

The Reaction of β -Amino Alcohols with 1,1'-Carbonyldiimidazole – Influence of the Nitrogen Substituent on the Reaction Course

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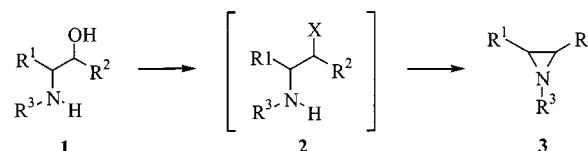
The reaction of β -amino alcohols with 1,1'-carbonyldiimidazole in dichloromethane is affected by the size of the nitrogen substituent. 1,3-Oxazolidin-2-ones are exclusively obtained from *N*-H, *N*-methyl and *N*-arylmethyl derivatives. *O*-(1-Imidazolyl)carbonyl derivatives are formed as intermediates

from *N*-[1-(2-pyridyl)alkyl]-(*S*)-valinol and are mainly or exclusively converted into aziridines in the presence of water, although the cyclization is impeded by large *N*-substituents such as triphenylmethyl.

Introduction

β -Amino alcohols **1** can be converted into aziridines **3** by a cyclodehydration reaction which usually takes place by the two step mechanism described in Scheme 1, where the intermediate **2** is either isolated or converted in situ into the target **3**. Enantiomerically pure, ring substituted aziridines can be prepared from β -amino alcohols available from the “chiral pool” or by asymmetric methodologies.^[1] Several methods and reagents have been described for this purpose. For example, the reaction of β -amino alcohols with sulfuric acid afforded the β -aminoalkyl sulfates **2** ($X = \text{OSO}_3\text{H}$), from which aziridines were obtained by alkali treatment at high temperature.^[2] On the other hand, the one-pot formation of the aziridines **3**, avoiding the isolation of intermediate **2**, was accomplished by the treatment of **1** with triphenylphosphane/carbon tetrachloride/triethylamine,^[3] diethyl azodicarboxylate (Mitsunobu reaction),^[3c,4] or dihalo-^[5] or dialkoxytriphenylphosphoranes.^[6] Moreover, starting from β -amino alcohols carrying bulky *N*-substituents, the corresponding *O*-tosyl and *O*-mesyl derivatives were prepared and then cyclized to aziridines by means of triethylamine in refluxing solvents,^[4g,7] although the one-pot formation of aziridines at low temperature was sometimes observed.^[4g,7d,7e] The reaction of β -amino alcohols with sulfuryl chloride generally afforded 2,2-dioxo-1,2,3-oxathiazolidines, but *N*-trityl-L-serine and -threonine benzyl esters were converted into the corresponding aziridines.^[8] The treatment of chiral β -amino alcohols with thionyl chloride gave 2-oxo-1,2,3-oxathiazolidines or β -chloro amines, which were then converted into aziridines.^[8,9] Finally, triflic anhydride has been used to convert valinol to 1-trifluoromethanesulfonyl-2-isopropylaziridine with excellent yield, although further examples were not provided.^[7e] These methods often give aziridines with high yields, but suffer from certain disadvantages, since they require acidic or

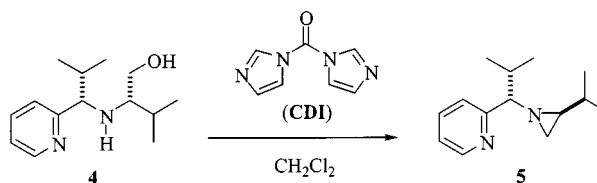
hard conditions, hazardous or poisonous reagents, tedious separation of by-products, or lack generality.



Scheme 1

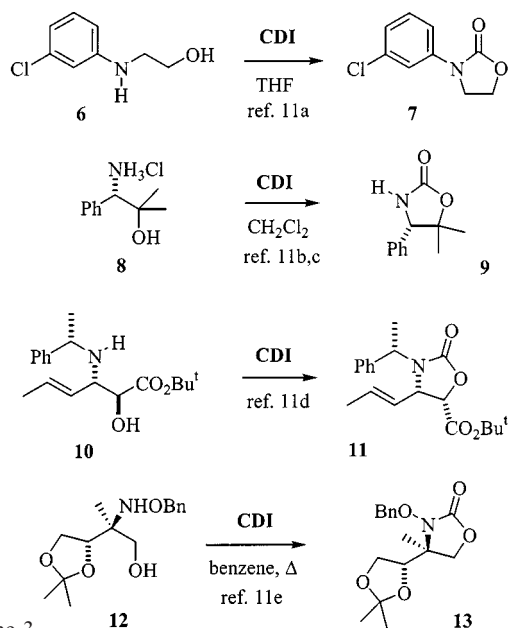
In the course of our studies directed towards the synthesis of enantiopure 1-(2-pyridyl)alkylamines,^[10] we discovered that the reaction of the β -amino alcohol **4** with 1,1'-carbonyldiimidazole (CDI) in dichloromethane unexpectedly yielded the aziridine **5** (Scheme 2).^[10e] This result has no precedent in the previously reported reactions of β -amino alcohols with CDI, as the 1,3-oxazolidin-2-ones **7**, **9**, **11** and **13** were obtained from the β -amino alcohols **6**, **8**, **10** and **12**, respectively (Scheme 3).^[11] Cyclic carbamates were recently prepared from 1,3-amino alcohols by reaction with CDI in the presence of triethylamine or imidazole.^[12] Moreover, the reaction of 1,2-diols^[13] and *N*-mono-substituted 1,2- and 1,4-diamines^[14a,14b] with CDI follows analogous pathways affording 1,3-oxazolidin-2-ones and cyclic ureas, respectively. On the other hand, primary 1,2- and 1,4-diamines did not afford the cyclic ureas by treatment with CDI, phosgene and other phosgene equivalents; this goal was achieved by the use of gaseous carbonyl sulfide.^[14c,14d]

