). – MS (CI, $NH_3$): *m*/*z* = 218 [$MNH_4^+$] (30), 201 [$MH^+$] (100). – HRMS (CI, $CH_4$): exact mass calcd. for $C_8H_{12}N_2O_2S$ + H 201.0697; found 201.0690.

**(4*R*)-3-(4-Methylpent-3-enyl)-2-oxothiazolidine-4-carbaldehyde Oxime (27):** Obtained according to Procedure III from **11** (0.53 g, 2.04 mmol) by reaction with DIBAL-H (1 M in hexane, 4 mL) for 4 h. Flash chromatography (EtOAc/hexane, 1:2 1:1) gave **27** as a white solid (0.17 g, 37%). – $^1$H NMR ([$D_6$]acetone) for a 3:1 mixture of *syn*/*anti* isomers: δ = 1.62 (s, 6 H, Me), 1.68 (s, 6 H, Me), 2.10–2.35 (m, 4 H, *syn*/*anti* $NCH_2CH_2CH$=), 2.98 (ddd, 1 H, *J* = 13.5, 8.5, 5.5 Hz, *syn* $NCH_2$), 2.99 (ddd, 1 H, *J* = 13.5, 8.0, 5.5 Hz, *anti* $NCH_2$), 3.18 (dd, 1 H, *J* = 11.5, 5.0 Hz, *anti* $SCH_2$), 3.28 (dd, 1 H, *J* = 11.5, 5.5 Hz, *syn* $SCH_2$), 3.47 (ddd, 2 H, *J* = 13.5, 8.5, 6.5 Hz, *syn*/*anti* $NCH_2$), 3.57 (dd, 1 H, *J* = 11.0, 7.5 Hz, *syn* $SCH_2$), 3.60 (dd, 1 H, *J* = 12.0, 8.0 Hz, *anti* $SCH_2$), 4.58 (dt, 1 H, *J* = 7.5, 5.5 Hz, *syn* CH), 5.09 (t sept., 2 H, *J* = 7.0, 1.5 Hz, *syn*/*anti* $CH=CMe_2$), 5.25 (ddd, 1 H, *J* = 7.5, 6.5, 5.0 Hz, *anti* CH), 6.94 (d, 1 H, *J* = 6.5 Hz, *anti* CH=NOH), 7.45 (d, 1 H, *J* = 7.5 Hz, *syn* CH=NOH), 10.41 (s, 1 H, *syn* NOH), 10.78 (s, 1 H, *anti* NOH). – $^{13}$C NMR ([$D_6$]acetone) for a 3:1 mixture of *syn*/*anti* isomers: δ = 17.7 (q, *syn*/*anti cis*-Me), 25.8 (q, *syn*/*anti trans*-Me), 27.0, 27.1 (t, *syn*/*anti* $CH_2CH$=), 29.7 ($SCH_2$), 44.0, 44.3 (2 t, *syn*/*anti* $NCH_2$), 53.9 (d, *anti* NCH), 59.5 (d, *syn* NCH), 121.3, 121.3 (d, *syn*/*anti* $CH=CMe_2$), 134.7 (s, *syn*/*anti* $CH=CMe_2$), 147.9 (d, *syn* CH=NOH), 149.5 (d, *anti* CH=NOH), 171.1 (s, *syn*/*anti* SCON). – MS (CI, $NH_3$): *m*/*z* = 246 [$MNH_4^+$] (5), 229 [$MH^+$] (100).

