Preparation of β^2-Amino Acid Derivatives (β^2hThr, β^2hTrp, β^2hMet, β^2hPro, β^2hLys, Pyrrolidine-3-carboxylic Acid) by Using DIOZ as Chiral Auxiliary[1])

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The title compounds were prepared from valine-derived *N*-acylated oxazolidin-2-ones, **1**–**3**, **7**, **9**, by highly diastereoselective (≥ 90%) *Mannich* reaction (→ **4**–**6**; *Scheme 1*) or aldol addition (→ **8** and **10**; *Scheme 2*) of the corresponding Ti- or B-enolates as the key step. The superiority of the '5,5-diphenyl-4-isopropyl-1,3-oxazolidin-2-one' (DIOZ) was demonstrated, once more, in these reactions and in subsequent transformations leading to various *t*-Bu-, Boc-, Fmoc-, and Cbz-protected β^2-homoamino acid derivatives **11**–**23** (*Schemes 3*–*6*). The use of ω-bromo-acyl-oxazolidinones **1**–**3** as starting materials turned out to open access to a variety of enantiomerically pure trifunctional and cyclic carboxylic-acid derivatives.

1. Introduction. – In contrast to β^3-homoamino acids, which are readily available in enantiomerically pure form from the natural proteinogenic amino acids by the *Arndt–Eistert* or *Kolbe* homologation strategy[7]) (18 of which are now commercially available[8])), the β^2-homoamino acids are much more challaging to prepare[7]). From the very beginning of our work on β-peptides containing β^2-amino acids [5][6], we decided to employ a uniform, general, synthetic approach towards derivatives of the 19 β^2-amino acids with proteinogenic side chains[9]): the reactions of chiral oxazolidinones, the *Evans* auxiliaries. With the valine-derived '5,5-diphenyl-4-isopropyl-1,3-oxazolidin-2-one' (DIOZ = 4-(1-methylethyl)-5,5-diphenyl-1,3-oxazolidin-2-one), we found a superior auxiliary [7–9], which we used whenever possible[10])[11]). The Li-, B-, and

[1]) Preliminary communication: [1].

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[6]) Postdoctoral Researcher at ETH Zürich (2004/2005), financed by a stipend of the *Deutsche Forschungsgemeinschaft*.

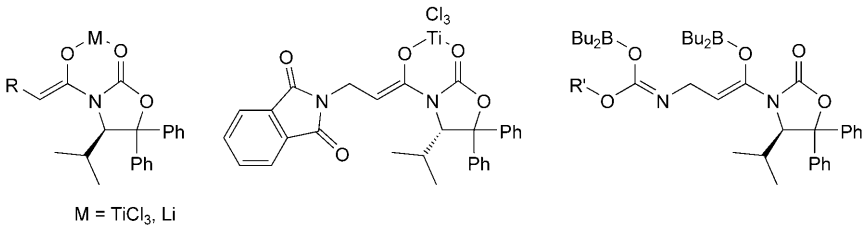
[7]) For an extensive review article on β- and γ-amino acids, and -peptide derivatives, see [2][3].

[8]) We thank *Fluka AG* (CH-Buchs) for generous discounts on purchases of Fmoc/acid-labile- and Boc/H_2-labile-protected β^3-amino acid derivatives. The preparation of Fmoc-β^3hCys(Tr)-OH and of Fmoc-β^3hHis(Tr)-OH is described in [4].

[9]) β^2hGly ≡ β^3hGly ≡ 'β-alanine' does not have a side chain.

[10]) Under certain hydrogenation conditions, DIOZ can undergo cleavage [10]. Aldol additions of DIOZ-derived enolates to aromatic aldehydes may occur with poor diastereoselectivities, *vide infra*, *Sect. 2*.

[11]) For a general review article on β^2-amino acid-containing peptides and natural products, see [11].

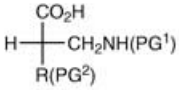


A **B** **C**

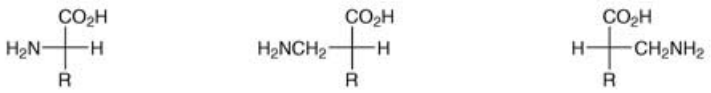
Ti-enolates of type **A**, **B**, and **C** were allowed to react with alkyl halides, aldehydes, aminomethylating reagents, or benzyliodoacetate, with generation of the sterogenic centers of the desired β^2-amino acid precursors.

