Claisen Rearrangements of Allylic and Propargylic Alcohols Prepared by an *N*-Boc-2-acyloxazolidine Methodology − Application to the Synthesis of Original Chiral Building Blocks

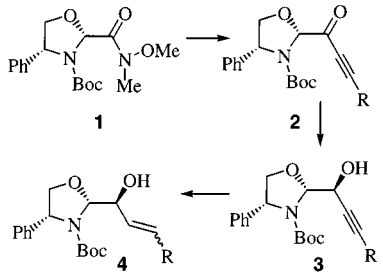
Claude Agami,[a] François Couty,*[a] and Gwilherm Evano[a]

Keywords: Asymmetric synthesis / Claisen rearrangement / Cyclopropanes / Oxazolidines

Stereodefined alkenols prepared in two steps from a Weinreb amide derived from (*R*)-phenylglycinol undergo highly stereoselective Claisen rearrangements. The masked aldehyde moiety of the produced *N*-Boc-alkenyloxazolidines can then be recovered *and reduced* without epimerization, to yield new enantiopure chiral building blocks. Alternatively, epoxidation of these *N*-Boc-2-alkenyloxazolidines by a well-established intramolecular bromocarbamation involving the Boc protecting group occurs stereoselectively. The resulting α,β-epoxyoxazolidines are then transformed into trisubstituted stereodefined cyclopropanes. Claisen rearrangements of propargylic alcohols, on the other hand, stereoselectively give α-allenyloxazolidines. These compounds follow a different pathway to α-alkenyloxazolidines as regards bromocarbamation. An original route to enantiopure 3-hydroxy-4-phenylpiperidine was found in the course of this study.

Introduction

Enantiopure 2-acyl-1,3-oxazolidines are useful heterocycles in asymmetric synthesis. Indeed, 1,2-asymmetric inductions occurring during nucleophilic attack of the carbonyl moiety adjacent to the oxazolidine heterocycle result with good stereocontrol in α-hydroxyoxazolidines.[1] These compounds can be considered as protected forms of α-hydroxy aldehydes and have found applications in asymmetric synthesis. In this field, we have previously developed a practical synthesis of *N*-Boc-2-acyloxazolidines; these compounds were shown to be useful chiral substrates for the synthesis of enantiopure 1,2-diols,[2] and also piperidinic heterocycles including (−)-desoxoprosopinine, (+)-pseudoconhydrine,[3] (+)-conhydrine, and analogues.[4] These acyloxazolidines encompass a particularly interesting family of ketones, of the general structure **2**. These ynones are easily prepared by treatment of the Weinreb amide **1** with a lithium acetylide and can be reduced in a highly stereoselective way (typically with *de* > 95%) by zinc borohydride. The produced alkynol **3** can then be reduced to either of the stereodefined (*E*)- or (*Z*)-allylic alcohols **4**, with Red-Al or H_2 in the presence of Lindlar's catalyst, respectively, while their mesyloxy derivatives were shown to undergo a 1,3-chirality transfer on reaction with organocuprates[5] (Scheme 1).



Scheme 1

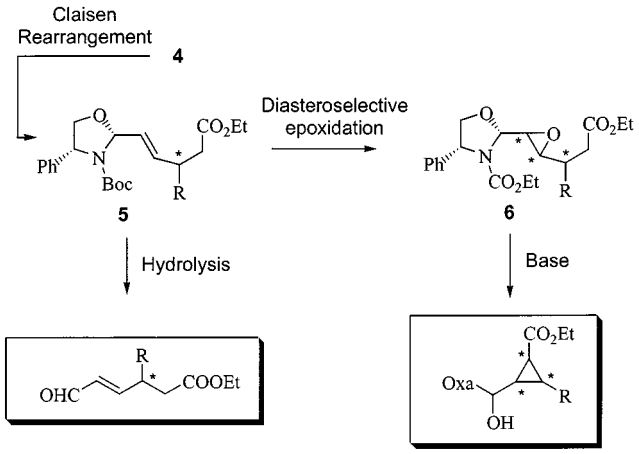
In this article[6] we wish to describe the Claisen rearrangement of allylic alcohols **4**, followed by the recovery of the masked aldehyde moiety present in the γ,δ-unsaturated esters **5** produced. This methodology is also especially well suited for the synthesis of trisubstituted cyclopropanes; the synthesis in this case involves a diastereoselective epoxidation of **5** to give α,β-epoxyoxazolidine **6**, followed by intramolecular nucleophilic opening of the epoxide, through reaction with the ester enolate moiety (Scheme 2).

Furthermore, in this paper we also report the Claisen rearrangements of propargylic alcohols **3**. This rearrangement stereoselectively gives α-allenyloxazolidines, and the chemical behavior of these allenic compounds was investigated.

Finally, in the course of this study, an unexpected intramolecular nucleophilic opening of a carbamate by an ester enolate resulted in an oxazoloazepinone. An intramolecular version of this reaction allowed us to devise a route to an oxazolopiperidinone. This was then transformed into (2*R*,3*R*)-2-hydroxy-3-phenylpiperidine, featuring the substi-

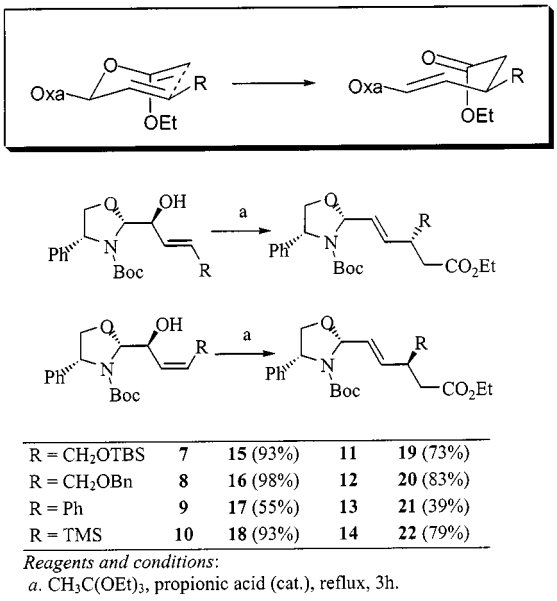
[a] Laboratoire de Synthèse Asymétrique associé au CNRS, Case courrier 47, Université Pierre et Marie Curie,
4 place Jussieu, 75005 Paris, France
Fax: (internat.) + 33-1/44272620
E-mail: couty@ccr.jussieu.fr

  1434−193X/02/0101−0029 $ 17.50+.50/0



Scheme 2

tution pattern found in a new class of antihypertensive compounds.



Scheme 3

Results and Discussion

I. Claisen Rearrangements of Allylic Alcohols Linked to Oxazolidine Rings

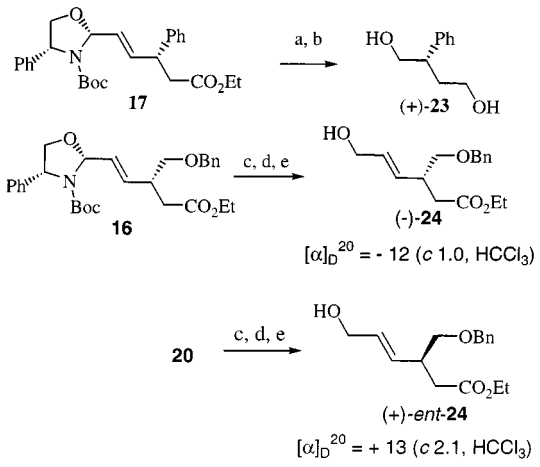
The (*E*)-allylic alcohols **7**−**10** and the (*Z*)-allylic alcohols **11**−**14** were prepared from Weinreb amide **1** by our previously reported three-step sequence.[5] This sequence enabled the hitherto unreported compounds **10**, **13**, and **14** to be synthesized (38, 80, and 48% overall yields, respectively). However, as regards the scope of this synthesis, it should be mentioned that an (*E*)-aliphatic alkenol (**4**, R = C_6H_{13}) was obtained only in a prohibitive 15% yield on Red-Al reduction of the corresponding carbinol (**3**, R = C_6H_{13}).

Claisen rearrangements were performed on these diastereoisomerically pure compounds to afford alkenyloxazolidines **15**−**22** with high levels of stereocontrol; no minor stereoisomer could be detected by NMR in the crude reaction product (Scheme 3). However, the yields of these reactions were low in the cases of compounds **9** and **13** (R = Ph).

The stereochemical course of this reaction is known to be governed by an equatorially substituted chair-like transition state[7] [depicted for an (*E*)-alkenol in Scheme 3], in which the configuration of the double bond in the starting alkenol dictates the configuration of the newly formed stereocenter.

Nevertheless, the sense of this 1,3-chirality transfer was confirmed through the sequence shown in Scheme 4. Oxidative cleavage of the alkenyl moiety in compound **17**, followed by reduction of the resulting aldehyde ester, gave diol (+)-**23**. Determination of the configuration of this diol[8] by examination of its optical rotation thus confirmed the stereochemical course of this reaction.

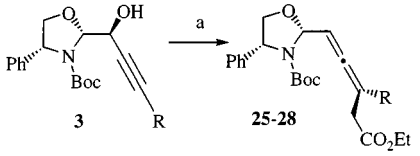
The recovery of the aldehyde moiety masked as an oxazolidine ring in the rearranged products was achieved with alkenyloxazolidines **16** and **20**. To this end, *N*-Boc deprotection (TFA) and mild hydrolysis of the produced ammonium salts gave the corresponding enals, with a concomitant release of (*R*)-phenylglycinol. In order to minimize the possibility of racemization of these enals, they were immediately reduced to allylic alcohols (−)-**24** and (+)-**24** (Scheme 4). The enantiomeric excesses of these alcohols were determined by chiral GC analysis [Chirasil-DEX-CB, 160 °C, t_R = 9.6 and 10.7 min for (−)-**24** and (+)-**24**, respectively] and found to be 98 and 93%, respectively. This demonstrates that little or no racemization occurs during these steps.



Scheme 4. Reagents and conditions: *a*. OsO_4 (cat.), $NaIO_4$, THF/H_2O; *b*. $NaBH_4$, EtOH, 53% overall yield; *c*. CF_3COOH, DCE; *d*. THF, H_2O; *e*. $NaBH_4$, $CeCl_3{\cdot}7H_2O$, EtOH, 0 °C; **24**: 72%, *ent*-**24**: 52%

II. Claisen Rearrangements of Propargylic Alcohols Linked to Oxazolidine Rings

We next turned our attention to Claisen rearrangements of alkynols[9] of general structure **3**. These substrates were found to be slightly less reactive than the allylic alcohols discussed above, and they required 4 h of reflux in triethyl



R:		Yield (%)
C_6H_{13}	**25**	67
CH_2OTBS	**26**	71
Ph	**27**	17
$Si(Me)_3$	**28**	50

Scheme 5. Reagents and conditions: *a*. $CH_3C(OEt)_3$, propionic acid (cat.), reflux, 4 h

orthoacetate to be converted into allenic oxazolidines. However, the rearrangement was again highly stereoselective and gave diastereoisomerically pure allenic compounds **25**−**28** (Scheme 5). A very modest yield, though, was observed when starting with the propargylic alcohol derived from phenylacetylene (**3**, R = Ph).