**(4*R*)-3-(But-3-enyl)thiazolidine-4-carbaldehyde Oxime (28):** Chromatography (EtOAc/hexane 1:2 neat EtOAc) of the crude oily residue of **26** gave the thiazolidin-2-one reduction side product **28** as

an oil (5%). – $[\alpha]_D^{20}$ = –65.0 (*c* = 0.014, $CHCl_3$). – $^1$H NMR ($CDCl_3$) for a 3.5:1 mixture of *syn*/*anti* isomers: δ = 2.30 (m, 4 H, *syn*/*anti* $NCH_2CH_2CH$=), 2.54 (t, 4 H, *J* = 7.0 Hz, *syn*/*anti* $NCH_2$), 2.95 (dd, 1 H, *J* = 10.0, 4.0 Hz, *anti* $SCH_2CH$), 3.02 (dd, 1 H, *J* = 10.0, 6.0 Hz, *syn* $SCH_2CH$), 3.12 (dd, 1 H, *J* = 10.0, 4.0 Hz, *syn* $SCH_2CH$), 3.21 (dd, 1 H, *J* = 10.0, 6.0 Hz, *anti* $SCH_2CH$), 3.94 (m, 2 H, *syn*/*anti* CH), 3.98 (d, 1 H, *J* = 10.0 Hz, *syn* $SCH_2N$), 3.99 (d, 1 H, *J* = 10.0 Hz, *anti* $SCH_2N$), 4.08 (d, 1 H, *J* = 10.0 Hz, *syn* $SCH_2N$), 4.19 (d, 1 H, *J* = 10.0 Hz, *anti* $SCH_2N$), 5.04 (dq, 2 H, *J* = 10.0, 1.0 Hz, *syn*/*anti* $CH=CH_2$), 5.10 (dq, 2 H, *J* = 15.0, 1.0 Hz, *syn*/*anti* $CH=CH_2$), 5.81 (ddt, 2 H, *J* = 15.0, 10.0, 5.0 Hz, *syn*/*anti* $CH=CH_2$), 6.66 (d, 1 H, *J* = 5.0 Hz, *anti* CH=NOH), 7.33 (d, 1 H, *J* = 5.0 Hz, *syn* CH=NOH), 8.00 (br. s, 1 H, NOH). – $^{13}$C NMR ($CDCl_3$) for the major *syn* isomer: δ = 32.0 (t, $SCH_2$), 33.4 (t, $CH_2CH$=), 52.6 (t, $NCH_2$), 58.0 (t, $SCH_2N$), 67.2 (d, CH), 116.3 (t, $CH=CH_2$), 135.8 (d, CH=$CH_2$), 150.3 (d, CH=NOH); for the minor *anti* isomer: δ = 32.0 (t, $SCH_2$), 33.3 (t, $CH_2CH$=), 53.4 (t, $NCH_2$), 58.0 (t, $SCH_2N$), 63.7 (d, CH), 116.5 (t, $CH=CH_2$), 135.6 (d, CH=$CH_2$), 151.3 (d, CH=NOH). – MS (CI, $CH_4$): *m*/*z* = 187 [$MH^+$] (100). – HRMS (CI, $CH_4$): exact mass calcd. for $C_8H_{14}N_2OS$ + H 187.0905; found 187.0800.

**Isoxazoline 29:** Obtained as described for **4a** from **25** (58 mg, 0.27 mmol) and $Et_3N$ (cat. amount). Purified by flash chromatography (EtOAc/hexane, 4:1) to give **29** as an oily solid (30 mg, 52%). – $[\alpha]_D^{20}$ = +38.57 (*c* = 0.021, $CHCl_3$). – $^1$H NMR: See Table 2. – $^{13}$C NMR: See Table 4. – MS (CI, $NH_3$): *m*/*z* = 228 [$MNH_4^+$] (100), 211 [$MH^+$] (30). – HRMS (CI, $CH_4$): exact mass calcd. for $C_{10}H_{14}N_2O_3$ + H 211.1082; found 211.1090.

**Isoxazoline 30:** Obtained as described for **4a** from **24** (0.10 g, 0.54 mmol) either with or without $Et_3N$ (cat. amount). Purified by flash chromatography on silica gel (EtOAc/hexane, 4:1) to give **30** as an oily solid (45 mg, 46%). – $[\alpha]_D^{20}$ = +48.09 (*c* = 0.021, $CDCl_3$). – $^1$H NMR: See Table 2. – $^{13}$C NMR: See Table 4.