The steric courses of the reactions follow the generally accepted mechanistic models [12], as confirmed by numerous X-ray crystal-structure analyses of the highly crystalline DIOZ derivatives [1][4][7][8][13][14]. Detailed procedures for the preparation by this method of most β^2-amino acids with appropriate N-terminal and side-chain functional-group protection for peptide syntheses have been previously published by us (*Table*) [15][16]. Those specified in the title are described herein; for nomenclature and symbols of β^2-amino acids, see **D**, **E**, and **F** in the *Table*. The incorporation into a β-peptide of all 20 β^2-amino acid moieties derived from the natural proteinogenic amino acids has been described recently [17]. For alternative enantioselective routes to certain β^2-amino acids, we refer to references in our review articles [2][3][11]. It is remarkable that it takes more than a dozen preparative steps to arrive at a building block for peptide synthesis, such as for instance Fmoc-β^2Gln(Tr)-OH [13], from simple, commercially available starting materials!

Table. *The Preparation of All 'Proteinogenic' β^2-Homoamino Acid β^2hXaa Derivatives, Suitably Protected for Solid-Phase Synthesis, Is Described in the Publications Referenced.* The present paper presents new or alternative procedures for the β^2-homoamino acids, the symbols of which are marked. If we consider the β^2-homoamino acids of type **E** (H-β^2hXaa-OH) as 'true' homologs of the proteinogenic amino acids **D** (H-Xaa-OH), we would have to specify the enantiomers **F**, as prepared by us, H-β^2hDXaa-OH; according to the *CIP* nomenclature, they will be H-(*S*)-β^2hXaa-OH, with the complication that the Ser, Trp, and Cys analogs have (*R*)-configuration (see also discussion in [1]).



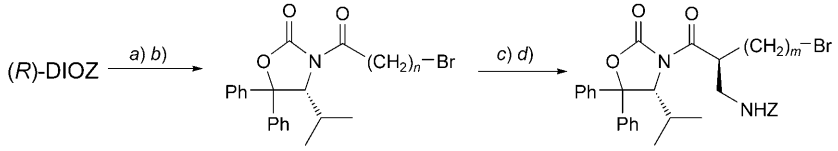
Xaa	Ala	Arg	Asp	Asn	Cys	His	Glu	Gln	Ile	Leu
Ref.	[7]	[15]	[13]	[13]	[4]	[4]	[7][13]	[13]	[14]	[7]
Xaa	Lys	Met	Phe	Pro	Ser	Thr	Trp	Tyr	Val	
Ref.	[16]	[14]	[7]		[4][7]		[10]	[7]	[7]	



D **E** **F**

2. Preparation of the Oxazolidinones 1–10 by DIOZ-Acylations, *Mannich* Reactions, and Aldol Additions. – The first step of execution of the *Evans* methodology is the acylation of the chiral oxazolidinone auxiliary. Due to steric protection of the DIOZ C=O group, this step can be carried out simply by treating a slurry in THF with BuLi, which leads to the soluble Li-DIOZ, and adding an acid chloride. In this way, we obtained the 3-(ω-bromoacyl)-oxazolidinones **1**–**3** in excellent yield (*Scheme 1*).

Scheme 1. *Preparation of ω-Bromoacyl-DIOZ Derivatives* **1**–**3** *and* Mannich *Reactions Thereof Rendering β^2-Amino Acid Derivatives* **4**–**6** *with ω-Bromoalkyl Side Chains*



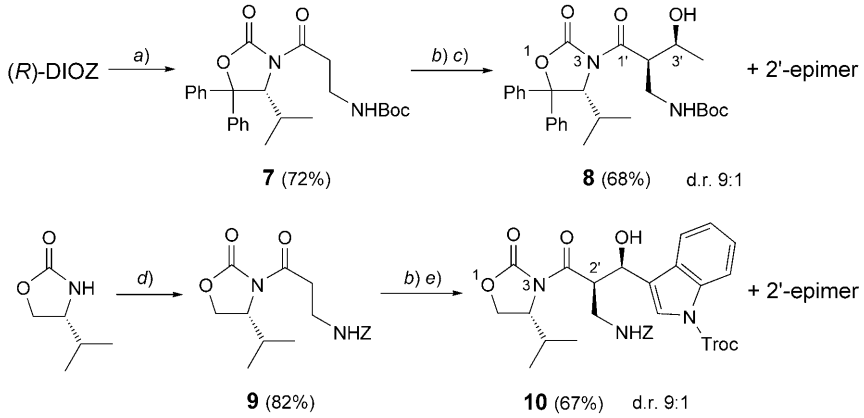
1 n = 3 (90%)
2 n = 4 (87%)
3 n = 5 (85%)

4 m = 2 (80%) d.r. 89:11
5 m = 3 (79%) d.r. 93:7
6 m = 4 (77%) d.r. 94:6

a) BuLi, THF, –30°. *b*) $Br(CH_2)_nCOCl$, 0°. *c*) $TiCl_4$, Et_3N, CH_2Cl_2, –15°. *d*) $ZHNCH_2OMe$, 0°. Z = $PhCH_2O–CO$.