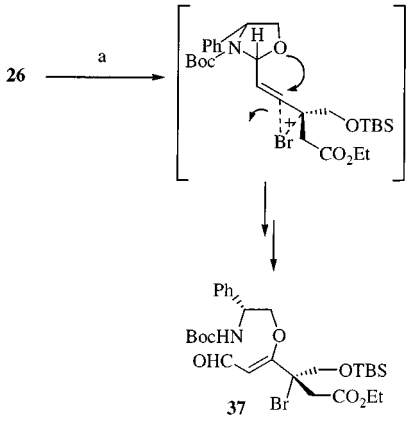
With the aim of recovering the aldehyde moiety from oxazolidine **25**, attempts like those described above in the case of alkenyloxazolidines were made. However, these experiments only produced polymeric compounds, probably because of the instability of the released allenal in acidic media.

III. Diastereoselective Epoxidation of Alkenyloxazolidines Resulting from Claisen Rearrangements

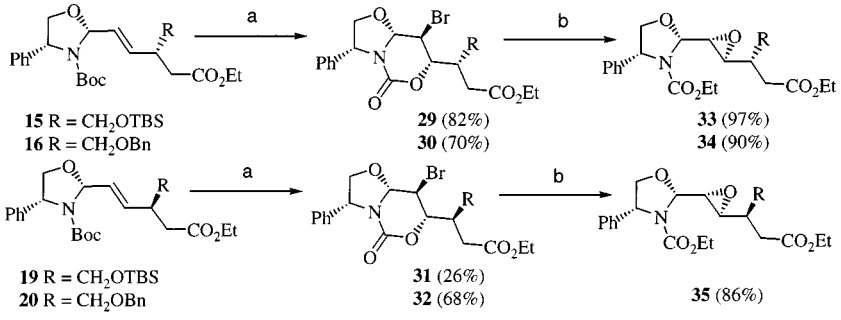
Epoxidation of alkenyloxazolidines **15**, **16**, **19**, and **20** by a two-step procedure was next studied.[10] This epoxidation consisted of an intramolecular bromocarbamation of the alkene moiety, followed by treatment of the resulting bicyclic urethane with sodium ethoxide, as depicted in Scheme 6. As previously reported with similar substrates,[5] the configuration of the stereocenter determined by the Claisen rearrangement does not influence the stereochemical course of the bromocarbamation: Urethanes **29**−**32** were in all cases obtained as unique stereoisomers, within ^{1}H NMR error limits. However, an unsatisfactory yield, most probably due to steric crowding, was obtained in the case of substrate **19**. The relative configurations of these urethanes were deduced from their ^{1}H NMR spectroscopic data and were consistent with previous results.[10,11] Particularly relevant were the ^3J values observed for the signals of the protons located on the bromine-substituted carbon atom; these large coupling constants (8.5 and 10.9 Hz in compound **29**, for example: see Exp. Sect.) unambiguously attested to a *trans*-diaxial geometry for this proton, which is in accordance with the depicted relative configuration in these urethanes. Epoxides **33**−**35** were then obtained in high yields from the corresponding urethanes by treatment with sodium ethoxide.

In the course of this study, iodolactonization[12] of carboxylic acid **36**, prepared by saponification of ester **16**, was investigated. However, this reaction was not chemoselective, and a mixture of uncharacterized compounds was produced, suggesting the occurrence of a competitive iodocarbamation.

As regards bromocarbamation, allenyloxazolidine **26** did not react in the same way as alkenyloxazolidine. In fact, treatment of **26** under the conditions described above gave enal **37** in good yield. This compound results from an opening of the bromonium ion − located on the double bond in a β-position to the oxazolidine ring by the lone pair of the oxygen atom[13] − followed by fragmentation, as depicted in Scheme 7. It should be noted, however, that the (*Z*) or (*E*) geometry of the enal in **37** was not proven unambiguously. The (*Z*) stereochemistry depicted should indeed be the result of the stereospecificity of this *anti*-nucleophilic attack, but a subsequent (*Z*) to (*E*) isomerization in the produced enal cannot be ruled out.



Scheme 7. Reagents and conditions: *a*. NBS, DME/H_2O, 80%

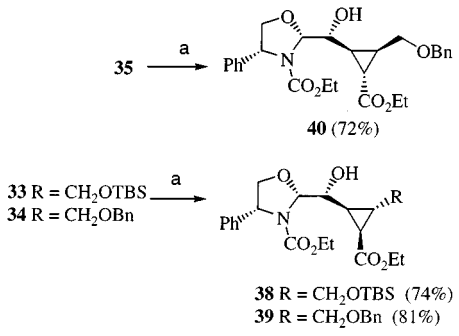


Scheme 6. Reagents and conditions: *a.* NBS, DME/H_2O; *b.* EtONa/EtOH

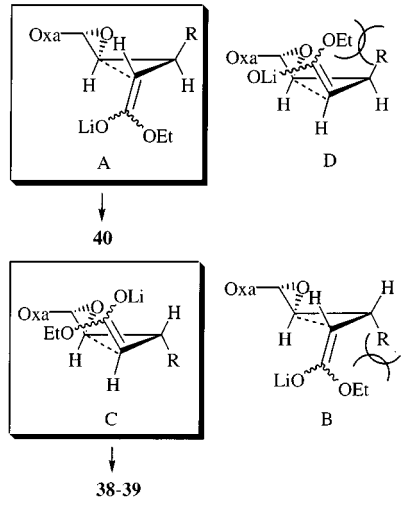
As a matter of fact, of the four diastereofaces of the allenyl moiety, only one gives a bromonium ion that would react further to produce **37**. No competitive intramolecular bromocarbamation of the double bond adjacent to the oxazolidine ring occurs in this reaction. This can be attributed to steric crowding of this double bond by the allene substituents, impeding the formation of the bromonium ion, and the subsequent attack of the bulky carbamate.

IV. Synthesis of Trisubstituted Cyclopropanes

Epoxy esters **33**−**35** were next transformed into trisubstituted cyclopropanes by treatment with LiHMDS at −50 °C (Scheme 8). This 3-*exo*-*trig* cyclisation[14] was highly stereoselective: Again, no minor isomers could be detected by ^{1}H NMR spectroscopy, and the relative configurations of the produced cyclopropanes **38**−**40** were assigned on the basis of the vicinal coupling values [^3J(*cis*) = 4−5 Hz, ^3J(*trans*) = 9 Hz; see Exp. Sect.]. In this reaction, the configuration of the stereocenter created during the Claisen rearrangement governs the stereochemical outcome of the intramolecular cyclopropanation; the ethoxycarbonyl moiety and the R group always show a *trans* relationship in the product. This stereoselectivity can easily be understood in terms of minimization of A$^{(1,3)}$ strain. Indeed, such minimization favors transition states A and C over B and D (Scheme 9.).



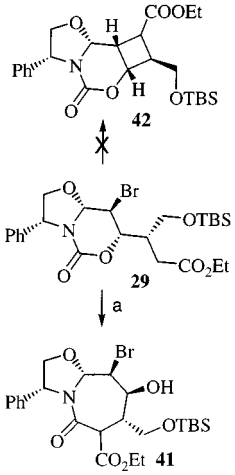
Scheme 8. Reagents and conditions: *a*. LiHMDS, THF, −50 °C



Scheme 9

V. Synthesis of Azepinones and Piperidinones

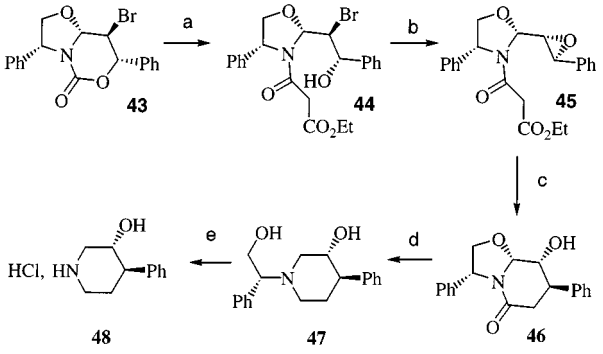
Finally, treatment of the bicyclic urethane **29** with LiHMDS was examined. This reaction gave oxazoloazepinone **41** through an intramolecular opening of the urethane ring by the enolate, instead of the expected intramolecular displacement of the bromine atom, which would yield compound **42** (Scheme 10). Compound **41** was produced as a single diastereomer in which the configuration of the newly created stereogenic center was not determined with certainty, although the value of the ^3J coupling for H(6) [δ = 5.39, ^3J H(6)−H(7) = 5.5 Hz; see Exp. Sect.] strongly suggests a *cis* relationship between H(6) and H(7). AM1 calculations were performed to minimize the conformations of both *cis* and *trans* isomers in **41**. In these minimized conformations, the values of the dihedral angle H(6)−C(6)−C(7)−H(7) are 45° in the *cis* isomer and 90° in the *trans* isomer; the former angle matches well with the observed ^3J value. This reaction represents a new route to polyhydroxylated azepanes, these compounds being good candidates for evaluation as glycosidase inhibitors.[15]



Scheme 10. Reagents and conditions: *a*. LiHMDS, THF, −50 °C, 61%

In order to examine the scope of this unexpected reaction, an intermolecular version was then studied. To this end, bicyclic urethane **43**, easily prepared by bromocarbamation of the corresponding cinnamaldehyde-derived *N*-Boc-alkenyloxazolidine[10] was treated with the lithium enolate of ethyl acetate to produce bromohydrin **44** in high yield, and this compound was then readily transformed into epoxide **45** (Scheme 11). In order to prepare a six-membered oxazolopiperidinone ring, intramolecular nucleophilic opening of this epoxide by the enolate of the β-amido ester was studied. However, this reaction proved to be quite sluggish, and among the numerous conditions investigated for this transformation,[16] NaH in DMF at 110 °C was found to be the best. Under these conditions, oxazolopiperidinone **46** could be isolated in a 41% yield, and deethoxycarbonylation of the ester moiety spontaneously occurred in the same pot. Transformation of this compound into (3*R*,4*R*)-3-hydroxy-4-phenylpiperidine (**48**) was effected in two steps: treatment with lithium aluminium hydride to afford **47**, fol-

lowed by hydrogenolysis. The substitution pattern of this heterocycle is currently of interest, since it has recently been shown that piperidines deriving from this basic framework display strong antihypertensive activity.[17]



Scheme 11. Reagents and conditions: *a*. LiHMDS, EtOAc, −50 °C, 97%; *b*. EtONa/EtOH, quant. yield; *c*. NaH, DMF, 100 °C, 41%; *d*. $LiAlH_4$, Et_2O, 63%; *e*. (i) HCl in EtOAc, (ii) Pd/C, MeOH, H_2, quant. yield

In conclusion, we have shown that Claisen rearrangements of allylic alcohols linked to *N*-Boc-oxazolidine rings provide a new route to enantiopure original chiral building blocks. When this rearrangement is combined with a diastereoselective epoxidation, this methodology permits the synthesis of trisubstituted cyclopropanes.

In the course of this work, during exploration of the reactivity of the esters resulting from the Claisen rearrangement, an unexpected intramolecular nucleophilic attack on a cyclic carbamate by an ester enolate was observed. An intermolecular version of this reaction was used as the key step to devise an original synthesis of (3*R*,4*R*)-3-hydroxy-4-phenylpiperidine, incorporating the basic skeleton of a new class of antihypertensive molecules. This work extends the scope of the use of *N*-Boc-acyloxazolidines in asymmetric synthesis, and further applications of this methodology are under study in our group.