**Isoxazoline 31:** Obtained as described for **4a** from **26** (90 mg, 0.45 mmol) and $Et_3N$ (cat. amount). Purified by flash chromatography (EtOAc/hexane, 4:1) to give **31** as a semi-solid (48 mg, 54%). – $[\alpha]_D^{20}$ = +48.09 (*c* = 0.021, $CDCl_3$). – $^1$H NMR: See Table 2. – $^{13}$C NMR: See Table 4. – HRMS (CI, $CH_4$): exact mass calcd. for $C_8H_{10}N_2O_2S$ + H 199.0541; found 199.0620.

**Isoxazoline 32:** Obtained as described for **4a** from **27** (0.14 g, 0.59 mmol) and $Et_3N$ (cat. amount). Purified by flash chromatography (EtOAc/hexane, 2:1 4:1) to give **32** as a white semi-solid (91 mg, 68%). – $^1$H NMR: See Table 2. – $^{13}$C NMR: See Table 4. – HRMS (CI, $CH_4$): exact mass calcd. for $C_{10}H_{14}N_2O_2S$ + H 227.0854; found 227.0891.

**Isoxazoline 33:** A suspension of **29** (30 mg, 0.14 mmol), $NaBH_4$ (10 mg, 0.26 mmol), and $LiAlH_4$ (25 mg, 0.66 mmol) in dry $Et_2O$ (2.5 mL) was stirred at 0 °C for 8 h (until TLC indicated complete consumption of the starting material). The mixture was then quenched with water (5 drops), aq. NaOH solution (20%, 3 drops), and further water (5 drops). The white precipitate obtained was separated from the organic layer and taken up in MeOH; filtration and concentration of the filtrate gave an oil. Evaporation of the solvent from the organic layer gave further oil. The combined oily residues were flash-chromatographed (MeOH) to give **33** (10 mg, 38%) as a colorless oil. – $^1$H NMR ($CDCl_3$): δ = 1.20 (s, 3 H, β-Me), 1.44 (s, 3 H, α-Me), 1.59 (qd, 1 H, *J* = 13.0, 4.0 Hz, $NCH_2CH_2$), 1.95 (dddd, 1 H, *J* = 13.0, 6.0, 4.0, 2.5 Hz, $NCH_2CH_2$), 2.71 (ddd, 1 H, *J* = 13.0, 12.5, 2.5 Hz, $NCH_2$), 3.08 (ddd, 1 H, *J* = 12.5, 6.0, 1.0 Hz, $CH_2CH$), 3.19 (ddd, 1 H, *J* = 13.0, 6.0, 4.0 Hz, $NCH_2$), 3.61 (ddd, 1 H, *J* = 6.0, 4.0, 1.0 Hz, $CH_2CH$), 3.80 (dd, 1 H, *J* = 11.5, 6.0 Hz, $CH_2OH$), 3.96 (dd, 1 H, *J* = 11.5, 4.0 Hz, $CH_2OH$). – $^{13}$C NMR ([$D_6$]acetone): δ = 22.1 (q, β-Me), 27.2 (q, α-Me), 27.5 (t, $NCH_2CH_2$), 43.8 (dd, $NCH_2$), 55.3 (d, CONCH), 56.3 (d, $CH_2CH$), 61.3 (t, $CH_2OH$), 86.7 (s, $NOCMe_2$), 160.8 (s, C=N). – MS (CI, $NH_3$): *m*/*z* = 185 [$MH^+$] (100).

