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Epoxyalcohol Route to Hydroxyethylene Dipeptide Isosteres. Stereodivergent Synthesis of the Diamino Alcohol Core of Ritonavir and Its C-2 Epimer

Fabio Benedetti,* Federico Berti, and Stefano Norbedo

Department of Chemical Sciences, University of Trieste, Via Giorgieri 1, I-34127 Trieste, Italy

benedett@univ.trieste.it

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A stereoselective synthesis of hydroxyethylene dipeptide isosteres based on the 1,4-diamino-2-hydroxybutane structure is described. Horner−Emmons olefination of phosphonates derived from α-amino acids, stereoselective reduction of the resulting enones to allylic alcohols, and *syn* epoxidation of the latter lead to enantiomerically pure 1-amino-2-hydroxy-3,4-epoxybutanes, key intermediates in the synthesis. Reductive cleavage of the epoxy alcohols with Red-Al proceeds in a highly regioselective way, giving 1-amino-2,4-dihydroxybutanes, from which diamino alcohol hydroxyethylene isosteres are obtained by selective protection of the secondary 2-hydroxy group, via cyclization to 1,3-oxazolidinone, and further elaboration of the 4-hydroxy. Both C-2 epimers of 1,4-diamino-2-hydroxybutanes are accessible by appropriate choice of the conditions for cyclization. The approach is demonstrated by the synthesis of a series of six hydroxyethylene dipeptide isosteres, including the diamino alcohol core of potent HIV-protease inhibitor ritonavir **18** and its C-2 epimer **11a**.

Introduction

Aspartyl proteases play a crucial role in the development and propagation of several disease states.[1] Renin for example, which is responsible for the conversion of angiotensinogen into angiotensin I, is involved in the development of hypertension, and cathepsin D, another endogenous protease, is thought to be involved in cancer and Alzheimer's disease. Among exogenous enzymes, plasmepsins are believed to be involved in the degradation of human hemoglobin, which is the main source of food for the malarial parasite *Plasmodium falciparum*. The human immunodeficiency virus protease (HIV-PR) is an essential enzyme for the replication of the virus responsible for AIDS, and aspartic proteases secreted into the host organism by strains of *Candida* may be connected with some of the effects caused by infections by these yeasts. The availability of structural information for many enzymes of this class has made them attractive targets for the rational design of potent and selective inhibitors, many of which show great promise as drugs.[1a,2] In particular, a number of designed inhibitors of HIV-PR have rapidly reached the market and are currently used in the therapy of AIDS,[3] in combination with inhibitors of reverse transcriptase, another retroviral enzyme. These combination therapies suppress viral replication for prolonged periods and have led to a significant decline in mortality related to AIDS.[4]

Peptidomimetic inhibitors based on hydroxyethylene dipeptide isosteres **A** show great efficacy against HIV-PR.[1−3,5] Ritonavir[6] and lopinavir,[7] both containing the 1,4-diamino-2-hydroxybutane core **A**, are among the most potent anti-AIDS drugs discovered so far, with excellent oral bioavailability, particularly when administered as an association of the two drugs (Kaletra).[4]

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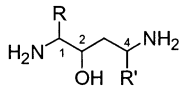
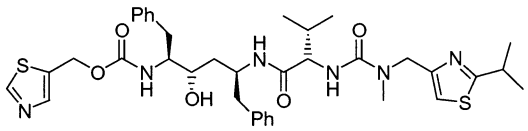
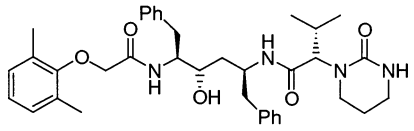
Nanomolar inhibitors of renin based on isosteres **A** have also been reported.[8]



A



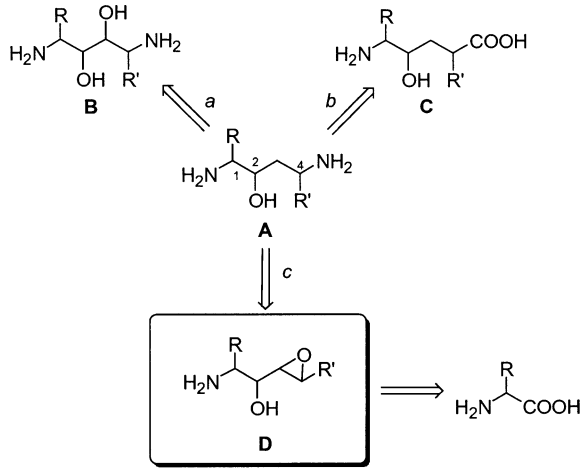
Ritonavir (ABT-538)



Lopinavir (ABT-378)

Due to the presence of the isolated chiral center on C-4, the synthesis of the diamino alcohol core **A** is not straightforward, and these isosteres are in general obtained by transformation of other, more accessible, dipeptide isosteres.[9] Thus, for example, the approach followed in the original synthesis of the diamino alcohol core of ritonavir[10] was based (route a, Scheme 1) on the deoxygenation of dihydroxyethylene isosteres **B** (diaminodiols), which, in turn, can be readily obtained by the pinacol homocoupling of α-aminoaldehydes[11] and from other chiral precursors such as sugars[12] or tartaric acid.[13]

SCHEME 1



This route, however, is practical only for C_2-symmetric diaminodiols, with identical R, R′ groups, the only case in which deoxygenation cannot lead to multiple products, due to the equivalency of the two symmetry-related hydroxy groups.

Another approach to diamino alcohols **A** (Scheme 1, route b) starts from hydroxyethylene isosteres **C** (5-amino-4-hydroxyacids), which are converted into **A** via the Curtius rearrangement of the corresponding acyl azides.[8,14] 4-Amino-3-hydroxybutyric acids **C** are accessible by a number of stereoselective strategies from chiral precursors such as α-amino acids[15] and sugars[16] or from achiral precursors by asymmetric synthesis.[17]

Despite the considerable synthetic effort in this area, however, few direct syntheses of the diamino alcohol core **A** have been reported and are limited to the dibenzyl derivative (R, R′ = CH_2Ph) mimicking the Phe-Phe dipeptide.[18] In this paper we describe a direct and general approach to diamino alcohol dipeptide isosteres **A** starting from α-amino acids (route c, Scheme 1).[19] The key

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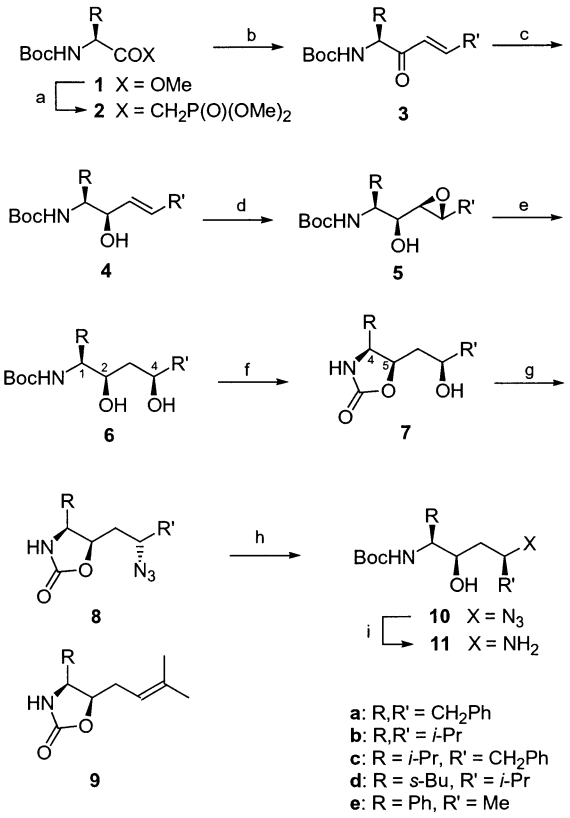
SCHEME 2[a]



[a] (a) $CH_3PO(OCH_3)_2$, n-BuLi, THF; 95%. (b) R′CHO, K_2CO_3, EtOH, 25 °C; 80%. (c) $NaBH_4$, MeOH, 0 °C; 67−79%. (d) mCPBA, CH_2Cl_2, 25 °C; 65−70%. (e) Red-Al, THF, 25 °C; 60−76%. (f) NaH, THF, 25 °C; 78−85%. (g): (i) MsCl, Et_3N, CH_2Cl_2, 0 °C; (ii) NaN_3, 18-crown-6, DMSO, 50 °C; 75−83% overall. (h): (i) Boc_2O, NaH, THF, 25 °C; (ii) K_2CO_3, MeOH/H_2O, 25 °C; 70−85% overall. (i) 1 atm H_2, 10% Pd/C, MeOH, 25 °C; 95−100%.

step in the synthesis is the reductive ring opening of epoxyalcohols **D,** which allows installing the isolated chiral center with the proper stereochemistry. Complete control of stereoselectivity in the formation of the isolated chiral center, access to both epimers at C-2, and the possibility to differentiate between R and R′ residues and between the two amino groups are the key features of this novel synthesis of the 1,4-diamino-2-hydroxybutane core unit.

