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S_N2' Regio and Stereoselective Alkylation of Allylic and Propargylic Mesylates Linked to a *N*-Boc Oxazolidine using Organocuprates

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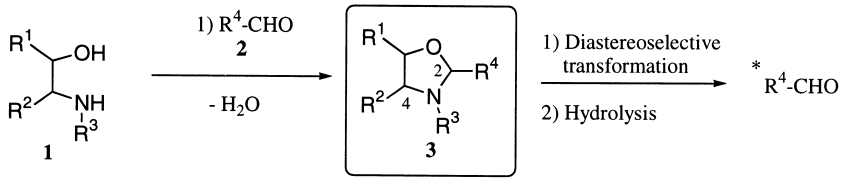
Abstract—***N***-Boc-oxazolidines derived from (***R***)-phenylglycinol and bearing a stereodefined propargylic or allylic alcohol side chain were transformed into the corresponding mesylates. Alkylation of these allylic mesylates by means of organocuprate reagents effected a regio and stereoselective 1,3-transfer of chirality. Similarly, alkylation of the propargylic mesylate gave a chiral allenyl oxazolidine. The ***N***-Boc-2-alkenyl oxazolidines resulting from an ***anti*** S_N2' addition underwent an intramolecular bromocarbamoylation with a high level of stereocontrol upon treatment with NBS. After reaction with sodium alkoxide, the resulting cyclic urethanes gave the corresponding epoxy oxazolidines whose reactivity towards organocuprates was studied. The sequence represents an efficient synthesis of enantiopure protected aldehydes bearing three contiguous chiral centers.

1,3-Oxazolidines **3** are easily prepared by condensation of an aldehyde with a chiral β-amino alcohol **1**. These heterocycles can be considered as a chiral protected form of the starting aldehyde **2**, and when R^4 is a prostereogenic group, its diastereoselective transformation, followed by hydrolysis eventually produces optically enriched aldehydes (Scheme 1).

Numerous applications of this strategy have been published.[1] Still the method relies upon an efficient stereocontrol during the first step, namely the formation of the C-2 stereocenter of the oxazolidine ring. We had previously shown that this new stereogenic center could be controlled efficiently to give diastereoisomerically pure *N*-Boc-*cis*-2,4 oxazolidines **3** (R^3=CO_2t-Bu). In the same context, our group recently developed two sets of diasteroselective transformations. On the one hand, diastereoisomerically pure α-hydroxy oxazolidines **5**, could be obtained from the reduction (or organometallic addition) of compound **4**. These could be transformed into two enantiomerically pure 1,2-diols by using a straightforward procedure (Scheme 2).[2] Furthermore, subsequent manipulation of these compounds allowed the asymmetric synthesis of piperidinic amino acids[3] or alkaloids.[4] On the other hand, when R^4 was an olefin, it underwent an efficient epoxidation via a two-step sequence involving treatment with *N*-bromosuccinimide followed by a sodium alkoxide-mediated cleavage of the resulting cyclic urethane **7**. The resulting epoxy oxazolidines **8** turned out to be very valuable synthons, as shown by their conversion into pheromones,[5] or into the *anti* isomer of the Taxol side chain.[6]

In order to extend the scope of these methodologies, we have combined them through an efficient 1,3-transfer of chirality[7] starting from an allylic alcohol such as **9**, the latter being synthesized through the diastereoselective reduction of an acyl oxazolidine. This transfer of chirality gives rise to an *N*-Boc-2-alkenyl oxazolidine **10**, which in turn, can be



Scheme 1.

Keywords: oxazolidine; asymmetric synthesis; organocuprates; epoxidation.
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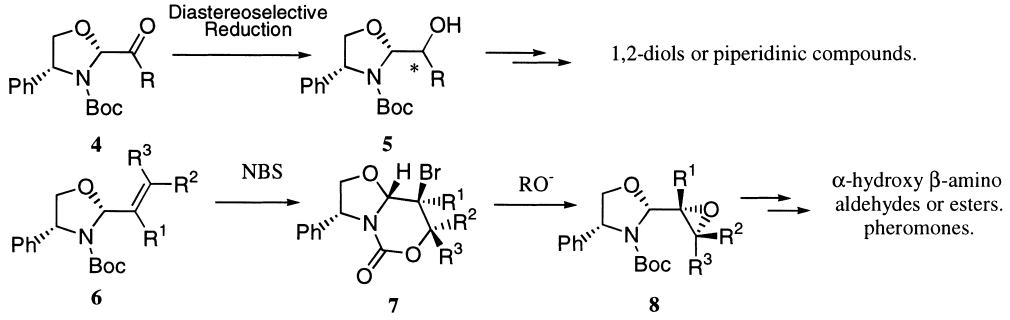
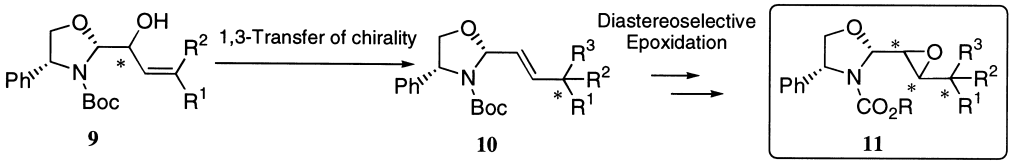


Scheme 2.



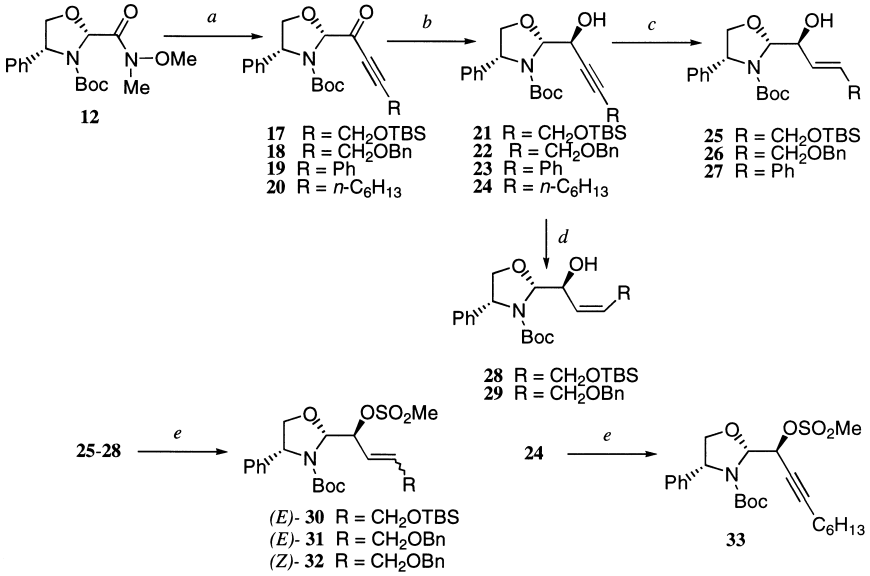
Scheme 3.

stereoselectively epoxidized, thus allowing the control of three contiguous stereogenic centers on the protected aldehyde **11** (Scheme 3).

This article describes: (i) the stereocontrolled synthesis of the required allylic alcohols **9**, (ii) a 1,3-transfer of chirality effected on the sulfonated allylic alcohols using organocopper reagents, (iii) the diastereoselective epoxidation of the resulting alkenyl oxazolidines, and (iv) a brief examination of the reactivity of the resulting epoxides.

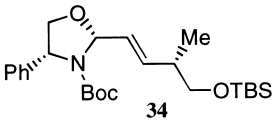
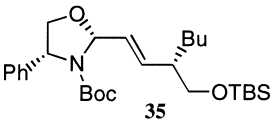
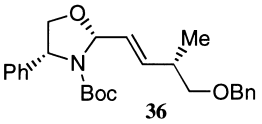
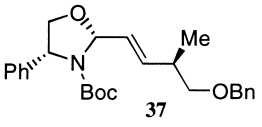
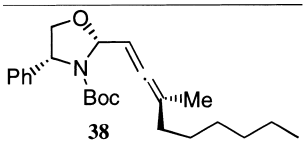
Synthesis of the α-hydroxy β-alkenyl oxazolidines

Allylic alcohols **25**–**29** linked to an *N*-Boc oxazolidine were synthesized as follows. Reaction of the Weinreb amide **12** with lithium acetylides **13**–**16** gave the desired 2-acyl oxazolidines **17**–**20** with yields ranging from 75 to 90%.[4] A reverse quench into a phosphate buffer was crucial to obtain good yields.[8] Reduction of these ynones by zinc borohydride in ether at −30°C gave carbinols **21**–**24** (de >95%).[9] These high selectivities can be rationalized by a model involving coordination of the metal cation with both oxygen atoms of the carbonyl and carbamate groups. Stereoselective reduction of these carbinols using Red-Al gave *E* allylic alcohols **25**–**27**, whereas hydrogenation in the presence of Lindlar's catalyst gave the *Z* isomers **28** and **29**. Alcohols **25**–**28** were then quantitatively converted into the corresponding mesylates **30**–**32**. The mesylate derived from alcohol **27** proved to be unstable at room temperature (RT) and could not be isolated. On the other hand, carbinol **24** could be converted into a stable mesyloxy derivative **33**

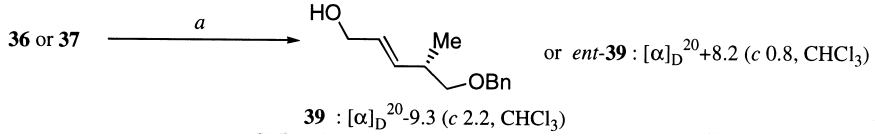


Scheme 4.