We envisioned that the nitrogen substituent must have a remarkable effect on the reaction course and decided to investigate in depth the reaction of β -amino alcohols with CDI. Especially, we aimed to verify the scope of this new method for the construction of the aziridine ring and to



Scheme 2

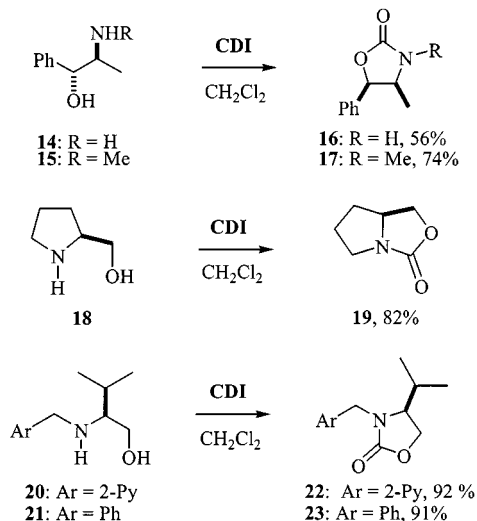
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prepare new optically pure aziridines useful in the field of asymmetric catalysis.^[10e]

Results

Despite the previously reported reactions of β -amino alcohols with CDI described in Scheme 3, we performed analogous reactions with the commercially available and optically pure β -amino alcohols (–)-norephedrine (**14**), (–)-ephedrine (**15**) and (*S*)-prolinol (**18**), and obtained the corresponding known oxazolidinones **16**,^[15] **17**^[15] and **19**,^[16] respectively, in good yields (Scheme 4).

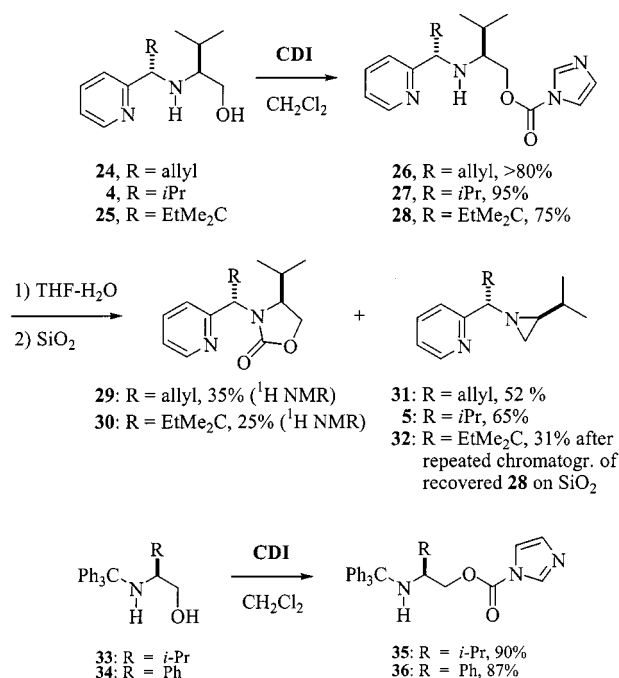


Scheme 4

Then we examined the reaction of (*S*)-valinol and (*S*)-phenylglycinol derivatives carrying different *N*-substituents; some of them were known compounds, others were prepared by routine methods, as described in the Experimental Section. In particular, the size of the *N*-substituent in the

(*S*)-valinol derivatives was finely tuned by the addition of different organometallic reagents to the imine derived from 2-pyridinaldehyde, according to the protocols described previously by us.^[10] The compounds **20** and **21**, carrying the 2-pyridylmethyl and benzyl groups as the *N*-substituent, were converted with high yields to the 1,3-oxazolidin-2-ones **22** and **23**, respectively (Scheme 4).

Different outcomes were obtained from the reaction of (*S*)-valinol derivatives having more bulky substituents, i.e. compounds **24** and **25** (Scheme 5). This lead us to repeat the reaction of **4**, but, to our great disappointment, we did not succeed in preparing the aziridine **5** in quantitative yield, as previously described:^[10e] instead, in different experiments apparently carried out by following the same experimental procedure, the yields were low to good. As a matter of fact, all the reaction mixtures derived from the β -amino alcohols **24**, **4** and **25** contained the *O*-(1-imidazolyl)-carbonyl derivatives **26–28** (Scheme 5). These compounds were identified only by ¹H NMR spectroscopy, since only low molecular weight products were revealed by GC-MS analyses.