Experimental Section

General: ^1H and ^{13}C spectra ($CDCl_3$ solution unless otherwise stated) were recorded with a Bruker ARX 250 spectrometer at 250 and 62.9 MHz, respectively; chemical shifts are reported in ppm from TMS. Optical rotations were determined with a Perkin−Elmer 141 instrument. All reactions were carried out under argon. Column chromatography was performed on silica gel 230−400 mesh with various mixtures of diethyl ether (Et_2O), ethyl acetate (EtOAc), and petroleum ether (PE). TLCs were run on Merck Kieselgel 60 F_{254} plates. Melting points are uncorrected. THF and ether were distilled from sodium/benzophenone ketyl. Dichloromethane was distilled from calcium hydride. "Usual workup" means: (i) decanting of the organic layer, (ii) extraction of the aqueous layer with ether, (iii) drying of the combined organic phases with $MgSO_4$, and (iv) solvent evaporation under reduced pressure. The compositions of stereoisomeric mixtures were determined by NMR analysis on crude products before any purification.

General Procedure for the Synthesis of Ynones 2: See ref.[5]

General Procedure for the $Zn(BH_4)_2$-Mediated Reduction of Ynones 2: See ref.[5]

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-[(1*S*)-1-hydroxy-3-trimethylsilyl-prop-2-ynyl]-4-phenyl-1,3-oxazolidine (3, R = TMS): Yield: 92%; R_f = 0.65 (Et_2O/PE, 1:1); m.p. 157 °C; $[\alpha]_D^{20}$ = +27 (*c* = 1.2, $CHCl_3$). ^1H NMR: δ = 0.14 (s, 9 H), 1.25 (br. s, 9 H), 4.19−4.35 (m, 2 H), 4.79 (dd, *J* = 8.9 and 2, 1 H), 4.84 (bm, 1 H), 4.87 (br. s, 1 H), 5.59 (d, *J* = 2, 1 H), 7.26−7.40 (m, 3 H), 7.48−7.57 (m, 2 H). ^{13}C NMR: δ = −0.1 (CH_3), 27.6 (CH_3), 61.0 (CH), 64.8 (CH), 65.3 (Cq), 74.0 (CH_2), 81.5 (Cq), 91.2, 91.7 (Cq), 126.7, 127.2, 128.0 (CH), 139.5 (Cq), 154.6 (Cq). IR: ν̃ = 3345, 2170, 1675. $C_{20}H_{24}NO_4Si$ (375.5): C 63.97, H 7.78, N 3.73; found C 63. 94, H 7.91, N 3.62.

General Procedure for the Red-Al-Mediated Reduction of Propargylic Alcohols 3: See ref.[5]

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-[(1*S*,2*E*)-1-hydroxy-3-trimethylsilylprop-2-enyl]-4-phenyl-1,3-oxazolidine (10): Yield: 52%; R_f = 0.56 (Et_2O/PE, 1:1); m.p. 131 °C; $[\alpha]_D^{20}$ = +40 (*c* = 0.7, $CHCl_3$). ^1H NMR: δ = 0.00 (s, 9 H), 1.23 (br. s, 9 H), 4.03 (dd, *J* = 8.9 and 4.9, 1 H), 4.23 (dd, *J* = 8.9 and 4.6, 1 H) 4.41 (br. s, 1 H), 4.63−4.79 (br. m, 1 H), 5.19 (br. s, 1 H), 6.00−6.19 (m, 2 H), 7.15−7.32 (m, 5 H). ^{13}C NMR: δ = −1.3 (CH_3), 28.1 (CH_3), 60.8 (CH), 73.5 (CH_2), 74.7 (CH), 81.5 (Cq), 93.0 (CH), 128.0, 128.6, 129.4, 132.2 (CH), 140.6 (Cq), 143.3 (CH), 154.6 (Cq). IR: ν̃ = 3380, 1675, 1625.

General Procedure for the Lindlar-Catalyzed Hydrogenation of Ynols 3: See ref.[5]

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-[(1*S*,2*Z*)-1-hydroxy-3-phenylprop-2-enyl]-4-phenyl-1,3-oxazolidine (13): Yield: 93%; R_f = 0.63 (Et_2O/PE, 2:8); oil; $[\alpha]_D^{20}$ = +22 (*c* = 0.6, $CHCl_3$). ^1H NMR: δ = 1.24 (s, 9 H), 3.97 (dd, *J* = 8.9 and 5.8, 1 H), 4.21 (dd, *J* = 8.9 and 7.1, 1 H), 4.73−4.87 (bm, 2 H), 5.25 (br. s, 1 H), 5.79 (dd, *J* = 11.7 and 9.9), 6.70 (d, *J* = 11.7, 1 H), 7.13−7.40 (m, 5 H). ^{13}C NMR: δ = 28.4 (CH_3), 60.9 (CH), 68.2 (CH), 73.3 (CH_2), 81.5 (Cq), 93.0 (CH), 126.7, 127.5, 128.5, 128.6, 128.9, 134.2 (CH), 136.5, 140.2 (Cq), 155.0 (Cq). IR: ν̃ = 3420, 1690, 1620.

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-[(1*S*,2*Z*)-1-hydroxy-3-trimethylsilylprop-2-enyl]-4-phenyl-1,3-oxazolidine (14): Yield: 65%; R_f = 0.75 (Et_2O/PE, 1:1); m.p. 76 °C; $[\alpha]_D^{20}$ = +39 (*c* = 1.0, $CHCl_3$). ^1H NMR: δ = 0.15 (s, 9 H), 1.33 (br. s, 9 H), 4.11 (dd, *J* = 8.7 and 5.1, 1 H), 4.25 (dd, *J* = 8.7 and 7.1, 1 H), 4.54−4.64 (br. m, 1 H), 4.84−4.93 (br. s, 1 H), 5.24 (br. s, 1 H), 5.85 (dd, *J* = 14.2 and 0.9), 6.39 (dd, *J* = 14.2 and 8.3, 1 H), 7.26−7.45 (m, 3 H), 7.47−7.53 (m, 2 H). ^{13}C NMR: δ = 0.5 (CH_3), 28.2 (CH_3), 60.9 (CH), 72.2 (CH_2), 73.4 (CH), 81.6 (Cq), 93.1 (CH), 127.1, 127.6, 128.4, 134.8 (CH), 140.8 (Cq), 144.9 (CH), 154.8 (Cq). R: ν̃ = 3400, 1692, 1622.

General Procedure for the Claisen Rearrangement of Propargylic Alcohols 3 and of Allylic Alcohols 7−14: A solution of propargylic alcohol or allylic alcohol (1.3 mmol) and propionic acid (3 drops) in triethyl orthoacetate (5 mL) was heated under reflux (Dean−Stark) while propionic acid (3 drops) was added every hour. The reaction was monitored by TLC and required ca. 4 h to reach completion for alkynols, and 3 h for allylic alcohols. At this time, concentration under reduced pressure was followed by flash chromatography to afford allenic or alkenyloxazolidines as clear oils.

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-[(1*E*,3*R*)-4-*tert*-butyldimethylsilyloxy-3-ethoxycarbonylmethylbut-1-enyl]-4-phenyl-1,3-oxazolidine (15): Yield: 93%; flash chromatography: Et_2O/PE, 1:9; oil;

R_f = 0.73 (Et_2O/PE, 1:1); $[\alpha]_D^{20}$ = −7 (*c* = 0.9; $CHCl_3$). ^1H NMR: δ = 0.00 (s, 6 H), 0.84 (s, 9 H), 1.18 (t, *J* = 7.1, 3 H), 1.30 (s, 9 H), 2.27 (dd, *J* = 15.5 and 8.2, 1 H), 2.58 (dd, *J* = 15.5 and 5.8, 1 H), 2.73−2.87 (m, 1 H), 3.49 (dd, *J* = 9.8 and 6.8, 1 H), 3.61 (dd, *J* = 9.8 and 5.2, 1 H), 3.87−3.94 (m, 1 H), 3.99−4.09 (m, 2 H), 4.17−4.26 (m, 1 H), 4.80−4.95 (bm, 1 H), 5.50−5.75 (m, 2 H), 5.82 (dd, *J* = 15.0 and 7.5, 1 H), 7.17−7.31 (m, 5 H). ^{13}C NMIR: δ = −5.3, 14.2 (CH_3), 18.3 (Cq), 25.9, 28.3 (CH_3), 36.0 (CH_2), 41.1 (CH), 60.2 (CH_2), 60.6 (CH), 65.4, 73.2 (CH_2), 80.4 (Cq), 89.6, 126.6, 127.4, 128.6, 128.9, 134.1 (CH), 140.7, 153.4, 172.3 (Cq). IR: ν̃ = 3030, 2930, 1720, 1700. − $C_{28}H_{45}NO_6Si$ (519.8): C 64.70, H 8.73, N 2.69; found C 64.61, H 8.82, N 2.71.

(2*R*,4*R*)-2-[(1*E*,3*R*)-4-Benzyloxy-3-ethoxycarbonylmethylbut-1-enyl]-3-*tert*-butoxycarbonyl-4-phenyl-1,3-oxazolidine (16): Yield: 98%; flash chromatography: EtOAc/PE, 2:8; oil; R_f = 0.5 (Et_2O/PE, 1:1); $[\alpha]_D^{20}$ = −13 (*c* = 2.6; $CHCl_3$). ^1H NMIR: δ = 1.20 (t, *J* = 7.1, 3 H), 1.32 (s, 9 H), 2.37 (dd, *J* = 15.4 and 8.0, 1 H), 2.61 (dd, *J* = 15.4 and 6.5, 1 H), 2.99 (sext, *J* = 6.5, 1 H), 3.40 (dd, *J* = 9.6, 6.9 Hz, 1 H), 3.50 (dd, *J* = 9.6 and 5.4, 1 H), 3.93 (dd, *J* = 8.6 and 5.2, 1 H), 4.03−4.13 (m, 2 H), 4.23 (dd, *J* = 8.6 and 6.8, 1 H), 4.47 (s, 2 H), 4.70−4.93 (br. s, 1 H), 5.54 (s, 1 H), 5.71 (dd, *J* = 15.0 and 4.6, 1 H), 5.88 (dd, *J* = 15.2 and 7.6, 1 H), 7.17−7.33 (m, 5 H). ^{13}C NMIR: δ = 14.3, 28.3 (CH_3), 36.7 (CH_2), 38.9 (CH), 60.3 (CH_2), 60.4 (CH), 65.4, 72.7, 73.1 (CH_2), 80.5 (Cq), 89.6, 126.7, 127.5, 128.4, 128.5, 129.0 134.2 (CH), 138.3, 140.7, 153.5, 172.3 (Cq). IR: ν̃ = 3030, 2980, 1730, 1700.