**Keto Alcohol 34:** To a solution of isoxazoline **30** (25 mg, 0.14 mmol) in dioxane/MeOH (1:3, 2 mL) were added $B(OH)_3$ (43 mg, 0.69 mmol), Raney Ni (1 drop of an aqueous suspension), and water (0.3 mL). An atmosphere of $H_2$ was introduced by repeated (3 times) evacuation and flushing with $H_2$ gas by means of a balloon. The mixture was then vigorously stirred at room temp. for 3.5 h (until TLC indicated complete consumption of the starting material). The catalyst was then filtered off and the filtrate was concentrated to leave a green oil, flash chromatography (EtOH/EtOAc, 1:4) of which gave **34** as a colorless oil (inseparable 5:1 mixture of isomers, 9 mg, 35%). – $^1$H NMR ($CDCl_3$) for the major diastereomer: δ = 1.87 (qd, 1 H, *J* = 13.0, 4.5 Hz, $NCH_2CH_2$), 2.12 (dddd, 1 H, *J* = 13.0, 5.0, 3.0, 2.0 Hz, $NCH_2CH_2$), 2.75 (dq, 1 H, *J* = 13.0, 5.0 Hz, $CH_2CHCH_2$), 3.36 (ddd, 1 H, *J* = 14.0, 12.5, 3.0 Hz, $NCH_2$), 3.75 (dd, 1 H, *J* = 11.5, 4.0 Hz, $CH_2OH$), 3.85 (dd, 1 H, *J* = 11.5, 6.5 Hz, $CH_2OH$), 4.12 (ddd, 1 H, *J* = 14.0, 4.5, 2.0 Hz, $NCH_2$), 4.17 (dd, 1 H, *J* = 9.0, 5.0 Hz, CONCH), 4.33 (t, 1 H, *J* = 9.0 Hz, $CO_2CH_2$), 4.71 (dd, 1 H, *J* = 9.0, 5.0 Hz, $CO_2CH_2$). – MS (CI, $NH_3$): *m*/*z* = 203 [$MNH_4^+$] (100), 186 [$MH^+$] (40).

**Alcohol 35:** To a solution of **31** (50 mg, 0.25 mmol) in dry DME (5 mL) was added $LiAlH_4$ (40 mg, 1.05 mmol) and the heterogeneous mixture was stirred for ca. 12 h at room temp. The reaction was then quenched with water (1 mL), the white precipitate obtained was separated from the aqueous DME and taken up in MeOH/EtOAc; filtration and concentration of the filtrate gave an oil. Evaporation of the aqueous DME layer gave further oil. The combined oily residues (65 mg) were flash chromatographed (EtOAc/hexane, 4:1, → $CHCl_3$/MeOH/$NH_4OH$, 70:10:1, → neat MeOH) and the collected fractions were left in the open air; slow evaporation of the solvents left **35** as a colorless oil (5 mg, 10%). – $^1$H NMR ($D_2O$): δ = 1.47 (qd, 1 H, *J* = 13.0, 3.5 Hz, $NCH_2CH_2$), 1.60 (dq, 1 H, *J* = 13.0, 3.5 Hz, $NCH_2CH_2$), 2.18 (dtt, 1 H, *J* = 12.5, 6.5, 4.0 Hz, $CH_2CHCH_2$), 2.20 (s, 3 H, NMe), 2.22 (td, 1 H, *J* = 12.5, 3.0 Hz, $NCH_2$), 2.84 (dd, 1 H, *J* = 14.5, 5.0 Hz, $CH_2SONH$), 2.85 (dt, 1 H, 12, 3.5 Hz, $NCH_2$), 3.11 (dd, 1 H, *J* = 5.0, 3.5, MeNCH), 3.62 (dd, 1 H, *J* = 11.5, 6.5 Hz, $CH_2OH$), 3.65 (dd, 1 H, *J* = 11.5, 7.0 Hz, $CH_2OH$), 4.00 (dd, 1 H, *J* = 14.5, 0.5 Hz, $CH_2SONH$), 4.22 (td, 1 H, *J* = 3.5, 1.0 Hz, CHNHSO). – $^{13}$C NMR ($D_2O$): δ = 22.4 (t, $NCH_2CH_2$), 38.2 (d, $CH_2CHCH_2$), 42.4 (q, NMe), 54.7 (dd, $NCH_2$), 60.5 (d, MeNCH), 63.2 (t, $CH_2OH$), 64.2 (dd, $CH_2SONH$), 66.7 (d, CHNHSO). – HRMS ($FAB^+$): *m*/*z* = 205.1634 [$MH^+$] (100), 189.1542 [M – Me] (51), 143.1039 [$MH^+$ – Me – SO] (51). – HRMS ($FAB^-$): *m*/*z* = 203.0060 [M – H] (100).