It should be underlined that the products were isolated after stirring or washing the reaction mixtures (CH_2Cl_2) with H_2O to remove the imidazole formed as a by-product. After considerable experimentation, we finally discovered that the aziridine **5** was formed during the aqueous treatment. In fact, when the aqueous workup was avoided and the solvent evaporated, ¹H NMR analyses of the crude mixtures coming from the substrates **24**, **4** and **25** indicated that the *O*-(1-imidazolyl)carbonyl derivatives were mainly or almost exclusively formed, being accompanied in all cases by imidazole. The mixture coming from **24** also contained traces amounts of the oxazolidinone **29** and about 15% of the aziridine **31**; the intermediate **28** was accompanied by

the oxazolidinone **30** (25%). On the other hand, only traces of the aziridine **5** were formed from **4**. The yield of the aziridine **5** was seemingly affected by the relative amounts of water in the workup and by the duration of stirring the heterogeneous mixture $\text{CH}_2\text{Cl}_2/\text{H}_2\text{O}$. In order to obtain reproducible results, it was preferable to evaporate the CH_2Cl_2 solvent and then stir the reaction residues in a diluted homogeneous medium $\text{THF}/\text{H}_2\text{O}$ (1:3). In this way, after 2 h, the complete cyclization of the intermediates **26–28** to 1,3-oxazolidin-2-ones and/or aziridines was observed. Starting from the compound **26** carrying the less bulky *N*-substituent, a mixture of oxazolidinone **29** and aziridine **31** was obtained, but only the aziridine **31** was isolated pure in 52% yield after column chromatography (SiO_2). On the other hand, the aziridine **5** was exclusively formed from **27**. It is noteworthy that from the compound **28**, with the most bulky *N*-substituent, the aziridine **32** was not formed in the aqueous medium, but during the attempted purification of **28** by chromatography on an SiO_2 column: an overall 31% yield of aziridine **32** was obtained by repeating the chromatography of recovered **28**.

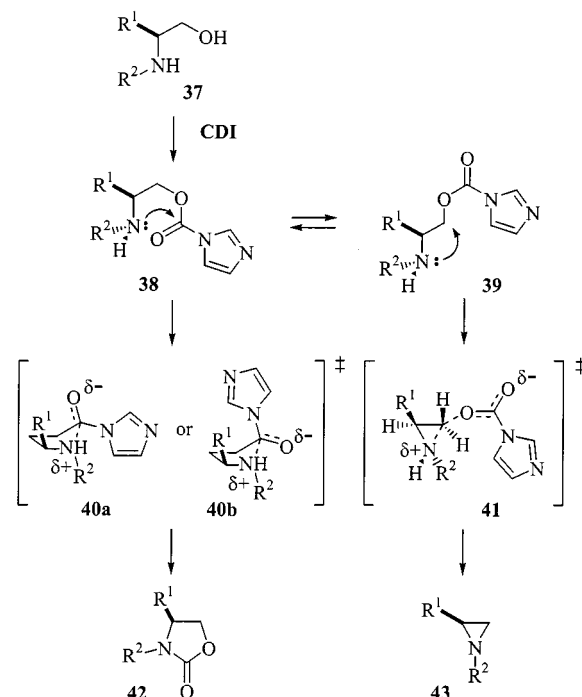
Finally, we carried out the reaction of *N*-triphenylmethyl-(*S*)-valinol (**33**) and *N*-triphenylmethyl-(*S*)-phenylglycinol (**34**), and observed the formation of the *O*-(1-imidazolyl)-carbonyl derivatives **35** and **36**, respectively, in high yields (Scheme 5). No cyclic product was obtained either by stirring **35,36** for several hours in the homogeneous system $\text{THF}/\text{H}_2\text{O}$ or by heating them in refluxing THF or toluene, even in the presence of triethylamine;^[12a] instead, unidentified by-products were sometimes formed.

Reaction Pathways

The construction of 1,3-oxazolidin-2-ones and aziridines by the reaction of chiral *N*-substituted β -amino alcohols **37** with CDI can be explained by the reaction course described in Scheme 6. The *O*-imidazolecarbonyl derivatives **40**^[17] can be envisaged as the preliminarily formed intermediates in the pathways leading to both the 1,3-oxazolidin-2-ones **42** and aziridines **43**. In fact, it is known that 3-methylamino-1,2-propandiol gives the cyclic carbonate instead of the cyclic carbamate, demonstrating that the primary hydroxyl function reacts preferentially to the secondary amine.^[13d]

The 1,3-Oxazolidin-2-ones **42** are then formed from **38** by the intramolecular attack of the secondary amine function at the carbonyl group of the carbamate moiety, through the diastereomeric transition states **40a,b**. On the other hand, aziridines **43** are formed from the conformers **39** of the same intermediates by an intramolecular $\text{S}_{\text{N}}2$ reaction in which nitrogen attacks the carbon atom bearing the *O*-imidazolecarbonyl leaving group, through the transition state **41**. This view is in agreement with the known reactivity of amines, since the presence of substituents at nitrogen favours the $\text{S}_{\text{N}}2$ displacement rather than attack at the carbonyl group.^[18,19]

Our results demonstrate that the rate of cyclization to 1,3-oxazolidin-2-ones is affected by the size of the *N*-substituent R^2 . This can be explained by considering the non-bonding interactions in the transition states, i.e. R^2 -imida-



Scheme 6

zole in **40a** and R^1 -imidazole in **40b**. However, the aziridines **43** were formed even with bulky R^2 substituents, although the cyclization required the presence of water, and did not occur at all when the size of R^2 was excessive, e.g. in **25**.