Table 1.

Entry	Substrate	Conditions	Yield (%)[a]	Product
1	**30**	$Me_2Cu(CN)(ZnCl)_2$, THF	30	 **34**
2	**30**	Me_2CuLi, THF	79	34
3	**30**	$Bu_2Cu(CN)(ZnCl)_2$, THF	61	 **35**
4	**30**	Bu_2CuLi, THF	0[b]	35
5	**31**	Me_2CuLi, THF	78	 **36**
6	**32**	Me_2CuLi, THF	72	 **37**
7	**33**	Me_2CuLi, THF	80	 **38**

[a] Yield of isolated product.
[b] No product **35** could be detected in ^1H NMR spectum of the crude material.



Scheme 5.

(Scheme 4: *Reagents and conditions*: *a*. Li≡CH_2OTBS (**13**), Li≡CH_2OBn (**14**), Li≡Ph (**15**) or Li≡C_6H_{13} (**16**), THF, −78°C to RT, 77% (**17**), 75% (**18**), 80% (**19**), quant. crude yield (**20**). *b*. $Zn(BH_4)_2$, Et_2O, −30°C, 95% (**21**), 94% (**22**), 95% (**23**), 62% (**24**). *c*. Red-Al, THF, RT; 85% (**25**), 80% (**26**), 75% (**27**). *d*. H_2, Lindlar's catalyst, EtOH, 90% (**28**), 80% (**29**). *e*. MsCl, Et_3N, CH_2Cl_2, quant. crude yields).

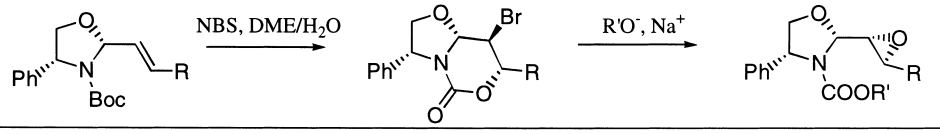
Having in hand the required mesylates, we next studied their alkylation using organocuprates.

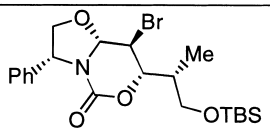
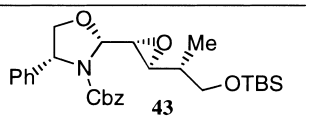
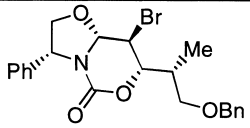
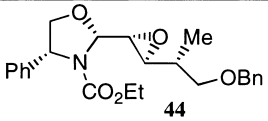
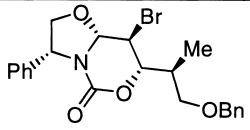
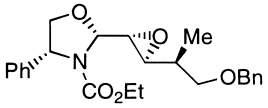
Action of organocuprate reagents

The *anti* S_N2' displacement of allylic[10] or propargylic[11] sulfonates by organocuprates is a well-known procedure and various experimental conditions have been described in order to improve the regioselectivity[10d] and/or the chemical yield,[10f] which is often low due to a competing reductive elimination. Experiments effected on oxazolidine **30**–**33** are listed in Table 1. Yamamoto's procedure which uses a higher order zinc cuprate reagent was unsatisfactory when it came to introducing a methyl group (entry 1), and simple Gilman's cuprates proved to be more reactive (entries 2 and 5–7). A butyl group was however successfully introduced using Yamamoto's reagent (compare entries 3 and 4).

The *anti* stereochemical outcome of this reaction was proved by a chemical correlation with known alkenol **39**.[12] With this objective, diastereomeric oxazolidines **36** and **37** were treated with trifluoroacetic acid in order to effect *N*-Boc deprotection. The corresponding enantiomeric aldehydes were then released by hydrolysis and reduced

Table 2.



Entry	Substrate	Yield (%)	Product	Yield (%)	Product
1	**34**	93	 **40**	68 (overall)	 **43**
2	**36**	89	 **41**	83	 **44**
3	**37**	70	 **42**	70	 **45**

with sodium borohydride. These reactions finally led to alkenols **39** and *ent*-**39** whose configurations were deduced from their optical rotation.The S_N2' substitution has therefore occurred with an *anti* stereochemical course (Scheme 5: *Reagents and conditions*: *a*. (i) CF_3CO_2H, CH_2Cl_2, (ii) THF, H_2O, (iii) $NaBH_4$, EtOH, 57% (**39**), 50% (*ent*-**39**)).

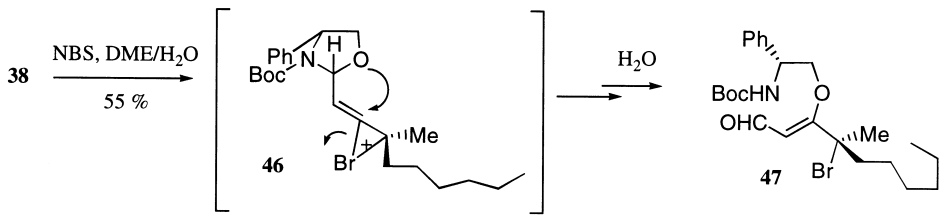
Epoxidation of the *N*-Boc alkenyl oxazolidines

The previously described[6] two-step epoxidation was next applied to alkenyl oxazolidines **34**, **36** and **37**. Treatment of these alkenyl oxazolidines with *N*-bromosuccinimide in a DME/water mixture provoked a regio and stereoselective intramolecular bromocarbamation and led to bicyclic urethanes **40**–**42**. From a mechanistical point of view, it should be noted that whereas bromocarbamation of **34** and **36** was complete after 10 min at RT, the reaction involving **37** was more sluggish and required 2 h to reach completion. This shows that reactivity is affected by the absolute configuration of the stereocenter α to the alkenyl moiety. However, high stereoselectivity was always observed, since no minor stereoisomer was ever detected in the ^1H NMR spectra of the crude products. Reaction of these bicyclic carbamates with sodium ethoxide in ethanol (compounds **41**, **42**) or with sodium phenylmethoxide in DMF (compound **40**) cleanly opened the urethane to give diastereoisomerically pure epoxy oxazolidines **43**–**45**. Consequently, it is possible to choose the nature of the protecting carbamate on the epoxy oxazolidine (Table 2).[13]

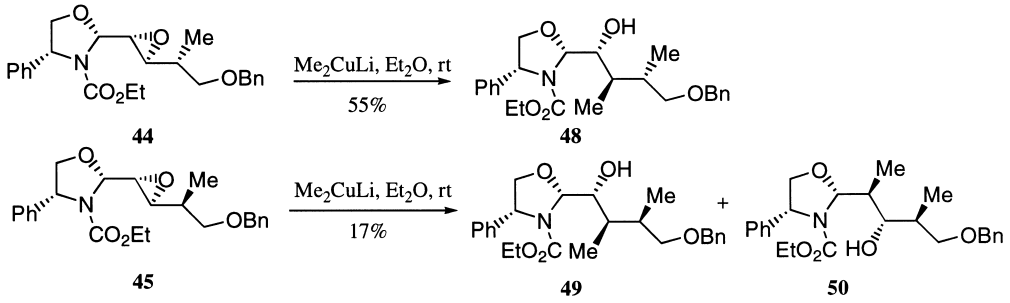
Unexpectedly, aldehyde **47** resulted from the bromocarbamation of the allenyl oxazolidine **38**. This compound is produced by a nucleophilic opening of the intermediate bromonium ion **46** by the oxygen atom[14] of the oxazolidine ring. Ring fragmentation followed by hydrolysis of the intermediate acyliminium ion then led to the diastereoisomerically pure enal **47** (Scheme 6).

Finally, epoxy oxazolidines **44** and **45** were reacted with Me_2CuLi in order to obtain a nucleophilic opening of their epoxide moieties (Scheme 7). Substrate **44** led to hydroxy oxazolidine **48** in an acceptable yield but, in the case of substrate **45**, both regioisomeric oxazolidines **49** and **50** were produced in low yield. High regioselectivity as observed in the first case has already been reported[5,6]in similar substrates devoid of an extra stereogenic center α to the epoxide.

The above difference of reactivity between compounds **44** and **45** can be rationalized by considering a chelation of the metal cation by the oxygen atom of the epoxide and of the benzylic ether (Fig. 1). Due to this chelation, the S_N2 approach is hindered by the methyl group in substrate **45**, thus lowering both its reactivity and regioselectivity.



Scheme 6.



Scheme 7.

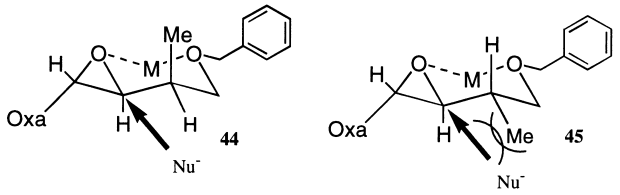


Figure 1.

In conclusion, this efficient 1,3-transfer of chirality involving organocopper reagents considerably enhances the usefulness of *N*-Boc-2-acyl oxazolidines in asymmetric synthesis. Explorations of other 1,3-transfers of chirality starting from enantiopure allylic alcohols linked to an oxazolidine ring are underway in our group.