Results and Discussion

The initial part of the synthesis (Scheme 2) is the preparation of the amino epoxyalcohol intermediates **5**, starting from α-amino acids and following a general approach that we developed as part of our work on dihydroxyethylene isosteres.[20] Aminoesters **1** were initially converted into the corresponding ketophosphonates **2** by reaction with lithiated methyl dimethylphosphonate.[21] Horner−Emmons olefination of the phosphonoketones **2** with the appropriate aldehyde under the conditions described by Mikolajczyk[22] ($EtOH/K_2CO_3$) gave the *trans* enones **3** characterized by a 15.5−16 Hz coupling constant between the vinyl protons. No *cis* isomers were detected, in agreement with the high stereoselectivity generally reported for this reaction.[22b]

The N-Boc aminoketones were then reduced with sodium borohydride in methanol, giving the *syn*-amino alcohols **4**. Hydride addition takes place according to Cram's model (BocNH = medium; R = large) with stereoselectivity ranging from 75% in the reduction of **3a** to over 95% in the reduction of aminoketones **3b**−**e** containing a branched substituent on the α-carbon.[20,23] In the latter case a single crystallization was sufficient to obtain amino alcohols **4** as single diastereoisomers. The enantiomeric purity was checked at this stage, by converting the N-Boc amino alcohols into the corresponding Mosher's esters and was found in every case to be the same as in the starting aminoesters **1**, indicating that no epimerization adjacent to the carbonyl takes place during the synthesis. *Syn* epoxidation[24] of the allylic alcohols **4** with *m*-chloroperoxybenzoic acid was the next step, giving the epoxyalcohols **5** as single stereoisomers. By this sequence of stereoselective reactions epoxyalcohols **5b**, **5d**, and **5e** were obtained in 32%, 40%, and 50% yield from the methyl esters of valine (**1b**), isoleucine (**1d**), and (*S*)-phenylglycine (**1e**), respectively; epoxides **5a** and **5c** were available from our previous investigation, in which the stereochemical course of this reaction sequence was analyzed and discussed in detail.[20]

Conversion of the epoxy alcohol intermediates **5** to hydroxyethylene isosters **11** was then carried out in four passages, as shown in Scheme 2. A regioselective reductive cleavage of the epoxide ring was required in order to set the correct functionalization on the four-carbon skeleton (Scheme 2). Red-Al is known to selectively transfer a hydride to the C-2 of 2,3-epoxy alcohols to give 1,3-diols;[25] accordingly, the reductive ring cleavage of epoxy alcohols **5** with this reagent proceeded successfully to give the *syn*,*syn*-aminodiols **6** in 60−76% isolated yield. Regioisomers derived from hydride attack at C-3 were never detected, irrespectively of the size of the R′ substituent. We have shown previously that, with a variety of nucleophiles under nonchelating conditions, ring opening of epoxides **5** takes place preferentially at the distal

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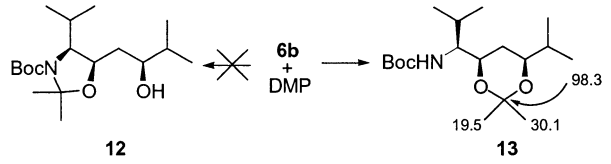
SCHEME 3



12 **13**

carbon.[20,26] The complete C-2 selectivity observed in this case is in agreement with the hypothesis that, in the reductive ring opening by Red-Al, selectivity is controlled by coordination of aluminum to the epoxy alcohol followed by intramolecular delivery of hydride onto C-2.[25a−e] Furthermore, the reduction of methyl epoxide **5e** clearly demonstrates that the scope of the reaction is not limited to substrates possessing bulky R′ substituents.

After establishing the desired functionalization on the butane skeleton, it was necessary to selectively protect the 2-hydroxy group in order to convert the newly formed 4-hydroxy into amine. The logical way to differentiate between the two secondary hydroxy groups was to exploit their different positional relationships with respect to the Boc-protected amino group in the formation of a cyclic N,O-protected derivative. In a first attempt, the aminodiol **6b** was treated with excess 2,2-dimethoxypropane (DMP) in the presence of *p*-toluenesulfonic acid; under these conditions, however, the 1,3-dioxane **13** was obtained rather than the desired oxazolidine **12** (Scheme 3). Although useless for the purpose of the synthesis, compound **13** allowed the confirmation of the *syn* stereochemistry of the parent 1,3-diol **6b**. In particular, in the ^{13}C NMR spectrum of **13** the large difference between the chemical shifts of the isopropylidene methyl groups (19.5 and 30.1 ppm, respectively) and the value of 98.3 ppm for the acetal quaternary carbon are diagnostic of a *syn* relationship between the two hydroxy groups.[27]

The desired intramolecular N,O-protection was eventually obtained by treating the N-Boc aminodiols **6** with sodium hydride in THF (Scheme 2), whereupon an intramolecular acyl transfer cyclization takes place smoothly, giving oxazolidinones **7** in good yields. Values of 7.3−8.0 Hz for the coupling constant $J_{(H4,H5)}$ between the vicinal oxazolidinone ring protons were measured in the ^{1}H NMR spectra of **7**, consistent with a *cis* disposition of the ring substituents.[28] Oxazolidinones **7** derive from L-amino acids via the epoxy alcohols **5**, and no racemization is observed in the early stages of the synthesis;[20] therefore, the *syn*-relationships between the ring substituents of **7** and between the oxygens of **13** (Scheme 3) unambiguously confirm the stereochemical assignments shown in Scheme 2.

Having accomplished the differentiation between the two secondary hydroxy groups, the next step in the synthesis was the conversion of the hydroxy group of **7**, activated as mesylate, into amino. This passage actually proved harder than expected due to the propensity of the intermediate mesylate to eliminate giving the alkene **9**. This was the main or sole product when direct displacement of the mesylate was attempted with concentrated NH_3 in THF or when sodium azide was used as the nucleophile in either aqueous methanol or DMSO. However, carrying out the displacement with sodium azide in dimethyl sulfoxide, in the presence of 18-crown-6, compounds **8** (Scheme 2) where obtained in 80−85% yield for the two passages. A small amount (8%) of elimination product **9** accompanied the formation of **8b** and **8d**, in which a bulky residue (R′ = isopropyl) is present on the carbon adjacent to the reaction center and partially hinders displacement of the leaving group by the nucleophile, while in the synthesis of benzyl derivatives **8a**,**c** and methyl derivative **8e** elimination to the alkene was not observed. The hydroxy and amino groups were then regenerated by treatment of the oxazolidinones **8** with di-*tert*-butyl dicarbonate, followed by hydrolysis of the more labile N-Boc-oxazolidinones thus obtained with potassium or cesium carbonate in aqueous methanol[29] to give N-Boc amino alcohols **10**. Finally, catalytic hydrogenation of the azides **10** gave the selectively monoprotected hydroxyethylene isosteres **11a**−**e**. Diamino alcohols **11** were obtained by this route in 27−38% yield from the epoxyalcohols **5**, while the overall yield from the starting N-Boc-aminoesters **1** was 11−17%. In view of the well-known preference of aspartic proteases for hydrophobic cleavage sites, dipeptide isosteres with aliphatic or aromatic side chains were selected as targets of the present study. However, the methodology is quite general and can be easily extended to other residues.

Dibenzyl diamino alcohol **11a** (Scheme 2) possesses the same structure of the diamino alcohol core of ritonavir and lopinavir, but has the opposite configuration at the alcoholic carbon, which is *R* in **11a** and *S* in ritonavir. Thus, an inversion of configuration at this carbon was required to extend our synthesis from the *syn*,*syn* to the *anti*,*anti* series of isosteres. The feasibility of this approach was demonstrated by the synthesis of the diamino alcohol core of ritonavir.

An initial attempt to invert the configuration of C-2 at a late stage in the synthesis was unsuccessful: when the azido alcohol **10a** was made to react with benzoic acid, under Mitsunobu conditions,[30] a mixture of products was formed, probably due to the presence of the reactive azido group. The solution, eventually, came again from oxazolidinone chemistry. We,[31] and others,[10,32] have shown that when the hydroxy group of chiral N-Boc-β-amino alcohols is converted into a suitable leaving group, cyclization to oxazolidinones can take place with inversion of configuration, by an S_N2 intramolecular displacement (Scheme 4) with concomitant loss of isobutene. The C-5 configuration of the resulting oxazolidinone is opposite with respect to that of the corresponding product

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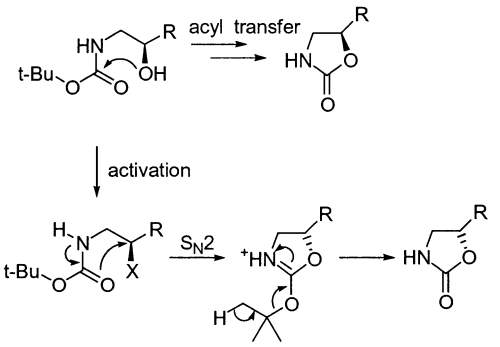
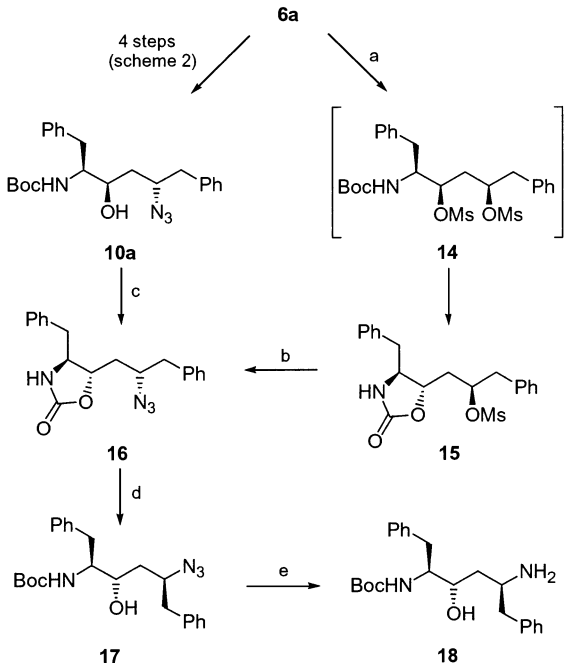
SCHEME 4



SCHEME 5[a]



[a] (a) MsCl, DIPEA, 1,2-dichloroethane, reflux. (b) NaN_3, 18-crown-6, DMSO, 50 °C; 50% for two steps. (c) $SOCl_2$, THF, 25 °C; 80%. (d) (i) Boc_2O, NaH, THF, 25 °C; (ii) K_2CO_3, MeOH/H_2O, 25 °C; 74%. (e) 1 atm H_2, 10% Pd/C, MeOH, 25 °C; 95%.

obtained by the more conventional base-catalyzed intramolecular acyl transfer mechanism.[33]

To apply this approach to the synthesis of the ritonavir core, the azide **10a** was treated with thionyl chloride, as recently described by Ghosh,[32a] to give the C-5 inverted oxazolidinone **16** in 80% yield (Scheme 5). The *trans* stereochemistry of this oxazolidinone was clearly established from a NOE experiment, which showed a 3% enhancement between the ring H-4 and H-5 against a 10% enhancement observed for the same protons in the corresponding *cis* oxazolidinone **8a**.