It is noteworthy that both the rate and the regioselectivity of the ring closure to aziridines **43** is enhanced by an aqueous medium. This outstanding solvent effect can be understood, in our opinion, by considering that the transition state **41** is more dipolar than the transition states **40a,b**, because the opposite charges are more separated; hence, it is better solvated and more stabilized by water, which has higher dipole moment and dielectric constant than aprotic organic solvents.

Conclusions

The nature of the *N*-substituent is the determining factor deciding the outcome of the reaction of β -amino alcohols with 1,1'-carbonyldiimidazole (CDI). 1,3-Oxazolidin-2-ones are exclusively produced from substrates having a small *N*-substituent, whereas the cyclization to aziridines is favoured by a larger *N*-alkyl substituent, e.g. 1-(2-pyridyl)alkyl, and requires the presence of H_2O . The *O*-imidazolecarbonyl derivatives of the β -amino alcohols (imidazole carboxylic esters) are the intermediates in these cyclizations. Only the latter compounds are isolated from β -amino alcohols carrying very bulky *N*-substituents, e.g. trityl, and do not undergo cyclization even at high temperature.

In our continuing efforts to synthesize other optically pure 1-[(2-pyridyl)alkyl]aziridines, we intend to verify if this procedure can be applied to other β -amino alcohols, especially (*S*)-phenylglycinol derivatives.

We wish to underline that the use CDI for the construction of aziridines and 1,3-oxazolidin-2-ones from β -amino alcohols, and similarly of cyclic ureas and carbonates from ω -amino alcohols and 1,n-diols, respectively, is convenient for the simplicity of the procedure and the mildness of the experimental conditions. Moreover, CDI is a stable (although hygroscopic), crystalline and safe reagent. These uses of CDI, despite a few reports,^[11–14] have been heretofore neglected with respect to other methods, which generally require phosgene or phosgene substitutes,^[20] which can result in better conversion and selectivity but are more hazardous. Recently developed procedures making use of CO/O₂/Pd-Cu,^[16c] CO/PdI₂/KI^[16e] or electrogenerated tetraethylammonium carbonate or peroxydicarbonate with a large excess of tosyl chloride^[20f] have drawbacks, too.

Experimental Section

General Conditions: Melting points are uncorrected. – Solvents were distilled under N₂ prior to use: THF over sodium benzophenone ketyl and then over LiAlH₄, and CH₂Cl₂ over P₂O₅. – Optical rotations were measured on a digital polarimeter in a 1-dm cell and $[\alpha]_D$ values are given in 10^{–1} deg cm³ g^{–1}. – ¹H NMR spectra were recorded on a Varian Gemini instrument at 300 or 200 MHz for samples in CDCl₃ which had been stored over Mg. ¹H Chemical shifts are reported in ppm relative to CHCl₃ (δ_H = 7.27) and *J* values are given in Hz. – MS spectra were taken at an ionizing voltage of 70 eV on a Hewlett-Packard 5970 or 5890 spectrometer with GLC injection. – Chromatographic purifications were carried out on columns of silica gel (Merck, 230–400 mesh) at medium pressure. – 2-Pyridinealdehyde and benzaldehyde (Aldrich) were distilled before use. – Chlorotriphenylmethane was purchased from Aldrich and used as received. – All organometallic reactions were performed in flame-dried apparatus under a static atmosphere of dry N₂. – (S)-N-Benzyl valinol (**21**) was prepared according to a reported procedure;^[21] the β -hydroxy amines **4**,^[10d,10e] **24**,^[10d,10e] and **25**^[10e] and aziridines **5**^[10e] and **32**^[10e] were prepared as previously described.