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-[(1*E*,3*R*)-4-ethoxycarbonyl-3-phenylbut-1-enyl]-4-phenyl-1,3-oxazolidine (17): Yield: 55%; flash chromatography: EtOAc/PE, 1:9; oil; R_f = 0.8 (Et_2O/PE, 1:1); $[\alpha]_D^{20}$ = −8 (*c* = 0.8; $CHCl_3$). ^1H NMIR: δ = 1.05 (t, *J* = 7.1, 3 H), 1.20 (s, 9 H), 2.68 (ABX, *J* = 15.1 and 8.0, 1 H), 3.82−4.06 (m, 4 H), 4.15 (dd, *J* = 8.6 and 6.8, 1 H), 4.70−4.90 (br. s, 1 H), 5.45−5.68 (m, 2 H), 6.00 (dd, *J* = 14.9 and 6.9, 1 H), 5.88 (dd, *J* = 15.2 and 7.6, 1 H), 7.09−7.24 (m, 10 H). ^{13}C NMIR: δ = 14.1, 28.2 (CH_3), 40.3 (CH_2), 44.2 (CH), 60.4 (CH_2), 60.5 (CH), 73.2 (CH_2), 80.5 (Cq), 89.4, 126.5, 126.8, 127.4, 127.6, 128.5, 128.6, 136.7 (CH), 140.7, 142.1, 153.4, 171.6 (Cq). IR: ν̃ = 3060, 3030, 1730.

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-[(1*E*,3*R*)-4-ethoxycarbonyl-3-trimethylsilylbut-1-enyl]-4-phenyl-1,3-oxazolidine (18): Yield: 93%; flash chromatography: Et_2O/PE, 1:9; oil; R_f = 0.76 (Et_2O/PE, 1:1); $[\alpha]_D^{20}$ = −3 (*c* = 0.8; $CHCl_3$). ^1H NMIR: δ = −0.03 (s, 9 H), 1.13 (t, *J* = 7.1, 3 H), 1.24 (s, 9 H), 2.11 (q, *J* = 7.4, 1 H) 2.38 (d, *J* = 7.1, 2 H), 3.87 (dd, *J* = 8.8 and 6.0, 1 H), 3.95−4.08 (m, 2 H), 3.99−4.09 (m, 2 H), 4.21 (dd, *J* = 8.8 and 6.9, 1 H), 4.78−4.88 (br. m, 1 H), 5.42 (dd, *J* = 15.4 and 5.8, 1 H), 5.57 (d, *J* = 5.8, 1 H), 5.83 (dd, *J* = 15.4 and 8.3, 1 H), 7.19−7.28 (m, 5 H). ^{13}C NMIR: δ = −3.1, 14.4, 28.4 (CH_3), 29.4 (CH), 34.0, 60.5 (CH_2), 60.7 (CH), 73.3 (CH_2), 80.4 (Cq), 90.2, 125.6, 126.4, 127.6, 128.6, 135.2 (CH), 140.9, 153.6, 173.4 (Cq). IR: ν̃ = 3030, 2980, 1720, 1700. GC (OV17, 250 °C), t_R = 7.45 min. MS (CI; NH_3): *m*/*z* (%): 464 (45), 392 (100), 348 (36), 302 (20), 258 (24), 236 (56), 148 (8), 60 (8). $C_{24}H_{37}NO_5Si$ (447.6): C 64.39, H 8.33, N 3.13; found C 64.46, H 8.29, N 3.04.

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-[(1*E*,3*S*)-4-*tert*-butyldimethylsilyloxy-3-ethoxycarbonylmethylbut-1-enyl]-4-phenyl-1,3-oxazolidine (19): Yield: 73%; flash chromatography: Et_2O/PE, 1:9; oil; R_f = 0.73 (Et_2O/PE, 1:1); $[\alpha]_D^{20}$ = +10 (*c* = 1.9; $CHCl_3$). ^1H NMIR: δ = 0.00 (s, 6 H), 0.84 (s, 9 H), 1.18 (t, *J* = 7.1, 3 H), 1.31 (s, 9 H), 2.29 (dd, *J* = 15.7 and 8.1, 1 H), 2.60 (dd, *J* = 15.7 and 6.2, 1 H), 2.74−2.86 (m, 1 H), 3.50−3.63 (m, 1 H), 3.63 (dd, *J* = 8.9 and 4.9, 1 H), 3.87−3.94 (m, 1 H), 3.99−4.09 (m, 2 H), 4.17−4.26 (m, 1 H) 4.80−4.95 (bm, 1 H), 5.50−5.75 (m, 2 H), 5.83 (dd, *J* = 15.4 and 7.5, 1 H), 7.19−7.33 (m, 5 H). ^{13}C NMIR: δ = −5.3, 14.2 (CH_3), 18.3 (Cq), 25.9, 28.2 (CH_3), 36.1 (CH_2), 41.8 (CH), 60.2 (CH_2), 60.6 (CH), 65.3, 73.2 (CH_2), 80.4 (Cq), 89.6, 126.6, 127.4, 128.6, 128.9, 134.2 (CH), 140.6, 153.4, 172.3 (Cq). IR: ν̃ = 3030, 2930, 1720, 1700.

(2*R*,4*R*)-2-[(1*E*,3*S*)-4-Benzyloxy-3-ethoxycarbonylmethylbut-1-enyl]-3-*tert*-butoxycarbonyl-4-phenyl-1,3-oxazolidine (20): Yield: 83%; flash chromatography: Et_2O/PE, 2:8; oil; R_f = 0.50 (Et_2O/PE, 6:4); $[\alpha]_D^{20}$ = +8 (*c* = 2.4; $CHCl_3$). ^1H NMIR: δ = 1.20 (t, *J* = 7.1, 3 H), 1.32 (s, 9 H), 2.37 (dd, *J* = 15.5 and 7.8, 1 H) 2.38 (dd, *J* = 15.5 and 6.2, 1 H), 2.99 (b sext, *J* = 6.7, 1 H), 3.40 (dd, *J* = 9.2 and 7.0, 1 H), 3.50 (dd, *J* = 9.2 and 5.5, 1 H), 3.93 (dd, *J* = 8.7 and 5.5, 1 H), 4.03−4.13 (m, 2 H), 4.24 (dd, *J* = 8.7 and 6.7, 1 H) 4.47 (s, 2 H) 4.70−4.93 (br. s, 1 H), 5.58 (br. s, 1 H), 5.71 (dd, *J* = 15.6 and 5.1, H), 5.86 (dd, *J* = 15.6 and 7.5, 1 H), 7.16−7.33 (m, 10 H),. ^{13}C NMIR: δ = 14.3, 28.3 (CH_3), 36.7 (CH_2), 38.9 (CH), 60.3 (CH_2), 60.4 (CH), 66.0, 72.6, 73.1 (CH_2), 80.6 (Cq), 89.6, 126.7, 127.5, 127.6, 128.4, 128.5, 129.0, 134.2 (CH), 138.3, 140.7, 153.5, 172.3 (Cq). IR: ν̃ = 3030, 2980, 1730, 1700. $C_{29}H_{37}NO_6$ (495.6): C 70.28, H 7.52, N 2.83; found C 70.62, H 7.55, N 2.70.

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-[(1*E*,3*S*)-4-ethoxycarbonyl-3-phenylbut-1-enyl]-4-phenyl-1,3-oxazolidine (21): Yield: 39%; flash chromatography: EtOAc/PE, 1:9; oil; R_f = 0.75 (Et_2O/PE, 1:1); $[\alpha]_D^{20}$ = +15 (*c* = 0.8; $CHCl_3$). ^1H NMIR: δ = 1.05 (t, *J* = 7.1, 3 H), 1.23 (s, 9 H), 2.68 (ABX, *J* = 15.1 and 7.7, 1 H), 3.82−4.01 (m, 4 H), 4.16 (dd, *J* = 8.8 and 6.9, 1 H), 4.70−4.90 (br. s, 1 H), 5.50−5.68 (m, 2 H), 6.00 (dd, *J* = 14.9 and 7.2, 1 H), 7.09−7.24 (m, 10 H). ^{13}C NMIR: δ = 14.1, 28.2 (CH_3), 40.3 (CH_2), 44.1 (CH), 60.4 (CH_2), 60.5 (CH), 73.3 (CH_2), 80.5 (Cq), 89.4, 126.5, 126.8, 127.4, 127.6, 128.5, 128.6, 136.4 (CH), 140.6, 142.1, 153.4, 171.6 (Cq). IR: ν̃ = 3060, 3030, 1730.

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-[(1*E*,3*S*)-4-ethoxycarbonyl-3-trimethylsilyl-but-1-enyl]-4-phenyl-1,3-oxazolidine (22): Yield: 79%; flash chromatography: Et_2O/PE, 1:9; oil; R_f = 0.75 (Et_2O/PE, 50:50); $[\alpha]_D^{20}$ = +11 (*c* = 0.8; $CHCl_3$). ^1H NMIR: δ = 1.19 (s, 9 H), 1.21 (t, *J* = 7.1, 3 H), 1.31 (s, 9 H), 2.15 (q, *J* = 7.7, 1 H), 2.42 (d, *J* = 6.5, 2 H), 3.85 (dd, *J* = 8.9 and 6.2, 1 H), 4.03−4.15 (m, 2 H), 4.28−4.31 (m, 1 H), 4.77−4.85 (br. m, 1 H), 5.39 (ddd, *J* = 15.4, 5.6 and 1.2, 1 H), 5.57 (d, *J* = 5.6, 1 H), 5.75−5.90 (br. m, 1 H), 7.17−7.26 (m, 5 H). ^{13}C NMIR: δ = − 3.0, 14.5, 28.5 (CH_3), 29.3 (CH), 34.2, 60.6 (CH_2), 60.9 (CH), 73.4 (CH_2), 80.5 (Cq), 90.0, 125.7, 126.8, 127.6, 128.6, 134.9 (CH), 140.8, 154.2, 173.4 (Cq). IR: ν̃ = 3030, 2980, 1710.

(*S*)-2-Phenylbutane-1,4-diol (23): An aqueous solution of OsO_4 (4 wt.%; 0.1 mL, 0.27 mmol) was added at 0 °C to a solution of **17** (120 mg, 0.27 mmol) in a THF/water mixture (1:1; 4 mL) . After 10 min, sodium periodate (300 mg, 1.4 mmol) was added and the mixture was stirred at room temp. for 8 h. Addition of an aqueous solution of sodium thiosulfate (10wt.%; 5 mL) was followed by the usual workup (Et_2O). The oily residue was then taken up in ethanol (4 mL) and treated with sodium borohydride (52 mg, 1.38 mmol). After 5 h, the reaction medium was hydrolyzed by addition of a saturated aqueous solution of NH_4Cl (5 mL) and the ethanol was distilled off under reduced pressure. The usual workup (Et_2O) was followed by flash chromatography (Et_2O/PE, 1:1) to give diol **23** as a clear oil (24 mg, 53%). $[\alpha]_D^{20}$ = +29.0 (*c* = 0.6; MeOH) {ref.[8] $[\alpha]_D^{20}$ = +29.4 (*c* = 0.7; MeOH)}. ^1H NMIR: δ = 1.84−2.07 m, 4 H), 2.95 (br. quint, *J* = 7.5, 1 H), 3.56−3.79 (m, 4 H), 7.19−7.36 (m, 5 H). ^{13}C NMIR: δ = 39.5 (CH_2), 46.1 (CH), 61.3, 67.7 (CH_2), 127.0, 127.8, 128.0, 128.9 (CH), 142.4 (Cq).