Experimental

General comments

^{1}H and ^{13}C spectra ($CDCl_3$ solution unless otherwise stated) were respectively recorded on a Bruker ARX 250 spectrometer at 250 and 62.9 MHz; 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 by using various mixtures of diethyl ether (E) and petroleum ether (EP). TLC was run on Merck Kieselgel $60F_{254}$ plates. Melting points are uncorrected. THF and ether were distilled from sodium/benzophenone ketyl. Dichloromethane was distilled from calcium hydride. Mention of "usual workup" means: (i) decantation of the organic layer, (ii) extraction of the aqueous layer with ether, (iii) drying of the combined organic phases over $MgSO_4$, and (iv) solvent evaporation under reduced pressure. Composition of stereoisomeric mixtures was determined by NMR analysis on crude products before any purification.

General procedure for the syntheses of ynones 17–20

To a solution of the required alkyne (27 mmol) in THF (50 mL) cooled to −78°C, was added dropwise *n*-butyllithium (1.6N solution in hexanes, 14.5 mL, 23 mmol). The solution was allowed to reach 0°C within 1 h and was cooled again at −78°C. To this solution was added dropwise a solution of Weinreb amide **12** (6 g, 17.8 mmol) in THF (25 mL). The reaction medium was slowly warmed to ca. −10°C (2 h). At this time, the reaction was quenched by pouring it with vigorous stirring into a biphasic layer made of 10 wt.% aqueous KH_2PO_4 (140 mL) and ether (140 mL), precooled at 0°C. Usual workup, followed by flash chromatography gave the following ynones.

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-(4-*tert*-butyldimethylsilyloxy-but-2-ynoil)-4-phenyl-1,3-oxazolidine 17. This compound was obtained as an oil (77%). Rf: 0.4 (E/EP: 20/80); IR (film): 1805, 1680; $[\alpha]_D^{20}$: +10 (*c* 1.2, $CHCl_3$); ^{1}H NMR: −0.05 (bs, 6H), 0.78 (bs, 9H), 1.04 and 1.14 (two bs, 9H), 3.90–3.95 (bm, 1H), 4.27–4.40 (bm, 3H), 4.70–4.78 (bm, 1H), 5.40 (s, 1H), 7.11–7.24 (m, 3H), 7.40 (dd, *J*=8.3 and 1.7, 2H); ^{13}C NMR: −5.0 (CH_3), 18.1 (Cq), 25.6 (CH_3), 27.9 (CH_3), 51.5 (CH_2), 60.7 (CH), 74.9 (CH_2), 81.4 (Cq), 82.2 (Cq), 90.4 (Cq), 92.8 (CH), 126.8 (CH), 127.6 (CH), 128.4 (CH), 138.6 (Cq), 153.0 (Cq), 182.2 (Cq). Anal. Calcd for $C_{24}H_{35}NSiO_5$: C, 64.69; H, 7.92; N 3.15. Found: C, 64.80; H, 7.89; N, 3.08.

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-(4-benzyloxy-but-2-ynoil)-4-phenyl-1,3-oxazolidine 18. This compound was obtained as an oil (75%). Rf: 0.55 (E/EP: 40/60); IR (film): 1805, 1680; $[\alpha]_D^{20}$: +3.1 (*c* 1.2, $CHCl_3$); ^{1}H NMR: 1.3 (bs, 9H), 3.87–4.02 (bm, 1H), 4.22 (s, 2H), 4.38 (dd, *J*=7.1 and 8.9, 1H), 4.49 (s, 2H), 4.75–4.84 (bm, 1H), 5.44 (bs, 1H), 7.15–7.45 (m, 10H); ^{13}C NMR 29.4 (CH_3), 58.3 (CH_2), 63.2 (CH), 71.2 (CH_2), 73.4 (CH_2), 81.0 (Cq), 81.2 (Cq), 81.6 (Cq), 91.9 (CH), 128.2 (CH), 128.3 (CH), 129.2 (CH), 129.5 (CH), 129.9 (CH), 137.9 (Cq), 140.1 (Cq), 153.4 (Cq), 183.7 (Cq).

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-(3-phenyl-prop-2-ynoil)-4-phenyl-1,3-oxazolidine 19. This compound was obtained as a pale yellow solid (80%). Rf: 0.6 (E/EP: 50/50); IR ($CHCl_3$): 1805, 1670; $[\alpha]_D^{20}$: +5.3 (*c* 1, $CHCl_3$); ^{1}H NMR: 1.22 (bs, 9H), 4.02 (t, *J*=7.2, 1H), 4.36 (dd, *J*=7.2 and 8.7, 1H), 4.84 (bs, 1H), 5.50 (bs, 1H), 7.15–7.25 (m, 6H), 7.34–7.42 (m, 4H, Ph); ^{13}C NMR: 28.0 (CH_3), 60.7 (CH), 75.1 (CH_2), 81.5 (Cq), 86.5 (Cq), 90.6 (CH), 95.3 (Cq), 119.7 (Cq), 126.9 (CH), 127.6 (CH), 128.4 (CH), 128.5 (CH), 129.7 (CH), 131.1 (CH), 133.2 (Cq), 138.9 (Cq), 153.1 (Cq), 182.3 (Cq).

(2*R*,4*R*)-3-*tert*-Butoxycarbonyl-2-(non-2-ynoil)-4-phenyl-1,3-oxazolidine 20. This compound was obtained as an oil (quantitative crude yield). Rf: 0.6 (E/EP: 40/60); IR (film): 1805, 1680; $[\alpha]_D^{20}$: +8.3 (*c* 0.52, $CHCl_3$); ^{1}H NMR: 0.78 (t,

J=6.8, 3H), 1.25 (bs, 9H), 1.2–1.55 (m, 8H), 2.24 (bt, J=6.9, 2H), 3.80–3.95 (bm, 1H), 4.30 (dd, J=7.2 and 8.9, 1H), 4.78 (bs, 1H), 5.40 (bs, 1H), 7.10–7.22 (m, 4H), 7.37 (dd, J=8.1 and 1.2, 2H); ^{13}C NMR: 14.4 (CH_3), 19.2 (CH_2), 22.6 (CH_2), 27.5 (CH_2), 28.1 (CH_3), 28.6 (CH_2), 31.2 (CH_2), 60.8 (CH), 75.2 (CH_2), 79.5 (Cq), 81.4 (Cq), 90.8 (CH), 99.5 (Cq), 127.1 (CH), 127.7 (CH), 128.5 (CH), 139.1 (Cq), 153.2 (Cq), 182.9 (Cq).

General procedure for the reduction of ynones 17–20 by zinc borohydride

To a solution of ynone (2.13 mmol) in ether (30 mL) was added dropwise at −30°C a solution of freshly prepared zinc borohydride in ether (0.5 M solution, 8.6 mL, 4.3 mmol). The mixture was warmed to 0°C and stirred for 1 h at this temperature. Hydrolysis by dropwise addition of a saturated aqueous solution of NH_4Cl (20 mL) was followed by usual workup to give carbinols **21**–**23** as solids that were washed with small portions of cold petroleum ether and used without further purification in the following steps. Analytical samples were purified by flash chromatography. Carbinol **24** was obtained as an oil and was purified by flash chromatography (E/EP: 40/60). It then crystallized on standing.

[2*R*,2(1*S*),4*R*]-3-*tert*-Butoxycarbonyl-2-(4-*tert*-butyldimethylsilyloxy-1-hydroxy-but-2-ynyl)-4-phenyl-1,3-oxazolidine 21. Yield 95%; mp 121°C; Rf: 0.6 (E/EP: 70/30); IR ($CHCl_3$): 3200, 2200, 1678; $[\alpha]_D^{20}$: +7 (*c* 0.8, $CHCl_3$); ^{1}H NMR: 0.01 (s, 6H), 0.79 (s, 9H), 1.18 (bs, 9H), 4.10 (dd, J=6 and 8.5, 1H), 4.18–4.22 (m, 3H), 4.7–4.80 (bm, 3H), 5.18 (d, J=1.1, 1H), 7.15–7.25 (m, 3H), 7.40 (d, J=7.8, 2H); ^{13}C NMR: −5.2 (CH_3), 18.1 (Cq), 25.7 (CH_3), 28.0 (CH_3), 51.7 (CH_2), 60.9 (CH), 64.5 (CH), 74.2 (CH_2), 81.6 (Cq), 82.5 (Cq), 85.0 (Cq), 92.0 (CH), 126.8 (CH), 127.4 (CH), 128.2 (CH), 139.8 (Cq), 154.6 (Cq). Anal. Calcd for $C_{24}H_{37}NSiO_5$: C, 64.39; H, 8.34; N 3.13. Found: C, 63.90; H, 8.28; N, 3.00.

[2*R*,2(1*S*),4*R*]-3-*tert*-Butoxycarbonyl-2-(4-benzyloxy-1-hydroxy-but-2-ynyl)-4-phenyl-1,3-oxazolidine 22. Yield 94%; mp 93°C; Rf: 0.55 (E/EP: 60/40); IR ($CHCl_3$): 3200, 2200, 1680; $[\alpha]_D^{20}$: +4.2 (*c* 0.6, $CHCl_3$); ^{1}H NMR:1.21 (bs, 9H), 1.55 (bs, 1H), 4.08 (bs, 2H), 4.13 (dd, J=6 and 8.5, 1H), 4.23 (t, J=8.5, 1H), 4.48 (s, 2H), 4.78–4.90 (bm, 2H), 5.23 (s, 1H), 7.10–7.25 (m, 8H), 7.45 (d, J=7.6, 2H); ^{13}C NMR: 28.1 (CH_3), 57.8 (CH_2), 61.2 (CH), 63.1 (CH), 71.5 (CH_2), 74.8 (CH_2), 82.5 (Cq), 82.0 (Cq), 84.9 (Cq), 85.0 (Cq), 92.5 (CH), 126.7 (CH), 126.8 (CH), 127.6 (CH), 128.2 (CH), 128.6 (CH), 128.8 (CH), 139.8 (Cq), 141.4 (Cq), 154.6 (Cq). Anal. Calcd for $C_{25}H_{29}NO_5$: C, 70.90; H, 6.90; N 3.31. Found: C, 70.85; H, 6.89; N, 3.30.