(S)-N-[(2-Pyridyl)methyl]valinol (20): To a solution of (S)-valinol (0.824 g, 8 mmol) in CH₂Cl₂ (10 mL) cooled at 0 °C was added anhydrous MgSO₄ (4 g) and freshly distilled 2-pyridinealdehyde (0.856 g, 8 mmol). The mixture was stirred for 2 h, then the solution was filtered and concentrated to leave an oily residue of the imine.^[10d] This was dissolved in MeOH (10 mL) and NaBH₄ (0.300 g, 8 mmol) was added. The mixture was stirred at room temp. for 4 h, then the solvent was evaporated at reduced pressure, H₂O (5 mL) was added, and the organic phase was extracted with Et₂O (3 $\times$ 10 mL). The collected organic layers were dried over Na₂SO₄ and concentrated to leave an oily residue. Chromatography on a short column of SiO₂ eluting with cyclohexane/ethyl acetate (60:40) gave compound **20** as an oil: 1.101 g (65%); $[\alpha]_D^{25}$ = +30.7 (*c* = 0.96, CHCl₃). – ¹H NMR (300 MHz, CDCl₃): δ = 8.55 (d, *J* = 5.7 Hz, 1 H, Py), 7.65 (m, 1 H, Py), 7.30 (d, *J* = 7.6 Hz, Py), 7.18 (m, 1 H, Py), 4.01 (q, 2 H, PyCH₂), 3.70 (dd, *J* = 3.9 and 11.4 Hz, 1 H, CHCH₂), 3.47 (dd, *J* = 7.2 and 11.4 Hz, 1 H, CHCH₂), 3.1 (br, 2 H, NH and OH), 2.50 (m, 1 H, CHCH₂), 1.85 (m, 1 H CHMe₂), 1.0 and 0.95 (2 d, *J* = 6.7 Hz, 6 H, CHMe₂). – MS: *m/z* (%) = 163 (100) [M⁺ – CH₂OH], 93 (92), 92 (46), 151 (38) [M⁺ – *i*Pr], 94 (24), 65 (20).

Preparation of N-Triphenylmethyl β -Amino Alcohols: To a solution of (S)-valinol or (S)-phenylglycinol (10 mmol) in dry CH₂Cl₂

(25 mL) cooled at 0 °C was added Et₃N (1.4 mL, 10 mmol), then diphenylmethyl bromide (2.480 g, 10 mmol) or triphenylmethyl chloride (2.800 g, 10 mmol). The mixture was stirred for 7–8 h, then filtered, washed with brine, dried over Na₂SO₄, and concentrated and the residue was chromatographed on an SiO₂ column (cyclohexane/ethyl acetate 90:10).

N-Triphenylmethyl-(S)-valinol (33): Yellowish oil; the compound was >95% pure by ¹H NMR analyses: 3.044 g, 90%; $[\alpha]_D^{20}$ = –20 (*c* = 1.16, CHCl₃). – ¹H NMR (CDCl₃, 300 MHz) δ = 7.6–7.05 (m, 15 H, Ph), 3.33 (dd, *J* = 3.7 and 11.0 Hz, 1 H, CHCH₂), 3.10 (dd, *J* = 5.4 and 11.0 Hz, 2 H, CHCH₂), 2.42 (m, 1 H, CHCH₂), 2.05 (broad, 2 H, NH and OH), 1.26 (m, 1 H, CHMe₂), 0.80 and 0.66 (2 d, *J* = 6.9 Hz, CHMe₂). – C₂₄H₂₇NO (345.48): calcd. C 83.44, H 7.88, N 4.05; found C 83.54, H 8.03, N 3.99.

(S)-N-Triphenylmethyl-phenylglycinol (34): White solid; 3.41 g (90%); m.p. 55–56 °C; $[\alpha]_D^{20}$ = –96 (*c* = 1, CHCl₃). – ¹H NMR (CDCl₃, 200 MHz) δ = 7.7–7.1 (m, 20 H, Ph), 3.81 (t, 1 H, CHN), 3.24 (dd, *J* = 4.1 and 10.5 Hz, 1 H, CHCH₂), 2.83 (dd, *J* = 5.4 and 10.5 Hz, 1 H, CHCH₂), 1.50 (broad, 2 H, NH and OH). – C₂₇H₂₅NO (379.49): calcd. C 85.45, H 6.64, N 3.69; found C 85.50, H 6.69, N 3.60.

Reactions of β -Amino Alcohols with 1,1'-Carbonyldiimidazole

A) Preparation of 1,3-Oxazolidin-2-ones: To a solution of the β -amino alcohol (5 mmol) in dry CH₂Cl₂ (20 mL) was added 1.1'-carbonyldiimidazole (0.810 g, 5 mmol) and the solution was stirred with a magnetic bar for 1–2 h, after which time the reaction was apparently complete, as judged by TLC analysis (sometimes the products and starting material were not well separated). The reaction mixture was washed with H₂O (2 $\times$ 10 mL), then dried (Na₂SO₄) and concentrated, and the residue was chromatographed on a column of SiO₂ eluting with cyclohexane/ethyl acetate mixtures.

(4S,5R)-4-Methyl-5-phenyl-1,3-oxazolidin-2-one (16): White solid; 0.523 g (56%); $[\alpha]_D^{20}$ = –170 (*c* = 1.2, CHCl₃), m.p. 116–117 °C {ref.^[15b] $[\alpha]_D^{20}$ = –158.4 (*c* = 0.44, CHCl₃), m.p. 116–117 °C; ref.^[15c] $[\alpha]_D^{20}$ = –149.6 (*c* = 0.51, CHCl₃), m.p. 102–105 °C}. – The ¹H NMR spectrum was identical to that reported in the literature. – MS: *m/z* (%) = 107 (100), 79 (55), 77 (23), 105 (20), 51 (18), 177 (17) [M⁺].