A more efficient synthesis of **16** was obtained by applying our conditions for N-Boc amino alcohol cyclization[31] directly to the N-Boc aminodiol **6a**, a precursor of the azide **10a**, which was also available from the synthesis of the hydroxyethylene isostere **11a**. When **6a** was treated with excess methanesulfonyl chloride and diisopropylethylamine, in 1,2-dichloroethane at 80 °C, the activated oxazolidinone **15** was smoothly obtained by cyclization of the intermediate bis-mesylate **14** (Scheme 5). It was thus possible, in a single step, to obtain (i) the desired inversion of configuration at the diol C-2; (ii) the selective protection of the first hydroxy group; and (iii) the activation of the second hydroxy group. The crude mesylate **15** was then subjected to the reaction with sodium azide and 18-crown-6, under the same conditions already described for the 2*R* series, to give the azide **16** with an overall yield of 50% for the two steps (Scheme 5). Although the yield for the cyclization step was somewhat lower in this case, the route is more direct and overall yields are better (50% for the pathway **6a** → **15** → **16** against 36% for the pathway **6a** → **10a** → **16**). The final steps of the synthesis, viz., Boc-protection and hydrolysis of the oxazolidinone **16** to give the protected amino alcohol **17** and catalytic hydrogenation of the azide to the (*S*,*S*,*S*)-diamino alcohol **18** (Scheme 5), are analogous to those already described for the epimeric (*S*,*R*,*S*)-isostere **11a**. By this route the Boc-monoprotected ritonavir core **18** was obtained from the diol **6a** in 35% and 25% overall yields for the two pathways described.

Conclusions

We have described a novel, stereoselective synthesis of diamino alcohol dipeptide isosteres based on epoxy alcohol intermediates (**5**) that can be obtained in good yields from α-amino acids. The high level of asymmetric induction observed in all steps ensures that the stereochemical information is efficiently transferred from the first stereogenic center, derived from the amino acid precursor, to the epoxide ring of intermediates **5**. Reductive cleavage of these epoxy alcohols is highly regioselective and generates 1-amino-2,3-diols, which are then elaborated to give the diamino alcohol isosteres, via the selective protection of the 2-hydroxy group as oxazolidinone. By tuning the conditions for N-Boc amino alcohol cyclization to 1,3-oxazolidinone it is further possible to control the configuration of the alcoholic carbon, thus giving access to both *syn*,*syn* and *anti*,*anti* isosteres. The possibility to introduce nonidentical R, R′ side chains, corresponding to natural and nonnatural amino acids, and the selective monoprotection of the amino groups are other valuable features of this approach, particularly for the synthesis of inhibitors in which the isostere is coupled to different peptide residues.[34]

Recently we have described the synthesis of dihydroxyethylene isosteres, based on the 1,4-diamino-2,3-dihydroxybutane[20] and 4-amino-2,3-dihydroxybutyrate[26] cores, via the ring opening of epoxyalcohols **5**. The extension of this approach to the 1,4-diamino-2-hydroxy isostere, described in this work, further demonstrates the utility of epoxy alcohols **5** as intermediates for the synthesis of building blocks of peptidomimetic aspartic protease inhibitors.

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(34) In the original synthesis of ritonavir, approximately 50% of the isostere was lost through statistical formation of the undesired product during the acylation of the unprotected diamino alcohol core. See ref 10.

Experimental Section

Moisture-sensitive reactions were carried out in oven-dried vessels under a positive argon pressure. THF was predried over KOH, fractionated, and redistilled from sodium benzophenone before use. Dichloromethane was dried over $CaCl_2$ and fractionated. Flash column chromatography was performed on silica gel 60 (230−400 mesh); silica gel 60_{F254} coated plastic sheets were used for TLC and developed with I_2 or with aqueous $KMnO_4/H_2SO_4$. Melting points were determined in an open capillary apparatus and are uncorrected. ^{1}H NMR spectra (400 MHz) and ^{13}C NMR spectra (100.4 MHz) were recorded for $CDCl_3$ solutions containing Me_4Si as an internal standard. Mass spectra were obtained by electron impact (MS) and/or electrospray ionization (ES-MS) at the University of Trieste Central Facility for Mass Spectrometry. Elemental analyses were obtained in-house at the Department of Chemical Sciences. Optical rotations were measured at 589 nm for MeOH solutions. Known phosphonates **2a**−**d** were obtained as described.[20,21] The synthesis of epoxyalcohols **5a** and **5c** has been reported previously.[20]

Dimethyl [(3*S*)-3-[*N*-(*tert*-Butyloxycarbonyl)amino]-3-phenyl-2-oxopropyl]phosphonate (2e). Following a reported procedure[20,21] and starting from 8.91 g (33.6 mmol) of (*S*)-*N*-Boc-2-phenylglycine methyl ester, 67.0 mL (168 mmol) of 2.5 M BuLi in hexane, and 18.2 mL (168 mmol) of dimethyl methylphosphonate, a crude oil was obtained, which was crystallized from isopropyl ether to afford 11.41 g (31.9 mmol, 95%) of white crystals; mp 89 °C; $[\alpha]^{25}_D$ +130 (*c* 0.2); IR (Nujol) 3242, 1703 cm^{-1}; ^{1}H NMR δ 1.38 (s, 9H), 2.86 (dd, 1H, J = 14.3, 21.6 Hz), 3.17 (dd, 1H, J = 14.3, 22.0 Hz), 3.61 (d, 3H, J = 11.0 Hz), 3.75 (d, 3H, J = 11.4 Hz), 5.44 (m, 1H), 5.88 (m, NH), 7.28−7.37 (m, 5H, Ar); ^{13}C NMR δ 28.3, 38.0 (d, J = 133 Hz), 53.2, 64.9, 80.1, 128.2, 128.8, 129.4, 136.1, 154.7, 197.6; ES-MS *m*/*z* 358 $[MH]^+$. Anal. Calcd for $C_{16}H_{24}NO_6P$: C 53.8, H 6.77, N 3.92. Found: C 53.9, H 6.38, N 3.92.

***tert*-Butyl (1*S*,3*E*)-1-Isopropyl-5-methyl-2-oxohex-3-enylcarbamate (3b).** Oven-dried K_2CO_3 (3.66 g, 26.5 mmol) was added in small portions, over 15 min, to a stirred solution of phosphonoketone **2b** (R = $CH(CH_3)_2$)[20,21] (8.57 g, 26.5 mmol) and isobutyric aldehyde (2.10 g, 29 mmol) in absolute ethanol (50 mL). After 3 h the reaction mixture was filtered and the solution was neutralized with glacial acetic acid. The solvent was rotary evaporated, and the residue was partitioned between ethyl acetate and saturated aqueous $NaHCO_3$. The aqueous phase was extracted with ethyl acetate, and the combined organic phases were washed with brine and dried over sodium sulfate. The solvent was rotary evaporated, and the crude oily product was purified by flash chromatography with 1:1 diethyl ether/petroleum ether as eluant (5.71 g, 80%): $[\alpha]^{25}_D$ +3.6 (*c* 0.4); IR (neat) 3427, 3335, 1716, 1693, 1626 cm^{-1}; ^{1}H NMR δ 0.71 (d, 3H, J = 7.0 Hz), 0.93 (d, 3H, J = 6.6 Hz), 1.01 (d, 6H, J = 6.6 Hz), 1.37 (s, 9H), 2.04 (m, 1H), 2.42 (m, 1H), 4.46 (dd, 1H, J = 4.0, 8.8 Hz), 5.22 (d, NH, J = 8.8 Hz), 6.08 (d, 1H, J = 15.7 Hz), 6.88 (dd, 1H, J = 6.6, 15.7 Hz); ^{13}C NMR δ 16.6, 19.8, 21.1, 28.2, 30.9, 31.2, 61.9, 79.4, 124.7, 155.3, 155.9, 198.7; ES-MS *m*/*z* 270 $[MH]^+$, 214, 170.

***tert*-Butyl (1*S*,3*E*)-5-Methyl-1-[(1*S*)-1-methylpropyl]-2-oxohex-3-enylcarbamate (3d).** With the same procedure, the phosphonoketone **2d**[20] (8.00 g, 23.7 mmol) and isobutyric aldehyde (1.95 g, 27 mmol) gave 5.37 g (19.0 mmol, 80%) of oily **5d**: $[\alpha]^{25}_D$ +1.1 (*c* 0.9); IR (neat) 3429, 3349, 1702, 1690, 1623 cm^{-1}; ^{1}H NMR δ 0.87 (d, 3H, J = 7.3 Hz), 0.96 (d, 3H, J = 6.8 Hz), 1.08 (d, 6H, J = 6.8 Hz), 1.08−1.32 (m, 2H), 1.43 (s, 9H), 1.82 (m, 1H), 2.49 (m, 1H), 4.52 (dd, 1H, J = 4.4, 8.3 Hz), 5.26 (d, NH, J = 8.3 Hz), 6.15 (d, 1H, J = 15.7 Hz), 6.94 (dd, 1H, J = 15.7, 6.5 Hz); ^{13}C NMR δ 11.6, 16.0, 21.1, 24.1, 28.3, 31.2, 37.7, 61.8, 79.4, 124.9, 155.2, 155.8, 198.9; ES-MS *m*/*z*: 284 $[MH]^+$, 228, 184.

***tert*-Butyl (1*S*,3*E*)-1-Phenyl-2-oxopent-3-enylcarbamate (3e).** With the same procedure, the phosphonoketone **2e** (9.50 g, 26.5 mmol) and acetaldehyde (7.90 g, 180 mmol) gave 6.11 g (22.3 mmol, 84%) of **3e**: needles, mp 80 °C; $[\alpha]^{25}_D$ +171 (*c* 0.2); IR (Nujol) 3417, 1721, 1688, 1630 cm^{-1}; ^{1}H NMR δ 1.39 (s, 9H), 1.79 (dd, 3H, J = 1.5, 7.0 Hz), 5.43 (d, 1H, J = 6.6 Hz), 5.97 (d, NH, J = 6.6 Hz), 6.10 (dd, 1H, J = 1.5, 15.4 Hz), 6.98 (dq, 1H, J = 7.0, 15.4 Hz), 7.26−7.35 (m, 5H, Ph); ^{13}C NMR 18.5, 28.4, 62.6, 79.8, 128.1, 128.2, 128.3, 129.1, 137.2, 145.2, 155.0, 194.3; ES-MS *m*/*z* 276 $[MH]^+$. Anal. Calcd for $C_{16}H_{21}NO_3$: C 69.8, H 7.69, N 5.09. Found: C 69.5, H 8.01, N 5.01.