Ethyl (*R*)-3-Benzyloxymethyl-6-hydroxyhex-3-enoate [(−)-24]: Trifluoroacetic acid (0.57 mL) was added to a solution of **16** (200 mg, 0.4 mmol) in 1,2-dichloroethane (3 mL). After 20 min, the solvent was removed under reduced pressure and the crude oil was taken up in a mixture of THF and water (1:1; 4 mL). After 1 h of stirring, the usual workup (Et_2O) gave an oil that was dissolved in ethanol (3 mL). $CeCl_3$ (7 H_2O) was added to this solution at 0 °C (180 mg, 0.48 mmol), followed after 10 min by sodium borohydride (18 mg, 0.48 mmol). After 1 h at 0 °C, the reaction medium was hydrolyzed by addition of a saturated aqueous solution of NH_4Cl (5 mL), and the ethanol was distilled off under reduced pressure. The usual workup (Et_2O) was followed by flash chromatography (EtOAc/PE, 3:7) and gave (−)-**24** as a clear oil (81 mg, 72%). R_f = 0.3 (Et_2O/PE, 7:3); $[\alpha]_D^{20}$ = −12 (*c* = 1.0; $CHCl_3$). ^1H NMIR: δ = 1.20 (t, *J* = 7.2, 3 H), 2.32 (dd, *J* = 15.2 and 8.0, 1 H), 2.56 (dd, *J* = 15.2 and 6.0, 1 H), 2.68 (br. s, 1 H), 2.90 (br. sext, *J* = 6.8, 1 H), 3.37 (dd, *J* = 9.2 and 7.0, 1 H), 3.46 (dd, *J* = 9.2 and 5.6, 1 H), 4.02−4.11 (m, 4 H), 4.48 (br. s, 2 H), 5.54−5.74 (m, 2 H), 7.25−7.33 (m, 5 H). ^{13}C NMIR: δ = 14.1 (CH_3), 36.8 (CH_2), 38.1 (CH), 60.3, 63.0, 72.7, 72.9 (CH_2), 127.6, 128.3, 131.0, 131.5 (CH), 138, 172.5 (Cq). IR: ṽ = 3435, 2860, 1730. GC (OV 17, 120 °C then gradient of 5 °C/min): t_R = 17.2 min. Chiral GC (Chirasil-DEX-CB, 156 °C): t_R = 9.6 min. MS (EI): *m*/*z* (%): 278 (3), 261 (100), 231 (18), 215 (3), 187 (6), 171 (47), 155 (88), 130 (31), 91 (35), 65 (16), 41 (3).

Ethyl (*S*)-2-Benzyloxymethyl-6-hydroxyhex-4-enoate [(+)-24]: This compound was prepared by the procedure described for (−)-**24**, starting with **20** (1 g, 2.09 mmol), and was obtained as an oil (305 mg, 52%). It displays the same spectroscopic data as described for (−)-**24**. $[\alpha]_D^{20}$ = +13 (*c* = 2.1; $CHCl_3$). Chiral GC (Chirasil-DEX-CB, 156 °C): t_R = 10.7 min. $C_{16}H_{22}O_4$ (278.3): C 69.04, H 7.97; found C 68.89, H 8.14.

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-[(2*R*)-3-ethoxycarbonylmethylnona-1,2-dienyl]-4-phenyl-1,3-oxazolidine (25): Yield: 67%; flash chromatography: Et_2O/PE, 1:9; R_f = 0.5 (Et_2O/PE, 4:6); $[\alpha]_D^{20}$ = +26 (*c* = 1.9, $CHCl_3$). ^1H NMIR: δ = 0.79 (t, *J* = 6.9, 3 H), 1.10−1.38 (m, 20 H), 2.00 (m, 2 H), 2.90 (dd, *J* = 15.4 and 1.8, 1 H), 2.99 (dd, *J* = 15.4 and 1.8, 1 H), 3.88 (dd, *J* = 8.9 and 6.8, 1 H), 4.04 (q, *J* = 6.9, 2 H), 4.25 (dd, *J* = 8.9 and 6.8, 1 H), 4.75−4.88 (br. m, 1 H), 4.36−5.43 (m, 1 H), 5.70 (d, *J* = 4.9, 1 H), 7.15−7.29 (m, 5 H). ^{13}C NMIR: δ = 14.2, 14.3 (CH_3), 22.7, 27.3, 28.3, 29.0, 31.8, 32.0, 38.8 (CH_2), 60.7 (CH), 60.8, 73.4 (CH_2), 80.5 (Cq), 87.9 (CH), 92.4 (CH), 102.0 (Cq), 126.5, 127.2, 128.5 (CH), 140.4 (Cq), 153.3 (Cq), 171.0 (Cq), 202.7 (Cq). IR: ṽ = 2930, 2855, 1717. $C_{27}H_{39}NO_5$ (457.6): C 70.87, H 8.59, N 3.06; found C 70.95, H 8.61, N 2.96.

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-[(2*S*)-3-*tert*-butyldimethylsilyloxymethyl-4-ethoxycarbonylbuta-1,2-dienyl]-4-phenyl-1,3-oxazolidine (26): Yield: 71%; flash chromatography: Et_2O/PE, 1:9; R_f = 0.8 (Et_2O/PE, 5:5); $[\alpha]_D^{20}$ = +44 (*c* = 1.3, $CHCl_3$). ^1H NMIR: δ = 0.07 (s, 6 H), 0.89 (s, 9 H), 1.24 (t, *J* = 7.1, 3 H), 1.32 (s, 9 H), 3.00 (dd, *J* = 16.0 and 2.2, 1 H), 3.09 (dd, *J* = 16.0 and 2.2, 1 H), 3.97 (dd, *J* = 8.9 and 6.8, 1 H), 4.10 (q, *J* = 7.1, 2 H), 4.27 (t, *J* = 2.3, 2 H), 4.31 (dd, *J* = 8.9 and 6.8, 1 H), 4.75−4.88 (bm, 1 H), 5.43−5.50 (m, 1 H), 5.77 (d, *J* = 4.6, 1 H), 7.22−7.36 (m, 5 H). ^{13}C NMIR: δ = −5.3, 14.3 (CH_3), 18.5 (Cq), 26.0, 28.3 (CH_3), 34.8 (CH_2), 60.8 (CH), 60.9, 63.2, 73.5 (CH_2), 80.5 (Cq), 87.6 (CH), 93.1 (CH), 102.0 (Cq), 126.7, 127.4, 128.6 (CH), 140.4 (Cq), 152.3 (Cq), 170.9 (Cq), 202.7 (Cq). IR: ṽ = 2930, 1979, 1700. $C_{28}H_{43}NO_6Si$ (517.7): C 64.96, H 8.37, N 2.71; found C 64.82, H 8.71, N 2.51.

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-[(2*S*)-4-ethoxycarbonyl-3-phenylbuta-1,2-dienyl]-4-phenyl-1,3-oxazolidine (27): Yield: 17%; flash chromatography: EtOAc/PE, 1:9; R_f = 0.5 (Et_2O/PE, 5:5); $[\alpha]_D^{20}$ = +41 (*c* = 0.6, $CHCl_3$). ^1H NMIR: δ = 1.07 (t, *J* = 6.9, 3 H), 1.21 (s, 9 H), 3.42 (s, 2 H), 3.85−4.29 (m,4 H), 4.80 (br. s, 1 H), 5.77−5.82 (m, 2 H), 7.10−7.95 (m, 10 H). ^{13}C NMIR: δ = 14.3, 28.3 (CH_3), 37.0 (CH_2), 60.4 (CH), 61.0, 73.6 (CH_2), 80.9 (Cq), 87.7, 89.4 (CH), 94.7 (Cq), 126.3, 126.5, 127.5, 128.3, 128.8, 128.9 (CH), 139.9, 140.5 (Cq), 154.1 (Cq), 170.8 (Cq), 205.8 (Cq).

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-[(2*S*)-4-ethoxycarbonyl-3-trimethylsilylbuta-1,2-dienyl]-4-phenyl-1,3-oxazolidine (28): Yield: 50%; flash chromatography: Et_2O/PE, 1:9; R_f = 0.7 (Et_2O/PE, 4:6); $[\alpha]_D^{20}$ = +53 (*c* = 0.9, $CHCl_3$). ^1H NMIR: δ = 0.16 (s, 9 H), 1.23 (t, *J* = 7.1, 3 H), 1.31 (s, 9 H), 2.99 (dd, *J* = 15.4 and 2.1, 1 H), 3.08 (dd, *J* = 15.4 and 2.4, 1 H), 3.96 (dd, *J* = 8.8 and 6.9, 1 H), 4.10 (q, *J* = 7.1, 2 H), 4.33 (dd, *J* = 8.8 and 7.1, 1 H) 4.80−4.92 (br. m, 1 H), 5.25−5.29 (m, 1 H), 5.83 (d, *J* = 5.2, 1 H), 7.25−7.29 (m, 5 H). ^{13}C NMIR: δ = −1.4, 14.2, 28.2 (CH_3), 35.8 (CH_2), 60.8 (2 CH), 73.6 (CH_2), 80.4 (Cq), 86.9, 87.8 (CH), 94.0 (Cq), 126.5, 127.5, 128.3 (CH), 140.6 (Cq), 153.2 (Cq), 171.4 (Cq), 206.2 (Cq).

(3*R*,7*S*,8*S*,9*R*)-8-Bromo-7-[(1*S*)-2-*tert*-butyldimethylsilyloxy-1-ethoxycarbonylmethylethyl]-3-phenyltetrahydrooxazolo[3,2-*c*][1,3]-oxazin-5-one (29): *N*-Bromosuccinimide (90 mg, 0.5 mmol) was added to a solution of **15** (200 mg, 0.38 mmol) in a mixture of DME/water (1:1; 2 mL). After this had stirred for 2 h at room temp., water (10 mL) was added. The usual workup (CH_2Cl_2), followed by flash chromatography (Et_2O/PE, 1:1), gave **29** as a clear oil (170 mg, 82%). R_f = 0.1 (Et_2O/PE, 1:1); $[\alpha]_D^{20}$ = +31 (*c* = 1.5; $CHCl_3$). ^1H NMIR: δ = 0.03 (s, 6 H), 0.9 (s, 9 H), 1.25 (t, *J* = 7.1, 3 H), 2.30−2.52 (m, 2 H), 2.92−3.05 (m, 1 H), 3.50 (dd, *J* = 10.6 and 4.5, 1 H), 3.80 (dd, *J* = 10.6 and 9.2, 1 H), 4.10−4.32 (m, 4 H), 4.51 (dd, *J* = 10.9 and 1.2, 1 H), 4.69 (dd, *J* = 10.9 and 8.7, 1 H), 4.94 (dd, *J* = 6.8 and 1.5, 1 H), 4.98 (d, *J* = 8.7, 1 H), 7.23−7.32 (m, 5 H). ^{13}C NMIR: δ = −5.3, 14.3 (CH_3), 18.2 (Cq), 26.0 (CH_3), 33.6 (CH_2), 37.5, 44.5, 60.8 (CH), 60.9, 61.6, 73.9 (CH_2), 79.6, 89.6, 126.5, 128.2, 128.8 (CH), 140.0, 149.0, 172.1 (Cq). IR: ṽ = 2927, 1730. $C_{24}H_{36}NO_6BrSi$ (542.5): C 53.13, H 6.69, N 2.58; found C 53.15, H 6.83, N 2.46.