[2*R*,2(1*S*),4*R*]-3-*tert*-Butoxycarbonyl-2-(1-hydroxy-3-phenyl-prop-2-ynyl)-4-phenyl-1,3-oxazolidine 23. Yield 95%; mp 101°C; $[\alpha]_D^{20}$: +19 (*c* 1.1, $CHCl_3$); ^{1}H NMR: 1.21 (bs, 9H), 4.15 (dd, J=6 and 8.6, 1H), 4.27 (dd, J=7.4 and 8.5, 1H), 4.79 (bs, 1H), 4.93 (bd, J=7.8, 1H), 5.15 (bs, 1H), 5.31 (s, 1H), 7.10–7.44 (m, 10H); ^{13}C NMR: 28.0 (CH_3), 61.2 (CH), 63.1 (CH), 65.3 (CH), 74.2 (CH_2), 81.9 (Cq), 86.5 (Cq), 87.4 (Cq), 85.0 (Cq), 92.4 (CH), 122.5 (CH), 126.9 (CH), 127.9 (CH), 127.6 (CH), 128.1 (CH), 128.3 (CH), 128.4 (CH), 131.8 (Cq), 139.9 (Cq), 154.7 (Cq).

[2*R*,2(1*S*),4*R*]-3-*tert*-Butoxycarbonyl-2-(1-hydroxy-non-2-ynyl)-4-phenyl-1,3-oxazolidine 24. Overall yield from **12** 62%; mp 73°C; Rf: 0.7 (E/EP: 60/40); IR ($CHCl_3$): 3150, 2110, 1680; $[\alpha]_D^{20}$: +8.3 (*c* 1.1, $CHCl_3$); ^{1}H NMR: 0.75 (t, J=6.8, 3H), 1.16 (bs, 9H), 1.05–1.30 (m, 8H), 2.04 (bt, J=6.9, 2H), 4.08 (dd, J=6 and 8.9, 1H), 4.19 (bt, J=8.6, 1H), 4.64–4.75 (bm, 1H), 5.15 (d, J=1.5, 1H), 7.10–7.22 (m, 3H), 7.38 (dd, J=6.9 and 1, 2H); ^{13}C NMR: 14.4 (CH_3), 19.3 (CH_2), 22.9 (CH_2), 28.4 (CH_3), 28.8 (CH_2), 29.0 (CH_2), 31.7 (CH_2), 61.5 (CH), 65.0 (CH), 74.5 (CH_2), 82.0 (Cq), 87.8 (Cq), 92.8 (CH), 127.3 (CH), 127.9 (CH), 128.6 (CH), 140.5 (Cq), 154.3 (Cq).

General procedure for the Red-Al-mediated reduction of carbinols 21–23

To a solution of carbinol (5 mmol) in THF (35 mL), was added dropwise at RT a solution of Red-Al in toluene (3.5 M solution, 2.25 mL, 7.9 mmol). Completion of the reduction was ascertained by TLC and required ca. 0.5 h. The mixture was then hydrolyzed by dropwise addition of a saturated aqueous solution of NH_4Cl (10 mL). Addition of water and ether, followed by usual workup gave (*E*)-allylic alcohols **25**–**27** as oils that were further purified by flash chromatography.

[2*R*,2(1*S*,2*E*),4*R*]-3-*tert*-Butoxycarbonyl-2-(4-*tert*-butyldimethylsilyloxy-1-hydroxy-but-2-enyl)-4-phenyl-1,3-oxazolidine 25. Yield 85%. Oil. Rf: 0.55 (E/EP: 70/30); IR ($CHCl_3$): 3400, 1620, 1690; $[\alpha]_D^{20}$: −21 (*c* 0.9, $CHCl_3$); ^{1}H NMR: 0.01 (s, 6H), 0.76 (s, 9H), 1.18 (bs, 9H), 3.85 (bs, 1H), 4.00 (dd, J=5.4 and 8.5, 1H), 4.15 (d, J=3.8, 2H), 4.21 (t, J=7.8, 1H), 4.42 (bm, 1H), 4.82 (bm, 1H), 5.15 (d, J=2.9, 1H), 5.74 (dd, J=5.4 and 15.7, 1H), 5.86 (dt, J=3.9 and 15.7, 1H) 7.15–7.25 (m, 3H), 7.29 (d, J=7.8, 2H); ^{13}C NMR: −5.2 (CH_3), 18.1 (Cq), 25.7 (CH_3), 28.0 (CH_3), 60.5 (CH), 63.1 (CH_2), 72.5 (CH), 73.5 (CH_2), 81.1 (Cq), 92.6 (CH), 126.5 (CH), 127.3 (CH), 127.6 (CH), 128.2 (CH), 132.2 (CH), 139.8 (Cq), 154.6 (Cq). Anal. Calcd for $C_{24}H_{39}NSiO_5$: C, 64.11; H, 8.74; N 3.11. Found: C, 64.09; H, 8.78; N, 3.01.

[2*R*,2(1*S*,2*E*),4*R*]-3-*tert*-Butoxycarbonyl-2-(4-benzyloxy-1-hydroxy-but-2-enyl)-4-phenyl-1,3-oxazolidine 26. Yield 80%. Oil. Rf: 0.59 (E/EP: 70/30); IR ($CHCl_3$): 3410, 1622, 1692; $[\alpha]_D^{20}$: −26.3 (*c* 0.52, $CHCl_3$); ^{1}H NMR: 1.24 (bs, 9H), 3.8–4.0 (bs, 1H), 3.97–4.06 (m, 3H), 4.21 (t, J=7.8, 1H), 4.43 (bs, 3H), 4.42 (bm, 1H), 4.84 (bs, 1H), 5.15 (d, J=2.5, 1H), 5.78 (dd, J=5.4 and 16, 1H), 5.90 (dt, J=5.4 and 16, 1H) 7.15–7.35 (m, 10H); ^{13}C NMR: 27.6 (CH_3), 60.1 (CH), 69.1 (CH_2), 71.7 (CH_2), 72.0 (CH), 72.9 (CH_2), 80.9 (Cq), 92.2 (CH), 126.2 (CH), 127.1 (CH), 127.3 (CH), 128.0 (CH), 129.0 (CH), 130.2 (CH), 137.8 (CH), 139.8 (Cq), 154.5 (Cq).

[2*R*,2(1*S*,2*E*),4*R*]-3-*tert*-Butoxycarbonyl-2-(1-hydroxy-3-phenyl-prop-2-enyl)-4-phenyl-1,3-oxazolidine 27. Yield 75%. Oil. Rf: 0.5 (E/EP: 70/30); IR ($CHCl_3$): 3420, 1620, 1690; $[\alpha]_D^{20}$: −28 (*c* 0.7, $CHCl_3$); ^{1}H NMR: 1.18 (bs, 9H), 4.01 (dd, J=4.8 and 8.8, 1H), 4.19 (t, J=7.6, 1H), 4.52 (bs, 1H), 4.82 (bs, 1H), 5.21 (bs, 1H), 6.18 (dd, J=6.1 and 16, 1H), 6.64 (d, J=16, 1H) 7.09–7.25 (m, 10H); ^{13}C NMR: 28.1 (CH_3), 60.7 (CH), 73.3 (CH), 73.5 (CH_2), 81.6 (Cq),

93.1 (CH), 126.7 (CH), 127.6 (CH), 128.5 (CH), 132.2 (CH), 136.8 (CH), 140.3 (Cq), 154.8 (Cq).

General procedure for the Lindlar-catalyzed hydrogenation of carbinols 21 and 22

In a solution of carbinol (2.3 mmol) in ethanol (20 mL), was suspended Lindlar's catalyst (155 mg, 15 wt. % of palladium). The vessel was flushed with hydrogen, and the mixture was vigorously stirred for 0.5 h. The mixture was then filtered over a short pad of Celite, and the catalyst was washed with ethanol. Evaporation of the solvent gave *Z*-allylic alcohols **28** and **29** as oils that were further purified by flash chromatography.

[2*R*,2(1*S*,2*Z*),4*R*]-3-*tert*-Butoxycarbonyl-2-(4-*tert*-butyldimethylsilyloxy-1-hydroxy-but-2-enyl)-4-phenyl-1,3-oxazolidine 28. Yield 90%. Oil. Rf: 0.53 (E/EP: 70/30); IR ($CHCl_3$): 3400, 1620, 1690; $[\alpha]_D^{20}$: +16 (*c* 0.7, $CHCl_3$); ^{1}H NMR: 0.04 (s, 6H), 0.83 (s, 9H), 1.26 (bs, 9H), 3.62 (bs, 1H), 4.04 (dd, *J*=5.8 and 8.7, 1H), 4.12–4.21 (m, 2H), 4.31 (dd, *J*=6 and 13.5, 1H), 4.65 (bd, *J*=5.7, 1H), 4.80 (bm, 1H), 5.09 (d, *J*=2.6, 1H), 5.54 (dd, *J*=5.6 and 5.9, 1H), 5. 63–5.72 (m, 1H) 7.13–7.25 (m, 3H), 7.31–7.35 (m, 2H); ^{13}C NMR: −5.5 (CH_3), 17.9 (Cq), 25.5 (CH_3), 27.7 (CH_3), 59.5 (CH), 60.4 (CH_2), 68.1 (CH), 73.2 (CH_2), 80.7 (Cq), 92.4 (CH), 126.5 (CH), 127.1 (CH), 127.9 (CH), 128.2 (CH), 133.1 (CH), 140.0 (Cq), 155.4 (Cq).