***tert*-Butyl (1*S*,2*R*,3*E*)-2-Hydroxy-1-isopropyl-5-methylhex-3-enylcarbamate (4b).** $NaBH_4$ (563 mg, 14.8 mmol) was added in small portions over 10 min, at 0 °C, to a stirred solution of enone **3b** (4.00 g, 14.8 mmol) in methanol (50 mL). After 1 h at 0 °C the solution was neutralized with glacial acetic acid, the solvent was rotary evaporated, and the residue was partitioned between ethyl acetate and saturated aqueous $NaHCO_3$. The aqueous phase was extracted with ethyl acetate, and the combined organic phases were washed with brine and dried over sodium sulfate. The solvent was rotary evaporated to give the crude product, which was recrystallized from isopropyl ether (2.69 g, 67%): mp 105−106 °C; $[\alpha]^{25}_D$ −31.5 (*c* 0.5); IR (Nujol) 3365, 1684 cm^{-1}; ^{1}H NMR δ 0.89 (d, 3H, J = 6.9 Hz), 0.92 (d, 3H, J = 6.8 Hz), 0.94 (d, 6H, J = 6.8 Hz), 1.37 (s, 9H), 1.71 (m, 1H), 2.24 (m, 1H), 2.61 (bs, OH), 3.46 (m, 1H), 4.07 (m, 1H), 4.38 (d, NH, J = 9.5 Hz), [5.34 (ddd, J = 15.4, 7.0, 1.1 Hz), 5.64 (dd, J = 15.4, 5.5 Hz), 2H]; ^{13}C NMR δ 18.2, 20.1, 22.2, 28.3, 28.9, 30.8, 60.4, 73.6, 79.4, 125.4, 141.1, 157.0; ES-MS *m*/*z* 272 $[MH]^+$, 216, 172. Anal. Calcd for $C_{15}H_{29}NO_3$: C 66.4, H 10.8, N 5.18. Found: C 66.9, H 11.1, N 5.27.

***tert*-Butyl (1*S*,2*R*,3*E*)-2-Hydroxy-5-methyl-1-[(1*S*)-1-methylpropyl]hex-3-enylcarbamate (4d).** With the same procedure, **3d** (3.00 g, 10.6 mmol) gave 2.39 g (8.37 mmol, 79%) of a white solid: mp 72−74 °C, from isopropyl ether; $[\alpha]^{25}_D$ −28.1 (*c* 0.4); IR (Nujol) 3382, 1683 cm^{-1}; ^{1}H NMR δ 0.87−1.01 (m, 12H), 1.09 (m, 1H), 1.44 (m, 10H), 1.56 (m, 1H), 2.29 (m, 1H), 2.75 (bs, OH), 3.59 (m, 1H), 4.20 (m, 1H), 4.45 (d, NH, J = 9.3 Hz), [5.39 (dd, J = 15.5, 6.9 Hz), 5.72 (dd, J = 15.5, 6.2 Hz), 2H]; ^{13}C NMR δ 11.1, 16.1, 22.2, 24.8, 28.3, 30.8, 35.6, 59.7, 73.4, 79.4, 125.1, 141.1, 157.1; ES-MS *m*/*z* 286 $[MH]^+$, 230, 186. Anal. Calcd for $C_{16}H_{31}NO_3$: C 67.31, H 10.95, N 4.93. Found: C 67.3, H 11.2, N 4.92.

***tert*-Butyl (1*S*,2*R*,3*E*)-2-Hydroxy-1-phenylpent-3-enylcarbamate (4e).** With the same procedure, **3e** (2.66 g, 9.67 mmol) gave 2.41 g (8.70 mmol, 90%) of a white solid: mp 128 °C, from isopropyl ether; $[\alpha]^{25}_D$ +31 (*c* 0.2); IR (Nujol) 3359, 1684 cm^{-1}; ^{1}H NMR δ 1.40 (s, 9H), 1.65 (d, 3H, J = 6.6 Hz), 2.17 (bs, OH), 4.32 (m, 1H), 4.71 (m, 1H), 5.29 (ddd, 1H, J = 1.5, 7.0, 15.4 Hz), 5.68 (dq, 1H, J = 6.6, 15.4 Hz), 7.25−7.34 (m, 5H, Ph); ^{13}C NMR δ 17.8, 28.4, 59.6, 75.5, 79.8, 127.6, 127.8, 128.4, 129.2, 129.5; ES-MS *m*/*z* 278 $[MH]^+$. Anal. Calcd for $C_{16}H_{23}NO_3$: C 69.3, H 8.36, N 5.05. Found: C 69.3, H 8.80, N 5.07.

***tert*-Butyl (1*S*,2*S*,3*R*,4*R*)-3,4-Epoxy-2-hydroxy-1-isopropyl-5-methylhexylcarbamate (5b).** 60% *m*-Chloroperoxybenzoic acid (3.17 g, 11.1 mmol) was added to a stirred solution of alkene **4b** (2.5 g, 9.21 mmol) in dichloromethane. After 24 h at room temperature, the solution was washed with 10% aqueous sodium metabisulfite, saturated aqueous $NaHCO_3$, and brine and dried over sodium sulfate. The solvent was rotary evaporated, and the crude product was purified by flash chromatography eluting with ethyl acetate/dichloromethane mixtures (1.72 g, 65%). Analytical samples were obtained by recrystallization from isopropyl ether/hexane: mp 80−81 °C; $[\alpha]^{25}_D$ +11.5 (*c* 0.7); IR (Nujol) 3371, 1686 cm^{-1}; ^{1}H NMR δ 0.84 (d, 3H, J = 7.0 Hz), 0.89−0.93 (m, 9H), 1.37 (s, 9H), 1.49 (m, 1H), 2.02 (m, 1H), 2.49 (bs, OH), 2.70 (m, 1H), 2.85 (m, 1H), 3.43 (m, 1H), 3.61 (m, 1H), 4.54 (d, NH, J = 10.3 Hz); ^{13}C NMR δ 16.0, 17.3, 17.9, 19.1, 27.3, 27.6, 29.0, 57.2, 57.6, 61.0, 70.0, 78.4, 155.2; ES-MS *m*/*z* 288 $[MH]^+$, 232, 188. Anal. Calcd for $C_{15}H_{29}NO_4$: C 62.7, H 10.2, N 4.87. Found: C 62.5, H 10.3, N 4.90.

***tert*-Butyl (1*S*,2*S*,3*R*,4*R*)-3,4-Epoxy-2-hydroxy-5-methyl-1-[(1*S*)-1-methylpropyl]hexylcarbamate (5d).** With the

same procedure, **4d** (2.00 g, 7.01 mmol) gave 1.48 g (4.91 mmol, 70%) of a white solid: mp 95−97 °C, from isopropyl ether/hexane; $[\alpha]^{25}_D$ +10.4 (*c* 0.4); IR (Nujol) 3363, 1691 cm^{-1}; ^1H NMR δ 0.83−0.94 (m, 13H), 1.36 (s, 9H), 1.45−1.52 (m, 2H), 1.73 (m, 1H), 2.51 (m, 1H), 2.71 (m, 1H), 2.84 (bs, OH), 3.51 (m, 1H), 3.65 (m, 1H), 4.54 (d, NH, J = 9.7 Hz); ^{13}C NMR δ 11.8, 16.4, 18.5, 19.1, 24.0, 28.5, 30.2, 35.6, 58.4, 58.9, 62.1, 70.9, 79.6, 156.5; ES-MS *m*/*z* 302 $[MH]^+$, 246, 202. Anal. Calcd for $C_{16}H_{31}NO_4$: C 63.74, H 10.36, N 4.67. Found: C 63.6, H 10.4, N 4.80.

***tert*-Butyl (1*S*,2*S*,3*R*,4*R*)-3,4-Epoxy-2-hydroxy-1-phenylpentylcarbamate (5e).** With the same procedure, **4e** (1.75 g, 6.32 mmol) gave 1.30 g (4.42 mmol, 70%) of a white solid: mp 135 °C, from isopropyl ether; $[\alpha]^{25}_D$ +53 (*c* 0.2); IR (Nujol) 3370, 1682 cm^{-1}; ^1H NMR δ 1.22 (d, 3H, J = 5.1 Hz), 1.41 (s, 9H), 2.42 (m, 1H), 2.62 (m, 1H), 2.96 (m, 1H), 3.87 (m, 1H), 4.91 (bs, OH), 5.56 (d, NH, J = 7.3 Hz), 7.27−7.37 (m, 5H, Ph); ^{13}C NMR δ 17.0, 28.4, 51.6, 58.5, 59.3, 72.2, 80.0, 127.1, 127.9, 128.7, 138.5, 155.6; ES-MS *m*/*z* 294 $[MH]^+$. Anal. Calcd for $C_{16}H_{23}NO_4$: C 65.5, H 7.90, N 4.77. Found: C 65.3, H 8.28, N 4.71.

General Procedure for the Reductive Ring Opening of Epoxides 5. *tert*-Butyl (1*S*,2*R*,4*R*)-1-Benzyl-2,4-dihydroxy-5-phenylpentylcarbamate (6a). A 70% solution of Red-Al in toluene (10 mL, 35 mmol) was added dropwise, at 0 °C, under an argon atmosphere to a solution of epoxide **5a**[20] (4.50 g, 11.7 mmol) in 60 mL of dry THF. The mixture was stirred at room temperature for 48 h and then cooled in an ice bath and quenched by dropwise addition of water (4.4 mL, 245 mmol) and NaF (10.3 g, 245 mmol). The mixture was stirred for 30 min, and the solid was filtered off and washed several times with ethyl acetate. The solution was dried over anhydrous Na_2SO_4, and the solvent was removed to obtain the crude product, which was purified by flash chromatography (ethyl acetate/petroleum ether, 3:7), giving a white solid (2.71 g, 7.02 mmol, 60%): mp 121−122 °C; $[\alpha]^{25}_D$ −18 (*c* 0.2); IR (Nujol) 3353, 1685 cm^{-1}; ^1H NMR δ 1.35 (s, 9H), 1.60 (m, 1H), 1.70 (m, 1H), 2.76 (m, 4H), 3.78 (m, 1H), 3.83 (m, 1H), 4.04 (m, 1H), 4.68 (d, NH, J = 8.4 Hz), 7.14−7.33 (m, 10H); ^{13}C NMR δ 28.2, 35.6, 38.2, 44.6, 56.5, 73.7, 74.5, 79.8, 126.4, 126.6, 128.3, 128.4, 128.6, 129.1, 129.2, 129.4, 137.8, 156.3; ES-MS *m*/*z* 386 $[MH]^+$, 330, 286. Anal. Calcd for $C_{23}H_{31}NO_4$: C 71.66, H 8.10, N 3.63. Found: C 71.6, H 8.14, N 3.68.