(3*R*,7*S*,8*S*,9*R*)-7-[(1*S*)-2-Benzyloxy-1-ethoxycarbonylmethylethyl]-8-bromo-3-phenyltetrahydrooxazolo[3,2-*c*][1,3]oxazin-5-one (30): This compound was prepared by the procedure described above, but with a reaction time of 4 h, and starting with **16** (183 mg, 0.37 mmol). It was isolated by flash chromatography (EtOAc/PE, 3:7) as a clear oil (135 mg, 70%). R_f = 0.5 (Et_2O); $[\alpha]_D^{20}$ = +51 (*c* = 1.1; $CHCl_3$). ^1H NMIR: δ = 1.51 (t, *J* = 7.0, 3 H), 2.65 (dd, *J* = 16.7 and 5.7, 1 H), 2.80 (dd, *J* = 16.7 and 8.2, 1 H), 3.37−3.49 (m, 1 H), 3.63 (dd, *J* = 9.7 and 5.0, 1 H), 3.91 (t, *J* = 9.2, 1 H), 4.35−4.44 (m, 3 H), 4.52 (dd, *J* = 9.0 and 6.5, 1 H), 4.69 (dd, *J* = 10.9 and 8.5, 1 H), 4.71 (AB syst., *J* = 13.0, 2 H), 4.82 (dd, *J* = 10.7 and 1.0, 1 H), 4.94 (dd, *J* = 10.9 and 8.5, 1 H), 5.21 (dd, *J* = 6.5 and 1.2, 1 H), 7.10−7.28 (m, 10 H). ^{13}C NMIR: δ = 14.2 (CH_3), 33.9 (CH_2), 35.4, 44.8, 60.7 (CH), 60.8, 68.6, 73.1, 73.8 (CH_2), 79.6, 89.1, 126.6, 127.3, 127.7, 128.2, 128.5, 128.8 (CH), 137.8, 139.9, 148.7, 171.8 (Cq). IR: ṽ = 2925, 1710.

(3*R*,7*S*,8*S*,9*R*)-8-Bromo-7-[(1*R*)-2-*tert*-butyldimethylsilyloxy-1-ethoxycarbonylmethylethyl]-3-phenyltetrahydrooxazolo[3,2-*c*][1,3]-oxazin-5-one (31): This compound was prepared by the procedure described above, but with a reaction time of 5 h, and starting with **19** (330 mg, 0.63 mmol). It was isolated after flash chromatography (EtOAc/PE, 2:8) as a clear oil (89 mg, 26%). R_f = 0.3 (Et_2O/PE, 1:1); $[\alpha]_D^{20}$ = +21 (*c* = 0.5; $CHCl_3$). ^1H NMIR: δ = 0.03 (s, 3 H), 0.04 (s, 3 H), 0.86 (s, 9 H), 1.19 (t, *J* = 7.1, 3 H), 2.18 (dd, *J* = 16.0 and 7.4, 1 H), 2.31 (dd, *J* = 16.0 and 5.4, 1 H), 2.79 (br. quint,

J = 6.5, 1 H), 3.63 (d, J = 7.4, 1 H), 4.01−4.15 (m, 4 H), 4.24 (dd, J = 9.2 and 6.5, 1 H), 4.69 (dd, J = 11.1 and 1.2, 1 H), 4.91 (d, J = 5.8, 1 H), 5.03 (d, J = 8.6, 1 H), 7.23−7.32 (m, 5 H). ^{13}C NMIR: δ = −5.3, 14.2 (CH_3), 18.3 (Cq), 26.0 (CH_3), 30.3 (CH_2), 38.8, 43.9, 60.8 (CH), 61.0, 62.4, 73.9 (CH_2), 77.2, 89.3, 126.65, 128.3, 128.9 (CH), 139.9, 148.7, 172.2 (Cq). IR: ν̃ = 2930, 1720.

(3*R*,7*S*,8*S*,9*R*)-7-[(1*R*)-2-Benzyloxy-1-ethoxycarbonylmethylethyl]-8-bromo-3-phenyltetrahydrooxazolo[3,2-*c*][1,3]oxazin-5-one (32): This compound was prepared by the procedure described above, but with a reaction time of 0.5 h, and starting with **20** (500 mg, 1.0 mmol). It was isolated by flash chromatography (CH_2Cl_2) as a solid (356 mg, 68%). M.p. 139 °C; R_f = 0.2 (Et_2O/PE, 7:3); $[\alpha]_D^{20}$ = +18 (c = 0.5; $CHCl_3$). ^{1}H NMIR: δ = 1.11 (t, J = 7.0, 3 H), 2.17 (dd, J = 16.0 and 7.2, 1 H), 2.31 (dd, J = 16.0 and 5.5, 1 H), 2.89−3.01 (m, 1 H), 3.42−3.60 (m, 2 H), 3.91−4.15 (m, 5 H), 4.45 (AB syst. J = 12.4, 2 H), 4.63 (dd, J = 11.2 and 1.6, 1 H), 4.83 (dd, J = 6.3 and 1.1, 1 H), 4.93 (d, J = 8.5, 1 H), 7.16−7.28 (m, 10 H). ^{13}C NMIR: δ = 14.0 (CH_3), 30.3 (CH_2), 36.2, 43.5, 60.6 (CH), 60.8, 69.4, 72.9, 73.7 (CH_2), 77.0, 89.0, 126.4, 127.5, 127.7, 128.3, 128.5, 128.7 (CH), 137.9, 139.79, 148.3, 171.8 (Cq). IR: ν̃ = 2925, 1710. $C_{25}H_{28}NO_6Br$ (518.4): C 57.92, H 5.44, N 2.70; found C 57.80, H 5.62, N 2.59.

(2*R*,4*R*)-2-[(1*R*,2*R*,3*S*)-4-*tert*-Butyldimethylsilyloxy-1,2-epoxy-3-ethoxycarbonylmethylbutyl]-3-ethoxycarbonyl-4-phenyl-1,3-oxazolidine (33): A solution of sodium ethoxide, prepared from sodium (80 mg, 3.5 mmol) in ethanol (2.5 mL), was added at room temp. to a solution of **29** (180 mg, 0.33 mmol) in ethanol (4 mL). The mixture was stirred for 1.5 h at room temp. and hydrolyzed by addition of a saturated aqueous solution of NH_4Cl (5 mL). The ethanol was then distilled off under reduced pressure, and the usual workup (Et_2O) followed by flash chromatography (Et_2O/PE, 6:4) gave epoxide **33** (162 mg, 97%) as a clear oil. R_f = 0.8 (Et_2O/PE, 6:4); $[\alpha]_D^{20}$ = +10 (c = 0.5; $CHCl_3$). ^{1}H NMIR: δ = 0.01 (s, 6 H), 0.83 (s, 9 H), 1.18 (t, J = 7.1, 3 H), 1.21 (t, J = 7.1, 3 H), 1.86−1.96 (m, 1 H), 2.30 (dd, J = 16.3 and 7.1, 1 H), 2.49 (dd, J = 8.0 and 2.2, 1 H), 2.99 (dd, J = 8.0 and 2.2, 1 H), 3.20 (t, J = 2.3, 1 H), 3.69 (b dd, J = 4.3 and 0.9, 1 H), 3.99−4.10 (m, 5 H), 4.25 (dd, J = 8.8 and 6.9, 1 H), 4.86 (t, J = 6.9, 1 H), 5.37 (d, J = 2.3, 1 H), 7.18−7.38 (m, 5 H). ^{13}C NMIR: δ = −4.9, 14.2, 14.5 (CH_3), 18.3 (Cq), 25.9 (CH_3), 32.8 (CH_2), 39.1, 55.2, 58.3 (CH), 60.5, 61.1 (CH), 61.9, 62.7, 73.9 (CH_2), 88.7, 126.8, 127.8, 128.6 (CH), 139.4, 155.2, 172.3 (Cq). IR: ν̃ = 2955, 2930, 1710. $C_{26}H_{41}NO_7Si$ (507.7): C 61.51, H 8.14, N 2.76; found C 61.14, H 8.21, N 2.79.

(2*R*,4*R*)-2-[(1*R*,2*R*,3*S*)-4-Benzyloxy-1,2-epoxy-3-ethoxycarbonylmethylbutyl]-3-ethoxycarbonyl-4-phenyl-1,3-oxazolidine (34): This compound was prepared by the procedure described above, starting with **30** (140 mg, 0.27 mmol). It was obtained as an oil (117 mg, 90%) after flash chromatography (EtOAc/PE, 2:8). R_f = 0.4 (Et_2O/PE, 5:5); $[\alpha]_D^{20}$ = −19 (c = 1.0; $CHCl_3$). ^{1}H NMIR: δ = 1.05−1.18 (m, 6 H), 2.09 −2.20 (m, 1 H), 2.31 (dd, J = 16.0 and 7.0, 1 H), 2.45 (dd, J = 16.2 and 7.0, 1 H), 3.01 (dd, J = 7.4 and 2.2, 1 H), 3.20 (t, J = 2.2, 1 H), 3.49 (d, J = 4.7, 1 H), 3.96−4.05 (m, 5 H), 4.22 (dd, J = 8.7 and 7.0, 1 H), 4.43 (s, 2 H), 4.84 (b t, J = 6.8, 1 H), 5.37 (br. s, 1 H), 7.17−7.34 (m, 10 H). ^{13}C NMIR: δ = 14.3, 14.5 (CH_3), 33.2 (CH_2), 37.8, 55.7, 58.0 (CH), 60.6 (CH_2), 61.0 (CH), 62.0, 70.1, 73.3, 73.9 (CH_2), 88.6, 127.6, 127.8, 128.4, 128.6 (CH), 138.3 139.5, 155.0, 172.1 (Cq). IR: ν̃ = 2985, 1715.

(2*R*,4*R*)-2-[(1*R*,2*R*,3*R*)-4-Benzyloxy-1,2-epoxy-3-ethoxycarbonylmethylbutyl]-3-ethoxycarbonyl-4-phenyl-1,3-oxazolidine (35): This compound was prepared by the procedure described above, starting with **32** (90 mg, 0.17 mmol). It was obtained as an oil (71 mg, 86%) after flash chromatography (EtOAc/PE, 2:8). R_f = 0.7 (Et_2O/PE, 6:4); $[\alpha]_D^{20}$ = −3 (c = 1.1; $CHCl_3$). ^{1}H NMIR: δ = 1.05−1.18 (m, 6 H), 2.22 (b sext, J = 6.3, 1 H), 2.50 (d, J = 6.7, 2 H), 3.09 (dd, J = 6.9 and 2.1, 1 H), 3.20 (t, J = 2.0, 1 H), 3.46−3.57 (m, 2 H), 3.98−4.13 (m, 5 H), 4.27 (dd, J = 8.7 and 7.0, 1 H), 4.42 (s, 2 H), 4.90 (t, J = 6.9, 1 H), 5.45 (br. s, 1 H), 7.20−7.40 (m, 10 H). ^{13}C NMIR: δ = 14.2, 14.4 (CH_3), 33.5 (CH_2), 38.0, 56.0, 58.2 (CH), 60.5 (CH_2), 60.8 (CH), 61.9, 69.8, 73.2, 73.9 (CH_2), 88.4, 126.7, 127.5, 127.6, 127.7, 128.4, 128.6 (CH), 138.1 139.4, 154.9, 172.1 (Cq). IR: ν̃ = 2980, 1715. $C_{27}H_{33}NO_7$ (483.6): C 67.06, H 6.88, N 2.90; found C 67.08, H 6.81, N 2.84.