For acylation with the Boc-protected 3-aminopropanoic acid, which cannot be converted to an acid chloride, we used the bifunctional-catalysis method [18–21], *i.e.*, *in situ* generation of a mixed anhydride and acylation in the presence of $LiCl/Et_3N$ [22] (*Scheme 2*) to form the DIOZ derivative **7**. The same procedure provided the classical *Evans* derivative **9**.

Scheme 2. *Preparation of* N-*Boc and* N-*Z-3-Aminopropanoyl-DIOZ Derivatives and Aldol Additions Thereof – Precursors of β^2hThr and β^2hTrp Derivatives*



7 (72%)
8 (68%) d.r. 9:1
9 (82%)
10 (67%) d.r. 9:1

a) $BocNH(CH_2)_2CO_2H$, PivCl, Et_3N, LiCl, THF, –30°. *b*) 2.2 equiv. Bu_2BOTf, Et_3N, CH_2Cl_2, –78°. *c*) MeCHO, –78°. *d*) $ZNH(CH_2)_2CO_2H$, PivCl, Et_3N, LiCl, THF, –30°. *e*) [(1-Troc)indol-3-yl]CHO, –78°. Boc = $^tBuO–CO$, Z = $PhCH_2O–CO$, Troc = $Cl_3CCH_2O–CO$.

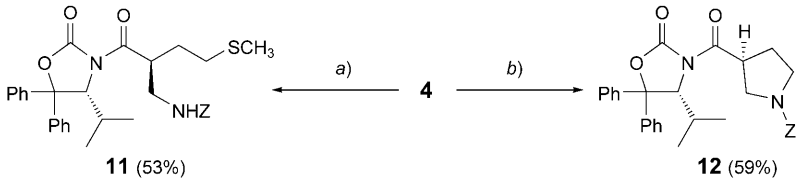
From the 3-(ω-bromoacyl)-oxazolidinones **1**–**3** Ti-enolates of type **A** can be generated, which are known to be nucleophilic only towards aldehydes and iminium

salts, but not towards alkyl halides: no cyclization to a three-, four-, or five-membered carbocyclic ring is observed upon treatment of **1**–**3** with $TiCl_4/Et_3N$. Likewise, B-enolate of type **C** can be generated from the the acyl-oxazolidinones **7** and **9**. Reactions of these enolate derivatives with benzyl *N*-(methoxymethyl)carbamate [23], acetaldehyde, and an *N*-protected indole-3-carbaldehyde, respectively, gave the β^2-amino acid derivatives **4**–**6**, **8**, and **10** in yields ranging from 90 to 94%. All products, except **10**, are crystalline and can be isolated in enantiomerically pure form by recrystallization; X-ray crystal structures of **6**, **7**, and **8** have been determined [1]. The classical *Evans* auxiliary (without the two Ph substituents) was used for the preparation of the β^2hTrp[12]) precursor **10**, because additions of DIOZ-derived B-enolates to aromatic aldehydes take place with poor diastereoselectivities[13]).

3. Conversion of the Oxazolidinones 4–6 to Various Other β^2-Amino Acid Derivatives. – The ω-bromoalkyl β^2-amino acid derivatives **4**–**6** are the most versatile intermediates on the way to a variety of β^2-amino acids with functionalized side chains or with a cyclic structure: Br/SCH_3 substitution in **4** provides a route to β^2hMet, Br/N_3 substitution in **4** provides a route to β^2hOrn, and hence to β^2hArg [15], the same transformation with **6** provides a route to β^2hLys, and *N*-deprotection, followed by cyclization, constitutes an access to pyrrolidine-3-carboxylic acid (a β-isoproline[14])) to β^2hPro, and to azepin-3-carboxylic acid [1] from **4**, **5**, and **6**, respectively[15]). Four of these transformations are described in the following sections.