***tert*-Butyl (1*S*,2*R*,4*S*)-2,4-Dihydroxy-1-isopropyl-5-methylhexylcarbamate (6b).** With the same procedure, **5b** (1.50 g, 5.22 mmol) gave **6b** (1.06 g, 3.65 mmol, 70%): white crystals, mp 126−128 °C; $[\alpha]^{25}_D$ −11 (*c* 0.3); IR (Nujol) 3400, 1690 cm^{-1}; ^1H NMR δ 0.83−0.89 (m, 12H), 1.38 (m, 10H), 1.55 (m, 1H), 1.58 (m, 1H), 1.89 (m, 1H), 3.39 (m, 1H), 3.56 (m, 1H), 3.76 (m, 1H), 4.49 (d, NH, J = 9.2 Hz); ^{13}C NMR δ 17.5, 18.3, 20.3, 27.9, 28.3, 34.2, 34.8, 60.3, 74.2, 77.7, 79.6, 157.0; MS (EI) *m*/*z* 289 ($M^{+\bullet}$, 0.05), 246 (0.2), 232 (0.2), 216 (1), 189 (2), 172 (12), 116 (44), 72 (100), 57 (79). Anal. Calcd for $C_{15}H_{31}NO_4$: C 62.24, H 10.79, N 4.86. Found: C 61.8, H 10.7, N 4.88.

***tert*-Butyl (1*S*,2*R*,4*R*)-2,4-Dihydroxy-1-isopropyl-5-phenylpentylcarbamate (6c).** With the same procedure, **5c**[20] (2.00 g, 5.96 mmol) gave **6c** (1.53 g, 4.53 mmol, 76%): oil; $[\alpha]^{25}_D$ −6.9 (*c* 0.3); IR (Nujol) 3363, 1691 cm^{-1}; ^1H NMR δ 0.87 (m, 6H), 1.43 (s, 9H), 1.54 (m, 1H), 1.68 (pseudo d, 1H, J = 14.2 Hz), 1.92 (m, 1H), 2.74 (dd, 1H, J = 5.9, 13.2 Hz), 2.80 (dd, 1H, J = 6.8, 13.2 Hz), 3.42 (m, 1H), 3.55 (bs, OH), 3.78 (m, 1H), 4.07 (m, 2H), 4.54 (d, NH, J = 9.8 Hz), 7.18−7.31 (m, 5H); ^{13}C NMR δ 17.2, 20.2, 27.7, 28.3, 37.9, 44.6, 60.0, 73.58, 73.62, 79.5, 126.4, 128.4, 129.3, 138.0, 156.9; ES-MS *m*/*z* 338 $[MH]^+$, 302.

***tert*-Butyl (1*S*,2*R*,4*S*)-2,4-Dihydroxy-5-methyl-1-[(1*S*)-1-methylpropyl]hexylcarbamate (6d).** With the same procedure, **5d** (2.00 g, 6.64 mmol) gave **6d** (1.29 g, 4.25 mmol, 64%): oil; $[\alpha]^{25}_D$ −7.7 (*c* 0.2); IR (neat) 3460, 1690 cm^{-1}; ^1H NMR δ 0.91 (m, 12H), 1.05 (m, 1H), 1.44 (m, 11H), 1.57−1.71 (m, 3H), 3.50 (m, 1H), 3.61 (m, 1H), 3.71 (bs, OH), 3.89 (m, 1H), 4.16 (bs, OH), 4.56 (d, NH, J = 9.3 Hz); ^{13}C NMR δ 11.3, 16.2, 17.5, 18.2, 24.3, 28.3, 34.1, 34.4, 34.8, 60.0, 73.9, 77.5, 79.7, 157.2; ES-MS *m*/*z* 304 $[MH]^+$, 248, 204.

***tert*-Butyl (1*S*,2*R*,4*S*)-2,4-Dihydroxy-1-phenyl-pentylcarbamate (6e).** With the same procedure, **5e** (800 mg, 2.73 mmol) gave **6e** (483 mg, 1.64 mmol, 60%): white solid; mp 116 °C; $[\alpha]^{25}_D$ +38 (*c* 0.1); IR (Nujol) 3363, 1683 cm^{-1}; ^1H NMR δ 1.13 (d, 3H, J = 6.2 Hz), 1.26 (m, 1H), 1.40 (s, 9H), 1.53 (m, 1H), 2.71 (bs, 2H, OH), 4.01 (m, 1H), 4.15 (m, 1H), 4.62 (m, 1H), 5.41 (d, NH, J = 5.5 Hz), 7.25−7.35 (m, 5H, Ph); ^{13}C NMR δ 24.3, 28.4, 40.7, 59.7, 68.8, 75.0, 80.0, 127.76, 127.81, 128.6, 138.6, 155.9; ES-MS *m*/*z* 296 $[MH]^+$. Anal. Calcd for $C_{16}H_{25}NO_4$: C 65.1, H 8.53, N 4.74. Found: C 65.3, H 8.44, N 4.75.

General Procedure for the Cyclization of N-Boc Amino Alcohols. (4*S*,5*R*)-4-Benzyl-5-[(2R)-2-hydroxy-3-phenylpropyl]-1,3-oxazolidin-2-one (7a). NaH (519 mg of a 60% dispersion in mineral oil, 13.0 mmol) was added portionwise to a solution of aminodiol **6a** (2.50 g, 6.49 mmol) in 50 mL of dry THF, at room temperature, under an argon atmosphere. The mixture was stirred overnight, quenched with 50 mL of a saturated NH_4Cl solution, and stirred for a further 30 min. The aqueous layer was extracted twice with ethyl acetate. The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The solvent was rotary evaporated, and the crude oil was purified by flash chromatography (ethyl acetate/petroleum ether, 1:1) to obtain 1.72 g (5.52 mmol, 85%) of colorless oil **7a**: $[\alpha]^{25}_D$ −42 (*c* 0.2); IR (neat) 3400, 1730 cm^{-1}; ^1H NMR δ 1.92 (m, 1H), 2.06 (m, 1H), 2.37 (bs, OH), 2.62 (dd, 1H, J = 11.0, 13.4 Hz), 2.82 (dd, 1H, J = 3.8, 13.4 Hz), 2.85 (d, 2H, J = 6.6 Hz), 3.96 (m, 1H), 4.08 (m, 1H), 4.88 (ddd, 1H, J = 4.4, 7.3, 11.5 Hz), 5.11 (bs, NH), 7.12−7.34 (m, 10H); ^{13}C NMR δ 35.5, 36.4, 43.5, 56.8, 70.6, 78.0, 126.7, 127.2, 128.7, 128.9, 129.0, 129.1, 129.37, 129.43, 136.3, 137.7, 158.1; ES-MS *m*/*z* 312 $[MH]^+$.

(4*S*,5*R*)-4-Isopropyl-5-[(2*S*)-2-hydroxy-3-methylbutyl]-1,3-oxazolidin-2-one (7b). With the same procedure, **6b** (1.00 g, 3.46 mmol) gave **7b** (610 mg, 2.83 mmol, 82%): mp 119−120 °C from pentane/diisopropyl ether; $[\alpha]^{25}_D$ −4.4 (*c* 0.3); IR (Nujol) 3200, 1730 cm^{-1}; ^1H NMR δ 0.92−1.00 (m, 12H), 1.75−1.96 (m, 4H), 2.42 (bs, OH), 3.62 (m, 2H), 4.77 (ddd, 1H, J = 3.8, 7.4, 10.2 Hz); ^{13}C NMR δ 16.9, 18.0, 18.6, 20.0, 27.9, 32.6, 33.0, 61.6, 74.6, 79.8, 160.0; MS (EI) *m*/*z* 215 ($M^{+\bullet}$, 0), 197 (2), 172 (81), 154 (33), 98 (100), 85 (43), 73 (35). Anal. Calcd for $C_{11}H_{21}NO_3$: C 61.35, H 9.83, N 6.53. Found: C 61.4, H 9.99, N 6.31.

(4*S*,5*R*)-4-Isopropyl-5-[(2*R*)-2-hydroxy-3-phenylpropyl]-1,3-oxazolidin-2-one (7c). With the same procedure, **6c** (1.40 g, 4.15 mmol) gave **7c** (918 mg, 3.48 mmol, 84%): mp 131−132 °C from pentane/diisopropyl ether; $[\alpha]^{25}_D$ −3.2 (*c* 0.2); IR (Nujol) 3300, 1730 cm^{-1}; ^1H NMR δ 0.86 (d, 3H, J = 6.8 Hz), 0.95 (d, 3H, J = 6.6 Hz), 1.81 (m, 2H), 2.01 (ddd, 1H, J = 6.8, 10.4, 14.5 Hz), 2.37 (bs, OH), 2.82 (dd, 1H, J = 7.5, 13.6 Hz), 2.87 (dd, 1H, J = 5.7, 13.6 Hz), 3.55 (pseudo t, 1H, J = 6.7 Hz), 4.09 (m, 1H), 4.75 (ddd, 1H, J = 3.3, 7.3, 10.4 Hz), 6.67 (bs, NH), 7.22−7.33 (m, 5H); ^{13}C NMR δ 18.0, 19.9, 27.8, 34.8, 43.2, 61.6, 70.7, 78.7, 126.6, 128.6, 129.4, 137.8, 159.9; ES-MS *m*/*z* 264 $[MH]^+$. Anal. Calcd for $C_{15}H_{21}NO_3$: C 68.40, H 8.04, N 5.34. Found: C 68.9, H 8.21, N 5.40.