(4S,5R)-3,4-Dimethyl-5-phenyl-1,3-oxazolidin-2-one (17): White solid; 0.707 g (74%); $[\alpha]_D^{20}$ = –122 (*c* = 1.2, CHCl₃), m.p. 91–92 °C {ref.^[15b] $[\alpha]_D^{20}$ = –118.3 (*c* = 0.23, CHCl₃), m.p. 91–92 °C; ref.^[15a] $[\alpha]_D$ = –110.6 (CHCl₃), m.p. 91–92 °C; ref.^[15d] $[\alpha]_D$ = –125 (*c* = 1.0, CHCl₃), m.p. 91–92 °C; ref.^[15f] $[\alpha]_D$ = –120 (*c* = 1.18, CHCl₃), m.p. 90–92 °C}. – The ¹H NMR spectrum was identical to that reported in the literature. – MS: *m/z* (%) = 57 (100) [MeCHNMe], 191 (30) [M⁺], 117 (28), 105 (25), 77 (24), 132 (20), 91 (14), 147 (10) [M⁺ – CO₂], 176 (9) [M⁺ – Me].

(S)-Tetrahydro-1H,3H-pyrrolo[1,2-c]oxazol-3-one 19: Yellowish oil; 0.521 g (82%); $[\alpha]_D^{20}$ = –33 (*c* = 1, CHCl₃) {ref.^[16a] $[\alpha]_D^{20}$ = –35.1 (*c* = 0.72, CHCl₃); ref.^[16b] $[\alpha]_D^{20}$ = +37.1 (*c* = 1.61, CHCl₃) for the (R)-enantiomer}. – The ¹H NMR spectrum was identical to that reported for the authentic compound.^[16c]

(4S)-Isopropyl-3-[(2-pyridyl)methyl]-1,3-oxazolidin-2-one (22): Yellowish oil; 1.011 g (92%). – $[\alpha]_D^{20}$ = –6.0 (*c* = 1.2, CHCl₃). – ¹H NMR (CDCl₃, 300 MHz): δ = 8.56 (d, *J* = 4.8 Hz, 1 H, Py), 7.75 (m, 1 H, Py), 7.44 (d, *J* = 8.1 Hz, 1 H, Py), 7.27 (m, 1 H, Py), 4.86 (d, *J* = 15.5 Hz, 1 H, PyCH₂), 4.32 (d, *J* = 15.5 Hz, 1 H, PyCH₂), 4.25 (dd, *J* = 9.0 and 12.0 Hz, 1 H, CHCH₂), 4.11 (dd, *J* = 14.7

and 9.0 Hz, 1 H, CHCH_2), 3.78 (m, 1 H, CHCH_2), 2.19 (m, 1 H, CHMe_2), 0.86 and 0.84 (2 d, $J = 7.0$ Hz, CHMe_2). – MS: m/z (%) = 93 (100), 92 (44), 177 (26) [$\text{M}^+ - \text{iPr}$], 65 (15), 133 (11). – $\text{C}_{12}\text{H}_{16}\text{N}_2\text{O}_2$ (220.27): calcd. C 65.43, H 7.32, N 12.72; found C 65.72, H 7.43, N 12.70.

3-Benzyl-(4S)-isopropyl-1,3-oxazolidin-2-one (23): Colourless oil; 0.996 g (91%); $[\alpha]_{\text{D}}^{20} = -25.5$ ($c = 1.1$, CHCl_3). – IR: $\tilde{\nu} = 1747$ (C=O). – ^1H NMR (CDCl_3 , 300 MHz): $\delta = 7.27$ (m, 5 H, Ph), 4.89 (d, $J = 15$ Hz, 1 H, PhCH_2), 4.19 (dd, $J = 9.0$ and 17.7 Hz, CHCH_2), 4.09 (dd, $J = 5.7$ and 9.0 Hz, CHCH_2), 3.98 (d, $J = 15$ Hz, 1 H, PhCH_2), 3.56 (m, 1 H, CHCH_2), 2.08 (m, 1 H, CHMe_2), 0.88 and 0.84 (2 d, $J = 6.9$ Hz, 6 H, CHMe_2). – MS: m/z (%) = 91 (100), 176 (18) [$\text{M}^+ - \text{iPr}$], 65 (10), 92 (8), 219 (4) [M^+]. – $\text{C}_{13}\text{H}_{17}\text{NO}_2$ (219.28): calcd. C 71.21, H 7.81, N 6.39; found C 71.29, H 7.85, N 6.35.

B) Preparation of *O*-[(1-imidazole)carbonyl] Derivatives: The same procedure previously described for the synthesis of 1,3-oxazolidin-2-ones was followed for the preparation of the compounds **26–28**, **35** and **36**. The reactions could not be monitored by GC-MS analyses because these high molecular weight compounds were not eluted. In order to detect the compounds **26** and **27**, which were more labile due to aqueous treatment, the reaction mixtures were analysed by ^1H NMR spectroscopy after evaporating the solvent and dissolving the residue in CDCl_3 ; in these cases, imidazole was present in the reaction mixtures.