[2*R*,2(1*S*,2*Z*),4*R*]-3-*tert*-Butoxycarbonyl-2-(4-benzyloxy-1-hydroxy-but-2-enyl)-4-phenyl-1,3-oxazolidine 29. Yield 80%. Oil. Rf: 0.55 (E/EP: 70/30); IR ($CHCl_3$): 3405, 1622, 1695; $[\alpha]_D^{20}$: +24 (*c* 0.54, $CHCl_3$); ^{1}H NMR: 1.24 (bs, 9H), 3.8–4.0 (bs, 1H), 3.9–4.18 (m, 3H), 4.18 (t, *J*=7.9, 1H), 4.43 (bs, 2H), 4.62 (bs, 1H), 4.84 (bs, 1H), 5.10 (bd, *J*=2.5, 1H), 5.60–5.82 (m, 2H) 7.15–7.30 (m, 10H); ^{13}C NMR: 28.1 (CH_3), 60.6 (CH), 66.2 (CH_2), 68.4 (CH_2), 72.3 (CH), 73.3 (CH_2), 81.4 (Cq), 92.7 (CH), 126.8 (CH), 127.1 (CH), 127.3 (CH), 127.9 (CH), 129.1 (CH), 130.1 (CH), 130.2 (CH), 138.1 (CH), 140.2 (Cq), 154.4 (Cq). Anal. Calcd for $C_{25}H_{31}NO_5$: C, 70.56; H, 7.34; N 3.29. Found: C, 69.61; H, 7.53; N, 3.15.

General procedure for the mesylation of allylic alcohols 25–28 and of carbinol 24

To a solution of the allylic alcohols **25**–**28** or of carbinol **24** (2.6 mmol) and triethylamine (0.5 mL, 3.5 mmol), in dichloromethane (30 mL) cooled at 0°C was added methanesulfonyl chloride (0.25 mL, 3.2 mmol). The solution was stirred at RT for 0.5 h and water was then added. Usual workup (dichloromethane) gave mesylates **30**–**33** as oils that were used without further purification. Mesylate derived from **27** proved to be unstable and could not be isolated.

[2*R*,2(1*S*,2*E*),4*R*]-3-*tert*-Butoxycarbonyl-2-(4-*tert*-butyldimethylsilyloxy-1-methanesulfonyloxy-but-2-enyl)-4-phenyl-1,3-oxazolidine 30. Yield 98%. Oil. Rf: 0.55 (E/EP: 70/30); $[\alpha]_D^{20}$: +75 (*c* 0.6, $CHCl_3$); ^{1}H NMR: 0.01 (s, 6H), 0.84 (s, 9H), 1.14 (bs, 9H), 2.70 (s, 3H), 4.10 (dd, *J*=6.4 and 8.9, 1H), 4.17 (bs, 2H), 4.27 (dd, *J*=7.3 and 8.9, 1H), 4.87 (bs, 1H), 5.20 (d, *J*=3.7, 1H), 5.35 (bs, 1H), 5.90 (dd, *J*=7.8 and 15, 1H), 6.18–6.24 (m, 1H), 7.15–7.23 (m, 3H), 7.29 (d, *J*=7.8, 2H); ^{13}C NMR: −5.3 (CH_3), 18.3 (Cq), 25.9 (CH_3), 28.1 (CH_3), 38.8 (CH_3), 60.6 (CH), 62.5 (CH_2), 72.8 (CH_2), 81.2 (CH), 81.5 (Cq), 90.7 (CH), 122.5 (CH), 126.9 (CH), 127.7 (CH), 128.5 (CH), 137.3 (CH), 139.2 (Cq), 154.6 (Cq).

[2*R*,2(1*S*,2*E*),4*R*]-3-*tert*-Butoxycarbonyl-2-(4-benzyloxy-1-methanesulfonyloxy-but-2-enyl)-4-phenyl-1,3-oxazolidine 31. Yield quant. Oil. Rf: 0.59 (E/EP: 70/30); $[\alpha]_D^{20}$: +60.5 (*c* 0.5, $CHCl_3$); ^{1}H NMR: 1.23 (bs, 9H), 2.66 (s, 3H), 3.8–4.0 (bs, 1H), 4.01 (d, *J*=3.7, 2H), 4.09 (dd, *J*=6.2 and 9, 1H), 4.26 (t, *J*=9, 1H), 4.45 (bs, 2H), 4.90 (bs, 1H), 5.20 (d, *J*=4.5, 1H), 5.90 (dd, *J*=4.5 and 16, 1H), 6.03 (dt, *J*=4 and 16, 1H), 7.15–7.35 (m, 10H); ^{13}C NMR: 28.1 (CH_3), 39.7 (CH_3), 60.6 (CH), 69.2 (CH_2), 71.5 (CH_2), 73.0 (CH_2), 80.8 (CH), 81.6 (Cq), 92.0 (CH), 125.1 (CH), 127.4 (CH), 127.3 (CH), 128.1 (CH), 128.2 (CH), 128.8 (CH), 128.9 (CH), 130.2 (CH), 134.3 (CH), 137.8 (Cq), 139.8 (Cq), 153.8 (Cq).

[2*R*,2(1*S*,2*Z*),4*R*]-3-*tert*-Butoxycarbonyl-2-(4-benzyloxy-1-methanesulfonyloxy-but-2-enyl)-4-phenyl-1,3-oxazolidine 32. Yield quant. Oil. Rf: 0.52 (E/EP: 70/30); $[\alpha]_D^{20}$: +58 (*c* 0.3, $CHCl_3$); ^{1}H NMR: 1.23 (bs, 9H), 2.65 (s, 3H), 4.0–4.22 (m, 4H), 4.42 (d, *J*=2.5, 2H), 4.85 (bs, 1H), 5.12 (d, *J*=2.8, 1H), 5.70 (bs, 1H), 5.76 (bt, *J*=7.2, 1H), 5.90–6.01 (m, 1H), 7.15–7.40 (m, 10H); ^{13}C NMR: 28.1 (CH_3), 38.6 (CH_3), 60.4 (CH), 66.0 (CH_2), 72.7 (CH_2), 72.8 (CH_2), 76.1 (CH), 81.3 (Cq), 90.4 (CH), 125.2 (CH), 127.0 (CH), 128.8 (CH), 128.0 (CH), 128.8 (CH), 128.3 (CH), 128.4 (CH), 133.0 (CH), 137.8 (Cq), 139.2 (Cq), 153.5 (Cq).

[2*R*,2(1*S*),4*R*]-3-*tert*-Butoxycarbonyl-2-(1-methanesulfonyloxy-non-2-ynyl)-4-phenyl-1,3-oxazolidine 33. Yield quant. Oil. Rf: 0.7 (E/EP: 60/40); $[\alpha]_D^{20}$: +15 (*c* 1.5, $CHCl_3$); ^{1}H NMR: 0.81 (t, *J*=6.8, 3H), 1.20–1.51 (bm, 17H), 2.21 (td, *J*=7.1 and 2.1, 2H), 2.93 (s, 3H), 4.04 (dd, *J*=7.5 and 8.7, 1H), 4.31 (dd, *J*=7.9 and 8.6, 1H), 4.90 (bs, 1H), 5.34 (d, *J*=2.9, 1H), 5.52 (bs, 1H), 7.10–7.40 (m, 5H); ^{13}C NMR: 14.4 (CH_3), 19.3 (CH_2), 22.9 (CH_2), 28.4 (CH_3), 28.5 (CH_2), 28.6 (CH_2), 31.6 (CH_2), 39.4 (CH_3), 53.9 (CH), 61.3 (CH), 71.6 (CH), 73.2 (CH_2), 74.7 (CH_2), 81.9 (Cq), 91.0 (CH), 91.9 (Cq), 127.2 (CH), 128.1 (CH), 128.9 (CH), 139.3 (Cq), 154.1 (Cq).

General procedure for the organocuprate alkylation of mesylates 30–32 with Me_2CuLi

To a suspension of copper iodide (1.56 g, 8.22 mmol) in THF (25 mL) was added dropwise at −78°C a solution of methyllithium (1.4N solution in ether, 9.4 mL, 13.2 mmol). The solution was allowed to reach −20°C and was then cooled again to −78°C. To this solution was added the required mesylate (3.3 mmol) in THF (10 mL). The mixture was stirred at ca. −60°C for 1 h and hydrolyzed by addition of a saturated aqueous solution of NH_4Cl (10 mL) and ammonia (30% aqueous solution, 3 mL). Addition of water and ether was followed by usual workup. Crude alkenyl oxazolidines were then purified by flash chromatography and were obtained as oils.