Thus, treatment of ([2-(2-bromoethyl)-3-aminopropanoyl]-DIOZ **4** with MeSNa in DMF gives the precursor **11** of H-(*S*)-β^2hMet-OH used in the synthesis of an all-β^2-icosapeptide [17], and deprotonation of **4** leads to the *N*-Z-protected pyrrolidine **12** (*Scheme 3*).

Scheme 3. *Conversion of the Bromoalkyl Derivative* **4** *to a Precursor for* (S)-β^2*hMet and for Pyrrolidine-3-carboxylic Acid*



a) MeSNa, DMF. *b*) NaH, cat. Bu_4NI, DMF, 70°. Z = $PhCH_2O-CO$.

Similarly, we have cyclized the ω-bromoalkyl derivative **5** (→ **13**; *Scheme 4*). The configuration of the product follows from an X-ray crystal structure of the corresponding *N*-Boc-protected compound (**13**, Boc instead of Z [1]). To prevent epimerization/racemization under the conditions of auxiliary removal, we used LiOH/H_2O_2 [24] for the conversion to Z-β^2hPro-OH (**14a**); normally, we hydrolize DIOZ

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12) For a route to β^2hTrp derivatives involving a *Curtius*-degradation step, see [10].

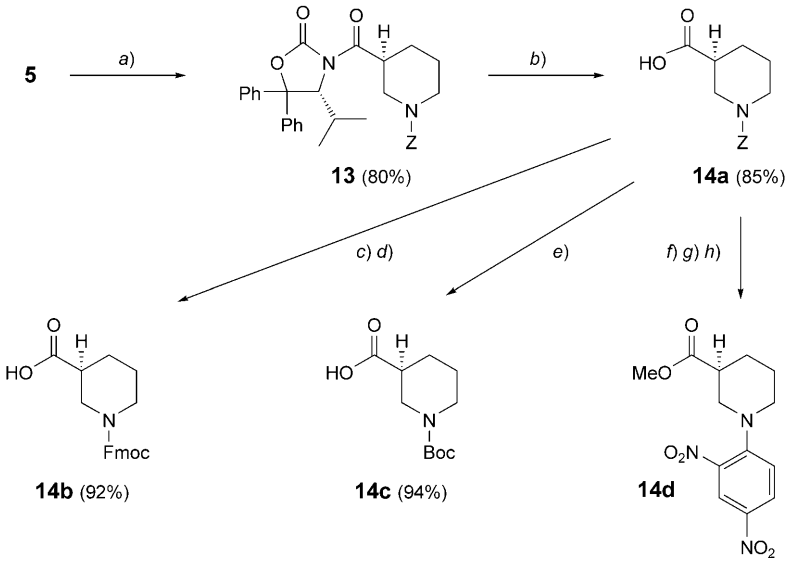
13) With the aldehyde used here, the selectivity of addition of the DIOZ analog of **9** is only 3:2, see also [1] and *Footnote 10*.

14) Proposals for the nomenclature of β-iso-Xaa, see *Fig. 5* and *Footnote 22* in [2].

15) Br/CN Substitution in **4** and hydrolysis should lead to β^2hGln or β^2hGlu derivatives.

derivatives with NaOH/H_2O/THF [7][8][16]). Subsequent protecting-group interchanges provided the acids Fmoc-β^2hPro-OH (**14b**) and Boc-β^2hPro-OH (**14c**).

Scheme 4. *Cyclization of the Bromoalkyl Derivative* **5** *to (*S*)-β^2hPro-Derivatives* **14**



a) NaH, cat. Bu_4NI, DMF, 70°. *b*) LiOH, H_2O_2, H_2O, THF, 0°. *c*) H_2, Pd/C, MeOH. *d*) (Fmoc)OSu, Na_2CO_3, dioxane, H_2O. *e*) H_2, Pd/C, Boc_2O, MeOH. *f*) Cat. CSA, EtOH. *g*) Pd/C, AcOH, EtOH. *h*) 2,4-Dinitro-1-fluorobenzene, EtOH, H_2O. Z = $PhCH_2O-CO$, Fmoc = 9*H*-fluoren-9-yl$-CH_2-CO$, Boc = ^{t}BuO$-$CO, Su = *N*-succinimidyl, CSA = campher sulfonic acid.

The enantiomeric purities of the β^2-homoproline derivatives **14a**–**14c** were determined by HPLC on chiral phases. Thus, compound **14b** was injected into a chiral HPLC column (*Chiralpak AD-H 1151*); in comparison with a racemic mixture, the enantiomer ratio was 93:7[17]). This is in agreement with the result of an analysis of ester **14d,** which was determined (on *Chiralcel OD-H*) to also have an enantiomeric purity of 93:7.