(4*S*,5*R*)-4-[(1*S*)-1-Methylpropyl]-5-[(2*S*)-2-hydroxy-3-methylbutyl]oxazolidin-2-one (7d). With the same procedure, **6d** (1.20 g, 3.95 mmol) gave **7d** (707 mg, 3.08 mmol, 78%): mp 66−69 °C from pentane/diisopropyl ether; $[\alpha]^{25}_D$ −10.5 (*c* 0.2); IR (neat) 3420, 1740 cm^{-1}; ^1H NMR δ 0.86−0.97 (m, 12H), 1.15 (m, 1H), 1.59 (m, 2H), 1.75−1.90 (m, 3H), 2.52 (bs, OH), 3.63 (m, 2H), 6.87 (s, NH); ^{13}C NMR δ 10.7, 16.0, 16.9, 18.6, 24.7, 32.6, 33.0, 34.3, 61.1, 74.5, 79.8, 160.0; ES-MS *m*/*z* 230 $[MH]^+$. Anal. Calcd for $C_{12}H_{23}NO_3$: C 62.84, H 10.11, N 6.13. Found: C 62.7, H 10.0, N 5.70.

(4*S*,5*R*)-4-Phenyl-5-[(2*S*)-2-hydroxypropyl]oxazolidin-2-one (7e). With the same procedure, **6e** (352 mg, 1.19 mmol) gave **7e** (244 mg, 1.10 mmol, 93%): mp 103 °C from pentane/diisopropyl ether; $[\alpha]^{25}_D$ +45 (*c* 0.2); IR (Nujol) 3405, 1723 cm^{-1}; ^1H NMR δ 1.07 (d, 3H, J = 6.2 Hz), 1.21 (pseudo t, 1H, J =

4.2, 14.6 Hz), 1.40 (ddd, 1H, J = 7.3, 9.7, 14.6 Hz), 2.21 (bs, OH), 3.83 (m, 1H), 4.88 (d, 1H, J = 8.0 Hz), 4.99 (ddd, 1H, J = 4.2, 8.0, 9.7 Hz), 6.03 (bs, NH), 7.22 (m, 2H), 7.37 (m, 3H); ^{13}C NMR δ 23.2, 39.9, 59.8, 65.7, 79.5, 127.2, 129.0, 136.6, 159.4; ES-MS m/z 222 $[MH]^+$. Anal. Calcd for $C_{12}H_{15}NO_3$: C 65.1, H 6.83, N 6.33. Found: C 65.2, H 7.18, N 6.17.

General Synthesis of Azides 8. (4*S*,5*R*)-4-Benzyl-5-[(2*S*)-2-azido-3-phenylpropyl]-1,3-oxazolidin-2-one (8a). Et_3N (2.14 mL, 15.4 mmol) and methane sulfonyl chloride (0.60 mL, 7.71 mmol) were added dropwise to alcohol **7a** (1.60 g, 5.14 mmol) in 25 mL of dry dichloromethane, at 0 °C, under an argon atmosphere. After 2 h the solution was diluted with 25 mL of dichloromethane and washed with ice cold water, ice cold 10% aqueous HCl, saturated aqueous $NaHCO_3$, and brine. After drying over anhydrous Na_2SO_4 the solvent was removed under reduced pressure to give the mesylate. NaN_3 (501 mg, 7.71 mmol) and 18-crown-6 (1.36 g, 5.14 mmol) were added to a DMSO solution (3 mL) of the crude mesylate, and the mixture was stirred for 24 h at 50 °C. Water (20 mL) was added, and the mixture was extracted several times with ethyl acetate. The combined organic layers were washed with water and brine and then dried over anhydrous Na_2SO_4. The solvent was rotary evaporated, and flash chromatography (1:1 ethyl acetate/petroleum ether) of the residue gave pure **8a** (1.30 g, 3.86 mmol, 75%): white solid, mp 74−76 °C; $[\alpha]^{25}_D$ +25 (c 0.2); IR (neat) 3300, 2105, 1750 cm^{-1}; ^{1}H NMR δ 1.62 (m, 1H), 1.99 (m, 1H), 2.58 (dd, 1H, J = 11.5, 13.4 Hz), 2.82 (dd, 1H, J = 3.7, 13.4 Hz), 2.94 (d, 2H), J = 6.6 Hz), 4.00 (m, 2H), 4.93 (m, 2H), 7.12−7.37 (m, 10H); ^{13}C NMR δ 34.4, 36.5, 41.7, 56.5, 60.4, 76.3, 127.1, 127.3, 128.7, 128.8, 129.1, 129.3, 136.2, 136.5, 157.9; ES-MS m/z 337 $[MH]^+$, 294, 216. Anal. Calcd for $C_{19}H_{20}N_4O_2$: C 67.84, H 5.99, N 16.66. Found: C 68.0, H 6.11, N 16.5.

(4*S*,5*R*)-4-Isopropyl-5-[(2*R*)-2-azido-3-methylbutyl]-1,3-oxazolidin-2-one (8b). Alcohol **7b** (550 mg, 2.55 mmol) gave azide **8b (**491 mg, 2.04 mmol, 80%), coeluting with a small amount (8%) of elimination product **9b**. **8b** was purified by crystallization: mp 48−50 °C; $[\delta]^{25}_D$ +93 (c 0.3); IR (CCl_4) 3250, 2100, 1760 cm^{-1}; ^{1}H NMR δ 0.92 (d, 3H, J = 6.4 Hz), 0.98 (m, 9H), 1.53 (pseudo t, 1H, J = 12.1 Hz), 1.76−1.92 (m, 3H), 3.53 (m, 1H), 3.63 (m, 1H), 4.80 (m, 1H), 6.79 (bs, NH); ^{13}C NMR δ 17.9, 19.0, 19.1, 19.7, 27.8, 30.8, 33.3, 61.9, 65.0, 77.1, 160.0; ES-MS m/z 241 $[MH]^+$, 213, 198.

(4*S*,5*R*)-4-Isopropyl-5-[(2*S*)-2-azido-3-phenylpropyl]-1,3-oxazolidin-2-one (8c). Alcohol **7c** (850 mg, 3.23 mmol) gave **8c** (772 mg, 2.68 mmol, 83%): white solid, mp 84 °C; $[\alpha]^{25}_D$ +111 (c 0.25); IR (Nujol) 3236, 2104, 1747 cm^{-1}; ^{1}H NMR δ 0.89 (d, 3H, J = 6.8 Hz), 0.96 (d, 3H, J = 6.6 Hz), 1.55 (ddd, 1H, J = 1.2, 2.0, 14.3 Hz), 1.75 (m, 1H), 1.91 (ddd, 1H, J = 2.4, 11.4, 14.3 Hz), 2.88 (dd, 1H, J = 7.8, 13.8 Hz), 2.91 (dd, 1H, J = 5.9, 13.8 Hz), 3.59 (pseudo t, 1H, J = 7.8 Hz), 3.92 (m, 1H), 4.81 (ddd, 1H, J = 2.0, 7.5, 11.4 Hz), 6.68 (bs, NH), 7.22−7.35 (m, 5H); ^{13}C NMR δ 19.1, 19.6, 27.8, 33.6, 41.8, 60.4, 61.8, 76.7, 127.0, 128.7, 129.3, 136.7, 159.9; ES-MS m/z 289 $[MH]^+$. Anal. Calcd for $C_{15}H_{20}N_4O_2$: C 62.43, H 6.99, N 19.5. Found: C 62.8, H 7.10, N 19.5.

(4*S*,5*R*)-4-[(1*S*)-1-Methylpropyl]-5-[(2*R*)-2-azido-3-methylbutyl]-1,3-oxazolidin-2-one (8d). Alcohol **7d (**650 mg, 2.83 mmol), with the same procedure, gave **8d** (577 mg, 2.27 mmol, 80%): oil; $[\alpha]^{25}_D$ +102 (c 0.2); IR (neat) 3450, 2105, 1740 cm^{-1}; ^{1}H NMR δ 0.88−1.02 (m, 12H), 1.17 (m, 1H), 1.54 (m, 3H), 1.85 (m, 2H), 3.54 (ddd, 1H, J = 2.1, 5.0, 11.4 Hz), 3.70 (dd, 1H, J = 7.5, 8.3 Hz), 4.80 (ddd, 1H, J = 2.0, 7.5, 11.4 Hz), 6.70 (s, NH); ^{13}C NMR δ 10.4, 15.6, 17.9, 19.0, 25.7, 30.8, 33.3, 33.8, 60.9, 65.0, 77.0, 160.1; ES-MS m/z 255 $[MH]^+$, 227, 212.

(4*S*,5*R*)-4-Phenyl-5-[(2*R*)-2-azido-propyl]-1,3-oxazolidin-2-one (8e). Alcohol **7e (**224 mg, 1.01 mmol), with the same procedure, gave **8e** (180 mg, 0.73 mmol, 72%): mp 106 °C; $[\alpha]^{25}_D$ +97 (c 0.2); IR (Nujol) 3269, 2106, 1747 cm^{-1}; ^{1}H NMR δ 1.02 (ddd, 1H, J = 2.0, 10.8, 14.5 Hz), 1.18 (d, 3H, J 6.6 Hz), 1.22 (m, 1H), 3.67 (m, 1H), 4.93 (d, 1H, J = 8.0 Hz), 5.03 (m, 1H), 5.96 (bs, NH), 7.22 (m, 2H), 7.38 (m, 3H); ^{13}C NMR δ 20.0, 38.2, 54.6, 59.3, 77.6, 126.9, 129.0, 129.1, 136.5, 159.3; ES-MS m/z 247 $[MH]^+$. Anal. Calcd for $C_{12}H_{14}N_4O_2$: C 58.5, H 5.73, N 22.8. Found: C 59.0, H 5.30, N 22.4.