[2*R*,2(1*E*,3*S*),4*R*]-3-*tert*-Butoxycarbonyl-2-(4-*tert*-butyldimethylsilyloxy-3-methyl-but-1-enyl)-4-phenyl-1,3-oxazolidine 34. Yield 79%. Oil. Rf: 0.5 (E/EP: 20/50); IR ($CHCl_3$): 2980, 1730; $[\alpha]_D^{20}$: −19 (*c* 0.7, $CHCl_3$); ^{1}H NMR: −0.02 (s, 6H), 0.83 (s, 9H), 0.99 (d, *J*=6.7, 3H), 1.30 (bs, 9H), 2.32–2.38 (m, 1H), 3.36 (dd, *J*=7.1 and 9.7, 1H), 3.51 (dd, *J*=5.8 and 9.7, 1H), 3.91 (dd, *J*=5.2 and 8.7, 1H), 4.20 (dd, *J*=6.8 and 8.7, 1H) 4.86 (bs, 1H), 5.54 (bs, 1H), 5.59 (dd, *J*=5.8 and 14.7, 1H), 5.81 (dd, *J*=7.1 and 14.7, 1H), 7.19–7.30 (m, 5H); ^{13}C NMR: −5.3 (CH_3), 16.5 (CH_3), 18.3 (Cq), 25.9 (CH_3), 28.3 (CH_3), 38.9 (CH_3), 60.5 (CH), 67.6 (CH_2), 73.1 (CH), 80.4 (Cq), 90.1 (CH), 126.6 (CH), 127.1 (CH), 127.3 (CH), 128.4 (CH), 137.8 (CH), 140.8 (Cq), 153.4 (Cq). Anal. Calcd for $C_{25}H_{41}NSiO_4$: C, 67.07; H, 9.23; N 3.13. Found: C, 67.01; H, 9.40; N, 3.16.

[2*R*,2(1*E*,3*S*),4*R*]-3-*tert*-Butoxycarbonyl-2-(4-benzyloxy-3-methyl-but-1-enyl)-4-phenyl-1,3-oxazolidine 36. Yield 78%. Oil. Rf: 0.3 (E/EP: 20/80); IR ($CHCl_3$): 2980, 1730; $[\alpha]_D^{20}$: −15.3 (*c* 1.1, $CHCl_3$); ^{1}H NMR: 1.02 (d, *J*=6.8, 3H), 1.27 (bs, 9H), 2.52 (hept, *J*=6.7, 1H), 3.25–35 (ABX, 2H), 3.90 (dd, *J*=5.2 and 8.7, 1H), 4.18 (dd, *J*=6.8 and 8.7, 1H), 4.43 (s, 2H), 4.85 (bs, 1H), 5.54 (bs, 1H), 5.57 (dd, *J*=15 and 5, 1H), 5.82 (dd, *J*=15 and 7, 1H), 7.15–7.28 (m, 10H); ^{13}C NMR: 17.4 (CH_3), 28.8 (CH_3), 37.0 (CH), 61.0 (CH), 73.5 (CH_2), 73.6 (CH_2), 75.3 (CH_2), 80.9 (Cq), 90.4 (CH), 127.1 (CH), 127.5 (CH), 127.9 (CH), 128.0 (CH), 128.1 (CH), 128.9 (CH), 138.1 (CH), 139.0 (Cq), 141.3 (Cq), 153.9 (Cq). Anal. Calcd for $C_{26}H_{33}NO_4$: C, 73.73; H, 7.85; N 3.31. Found: C, 73.58; H, 7.88; N, 3.32.

[2*R*,2(1*E*,3*R*),4*R*]-3-*tert*-Butoxycarbonyl-2-(4-benzyloxy-3-methyl-but-1-enyl)-4-phenyl-1,3-oxazolidine 37. Yield 72%. Oil. Rf: 0.3 (E/EP: 20/80); IR ($CHCl_3$): 2980, 1730; $[\alpha]_D^{20}$: −18.6 (*c* 1.2, $CHCl_3$); ^{1}H NMR: 1.05 (d, *J*=6.8, 3H), 1.28 (bs, 9H), 2.55 (hept, *J*=6.7, 1H), 3.60–3.75 (ABX, 2H), 3.93 (dd, *J*=5.2 and 8.7, 1H), 4.21 (dd, *J*=6.0 and 8.7, 1H), 4.35 (s, 2H), 4.76 (bs, 1H), 5.46 (bs, 1H), 5.50 (dd, *J*=15 and 5, 1H), 5.76 (dd, *J*=15 and 7, 1H), 7.15–7.30 (m, 10H); ^{13}C NMR: 17.0 (CH_3), 28.7 (CH_3), 36.5 (CH), 60.6 (CH), 73.1 (CH_2), 73.2 (CH_2), 75.0 (CH_2), 80.4 (Cq), 90.1 (CH), 126.4 (CH), 127.0 (CH), 127.4 (CH), 127.5 (CH), 128.5 (CH), 128.6 (CH), 138.1 (CH), 138.9 (Cq), 141.2 (Cq), 153.9 (Cq).

[2*R*,2(1*E*,3*S*),4*R*]-3-*tert*-Butoxycarbonyl-2-(4-*tert*-butyldimethylsilyloxy-3-butyl-but-1-enyl)-4-phenyl-1,3-oxazolidine 35. To a solution of zinc chloride in THF (0.63N, 9.5 mL, 6 mmol) was added dropwise at −78°C a solution of *n*-butyllithium in hexanes (1.58N solution, 3.8 mL, 6 mmol). The solution was warmed to 0°C, cooled again at −78°C, and cannulated into a suspension of copper cyanide (270 mg, 3 mmol) in THF (4 mL) at −78°C. The mixture was warmed at 0°C and the resulting greenish solution was cooled again at −78°C. To this solution was added mesylate **30** (527 mg, 1 mmol) in THF (3 mL). The reaction mixture was allowed to progressively reach 0°C and was stirred for 2 h at this temperature. Hydrolysis was effected by addition of a saturated aqueous solution of NH_4Cl (10 mL) and ammonia (30% aqueous solution, 3 mL). Addition of water and ether was followed by usual workup. Crude alkenyl oxazolidine was then purified by flash chromatography (E/EP: 15/85) and was obtained as an oil. Yield 61%.Rf: 0.35 (E/EP: 20/80); IR ($CHCl_3$): 2980, 1730; $[\alpha]_D^{20}$ −3.7 (*c* 0.65, $CHCl_3$); ^{1}H NMR: 0.35 (s, 6H), 1.04–1.15 (m, 12H), 1.40–1.91 (m, 15H), 2.4–2.6 (m, 1H), 3.77 (dd, *J*=6.4 and 9.8, 1H), 3.85 (dd, *J*=6.4 and 9.8, 1H), 4.25 (dd, *J*=5.6 and 8.7, 1H), 4.55 (dd, *J*=6.9 and 8.7, 1H), 5.05–5.30 (bm, 1H), 5.82–5.92 (m, 2H), 6.03 (dd, *J*=8 and 15.7, 1H), 7.50–7.70 (m, 5H); ^{13}C NMR: −5.6 (CH_3), 14.1 (CH_3), 18.4 (Cq), 23.4 (CH_2), 26.5 (CH_2), 28.8 (CH_3), 29.3 (CH_2), 30.7 (CH_2), 45.1 (CH), 60.6 (CH), 66.4 (CH_2), 73.2 (CH_2), 80.4 (Cq), 90.1 (CH), 126.5 (CH), 127.4 (CH), 128.1 (CH), 128.3 (CH), 136.6 (CH), 140.6 (Cq), 153.5 (Cq). Anal. Calcd for $C_{28}H_{47}NSiO_4$: C, 68.52; H, 9.65; N 2.85. Found: C, 68.60; H, 9.83; N, 2.78.

[2*R*,2(2*R*),4*R*]-3-*tert*-Butoxycarbonyl-2-(3-methylnona-1,2-dienyl)-4-phenyl-1,3-oxazolidine 38. To a solution of copper bromide (430 mg, 3 mmol) and lithium bromide (260 mg, 3 mmol) in THF (15 mL) cooled at −78°C, was added dropwise a solution of methylmagnesium bromide in ether (3N solution, 1 mL, 3 mmol). The mixture was warmed to −20°C within 0.5 h and cooled again at −78°C. To this solution was then added mesylate **33** (700 mg, 1.5 mmol) in THF (5 mL). The mixture was allowed to slowly reach 0°C (1 h) and then quenched by addition of a saturated aqueous solution of NH_4Cl (10 mL) and ammonia (30% aqueous solution, 3 mL). Addition of water and ether was followed by usual workup. Crude allenyl oxazolidine was then purified by flash chromatography (E/EP: 20/80) and was obtained as an oil (463 mg: 80%). Rf: 0.70 (E/EP: 40/60); IR ($CHCl_3$): 2925, 1997, 1703, 1370; $[\alpha]_D^{20}$: −8.5 (*c* 1, $CHCl_3$); ^{1}H NMR: 0.80 (t, *J*=6.9, 3H), 1.20–1.70 (m, 17H), 1.65 (d, *J*= 2.8, 3H), 1.9–2.0 (m, 2H), 3.87 (dd, *J*=6.7 and 8.8, 1H), 4.22 (dd, *J*=6.9 and 8.8, 1H), 4.81 (bs, 1H), 5.19–5.23 (bm, 1H), 5.64 (bd, *J*=5, 1H), 7.10–7.40 (m, 5H); ^{13}C NMR: 14.5 (CH_3), 19.3 (CH_3), 23.0 (CH_2), 27.8 (CH_2), 28.6 (CH_3), 29.4 (CH_2), 32.1 (CH_2), 34.3 (CH_2), 61.1 (CH), 73.5 (CH_2), 80.7 (Cq), 88.8 (CH), 90.9 (CH), 103.6 (Cq), 126.9 (CH), 128.8 (CH), 140.7 (Cq), 153.8 (Cq), 202.3 (Cq). Anal. Calcd for $C_{24}H_{35}NO_3$: C, 74.76; H, 9.15; N 3.63. Found: C, 74.94; H, 9.28; N, 3.72.