To further demonstrate the synthetic potential of the amido-methylated ω-bromoacyl-DIOZ derivatives, we have substituted Br by N_3 in **6** (→ **15**). Reduction of the N_3 group under 'bocylating' conditions gave the Z-β^2hLys(Boc)-DIOZ **16** (*Scheme 5*), which had been used as the precursor for the β^2-dipeptide Fmoc-β^2hIle-β^2hLys(Boc)-OH employed in the β^2-icosapeptide synthesis mentioned above [17].

4. Preparation of Z-(*R*,*S*)-β^2Thr(*t*-Bu)-OH and of Fmoc-(*R*)-β^2Trp(Boc)-OH from the Oxazolidinones 8 and 10. – The conversion of the aldol adducts **8** and **10** to building

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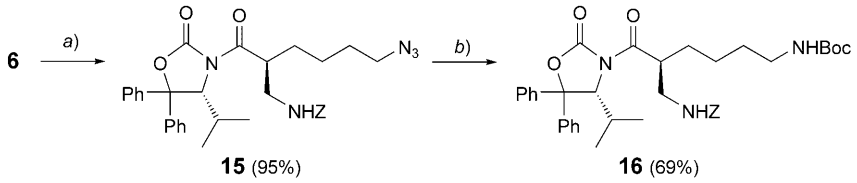
[16]) In esterifying DIOZ removals, for instance with $PhCH_2OLi$, we have observed extensive racemizations of the resulting esters. When an ester must be prepared from a product of alkylation or aldol addition of an acylated DIOZ, it is preferable to first prepare the acid and subsequently esterify it.

[17]) We thank Dr. *Eric Francotte* of *Novartis AG*, Basel, CTA/PSB, for determination of the enantiomeric purity of **14b**.

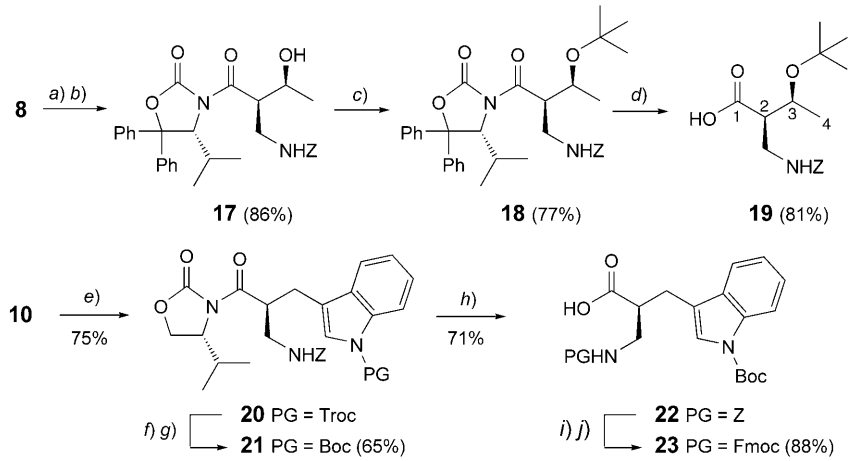
Scheme 5. *(S)-β²hLys Derivatives* **15** *and* **16** *from the Bromoalkyl Precursor* **6** *by Br/N_3-Substitution as Key Step*



a) NaN_3, DMF. *b*) *Lindlar* cat., H_2, Boc_2O, MeOH. Boc = ^{t}BuO–CO, Z = $PhCH_2O$–CO.

blocks suitably protected for solid-phase peptide synthesis is outlined in *Scheme 6*. Thus, Boc/Z protecting-group exchange in **8** (→ **17**), *tert*-butylation of the OH group (→ **18**), and cleavage from the auxiliary group, this time with Bu_4NOH, provided Z-β²hThr(*t*-Bu)-OH (**19**) in an overall yield of 54%.

Scheme 6. *Functional-Group Manipulations for the Conversion of DIOZ Derivatives* **8** *and* **10** *to Protected (R,S)-β²hThr-OH* **19** *and (S)-β²hTrp-OH* **23**



a) TFA, CH_2Cl_2, 0°. *b*) Z–Cl, $NaHCO_3$. CH_2Cl_2, H_2O. *c*) Isobutylene, H_2SO_4, CH_2Cl_2. *d*) Bu_4NOH, THF, H_2O. *e*) $BF_3 \cdot Et_2O$, Et_3SiH. *f*) Zn, AcOH. *g*) Boc_2O, DMAP, MeCN. *h*) LiOH, H_2O_2, H_2O, THF, 0°. *i*) H_2, Pd/C, EtOH. *j*) (Fmoc)OSu, Na_2CO_3, acetone, H_2O. Z = $PhCH_2O$–CO, Boc = ^{t}BuO–CO, Troc = Cl_3CCH_2O–CO, Fmoc = 9*H*-fluoren-9-yl–CH_2O–CO, Su = *N*-succinimidyl.