(2*Z*,4*S*)-4-Bromo-5-*tert*-butyldimethylsilyloxy-4-ethoxycarbonylmethyl-3-{[(2*R*)-2-phenyl-2-*N*-*tert*-butoxycarbonylethyl]oxy}pent-2-enal (37): This compound was prepared by the procedure described for the bromocarbamation of **15**, starting with allene **26** (310 mg, 0.59 mmol). It was obtained as an oil (290 mg, 80%) after flash chromatography (Et_2O/PE, 3:7). R_f = 0.4 (Et_2O/PE, 4:6); $[\alpha]_D^{20}$ = +7 (c = 1.5; $CHCl_3$). ^{1}H NMIR: δ = 0.00 (s, 6 H), 0.82 (s, 9 H), 1.18 (t, J = 7.1, 3 H), 1.34 (s, 9 H), 2.86 (AB syst., J = 15, 2 H), 3.66−3.83 (m, 2 H), 3.82 (AB syst., J = 11.1, 2 H), 4.03−4.15 (m, 2 H), 4.77 (br. s, 1 H), 5.51 (d, J = 6.5, 1 H), 6.50 (d, J = 6.5, 1 H), 7.19−7.27 (m, 5 H), 9.73 (d, J = 6.5, 1 H). ^{13}C NMIR: δ = −5.4, 14.1 (CH_3), 18.1 (Cq), 25.8, 28.3 (CH_3), 38.2 (CH_2), 54.8 (CH), 61.2, 64.7 (CH_2), 79.5, 85.8 (Cq), 126.2, 127.6, 128.6, 138.0 (CH), 139.6, 155.3, 168.9 (Cq), 191.0 (CH). IR: ν̃ = 3390, 3065, 2930, 1682.

(2*R*,4*R*)-2-{(*R*)-[(1*S*,2*S*,3*R*)-2-*tert*-Butyldimethylsilyloxymethyl-3-ethoxycarbonylcyclopropyl](hydroxy)methyl}-3-ethoxycarbonyl-4-phenyl-1,3-oxazolidine (38): A solution of lithium bis(trimethylsilylamide) (1 M solution in THF, 0.35 mL, 0.35 mmol) was added at −78 °C to a solution of **32** (76 mg, 0.15 mmol) in THF (3 mL). The solution was stirred for 6 h at −50 °C and hydrolyzed by addition of a saturated aqueous solution of NH_4Cl (5 mL). The usual workup, followed by flash chromatography (EtOAc/PE, 3:7) gave cyclopropane **38** as an oil (56 mg, 74%). R_f = 0.4 (Et_2O/PE, 6:4); $[\alpha]_D^{20}$ = +32 (c = 1.3; $CHCl_3$). ^{1}H NMIR: δ = 0.00 (s, 6 H), 0.83 (s, 9 H), 1.07 (t, J = 6.9, 3 H), 1.12 (t, J = 6.9, 3 H), 1.47 (td, J = 9.0 and 6.0, 1 H), 1.75 (dd, J = 9.0 and 5.2, 1 H), 1.86 (br. quint, J = 5.2, 1 H), 3.53 (dd, J = 10.7 and 5.2, 1 H), 3.80 (dd, J = 10.7 and 4.9, 1 H), 3.85−4.09 (m, 6 H), 4.21 (dd, J = 8.7 and 7.2, 1 H), 4.93 (t, J = 6.6, 1 H), 5.23 (d, J = 7.2, 1 H), 7.18−7.33 (m, 5 H). ^{13}C NMIR: δ = −5.2, 14.3, 14.4 (CH_3), 18.4 (Cq), 22.4 (CH), 26.0 (CH_3), 27.0, 28.1 (CH), 60.5 (CH_2), 61.0 (CH), 62.4, 62.7 (CH_2), 70.7 (CH), 73.7 (CH_2), 93.1, 126.6, 127.7, 128.7 (CH), 139.7, 156.7, 173.0 (Cq). IR: ν̃ = 3420, 2955, 1680. $C_{26}H_{41}NO_7Si$ (507.7): C 61.51, H 8.14, N 2.76; found C 61.79, H 8.57, N 2.56.

(2*R*,4*R*)-2-{(*R*)-[(1*S*,2*S*,3*R*)-2-Benzyloxymethyl-3-ethoxycarbonylcyclopropyl](hydroxy)methyl}-3-ethoxycarbonyl-4-phenyl-1,3-oxazolidine (39): This compound was prepared by the procedure described above, starting with **34** (65 mg, 0.13 mmol). It was obtained as an oil (53 mg, 81%) after flash chromatography (EtOAc/PE, 1:1). R_f = 0.2 (Et_2O/PE, 6:4); $[\alpha]_D^{20}$ = +32 (c = 1.2; $CHCl_3$). ^{1}H NMIR: δ = 1.04 (t, J = 7.0, 3 H), 1.07 (t, J = 7.0, 3 H), 1.39 (td, J = 8.9 and 5.6, 1 H), 1.70 (dd, J = 8.9 and 5.1, 1 H), 1.95 (br. quint, J = 5.5, 1 H), 3.30 (dd, J = 10.4 and 6.5, 1 H), 3.53 (dd, J = 10.4 and 5.4, 1 H), 3.83−4.05 (m, 6 H), 4.16 (dd, J = 8.7 and 7.2, 1 H), 4.47 (s, 2 H), 4.89 (t, J = 6.2, 1 H), 5.19 (d, J = 7.0, 1 H), 7.18−7.26 (m, 10 H). ^{13}C NMIR: 14.2, 14.3 (CH_3), 22.4, 24.5, 29.1 (CH), 60.5 (CH_2), 61.0 (CH), 62.4 (CH_2), 70.6 (CH), 70.8, 73.6 (CH_2), 93.0, 126.6, 127.6, 127.8, 128.4, 128.7 (CH), 138.3, 139.7, 156.6, 172.6 (Cq). IR: ν̃ = 3410, 2980, 1715.

(2*R*,4*R*)-2-{(*R*)-[(1*S*,2*R*,3*S*)-2-Benzyloxymethyl-3-ethoxycarbonylcyclopropyl)(hydroxy)methyl}-3-ethoxycarbonyl-4-phenyl-1,3-oxazolidine (40): This compound was prepared by the procedure described above, starting with **35** (72 mg, 0.15 mmol). It was obtained as an oil (52 mg, 72%) after flash chromatography (EtOAc/PE, 4:6). R_f = 0.4 (EtOAc/PE, 4:6); $[\alpha]_D^{20}$ = +3 (*c* = 0.5; $CHCl_3$). ^1H NMIR: δ = 1.05 (t, *J* = 7.0, 3 H), 1.06 (t, *J* = 7.0, 3 H), 1.64 (t, *J* = 4.7, 1 H), 1.81−1.95 (m, 2 H), 3.40−3.51 (m, 1 H), 3.73−3.81 (m, 2 H), 3.83−4.15 (m, 5 H), 4.23 (dd, *J* = 8.9 and 7.1, 1 H), 4.49 (AB syst., *J* = 12.1, 2 H), 4.91 (dd, *J* = 6.7 and 5.2, 1 H), 5.28 (d, *J* = 5.0, 1 H), 7.18−7.33 (m, 10 H). ^{13}C NMIR: δ = 14.2, 14.5 (CH_3), 23.9, 24.0, 27.8 (CH), 60.6 (CH_2), 61.0 (CH), 62.1, 68.5 (CH_2), 72.4 (CH), 73.1, 73.7 (CH_2), 92.0, 126.8, 127.7, 128.0, 128.6 (CH), 137.6, 140.3, 156.1, 172.9 (Cq). IR: ṽ = 3428, 2980, 1650.

(3*R*,7*S*,8*S*,9*S*,10*R*)-9-Bromo-7-*tert*-butyldimethylsilyloxymethyl-6-ethoxycarbonyl-8-hydroxy-5-oxo-3-phenyloctahydrooxazolo[3,2-*a*]-azepine (41): This compound was prepared by the procedure described above, starting with **29** (317 mg, 0.58 mmol) and with a reaction time of 1.5 h. It was obtained as an oil (191 mg, 61%) after flash chromatography (EtOAc/PE, 2:8). R_f = 0.5 (Et_2O/PE, 6:4); positive Beilstein test. ^1H NMIR: δ = −0.24 (s, 3 H), −0.09 (s, 3 H), 0.81 (s, 9 H), 1.32 (t, *J* = 7.1, 3 H), 2.69−2.78 (m, 1 H), 2.94 (t, *J* = 10.5, 1 H), 3.25 (br. s, 1 H), 4.07 (dd, *J* = 10.3 and 5.0, 1 H), 4.13−4.19 (m, 5 H), 4.40 (d, *J* = 9.0, 1 H), 4.55 (br. s, 1 H), 5.39 (d, *J* = 5.5, 1 H), 5.59 (d, *J* = 9.5, 1 H), 7.26−7.40 (m, 3 H), 7.53−7.57 (m, 2 H). ^{13}C NMIR: δ = 1.3, 1.9, 14.0, 25.7 (CH_3), 43.7, 46.9, 55.9 (CH), 59.6 (CH_2), 60.1 (CH), 61.4, (CH_2), 69.3, 71.6, 89.4, 127.4, 128.2, 128.8 (CH), 139.2, 165.8, 169.0 (Cq). IR: ṽ = 3420, 1750, 1675.

(2*R*,4*R*)-2-[(1*S*,2*R*)-1-Bromo-2-hydroxy-2-phenylethyl]-3-(2-ethoxycarbonyl-1-oxoethyl)-4-phenyl-1,3-oxazolidine (44): A solution of LiHMDS in THF (35 mL, 1 M solution, 35 mmol) was added dropwise at −78 °C to a solution of ethyl acetate (3.9 mL, 40 mmol) in THF (20 mL). The solution was warmed to −50 °C over 1 h and recooled to −78 °C. To this solution was then added dropwise a solution of **43** (3 g, 8.01 mmol) in THF (30 mL). The reaction mixture was stirred at −50 °C for 1.5 h and hydrolyzed with an aqueous saturated solution of NH_4Cl. The usual workup, followed by flash chromatography (EtOAc/PE/CH_2Cl_2), gave bromohydrin **44** as a white solid (3.6 g, 97%). R_f = 0.5 (EtOAc/PE, 1:1); m.p. 120 °C; $[\alpha]_D^{20}$ = +11 (*c* = 0.7; $CHCl_3$). ^1H NMIR: δ = 1.47 (t, *J* = 7, 3 H), 3.28 (d, *J* = 15.7, 1 H), 3.43 (d, *J* = 15.7, 1 H), 3.59 (d, *J* = 6.2, 1 H), 4.37 (q, *J* = 7.0, 2 H) 4.61−4.73 (m, 2 H), 5.24 (t, *J* = 7.2, 1 H), 5.41 (t, *J* = 6.5, 1 H), 5.53 (dd, *J* = 2 and 7.2, 1 H), 6.05 (d, *J* = 2, 1 H), 7.29−7.60 (m, 10 H). ^{13}C NMIR: δ = 14.4 (CH_3), 43.3 (CH_2), 58.1, 61.8 (CH), 61.9, 75.2 (CH_2), 76.8, 90.2, 127.1, 127.7, 128.7, 129.0, 129.6 (CH), 137.8, 141.4, 167.2, 167.9 (Cq). IR: ṽ = 3420, 2955, 1680. $C_{22}H_{24}NO_5Br$ (462.3): C 57.15, H 5.23, N 3.03; found C 57.13, H 5.37, N 2.87.