(4*S*) and (4*R*) 5-Benzyloxy-4-methyl-pent-2-enol 39 and *ent*-39. To a solution of **36** or **37** (0.7 mmol) in dichloroethane (5 mL) was added at rt trifluoroacetic acid (1 mL). The solution was stirred for 0.5 h and concentrated under reduced pressure. The crude deprotected oxazolidine was then taken up in THF (4 mL) and water (4 mL) and stirred for 1 h. Usual workup gave an oil that was dissolved in EtOH (10 mL) and sodium borohydride (54 mg, 1.4 mmol) was added portionwise at 0°C. After 0.5 h, the mixture was hydrolyzed by addition of a saturated aqueous solution of NH_4Cl (5 mL), and the ethanol was evaporated under reduced pressure. Addition of water and ether, followed by usual work up and flash chromatography (E/EP: 50/50) gave title alkenols as oils. **39**: 83 mg, 57%. Rf: 0.2 (E/EP: 50/50); $[\alpha]_D^{20}$: −9.3 (*c* 2.25, $CHCl_3$); GC (OV17, 60 to 220°C, rate: 10°C/mn): tr 11.3 mn (98%); ^{1}H NMR: 0.95 (d, *J*=6.8, 3H), 1.90 (bs, 1H), 2.42 (hept, *J*=6.5, 1H), 3.22 (dd, *J*=6.5 and 9.1, 1H), 3.29 (dd, *J*=6.5 and 9.1, 1H), 3.98 (d, *J*=4.2, 2H), 4.42 (s, 2H), 5.56–5.90 (m, 2H), 7.22–7.35 (m, 5H); ^{13}C NMR: 17.3 (CH_3), 36.8 (CH), 63.9 (CH), 73.3 (CH_2), 75.4 (CH_2), 127.9 (CH), 128.0

(CH), 128.7 (CH), 129.2 (CH), 135.5 (CH), 138.7 (Cq). *ent*-**39**: 73 mg, 50%; $[\alpha]_D^{20}$: +8.2 (*c* 0.8, $CHCl_3$).

General procedure for the bromocarbamation of alkenyloxazolidines 34, 36 and 37

To a solution of alkenyl oxazolidine (1 mmol) in a mixture of water (5 mL) and dimethoxyethane (5 mL) was added *N*-bromosuccinimide (202 mg, 1.15 mmol). The mixture was stirred for 45 min (2 h in case of substrate **37**) and water was added. Usual workup (dichloromethane) gave **40** and **41** as solids that were triturated with small portions of petroleum ether and used as such in the following step. Analytical samples were purified by flash chromatography. Compound **42** was obtained as an oil and was purified by flash chromatography (E/EP: 60/40).

[3*R*,7*S*,7(1*R*),8*S*,9*R*]-8-Bromo-7-(2-*tert*-butyldimethylsilyloxy-1-methylethyl)-3-phenyl-tetrahydrooxazolo [3,2-c] [1,3]oxazin-5-one 40. Yield 93%. mp: 136°C; Rf: 0.30 (E/EP: 70/30); $[\alpha]_D^{20}$: +15 (*c* 0.4, $CHCl_3$); ^{1}H NMR: 0.02 (s, 6H), 0.76 (d, *J*=6.8, 3H), 0.82 (s, 9H), 2.35–2.41 (m, 1H), 3.44 (dd, *J*=5.8 and 9.9, 1H), 3.59 (t, *J*=9.8, 1H), 3.92 (dd, *J*=8.7 and 11, 1H), 4.09 (t, *J*=9.2, 1H), 4.20 (dd, *J*=6.6 and 9.2, 1H), 4.61 (dd, *J*=1.6 and 11, 1H), 4.88 (d, *J*=6.4, 1H), 5.01 (d, *J*=8.7, 1H), 7.20–7.43 (m, 5H); ^{13}C NMR: −5.5 (CH_3), 8.2 (CH_3), 18.1 (Cq), 25.8 (CH_3), 36.2 (CH), 43.6 (CH), 60.5 (CH), 63.8 (CH_2), 73.7 (CH_2), 77.2 (CH), 89.1 (CH), 126.3 (CH), 128.0 (CH), 128.6 (CH), 139.8 (Cq), 149.0 (Cq). Anal. Calcd for $C_{21}H_{32}NSiBrO_4$: C, 53.61; H, 6.86; N 2.98. Found: C, 54.10; H, 7.14; N, 3.04.

[3*R*,7*S*,7(1*R*),8*S*,9*R*]-8-Bromo-7-(2-benzyloxy-1-methylethyl)-3-phenyl-tetrahydrooxazolo[3,2-c][1,3] oxazin-5-one 41. Yield 89%. mp: 140°C; Rf: 0.24 (E/EP: 70/30); $[\alpha]_D^{20}$: +18 (*c* 0.5, $CHCl_3$); ^{1}H NMR: 0.81 (d, *J*= 7, 3H), 2.49–2.60 (m, 1H), 3.33 (dd, *J*=5.5 and 9.9, 1H), 3.49 (t, *J*=9.9, 1H), 3.90 (dd, *J*=8.6 and 11, 1H), 4.05 (dd, *J*=9.2 and 1.2, 1H), 4.15 (dd, *J*=6.5 and 9.2, 1H), 4.41 (d, *J*=12, 1H), 4.43 (d, *J*=12, 1H), 4.62 (dd, *J*=11 and 2, 1H), 4.88 (dd, *J*=6.5 and 1.2, 1H), 4.99 (d, *J*=8.6, 1H), 7.25–7.55 (m, 10H); ^{13}C NMR: 9.1 (CH_3), 34.4 (CH), 43.9 (CH), 61.1 (CH), 71.5 (CH_2), 73.5 (CH_2), 74.3 (CH_2), 77.6 (CH), 89.6 (CH), 126.8 (CH), 128.0 (CH), 128.6 (CH), 128.8 (CH), 138.6 (Cq), 140.3 (Cq), 149.5 (Cq).

[3*R*,7*S*,7(1*S*),8*S*,9*R*]-8-Bromo-7-(2-benzyloxy-1-methylethyl)-3-phenyl-tetrahydrooxazolo[3,2-c][1,3] oxazin-5-one 42. Yield 70%. Oil. Rf: 0.17 (E/EP: 70/30); $[\alpha]_D^{20}$: +13 (*c* 0.4, $CHCl_3$); ^{1}H NMR: 0.96 (d, *J*=7, 3H), 2.65–2.75 (m, 1H), 3.23 (dd, *J*=4.5 and 9.9, 1H), 3.54 (t, *J*=9.9, 1H), 4.03 (dd, *J*=1.2 and 8.9, 1H), 4.15 (dd, *J*=8.6 and 11, 1H), 4.24 (dd, *J*=1.2 and 10, 1H), 4.33 (s, 2H), 4.70 (dd, *J*=8.9 and 10, 1H), 4.87 (dd, *J*=1.2 and 8.6, 1H), 4.90 (d, *J*=9, 1H), 7.25–7.55 (m, 10H); ^{13}C NMR: 9.1 (CH_3), 34.4 (CH), 43.9 (CH), 61.1 (CH), 71.5 (CH_2), 73.5 (CH_2), 74.3 (CH_2), 77.6 (CH), 89.6 (CH), 126.8 (CH), 128.0 (CH), 128.6 (CH), 128.8 (CH), 138.6 (Cq), 140.3 (Cq), 149.5 (Cq).

[2*R*,2(1*R*,2*R*,3*R*),4*R*]-3-Benzyloxycarbonyl-2-(4-*tert*-butyldimethylsilyloxy-1,2-epoxy-3-methylbutyl)-4-phenyl-1,3-oxazolidine 43. To a suspension of sodium hydride (60 wt. %, 60 mg, 1.5 mmol) in DMF (5 mL), cooled at 0°C, was added dropwise benzyl alcohol (0.155 mL, 1.5 mmol). After 0.5 h, a solution of **38** (471 mg, 1 mmol) in DMF (4 mL) was added dropwise and the mixture was stirred for 0.5 h at 0°C. Addition of water and ether was followed by usual workup and purification by flash chromatography (E/EP: 15/85). Epoxide **43** was obtained as an oil (338 mg, 68% overall yield from **34**). Rf: 0.6 (E/EP: 70/30); $[\alpha]_D^{20}$: −8 (*c* 0.5, $CHCl_3$); ^{1}H NMR: −0.01 (bs, 6H), 0.82 (bs, 9H), 0.91 (d, *J*=7, 3H), 1.62–1.70 (m, 1H), 2.92 (dd, *J*=2 and 6, 1H), 3.21 (bs, 1H), 3.40–3.50 (m, 2H), 4.01 (dd, *J*=7.5 and 8.7, 1H), 4.26 (dd, *J*=7 and 8.8, 1H), 4.88 (bt, *J*=6.8, 1H), 4.98 and 5.04 (AB, *J*=11, 2H), 5.48 (bs, 1H), 6.85–7.38 (m, 10H); ^{13}C NMR: −5.5 (CH_3), 12.9 (CH_3), 18.2 (CH_3), 25.8 (CH_3), 37.5 (CH), 57.2 (CH), 57.4 (CH), 61.4 (CH), 67.3 (CH_2), 74.0 (CH_2), 88.7 (CH), 126.7 (CH), 127.7 (CH), 127.9 (CH), 128.4 (CH), 128.6 (CH), 135.9 (Cq), 139.1 (Cq), 154.7 (Cq). Anal. Calcd for $C_{28}H_{39}NSiO_5$: C, 67.57; H, 7.90; N 2.81. Found: C, 67.73; H, 7.82; N, 2.73.