Deoxygenation with silane converted compound **10** (containing five functional groups!) to the Fmoc-β²hTrp derivative **20**, which was converted to Fmoc-β²hTrp(Boc)-OH (**23**) by a series of three functional-group manipulations: Troc removal and Boc introduction on the indole N-atom (→ **21**), liberation of the carboxylic acid group (→ **22**), and Z/Fmoc interchange on the amino N-atom (→ **23**), in a total yield of 30% over six steps.

5. Conclusions. – Two types of reactions have been employed for the assembly of side-chain functionalized β²-homoamino acids with selective formation of the stereogenic center in the α-carbonyl position: the amidomethylation, a kind of *Mannich*

reaction, of ω-bromoacyl-DIOZ and the hydroxyalkylation, *i.e.*, aldol addition, of *N*-Boc or *N*-Z-protected 3-aminopropanoyl-oxazolidinones. In the first case Cl_3Ti-enolates and in the second case Bu_2B-enolates were applied. Throughout, the desired stereogenic center was created with stereoselectivities $\geq 90\%$, and purification procedures (crystallization with DIOZ derivatives) provided enantiomerically pure samples on a preparative scale.

The usefulness of ω-bromoacyl-oxazolidinones **1**–**3** was demonstrated; DIOZ derivatives of this type serve as starting materials not only for the preparation of the β^2-homoamino acids described herein, but for many other targets as well, due to the fact that there are numerous synthetically useful C-, N-, P-, S-, Se-nucleophiles, by which a primary bromide can be substituted.

The overall benzylation-type reaction, **9** → **10** → **20**, consisting of an aldol addition and a deoxygenation can be superior to direct benzylations in the case of functionalized reactants, such as the amino-acyl-oxazolidinone and the indole-carbaldehyde. Still, it is striking to realize that the β^2hTrp amino acid **23**, with a single stereogenic center and two orthogonally protected functionalized side chains, requires nine steps to be synthesized.

Experimental Part

1. *General. Abbreviations*: Boc: (*tert*-butoxy)carbonyl, Boc_2O: di-(*tert*-butyl) dicarbonate, Z: (benzyloxy)carbonyl, h.v.: high vacuum, 0.01–0.1 Torr, Troc: (2,2,2-trichloroethoxy)carbonyl. Solvents for chromatography and workup procedures were distilled from *Sikkon* (anh. $CaSO_4$; *Fluka*) and from KOH (Et_2O). Et_3N was distilled from CaH_2 and stored over 4-Å molecular sieves. Amino acids were purchased from *Fluka* or *Senn*. BuLi was used as a *ca*. 1.6M soln. in hexane, Bu_2BOTf as 1M soln. in CH_2Cl_2. THF was freshly distilled over Na under Ar before use. LiCl was dried under h.v. at 150° overnight. 4-Bromobutanoyl chloride, 5-bromopentanoyl chloride, and 6-bromohexanoyl chloride were freshly prepared from the corresponding carboxylic acids by treatment with oxalyl chloride [25]. All other reagents were used as received from *Fluka* or *Aldrich*. DIOZ and benzyl *N*-(methoxymethyl)carbamate ($ZHNCH_2OMe$) were prepared according to [9] and [23], resp. TLC: *Merck* silica gel *60* F_{254} plates; detection with UV, anisaldehyde soln. (9.2 ml of anisaldehyde, 12.5 ml of conc. H_2SO_4, 3.75 ml of AcOH, 340 ml of EtOH), or 'Mo-stain' soln. (25 g of phosphormolybdic acid, 10 g of $Ce(SO_4)_2 \cdot H_2O$, 60 ml of conc. H_2SO_4, 940 ml of H_2O). Flash Chromatography (FC): *Fluka* silica gel *60* (40–63 μm); at *ca.* 0.3 bar. IR Spectra: *Perkin-Elmer 1600 FT-IR* spectrophotometer. NMR Spectra: *Bruker AMX II 500* (^{1}H: 500 MHz, ^{13}C: 125 MHz), *AMX-400* (^{1}H: 400 MHz, ^{13}C: 100 MHz), *AMX-300* (^{1}H: 300 MHz, ^{13}C: 75 MHz), *Varian Mercury XL 300* (^{1}H: 300 MHz, ^{13}C: 75 MHz); chemical shifts δ in ppm downfield from internal Me_4Si (= 0 ppm); *J* values in Hz. Mass Spectra: *IonSpec Ultima 4.7 T FT* ion cyclotron resonance (ICR, HR-MALDI, in 2,5-dihydroxybenzoic acid matrix) spectrometer; in *m*/*z* (% of basis peak). Elemental analyses were performed by the Microanalytical Laboratory of the Laboratorium für Organische Chemie, ETH-Zürich.