General Synthesis of Azido Alcohols 10. *tert*-Butyl (1*S*,2*R*,4*S*)-4-Azido-1-benzyl-2-hydroxy-5-phenylpentylcarbamate (10a). NaH (157 mg of a 60% dispersion in mineral oil, 3.92 mmol) was added to **8a** (1.20 g, 3.57 mmol) in 20 mL of dry THF, under an argon atmosphere, and the mixture was stirred at room temperature for 1 h. Boc anhydride (935 mg, 4.28 mmol) was then added in small portions, and stirring was continued for 2 h. 20% aqueous citric acid (20 mL) was then added, and the aqueous layer was separated and extracted twice with ethyl acetate. The combined organic phases were washed with a saturated $NaHCO_3$ solution, the solvent was rotary evaporated, and the residue was taken up in 50 mL of a 4:1 mixture of methanol and water. K_2CO_3 (987 mg, 7.14 mmol) was added, and the mixture was stirred overnight, neutralized with glacial acetic acid, concentrated to one-fifth of its original volume, and extracted twice with ethyl acetate. The combined organic layers were washed with saturated $NaHCO_3$ and brine and dried over anhydrous Na_2SO_4. The solvent was rotary evaporated, and the crude product was purified by flash chromatography (ethyl acetate/petroleum ether mixtures), giving pure **10a** (1.03 g, 2.50 mmol, 70%): white solid, mp 121−123 °C; $[\alpha]^{25}_D$ −5.0 (c 0.2); IR (Nujol) 3376, 3310, 2103, 1686 cm^{-1}; ^{1}H NMR δ 1.35 (s, 9H), 1.50 (m, 1H), 1.65 (ddd, 1H, J = 2.8, 10.1, 13.2 Hz), 2.71 (m, 1H), 2.87 (m, 3H), 3.49 (bs, OH), 3.82 (m, 1H), 3.88 (m, 1H), 3.95 (m, 1H), 4.54 (m, NH), 7.17−7.33 (m, 10H); ^{13}C NMR δ 28.2, 36.3, 37.3, 41.6, 57.1, 60.8, 70.8, 80.0, 126.6, 126.8, 128.3, 128.6, 129.1, 129.3, 137.4, 137.6, 156.6; ES-MS m/z 411 $[MH]^+$, 355, 311. Anal. Calcd for $C_{23}H_{30}N_4O_3$: C 67.29, H 7.37, N 13.65. Found: C 67.5, H 7.45, N 13.7.

***tert*-Butyl (1*S*,2*R*,4*R*)-4-Azido-1-isopropyl-2-hydroxy-5-methylhexylcarbamate (10b).** Oxazolidinone **8b (**450 mg, 1.87 mmol) gave, with the same procedure, the protected amino alcohol **10b** (471 mg, 1.50 mmol, 80%): oil; $[\alpha]^{25}_D$ +14 (c 0.2); IR (neat) 3330, 3440, 2100, 1690 cm^{-1}; ^{1}H NMR δ 0.89−0.99 (m, 12H), 1.45 (m, 10H), 1.84 (m, 3H), 2.88 (d, OH, J = 6.6 Hz), 3.52 (m, 1H), 3.56 (m, 1H), 3.82 (m, 1H), 4.42 (d, NH, J = 8.8 Hz); ^{13}C NMR δ 18.0, 18.1, 19.1, 20.0, 28.3, 28.7, 33.2, 34.2, 60.8, 65.4, 69.6, 79.8, 157.1; ES-MS m/z 315 $[MH]^+$, 259, 215.

***tert*-Butyl (1*S*,2*R*,4*S*)-4-Azido-1-isopropyl-2-hydroxy-5-phenylpentylcarbamate (10c).** Oxazolidinone **8c** (700 mg, 2.43 mmol) gave, with the same procedure, the protected amino alcohol **10c** (669 mg, 1.84 mmol, 76%): white solid, mp 67 °C; $[\alpha]^{25}_D$ +21 (c 0.4); IR (Nujol) 3392, 3378, 2103, 1689 cm^{-1}; ^{1}H NMR δ 0.92 (d, 3H, J = 6.8 Hz), 0.96 (d, 3H, J = 6.8 Hz), 1.43 (s, 9H), 1.43−1.57 (m, 2H), 1.82 (m, 1H), 2.88 (m, 3H), 3.49 (m, 1H), 3.85 (m, 1H), 3.98 (m, 1H), 4.38 (d, NH, J = 8.8 Hz), 7.22−7.31 (m, 5H); ^{13}C NMR δ 18.1, 20.0, 28.3, 28.7, 37.0, 41.7, 60.7, 60.8, 69.4, 79.8, 126.8, 128.6, 129.3, 137.4, 157.1; ES-MS m/z 363 $[MH]^+$, 307. Anal. Calcd for $C_{19}H_{30}N_4O_3$: C 62.92, H 8.34, N 15.5. Found: C 63.3, H 8.49, N 15.2.

***tert*-Butyl (1*S*,2*R*,4*R*)-4-Azido-2-hydroxy-5-methyl-1-[(1*S*)-1-methylpropyl]hexylcarbamate (10d).** Oxazolidinone **8d (**500 mg, 1.97 mmol) gave, with the same procedure, the protected amino alcohol **10d** (549 mg, 1.67 mmol, 85%): oil; $[\alpha]^{25}_D$ +18 (c 0.2); IR (neat) 3450, 3353, 2105, 1691 cm^{-1}; ^{1}H NMR δ 0.90−0.99 (m, 12H), 1.12 (m, 1H), 1.44 (m, 11H), 1.56 (m, 2H), 1.84 (m, 1H), 3.12 (d, OH, J = 6.6 Hz), 3.57 (m, 2H), 3.87 (m, 1H), 4.45 (d, NH, J = 9.0 Hz); ^{13}C NMR δ 11.2, 16.0, 18.0, 19.1, 24.7, 28.3, 33.2, 34.0, 35.4, 60.1, 65.4, 69.2, 79.8, 157.2; ES-MS m/z 329 $[MH]^+$, 286, 273, 239, 216.

***tert*-Butyl (1*S*,2*R*,4*R*)-4-Azido-2-hydroxy-1-phenylpentylcarbamate (10e).** Oxazolidinone **8e (**160 mg, 0.65 mmol) gave, with the same procedure, the protected amino alcohol **10e** (177 mg, 0.55 mmol, 85%): mp 89 °C; $[\alpha]^{25}_D$ +63 (c 0.2); IR (Nujol) 3384, 2103, 1685 cm^{-1}; ^{1}H NMR δ 1.25 (d, 3H, J = 6.6 Hz), 1.28 (m, 1H), 1.40 (s, 9H), 1.53 (m, 1H), 2.13 (bs, OH), 3.73 (m, 1H), 4.07 (ddd, 1H, J = 2.2, 4.8, 10.6 Hz), 4.59 (m, 1H), 5.30 (bs, NH), 7.30 (m, 5H); ^{13}C NMR δ 20.0, 28.4, 40.2, 54.7,

59.6, 71.0, 80.1, 127.7, 127.9, 128.8, 138.6, 155.7; ES-MS *m*/*z* 321 $[MH]^+$. Anal. Calcd for $C_{16}H_{24}N_4O_3$: C 60.0, H 7.55, N 17.5. Found: C 59.8, H 7.99, N 17.2.

General Procedure for the Reduction of Azides. *tert*-Butyl (1*S*,2*R*,4*S*)-4-Amino-1-benzyl-2-hydroxy-5-phenylpentylcarbamate (11a). Azide **10a** (800 mg, 1.95 mmol) in 30 mL of methanol was stirred overnight under a H_2 atmosphere in the presence of 10% Pd/C. The mixture was filtered through a short pad of Celite, and the solvent was removed under reduced pressure to obtain pure **11a** (750 mg, 1.95 mmol, 100%): white solid, mp 130−132 °C; $[\alpha]^{25}_D$ +1.0 (*c* 2); IR (Nujol) 3380, 3340, 3280, 1687 cm^{-1}; ^1H NMR δ 1.34 (s, 9H), 1.59 (m, 1H), 1.75 (ddd, 1H, J = 2.9, 7.3, 14.2 Hz), 2.53 (m, 1H), 2.80 (m, 2H), 3.08 (dd, 1H, J = 3.9, 13.7 Hz), 3.52 (m, 1H), 3.82 (m, 1H), 3.88 (m, 1H), 4.46 (d, NH, J = 8.8 Hz), 7.16−7.32 (m, 10H); ^{13}C NMR δ 28.3, 36.5, 37.4, 44.5, 50.5, 55.2, 71.6, 79.1, 126.1, 126.4, 128.2, 128.6, 129.2, 129.6, 138.3, 138.7, 155.6; ES-MS *m*/*z* 385 $[MH]^+$. Anal. Calcd for $C_{23}H_{32}N_2O_3$: C 71.84, H 8.39, N 7.29. Found: C 71.7, H 8.32, N 7.33.

***tert*-Butyl (1*S*,2*R*,4*R*)-4-Amino-1-isopropyl-2-hydroxy-5-methylhexylcarbamate (11b).** Hydrogenation of **10b** (300 mg, 0.95 mmol), under the same conditions, gave **11b** (261 mg, 0.91 mmol, 95%): oil; $[\alpha]^{25}_D$ +15 (*c* 0.2); IR (neat) 3310, 1690 cm^{-1}; ^1H NMR δ 0.84 (d, 3H, J = 6.8 Hz), 0.88 (d, 6H, J = 6.8 Hz), 0.94 (d, 6H, J = 6.8 Hz), 1.43 (s, 9H), 1.45−1.57 (m, 2H), 1.63 (m, 1H), 2.29 (dd, 1H, J = 3.4, 6.8 Hz), 2.96 (bs, OH, NH_2), 3.01 (m, 1H), 3.60 (pseudo dt, 1H, J = 3.4, 10.2 Hz), 3.69 (m, 1H), 4.34 (d, NH, J = 10.2 Hz); ^{13}C NMR δ 15.3, 17.8, 18.6, 20.3, 27.2, 28.4, 33.8, 34.3, 54.0, 57.8, 70.6, 79.0, 156.1; ES-MS *m*/*z* 289 $[MH]^+$, 233, 189.