(S)-O-[(1-Imidazolyl)carbonyl]-N-[(1S)-1-(2-pyridyl)but-3-en-1-yl]valinol (26): The crude oily product contained also the aziridine **31** (ca. 15%) and trace amounts of the starting material **24**.

26: ^1H NMR (CDCl_3 , 300 MHz): $\delta = 8.56$ (m, 1 H, Py), 8.16 (s, 1 H, Im), 7.64 (m, 1 H, Py), 7.44 (s, 1 H, Im), 7.36 (d, $J = 4.3$ Hz, 1 H, Py), 7.20–7.05 (m, 2 H, Py and Im), 5.70 (m, 1 H, $\text{CH}=\text{CH}_2$), 5.12–4.86 (m, 2 H, $\text{CH}=\text{CH}_2$), 4.53 and 4.36 (2 m, 2 H, CH_2O), 3.91 (t, 1 H, PyCHN), 2.56–2.28 (m, 4 H, $\text{CH}_2=\text{CHCH}_2$, NCHCH_2O and NH), 1.74 (m, 1 H, CHMe_2), 0.93 and 0.86 (2 d, $J = 6.6$ Hz, 6 H, CHMe_2).

(S)-O-[(1-Imidazolyl)carbonyl]-N-[(1S)-1-(2-pyridyl)-2-methylpropyl]valinol (27): The crude oily product contained imidazole and trace amounts of the starting material **4** and aziridine **5**.

27: ^1H NMR (CDCl_3 , 200 MHz): $\delta = 8.58$ (d, $J = 4.3$ Hz, 1 H, Py), 8.17 (s, 1 H, Im), 7.64 (m, 1 H, Py), 7.46 (s, 1 H, Im), 7.30–7.10 (m, 3 H, Py and Im), 4.45 (m, 2 H, CH_2O), 3.48 (d, $J = 6.8$ Hz, 1 H, PyCHN), 2.39 (q, 1 H, NCHCH_2O), 1.93 and 1.75 (2 m, 2 H, CHMe_2), 1.27 (broad, 1 H, NH), 1.0, 0.91, 0.84 and 0.75 (4 d, $J = 6.6$ Hz, 12 H, CHMe_2).

(S)-O-[(1-Imidazolyl)carbonyl]-N-[(1S)-1-(2-pyridyl)-2,2-dimethylbutyl]valinol (28): The crude oily product contained about 25% of the oxazolidinone **30**.

28: ^1H NMR (CDCl_3 , 200 MHz): $\delta = 8.56$ (m, 1 H, Py), 8.15 (s, 1 H, Im), 7.6 (m, 1 H, Py), 7.44 (s, 1 H, Im), 7.25–7.10 (m, 2 H, Py), 7.08 (s, 1 H, Im), 4.42 (d, $J = 4.9$ Hz, CH_2O), 3.58 (s, 1 H, PyCHN), 2.16 (m, 1 H, NCHCH_2), 1.72 (m, 1 H, CHMe_2), 1.35 (m, 2 H, CH_2Me), 0.85–1.0 (m, 15 H, CHMe_2 , $\text{MeCH}_2\text{CMe}_2$).

(S)-O-[(1-Imidazolyl)carbonyl]-N-triphenylmethylvalinol (35): White solid, 1.980 g (90%); m.p. 106–107 °C (cyclohexane). – $[\alpha]_{\text{D}}^{20} = -50.4$ ($c = 0.96$, CHCl_3). – IR (nujol): $\tilde{\nu} = 3252$ (N–H), 1769 (C=O) cm^{-1} . – ^1H NMR (CDCl_3 , 300 MHz): $\delta = 8.04$ (s, 1 H, Im), 7.57 (m, 5 H, Ph), 7.35 (m, 1 H, Im), 7.31–7.16 (m, 10 H, Ph), 7.08 (m, 1 H, Im), 4.10 (dd, $J = 4.2$ and 10.8 Hz, 1 H, CHCH_2), 3.94 (dd, $J = 5.4$ and 11.1 Hz, 1 H, CHCH_2), 2.66 (m, 1 H, CHCH_2), 2.03 (m, 1 H, NH), 1.60 (m, 1 H, CHMe_2), 0.90

and 0.86 (2 d, $J = 6.9$ Hz, CHMe_2). – $\text{C}_{28}\text{H}_{29}\text{N}_3\text{O}_2$ (439.55): calcd. C 76.51, H 6.65, N 9.56; found C 76.55, H 6.70, N 9.51.