2. *Acylation of the Auxiliary with Acyl Chlorides. General Procedure 1* (*GP 1*). To a suspension of the auxiliary (1 equiv.) in THF (0.25M), BuLi (1.05 equiv.) was slowly added at − 30°. After stirring for 10 min, a soln. of the acyl chloride (1.2 equiv.) in THF (0.8 ml/mmol) was added. The mixture was stirred at 0° for 2 h, allowed to warm slowly to r.t. over 14 h, hydrolyzed by the addition of sat. NH_4Cl soln., and diluted with Et_2O. The org. phase was washed with 1M HCl (2 ×), 1M NaOH (2 ×), and brine, dried ($MgSO_4$), and evaporated. The crude product was purified by FC.

3. *Amidoalkylation of Acyl-Oxazolidinones. General Procedure 2* (*GP 2*). To a soln. of the acyl-oxazolidinone (1 equiv.) in CH_2Cl_2 (0.2M), $TiCl_4$ (1.05 equiv.) and Et_3N (1.10 equiv.) were added at − 15° (ice/MeOH bath). The deep-red soln. was stirred at − 15° for 30 min, treated with a soln. of benzyl *N*-(methoxymethyl)carbamate (1.05 equiv.) in CH_2Cl_2 (0.5M) and additional $TiCl_4$ (1.1 equiv.). The mixture was stirred at 0° (ice bath) for 3 h, hydrolyzed by the addition of sat. NH_4Cl soln., and diluted with CH_2Cl_2 or Et_2O. The org. phase was washed with 1M HCl (2 ×), 1M NaOH, and brine, dried ($MgSO_4$), and evaporated. The crude product was purified by FC.

4. *Acylation of the Auxiliary with Mixed Anhydrides. General Procedure 3* (*GP 3*). To a soln. of the appropriate acid (1.05 equiv.) in THF (0.2M), Et_3N (2.5 equiv.) and pivaloyl chloride (1 equiv.) were added at $-30°$. The resulting white suspension was stirred at $-30°$ for 2 h, LiCl (1.1 equiv.) and the auxiliary (0.95 equiv.) were added, and stirring was continued for 1–2 d as the mixture was allowed to warm to r.t. The mixture was diluted with Et_2O, washed with sat. NH_4Cl soln. (2 ×), 1M NaOH (2 ×), and sat aq. NaCl soln., dried ($MgSO_4$), and concentrated under reduced pressure. FC of the crude product yielded the pure compound.

5. *Aldol Reaction* via *Boron-Enolate. General Procedure 4* (*GP 4*). To a soln. of the acyl-oxazolidinone (1 equiv.) in CH_2Cl_2 (0.4M), Bu_2BOTf (2.2 equiv.) and Et_3N (2.4 equiv.) were added at $-78°$. After stirring at $-78°$ for 1 h and 15 min at 0°, the mixture was cooled again to $-78°$, treated with the appropriate aldehyde (2.5 equiv.), and stirred at the indicated temp. and time. After addition of a phosphate buffer (pH 7, 1 ml/mmol), MeOH (3 ml/mmol), and H_2O_2/MeOH 1:2 (3 ml/mmol), the mixture was stirred at r.t. for 1 h, diluted with Et_2O, washed with 0.5M HCl, sat. $NaHCO_3$ soln., and brine. The org. phase was dried ($MgSO_4$) and evaporated, and the crude product was purified by FC.

6. *Bromide Substitution. General Procedure 5* (*GP 5*). A mixture of the brominated acyl-oxazolidinone (1 equiv.) and NaN_3 (1.2 equiv.) or MeSNa (1–3 equiv.) in DMF (0.5M) was stirred at r.t. for 14 h, diluted with Et_2O, and washed with H_2O (2 ×). The org. phase was separated, dried ($MgSO_4$), and evaporated, and the crude product was purified by FC or recrystallization.