[2*R*,2(1*R*,2*R*,3*R*),4*R*]-3-Ethyloxycarbonyl-2-(4-benzyloxy-1,2-epoxy-3-methylbutyl)-4-phenyl-1,3-oxazolidine 44. To a suspension of **39** (364 mg, 0.82 mmol) in ethanol (10 mL) was added at RT a solution of sodium ethoxide (prepared from sodium: 188 mg, 8.2 mmol) in ethanol (6 mL). The mixture was stirred at RT for 1 h, and quenched by addition of an aqueous saturated solution of NH_4Cl (5 mL). The ethanol was evacuated under reduced pressure followed by addition of water and ether then usual workup and flash chromatography (E/EP: 60/40) to give title epoxide **44** as an oil (280 mg, 83%). Rf: 0.5 (E/EP: 70/30); $[\alpha]_D^{20}$: −4.8 (*c* 0.5, $CHCl_3$); ^{1}H NMR: 0.94 (d, *J*=6.3, 3H), 1.10 (bs, 3H), 1.74 (hept, *J*=6.8, 1H), 2.88 (dd, *J*=2 and 7, 1H), 3.16 (t, *J*=2.2, 1H), 3.23–3.42 (m, 2H), 3.87–4.01 (m, 2H), 4.17 (dd, *J*=7 and 8.6, 1H), 4.32 (d, *J*=3, 2H), 4.80 (bt, *J*=6.8, 2H), 5.37 (bs, 1H), 7.20–7.41 (m, 10H); ^{13}C NMR: 13.6 (CH_3), 11.4 (CH_3), 35.7 (CH), 57.6 (CH), 57.7 (CH), 60.8 (CH), 61.7 (CH_2), 72.4 (CH_2), 73.0 (CH_2), 73.8 (CH_2), 88.5 (CH), 127.1 (CH), 127.9 (CH), 128.1 (CH), 128.8 (CH), 128.9 (CH), 138.9 (Cq), 139.8 (Cq), 155.3 (Cq). Anal. Calcd for $C_{24}H_{29}NO_5$: C, 70.05; H, 7.10; N, 3.40. Found: C, 68.87; H, 7.22; N, 3.35.

[2*R*,2(1*R*,2*R*,3*S*),4*R*]-3-Ethyloxycarbonyl-2-(4-benzyloxy-1,2-epoxy-3-methylbutyl)-4-phenyl-1,3-oxazolidine 45. Following the procedure for the preparation of **44**, epoxide **45** was obtained as an oil (70%). Rf: 0.5 (E/EP: 70/30); $[\alpha]_D^{20}$: −2.5 (*c* 0.7, $CHCl_3$); ^{1}H NMR: 0.95 (d, *J*=6.8, 3H), 1.10 (bs, 3H), 1.78 (hept, *J*=6.8, 1H), 2.97 (dd, *J*=2 and 7, 1H), 3.16 (t, *J*=2.2, 1H), 3.40–3.50 (m, 2H), 3.98–4.06 (m, 2H), 4.25 (dd, *J*=7 and 8.6, 1H), 4.46 (s, 2H), 4.83 (bt, *J*=6.8, 2H), 5.41 (bs, 1H), 7.15–7.40 (m, 10H); ^{13}C NMR: 13.9 (CH_3), 14.8 (CH_3), 36.2 (CH), 57.6 (CH), 57.7 (CH), 61.2 (CH), 62.2 (CH_2), 72.9 (CH_2), 73.5 (CH_2), 74.3 (CH_2), 88.9 (CH), 127.1 (CH), 127.9 (CH), 128.1 (CH), 128.8 (CH), 128.9 (CH), 138.9 (Cq), 139.8 (Cq), 155.4 (Cq).

[2*Z*, 4*R*, 3(3*R*)]-4-Bromo-4-methyl-3-(3-phenyl-3-*N*-*tert*-butoxycarbonyl-ethyloxy)-dec-2-enal 47. To an emulsion of allenyl oxazolidine **38** (162 mg, 0.42 mmol) in a mixture of water (3 mL) and dimethoxyethane (3 mL) was added *N*-bromosuccinimide (89 mg, 0.54 mmol). The mixture was stirred for 45 mn and water was added. Usual workup

(dichloromethane) gave **47** as an oil that was purified by flash chromatography (E/EP: 50/50).The title compound was obtained as an oil (112 mg, 55%): Rf: 0.5 (E/EP: 70/30); $[\alpha]_D^{20}$: −10.4 (*c* 0.25, $CHCl_3$) IR (film): 2980, 1722; ^{1}H NMR: 0.81 (t, *J*=6.1, 3H), 1.18 (bs, 8H), 1.34 (bs, 9H), 1.43 (s, 3H), 1.55–1.73 (m, 2H) 3.59 (bd, *J*=5, 2H), 4.75 (bs, 1H), 4.92–5.02 (bm, 1H), 6.39 (d, *J*=6.5, 1H), 7.20–7.42 (m, 5H), 9.82 (bd, *J*=6.5, 1H); ^{13}C NMR: 14.1 (CH_3), 22.6 (CH_2), 23.3 (CH_2), 25.1 (CH_3), 28.3 (CH_3), 28.8 (CH_2), 29.2 (CH_2), 39.5 (CH_2), 54..8 (CH), 66.6 (CH2), 79.9 (Cq), 85.0 (Cq), 126.5 (CH), 127.8 (CH), 128.7 (CH), 135.6 (CH), 139.6 (Cq), 152.2 (Cq), 155.2 (Cq), 191.3 (CH). Anal. Calcd for $C_{24}H_{36}NBrO_4(H_2O)$: C, 57.79; H, 7.65; N, 2.79. Found: C, 57.70; H, 7.39; N, 2.53.

[2*R*,2(1*R*,2*R*,3*S*),4*R*]-3-Ethyloxycarbonyl-2-(4-benzyloxy-1-hydroxy-2,3-dimethylbutyl)-4-phenyl-1,3-oxazolidine 48. To a suspension of copper iodide (304 mg, 1.6 mmol) in ether (5 mL) cooled at −78°C was added dropwise a solution of methyllithium (1.4N solution in ether, 2.3 mL, 3 mmol). The mixture was allowed to slowly reach 0°C and a solution of epoxide **44** (220 mg, 0.53 mmol) in ether (5 mL) was then added. The solution was stirred for 12 h at 0°C and hydrolyzed by addition of a saturated aqueous solution of NH_4Cl (10 mL) and ammonia (30% aqueous solution, 3 mL). Addition of water and ether was followed by usual workup. Flash chromatography of the residue (E/EP: 20/80) gave two fractions. The first fraction eluted was the title compound (50 mg, 22%), the second one consisted of a mixture of the title compound and starting material in a respective 80/20 ratio (85 mg). First fraction: oil; Rf: 0.70 (E/EP: 70/30); $[\alpha]_D^{20}$ −17.7 (*c* 1.5, $CHCl_3$); ^{1}H NMR: 0.89 (d, *J*=8, 3H), 0.98 (d, *J*=8, 3H), 1.05 (t, *J*=7.9, 3H), 1.42 (d, *J*=6.5, 0.6H), 1.63 (bs, 0.4H), 1.79–1.90 (m, 1H), 2.20–2.35 (m, 1H), 3.18 (dd, *J*=5 and 9, 1H), 3.46 (bt, *J*=9.2, 1H), 3.53 (bq, *J*= 6.8, 1H), 3.94 (dd, *J*=6.8 and 8.6, 1H), 4.00 (q, *J*=7.9, 2H), 4.23 (t, *J*=8, 1H), 4.45 (s, 2H), 4.98 (bt, 1H), 5.40 (d, *J*=7.4, 1H), 7.15–7.35 (m, 10H); ^{13}C NMR: 11.8 (CH_3), 14.8 (CH_3), 17.4 (CH_3), 32.9 (CH), 40.0 (CH), 61.2 (CH), 62.3 (CH), 72.6 (CH_2), 73.7 (CH_2), 76.4 (CH_2), 73.8 (CH_2), 91.9 (CH), 126.6 (CH), 127.8 (CH), 128.1 (CH), 128.2 (CH), 128.8 (CH), 138.3 (Cq), 140.6 (Cq), 156.9 (Cq).

[2*R*,2(1*R*,2*R*,3*R*),4*R*]-3-Ethyloxycarbonyl-2-(4-benzyloxy-1-hydroxy-2,3-dimethylbutyl)-4-phenyl-1,3-oxazolidine 49 and [2*R*,2(1*S*,2*S*,3*S*),4*R*]-3-Ethyloxycarbonyl-2-(4-benzyloxy-1,3-dimethyl-2-hydroxy-butyl)-4-phenyl-1,3-oxazolidine 50. Following the procedure for the preparation of **48** and starting from **45** (230 mg, 0.56 mmol), an inseparable mixture of **49** and **50** was obtained (30 mg, 17%) Rf: 0.70 (E/EP: 70/30). The ratio of **49** and **50** was determined by integration of the following signals: ^{1}H NMR: 0.86 (d, *J*=8, 2.46H), 0.90 (d, *J*=8, 2.46H), 0.97 (d, *J*=8, 0.54H), 0.98 (d, *J*=8, 0.54H), 1.05 (t, *J*=7.9, 2.46H), 1.14 (t, *J*=7.9, 0.54H).

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