(2*R*,4*R*)-3-(2-Ethoxycarbonyl-1-oxoethyl)-2-[(1*R*,2*R*)-2-phenyl-1,2-epoxyethyl]-4-phenyl-1,3-oxazolidine (45): Compound **44** (1 g, 2.16 mmol) was added to a solution of sodium ethoxide, prepared from sodium (260 mg, 10.8 mmol) in ethanol (20 mL). The solution was stirred for 15 min and quenched by addition of a saturated aqueous solution of NH_4Cl. The ethanol was then distilled off. Addition of water and dichloromethane followed by the usual workup gave epoxide **45** as a solid (820 mg, quant. yield). R_f = 0.58 (EtOAc/PE, 1:1); m.p. 72 °C; $[\alpha]_D^{20}$ = +11.7 (*c* = 1.1; $CHCl_3$). ^1H NMR (two rotamers, in a 82:18 ratio): δ = 1.35 and 1.40 (2 t, *J* = 7, 3 H), 3.38 (d, *J* = 15.7, 0.82 H), 3.51 (d, *J* = 15.7, 1 H), 3.45 (t, *J* = 1.5, 0.82 H), 3.85−4.05 (m, 0.36 H), 4.25 (d, *J* = 1.7, 1 H), 4.32 (q, *J* = 7.3, 2 H), 4.48 (dd, *J* = 7.5 and 8.5, 1 H), 4.73 (dd, *J* = 6.7 and 8.5, 1 H), 5.25 (t, *J* = 7, 0.8 H), 5.38 (d, *J* = 6.7, 0.2 H), 5.75 (b t, *J* = 6, 0.2 H), 6.23 (s, 0.8 H)7.52−7.73 (m, 10 H). ^{13}C NMR (major rotamer): δ = 14.4 (CH_3), 42.9 (CH_2), 55.1 (CH), 61.6 (CH_2), 61.7, 62.2, 75.4, 88.0, 125.8, 126.4, 126.9, 127.8, 128.4, 128.6, 128.7, 129.3 (CH), 136.3, 137.8, 166.6, 166.8 (Cq). IR: (Nujol) ṽ = 1658, 1733, 2924.

(7*R*,8*R*,9*R*)-8-Hydroxy-3,7-diphenyloxazolo[3,2-*a*]pyridin-5-one (46): Sodium hydride (60 wt.%; 14 mg, 0.3 mmol) was added to a solution of epoxide **45** (97 mg, 0.254 mmol) in dry DMF (3 mL). The solution was stirred at 50 °C for 1 h and then at 100 °C for 2 h 15. The mixture was then cooled to room temp. and hydrolyzed by addition of a saturated aqueous solution of NH_4Cl. The usual workup (CH_2Cl_2) was followed by flash chromatography (EtOAc/PE, 4:6) and gave **46** as a white solid (32 mg, 41%). R_f = 0.75 (EtOAc/PE, 7:3); m.p. 215 °C; $[\alpha]_D^{20}$ = −120 (*c* = 1.6; $CHCl_3$). ^1H NMIR: δ = 2.56 (dd, *J* = 1.5 and 17.5, 1 H), 2.95 (dd, *J* = 7.2 and 17.5, 1 H), 3.05 (br. s, 1 H), 3.50−3.55 (m, 1 H), 3.95 (dd, *J* = 1.7 and 9.0, 1 H), 4.04 (dd, *J* = 7.0 and 9.0, 1 H), 4.31 (br. s, 1 H), 4.46 (d, *J* = 2.0, 1 H), 4.95 (b d, *J* = 7.0, 1 H), 7.15−7.34 (m, 10 H). ^{13}C NMIR: δ = 32.1 (CH_2), 42.2, 58.5, 69.3 (CH), 74.7 (CH_2), 86.8, 126.2, 127.3, 127.4, 128.7, 128.8, 129.4 (CH), 140.2, 140.9, 167.4 (Cq). IR: (Nujol) ṽ = 1628, 2920, 3278. $C_{19}H_{19}NO_3$ (309.4): C 73.76, H 6.19, N 4.52; found C 73.60, H 6.39, N 4.37.

(1*R*,3*R*,4*R*)-1-(2-Hydroxy-1-phenylethyl)-4-phenylpiperidin-2-ol (47): $LiAlH_4$ (70 mg, 2 mmol) was added portionwise to a solution of **46** (110 mg, 0.35 mmol) in THF (5 mL). The suspension was stirred at room temp. for 3 h and quenched by pouring it into an aqueous solution of NaOH (4 wt.%; 4 mL). Addition of water (5 mL) with vigorous stirring was followed by filtration through a Celite pad. Concentration under reduced pressure gave an oil that was purified by flash chromatography (EtOAc/PE, 7:3). Diol **47** was obtained as a clear oil (67 mg, 63%). R_f = 0.45 (EtOAc/PE, 8:2); $[\alpha]_D^{20}$ = +21.4 (*c* = 0.5; $CHCl_3$). ^1H NMIR: δ = 1.97 (t, *J* = 10.2, 1 H), 2.01−2.15 (m, 2 H), 2.41−2.52 (m, 1 H), 2.53−2.72 (m, 1 H), 2.90 (br. s, 2 H), 3.21 (b dd, *J* = 1.5 and 10.7, 1 H), 3.45 (ddd, *J* = 1.5, 4.2, and 10.7, 1 H), 3.91 (dd, *J* = 4.5 and 9.7, 1 H), 4.00 (dd, *J* = 4.5 and 9.7, 1 H), 4.01−4.10 (m, 1 H), 4.30 (t, *J* = 9.9, 1 H), 7.46−7.67 (m, 10 H). ^{13}C NMIR: δ = 32.4 (CH_2), 51.4 (CH), 52.8, 52.9, 60.3 (CH_2), 69.8, 72.2, 127.1, 127.9, 128.1, 128.4, 128.8, 128.9 (CH), 135.2, 142.1 (Cq).

(3*R*,4*R*)-4-Phenylpiperidin-3-ol (48): Pd/C (10%; 10 mg) was added to a solution of **47**·HCl (56 mg, 0.168 mmol) in MeOH (3 mL), and the suspension was stirred at room temp. under hydrogen for 24 h. The suspension was then filtered through Celite (washed with hot MeOH), and the filtrate was concentrated under reduced pressure to give **48**·HCl as crystals, which were washed with small portions of acetone (38 mg, quant. yield). M.p. 186 °C; $[\alpha]_D^{20}$ = +40.2 (*c* = 0.5; $CHCl_3$). ^1H NMR (D_2O): δ = 2.08−2.23 (m, 2 H), 2.92−3.00 (m, 1 H), 3.07 (t, *J* = 11.2, 1 H), 3.28 (td, *J* = 12.0 and 2.0, 1 H), 3.63 (b d, *J* = 12.5, 1 H), 3.74 (dd, *J* = 3.5 and 12.2, 1 H), 4.21 (td, *J* = 11.5 and 6.2, 1 H), 7.43−7.62 (m, 5 H). ^{13}C NMIR: δ = 29.1, 44.1 (CH_2), 48.4 (CH), 48.5 (CH_2), 67.9, 127.8, 128.1, 129.4 (CH), 141.1 (Cq). IR: ṽ = 2923, 1459, 1376. $C_{10}H_{15}NO{\cdot}HCl{\cdot}H_2O$ (231.7): calcd. C 57.02, H 7.83, N 6.04; found C 57.01, H 7.36, N 5.97.

[1] [1a] L. Colombo, M. D. Giacomo, D. Brusotti, E. Milano, *Tetrahedron Lett.* **1995**, *36*, 2863−2866. [1b] G. Poli, E. Maccagni, L. Manzoni, T. Pilati, C. Scolastico, *Tetrahedron* **1997**, *53*, 1759. [1c] T. Harder, T. Löhl, M. Bolte, K. Wagner, D. Hoppe,

Tetrahedron Lett. **1994**, *35*, 7365−7368. [1d] P. O'Brien, S. Warren, *Tetrahedron Lett.* **1996**, *37*, 3051−3054.
[2] C. Agami, F. Couty, C. Lequesne, *Tetrahedron* **1995**, *51*, 4043−4056.
[3] C. Agami, F. Couty, H. Lam, H. Mathieu, *Tetrahedron* **1998**, *54*, 8783−8796.
[4] C. Agami, F. Couty, N. Rabasso, *Tetrahedron Lett.* **2000**, *41*, 4113−4116.
[5] C. Agami, C. F. Couty, G. Evano, H. Mathieu, *Tetrahedron* **2000**, *56*, 367−376.
[6] For a preliminary communication of this work, see: C. Agami, F. Couty, G. Evano, *Tetrahedron Lett.* **2000**, *41*, 8301−8305.
[7] [7a] P. Vittorelli, T. Winkler, H. J. Hansen, H. Schmid, *Helv. Chim. Acta* **1968**, *51*, 1457−1461. [7b] H. J. Hansen, H. Schmid, *Tetrahedron* **1974**, *30*, 1959−1969. [7c] R. L. Vance, N. G. Rondan, K. N. Houk, F. Jensen, W. T. Borden, A. Komornicki, E. Wimmer, *J. Am. Chem. Soc.* **1988**, *110*, 2314−2315. [7d] W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T. Li, J. Faulkner, M. R. Petersen, *J. Am. Chem. Soc.* **1970**, *92*, 741−742.
[8] G. Bettoni, C. Celluci, V. Tortorella, *J. Heterocycl. Chem.* **1976**, *13*, 1053−1055.
[9] M. A. Henderson, C. H. Heathcock, *J. Org. Chem.* **1988**, *53*, 4736−4745. For a recent example of the use of this reaction in synthesis, see: J. D. Ha, J. K. Cha, *J. Am. Chem. Soc.* **1999**, *121*, 10012−10020.
[10] C. Agami, F. Couty, O. Venier, L. Hamon, *J. Org. Chem.* **1997**, *62*, 2107−2113.
[11] [11a] C. Agami, F. Couty, O. Venier, *Synlett* **1995**, 1027−1028. [11b] C. Agami, F. Couty, O. Venier, *Synlett* **1996**, 511−512.
[12] N. J. Barnes, A. H. Davidson, L. R. Hughes, G. Procter, V. Rajcoomar, *Tetrahedron Lett.* **1981**, *22*, 1751−1754.
[13] For a similar behavior involving an acetal instead of an oxazolidine ring, see: H. Fujioka, Y. Nagatomi, H. Kitagawa, Y. Kita, *J. Am. Chem. Soc.* **1997**, *119*, 12016−12017. See also ref.[4]
[14] [14a] J. H. Babler, A. J. Tortorello, *J. Org. Chem.* **1976**, *41*, 885−887. [14b] J. Ficini, J. d′Angelo, *Tetrahedron Lett.* **1976**, *28*, 2441−2444. [14c] S. Takano, N. Sato, M. Akiyama, K. Ogasawara, *Heterocycles* **1985**, *23*, 2859−2872.
[15] L. Poitout, LeY. Merrer, J. C. Depezay, *Tetrahedron Lett.* **1996**, *37*, 1613−1616.
[16] S. K. Taylor, *Tetrahedron* **2000**, *56*, 1149−1163.
[17] E. Vieira, A. Bingelli, V. Breu, D. Bur, W. Fischli, R. Güller, G. Hirth, H. P. Märky, M. Müller, C. Oefner, M. Scalone, H. Stadler, M. Wihelm, W. Wostl, *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1397−1402.

Received March 20, 2001
[O01138]