(S)-O-[(1-Imidazolyl)carbonyl]-N-triphenylmethylphenylglycinol (36): White solid; 2.065 g (87%); m.p. 132 °C. – $[\alpha]_{\text{D}}^{20} = -46$ ($c = 1$, CHCl_3). – IR: $\tilde{\nu} = 3298$, 3156, 1760 cm^{-1} . – ^1H NMR (CDCl_3 , 300 MHz): $\delta = 7.89$ (m, 1 H, Im), 7.48 (m, 5 H, Ph), 7.27 (s, 1 H, Im), 7.25–7.06 (m, 15 H, Ph), 7.0 (m, 1 H, Im), 4.05 (m, 2 H, CHCH_2), 3.88 (dd, $J = 6.0$ and 9.6 Hz, 1 H, CHCH_2), 2.60 (d, $J = 7.2$ Hz, 1 H, NH). – MS: m/z (%) = 243 (100) [CPh_3], 165 (23), 244 (20), 348 (9) [$\text{M}^+ - \text{CH}_2\text{OCOIm}$], 91 (5), 360 (4). – $\text{C}_{31}\text{H}_{27}\text{N}_3\text{O}_2$ (473.57): calcd. C 78.62, H 5.75, N 8.87; found C 78.71, H 5.85, N 8.80.

C) Preparation of the Aziridines 5, 31 and 32: The procedure previously described for the preparation of oxazolidinones was followed. After the reaction was complete, as indicated by disappearance of the starting β -amino alcohol (TLC analysis), the solvent was evaporated and the residue was taken up with 120 mL of a THF/ H_2O mixture (1:3). After stirring for 2 h, most of the THF was evaporated at reduced pressure and the aqueous phase extracted with Et_2O (3×50 mL), the collected ethereal layers were dried (Na_2SO_4) and concentrated.

(2R)-Isopropyl-1-[(S)-1-(2-pyridyl)but-3-en-1-yl]aziridine (31): Yellowish oil; 0.571 g (52%) was obtained after column chromatography (SiO_2) eluting with cyclohexane/ethyl acetate (80:20); $[\alpha]_{\text{D}}^{20} = -45.1$ ($c = 0.96$, CHCl_3). – ^1H NMR (CDCl_3 , 200 MHz): $\delta = 8.57$ (d, $J = 4.2$ Hz, 1 H, Py), 7.70 (m, 1 H, Py), 7.46 (d, $J = 8.2$ Hz, 1 H, Py), 7.08 (m, 1 H, Py), 5.70 (m, 1 H, $\text{CH}=\text{CH}_2$), 5.06–4.84 (m, 2 H, $\text{CH}=\text{CH}_2$), 2.68 (m, 2 H, PyCHCH_2), 2.57 (m, 1 H, PyCH), 1.72 (d, $J_{\text{cis}} = 3.4$ Hz, 1 H, NCH_2), 1.50 (d, $J_{\text{trans}} = 6.6$ Hz, 1 H, NCH_2), 1.36–1.22 (m, 2 H, NCH-iPr and CHMe_2), 0.79 and 0.49 (2 d, $J = 6.6$ and 6.2 Hz, 6 H, CHMe_2). – $\text{C}_{14}\text{H}_{20}\text{N}_2$ (216.32): calcd. C 77.73, H 9.32, N 12.95; found C 77.77, H 9.36, N 12.90.

0.450 g of a 2:1 mixture of 1,3-oxazolidin-2-one (**29**) and aziridine **31** was also obtained by column chromatography; from the ^1H NMR spectrum (CDCl_3 , 200 MHz), the signals due to the oxazolidinone **29** could be discerned: $\delta = 8.57$ (d, $J = 4.3$ Hz, 1 H, Py), 7.65 (m, 2 H, Py), 7.10 (m, 1 H, Py), 5.82 (m, $\text{CH}=\text{CH}_2$), 5.31–4.95 (m, 3 H, $\text{CH}=\text{CH}_2$ and PyCH), 4.11 (dd, $J = 8.8$ and 12.4 Hz, 1 H, CH_2O), 4.07 (dd, $J = 8.8$ and 4.8 Hz, 1 H, CH_2O), 3.82 (m, 1 H, NCHCH_2O), 3.04 (m, 2 H, $\text{CH}_2=\text{CHCH}_2$), 1.74 (m, 1 H, CHMe_2), 0.75 and 0.47 (2 d, $J = 7.4$ and 6.6 Hz, 6 H, CHMe_2).

(2R)-Isopropyl-1-[(S)-1-(2-pyridyl)-2-methylpropyl]aziridine (5): Yellowish oil; 1.029 g (95%, >95% pure by GC-MS and ^1H NMR analyses); chromatography on a SiO_2 column eluting with cyclohexane/ethyl acetate (85:15) gave pure **5** as a colourless oil; 0.708 g (65%); $[\alpha]_{\text{D}}^{20} = -19.1$ ($c = 0.96$, CHCl_3). – The ^1H NMR spectrum was identical to that previously described.^[10e]

(2R)-Isopropyl-1-[(S)-1-(2-pyridyl)-2,2-dimethylbutyl]aziridine (32): Chromatography of the crude reaction product on an SiO_2 column eluting with cyclohexane/ethyl acetate (80:20) gave a small amount of the aziridine **32**; the fractions mainly containing recovered compound **28** were concentrated and the residue was again chromatographed to obtain further aziridine; the collected aziridine **32**, obtained as a yellowish oil, weighed 0.382 g (31%) and was identical to that previously described.^[10e]

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