**(2*R*,3*S*,4*S*)-2-(3-Amino-2-mercaptomethyl-1-methylpiperidin-4-yl)propan-2-ol (36):** To a solution of **32** (86 mg, 0.38 mmol) in dry $Et_2O$ (8 mL) was added $LiAlH_4$ (72 mg, 1.89 mmol) and the heterogeneous mixture was stirred at 0 °C for 15 min. and then at room temp. for 7 h. The reaction was subsequently quenched with MeOH/water (1:1, 5 mL) and the white precipitate obtained was separated from the aqueous $Et_2O$ and washed with MeOH/water. Filtration and concentration of the washings gave an oil. Evaporation of the solvents from the aqueous $Et_2O$/MeOH layer gave further oil. The combined oily residues (88 mg) were flash-chromatographed (MeOH/$CHCl_3$, 1:7, → $CHCl_3$/MeOH/$NH_4OH$, 70:10:1) to give **36** as a colorless oil (20 mg, 24%). – $^1$H NMR ($D_2O$): δ = 1.21 (s, 3 H, Me), 1.36 (s, 3 H, Me), 1.41 (dt, 1 H, *J* = 12.5, 3.0 Hz,

C*H*CMe$_2$OH), 1.64 (qd, 1 H, $J$ = 13.0, 4.0 Hz, NCH$_2$C*H*$_2$), 1.78 (dq, 1 H, $J$ = 13.5, 3.0 Hz, NCH$_2$C*H*$_2$), 2.22 (td, 1 H, $J$ = 11.5, 3.5 Hz, NCH$_2$), 2.32 (s, 3 H, NMe), 2.34 (ddd, 1 H, $J$ = 9.0, 4.0, 2.0 Hz, C*H*CH$_2$SH), 2.90 (dd, 1 H, $J$ = 13.5, 9.0 Hz, C*H*$_2$SH), 3.00 (dt, 1 H, $J$ = 11.5, 3.0 Hz, NCH$_2$), 3.26 (dd, 1 H, $J$ = 13.5, 4.0 Hz, C*H*$_2$SH), 3.60 (br. s, 1 H, C*H*NH$_2$). – $^{13}$C NMR (D$_2$O): δ = 21.3 (t, NCH$_2$C*H*$_2$), 28.4 (q, Me), 29.6 (q, Me), 40.1 (dd, CH$_2$SH), 43.9 (q, NMe), 48.2 (d, *C*HCMe$_2$OH), 49.7 (d, CHNH$_2$), 58.2 (dd, NCH$_2$), 69.1 (d, *C*HCH$_2$SH), 74.4 (s, *C*Me$_2$OH). – HRMS (CI, CH$_4$): exact mass calcd. for C$_{10}$H$_{22}$N$_2$OS + H 219.1531; found 219.1526.

## Acknowledgments

Generous support for this work by the "Minerva Foundation Otto Mayerhoff Center for the Study of Drug–Receptor Interactions" at Bar Ilan University, the "Marcus Center for Pharmaceutical and Medicinal Chemistry", and the "Bronia Hacker Fund for Scientific Instrumentation" at Bar Ilan University is gratefully acknowledged.

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Received June 25, 1999
[O99379]