***tert*-Butyl (1*S*,2*R*,4*S*)-4-Amino-1-isopropyl-2-hydroxy-5-phenylpentylcarbamate (11c).** Hydrogenation of **10c** (500 mg, 1.38 mmol) gave **11c** (441 mg, 1.31 mmol, 95%): white solid, mp 158−162 °C; $[\alpha]^{25}_D$ +1.7 (*c* 0.2); IR (Nujol) 3350, 1695 cm^{-1}; ^1H NMR δ 0.85 (d, 3H, J = 7.0 Hz), 0.94 (d, 3H, J = 7.0 Hz), 1.45 (s, 9H), 1.63 (m, 1H), 1.73 (m, 1H), 2.25 (m, 1H), 2.57 (dd, 1H, J = 9.3, 13.4 Hz), 2.84 (dd, 1H, J = 4.0, 13.4 Hz), 3.1 (bs, OH, NH_2), 3.57 (m, 2H), 3.78 (m, 1H), 4.37 (d, NH, J = 10.2 Hz), 7.19−7.32 (m, 5H); ^{13}C NMR δ 15.5, 20.3, 26.9, 28.4, 37.4, 44.8, 50.3, 58.4, 70.4, 79.0, 126.4, 128.5, 129.2, 138.6, 156.2; ES-MS *m*/*z* 337 $[MH]^+$, 281. Anal. Calcd for $C_{19}H_{32}N_2O_3$: C 67.80, H 9.58, N 8.36. Found: C 68.1, H 9.72, N 8.21.

***tert*-Butyl (1*S*,2*R*,4*R*)-4-Azido-2-hydroxy-5-methyl-1-[(1*S*)-1-methylpropyl]hexylcarbamate (11d).** Hydrogenation of **10d** (400 mg, 1.22 mmol) gave **11d** (354 mg, 1.17 mmol, 96%): mp 158−162 °C; $[\alpha]^{25}_D$ +6.2 (*c* 0.2); IR (Nujol) 3452, 3332, 1695 cm^{-1}; ^1H NMR δ 0.87−0.95 (m, 12H), 1.42 (s, 9H), 1.40−1.64 (m, 5H), 1.97 (m, 1H), 2.99 (m, 1H), 3.62 (m, 1H), 3.76 (m, 1H), 4.33 (d, NH, J = 10.1 Hz); ^{13}C NMR δ 11.9, 16.4, 17.7, 18.7, 22.5, 28.3, 34.0, 34.3, 34.5, 53.8, 58.3, 70.3, 78.9, 156.1; ES-MS *m*/*z* 303 $[MH]^+$.

***tert*-Butyl (1*S*,2*R*,4*R*)-4-Azido-2-hydroxy-1-phenylpentylcarbamate (11e).** Hydrogenation of **10e** (80 mg, 0.25 mmol) gave **11e** (74 mg, 0.25 mmol, 100%): oil; $[\alpha]^{25}_D$ +38 (*c* 0.2); IR (neat) 3450, 1690 cm^{-1}; ^1H NMR δ (50 °C) 1.16 (d, 3H, J = 6.6 Hz), 1.22 (m, 1H), 1.36 (s, 9H), 1.48 (m, 1H), 3.31 (m, 4H), 4.23 (m, 1H), 4.50 (m, 1H), 5.63 (bs, NH), 7.29 (m, 5H); ^{13}C NMR (50 °C) δ 22.1, 28.2, 39.3, 44.8, 59.6, 70.5, 79.6, 127.4, 128.1, 128.2, 139.8, 155.6; ES-MS *m*/*z* 295 $[MH]^+$.

***tert*-Butyl (1*S*)-1-[(4*R*,6*S*)-6-Isopropyl-2,2-dimethyl-1,3-dioxan-4-yl]-2-methylpropylcarbamate (13).** Aminodiol diol **6b** (240 mg, 0.83 mmol) and *p*-toluensulfonic acid (15 mg, 0.079 mmol) were refluxed in 5 mL of dimethoxypropane. The solvent was rotary evaporated and the residue partitioned between diethyl ether and a saturated $NaHCO_3$ solution. The aqueous layer was extracted again with ether. The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The solvent was rotary evaporated and the crude product purified by flash chromatography (15% ethyl acetate in petroleum ether) to give white crystals (210 mg, 77%): mp 75−80 °C; $[\delta]^{25}_D$ −15 (*c* 0.4); IR (Nujol) 3300, 1690 cm^{-1}; ^1H NMR δ 0.80 (d, 3H, J = 6.8 Hz), 0.85 (d, 3H, J = 6.8 Hz), 0.91 (m, 6H), 1.21 (m, 1H), 1.37 (s, 6H), 1.44 (s, 9H), 1.54 (m, 1H), 1.61 (m, 1H), 2.16 (m, 1H), 3.42 (m, 1H), 3.50 (m, 1H), 3.63 (m, 1H), 4.40 (d, NH, J = 10.3 Hz); ^{13}C NMR δ 15.6, 17.6, 18.5, 19.5, 20.2, 26.6, 28.4, 30.1, 30.9, 33.0, 58.4, 70.0, 74.3, 79.0, 98.3, 156.1; MS (EI) *m*/*z* 329 ($M^{+\bullet}$, 0.01%), 314 (0.01), 172 (11), 157 (33), 116 (29), 99 (100), 57 (92). Anal. Calcd for $C_{18}H_{35}NO_4$: C 65.61, H 10.71, N 4.27. Found: C 65.8, H 11.0, N 4.28.

(4*S*,5*S*)-4-Benzyl-5-[(2*S*)-2-azido-3-phenylpropyl]-1,3-oxazolidin-2-one (16). Method A. Diisopropyl ethylamine (2.2 mL, 12.5 mmol) and methanesulfonyl chloride (0.48 mL, 6.24 mmol) were added, in order, to a solution of diol **6a** (800 mg, 2.08 mmol) in 20 mL of 1,2-dichloroethane, under an argon atmosphere. The mixture was refluxed for 5 h, cooled to room temperature, diluted with 20 mL of dichloromethane, and washed with ice cold water, ice cold 10% aqueous HCl, saturated aqueous $NaHCO_3$, and brine. The organic layer was dried over anhydrous Na_2SO_4, and the solvent was evaporated to give the crude mesylate **15**. To a solution of crude **15** in 2 mL of DMSO were then added NaN_3 (203 mg, 3.12 mmol) and 18-crown-6 (550 mg, 2.08 mmol), and the reaction was carried out as previously described for the synthesis of **8a**, affording 350 mg (1.04 mmol, 50%) of azide **16** as an oil: $[\alpha]^{25}_D$ −35 (*c* 0.2); IR (neat) 3285, 2106, 1755 cm^{-1}; ^1H NMR δ 1.62 (m, 1H), 1.86 (m, 1H), 2.74−2.91 (m, 4H), 3.54 (m, 1H), 3.66 (m, 1H), 4.42 (m, 1H), 6.02 (bs, NH), 7.13−7.36 (m, 10H); ^{13}C NMR δ 38.2, 40.2, 41.4, 59.2, 59.5, 78.5, 127.0, 127.4, 128.6, 129.00, 129.04, 129.3, 135.5, 136.6, 158.4; ES-MS *m*/*z* 337 $[MH]^+$.

Method B. Thionyl chloride (145 mg, 1.22 mmol) was added to a solution of azide **10a** (100 mg, 0.24 mmol) in 2 mL of dry THF under an argon atmosphere, and the reaction mixture was kept at room temperature for 18 h. Evaporation of the solvent under reduced pressure gave the crude azide **16**, which was purified by flash chromatography (1:1 ethyl acetate/petroleum ether) (65 mg, 0.19 mmol, 80%).

***tert*-Butyl (1*S*,2*S*,4*S*)-4-Azido-1-benzyl-2-hydroxy-5-phenylpentylcarbamate (17).** With the same procedure described for the synthesis of **10a**, oxazolidinone **16** (300 mg, 0.89 mmol) gave the N-Boc amino alcohol **17** (271 mg, 0.66 mmol, 74%): oil; $[\alpha]^{25}_D$ −19 (*c* 0.2); IR (neat) 3350, 2105, 1690 cm^{-1}; ^1H NMR δ 1.24−1.52 (m, 10H), 1.62 (m, 1H), 2.85 (m, 4H), 3.72 (m, 2H), 3.85 (m, 1H), 4.89 (d, NH, J = 8 Hz), 7.15−7.28 (m, 10H); ^{13}C NMR δ 28.3, 38.4, 41.2, 55.5, 62.0, 69.8, 79.4, 126.3, 126.7, 126.8, 128.3, 128.4, 128.6, 129.2, 129.3, 136.9, 138.2, 156.0; ES-MS *m*/*z* 412 $[MH]^+$, 384, 355, 311.

***tert*-Butyl (1*S*,2*S*,4*S*)-4-Amino-1-benzyl-2-hydroxy-5-phenylpentylcarbamate (18).** Hydrogenation of **17** (200 mg, 0.49 mmol), as described for the synthesis of **11a**, gave **18** (178 mg, 0.46 mmol, 95%): white solid, mp 58−60 °C; $[\alpha]^{25}_D$ −19 (*c* 0.2); IR (neat) 3438, 3365, 1700 cm^{-1}; ^1H NMR δ 1.24−1.52 (m, 2H), 1.42 (s, 9H), 2.48 (dd, 1H, J = 8.2, 13.6 Hz), 2.80 (dd, 1H, J = 4.9, 13.6 Hz), 2.86 (d, 2H, J = 7.5 Hz), 3.06 (m, 1H), 3.4 (bs, NH_2, OH), 3.66 (m, 1H), 3.78 (m, 1H), 5.10 (d, NH, J = 9.7 Hz), 7.08−7.30 (m, 10H); ^{13}C NMR δ 28.4, 38.8, 38.9, 46.8, 53.9, 56.3, 71.4, 78.9, 126.0, 126.6, 128.3, 128.6, 129.0, 129.3, 129.5, 129.6, 137.7, 138.8, 155.9; ES-MS *m*/*z* 385 $[MH]^+$, 329. Anal. Calcd for $C_{23}H_{32}N_2O_3$: C 71.84, H 8.39, N 7.29. Found: C 72.0, H 8.48, N 7.12.

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Supporting Information Available: Copies of the ^1H NMR and ^{13}C NMR of compounds **2e**, **3**, **4**, **5**, **6**, **7**, **8**, **10**, **11**, **13**, **16**, **17**, and **18**. This material is available free of charge via the Internet at http://pubs.acs.org.

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