*(4*R*)-3-(4-Bromo-1-oxobutyl)-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* (**1**). (*R*)-DIOZ (11.3 g, 40 mmol) was treated with BuLi (28.0 ml, 42 mmol) and 4-bromobutanoyl chloride (8.9 g, 48 mmol) according to *GP 1*. FC (pentane/Et_2O 9:1) yielded **1** (15.59 g, 90%). Colorless solid. M.p. 105–107°. R_f (pentane/Et_2O 6:4) 0.70. $[\alpha]_D^{r.t.} = +207.9$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3011*w*, 2969*w*, 1779*s*, 1691*m*, 1494*w*, 1450*m*, 1399*m*, 1365*m*, 1319*m*, 1177*m*, 1092*w*, 1052*w*, 1036*w*, 1001*w*, 961*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.78 (*d*, $J = 6.8$, Me); 0.85 (*d*, $J = 7.0$, Me); 1.92–2.02 (*m*, Me_2CH); 2.08–2.19 (*m*, CH_2); 2.87–2.95, 3.03–3.12 (*m*, CH_2CO); 3.38 (*t*, $J = 6.6$, CH_2Br); 5.39 (*d*, $J = 3.4$, CHN); 7.26–7.48 (*m*, 10 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.4, 21.7 (Me); 27.3 (CH_2); 30.0 (CH); 32.3, 33.7 (CH_2); 64.5 (CH); 89.2 (C); 125.8, 126.0, 128.3, 128.4, 128.5, 128.9 (CH); 138.4, 142.4, 153.4, 174.1 (C). MALDI-MS: 452.1 (34, $[M + Na]^+$), 372.2 (100, $[M - Br + Na]^+$). Anal. calc. for $C_{22}H_{24}BrNO_3$ (430.34): C 61.40, H 5.62, N 3.25, Br 18.57; found: C 61.38, H 5.49, N 3.23, Br 18.24.

*(4*R*)-3-(5-Bromo-1-oxopentyl)-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* (**2**). (*R*)-DIOZ (20.0 g, 71 mmol) was treated with BuLi (49.7 ml, 74.6 mmol) and 5-bromopentanoyl chloride (17.0 g, 85.3 mmol) according to *GP 1*. FC (pentane/Et_2O 9:1) yielded **2** (21.71 g, 87%). Colorless oil. R_f (pentane/Et_2O 6:4) 0.70. $[\alpha]_D^{r.t.} = +172.1$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3025*w*, 2967*w*, 1781*s*, 1494*w*, 1450*m*, 1366*m*, 1320*m*, 1177*m*, 1120*w*, 1051*w*, 1002*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.76 (*d*, $J = 6.8$, Me); 0.87 (*d*, $J = 7.0$, Me); 1.68–1.81 (*m*, 2 CH_2); 1.95–2.02 (*m*, Me_2CH); 2.77–2.94 (*m*, CH_2CO); 3.32 (*t*, $J = 6.4$, CH_2Br); 5.36 (*d*, $J = 3.4$, CHN); 7.26–7.49 (*m*, 10 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.5, 21.8 (Me); 23.2 (CH_2); 29.8 (CH); 31.8, 33.0, 34.2 (CH_2); 64.6 (CH); 89.5 (C); 125.6, 125.9, 128.0, 128.4, 128.6, 128.9 (CH); 138.1, 142.3, 153.1, 172.5 (C). MALDI-MS: 468.1 (88, $[M + Na]^+$), 402.1 (21), 320.2 (41). Anal. calc. for $C_{23}H_{26}BrNO_3$ (444.37): C 62.17, H 5.90, N 3.15, Br 17.98; found: C 62.30, H 6.03, N 3.41, Br 17.96.

*(4*R*)-3-(6-Bromo-1-oxohexyl)-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* (**3**). (*R*)-DIOZ (5.6 g, 20 mmol) was treated with BuLi (14.0 ml, 21 mmol) and 6-bromohexanoyl chloride (5.1 g, 24 mmol) according to *GP 1*. FC (pentane/Et_2O 9:1) yielded **3** (7.82 g, 85%). Colorless solid. M.p. 74–75°. R_f (pentane/Et_2O 6:4) 0.70. $[\alpha]_D^{r.t.} = +165.6$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3026*w*, 2967*w*, 1781*s*, 1702*s*, 1494*w*, 1450*m*, 1366*m*, 1320*m*, 1177*m*, 1120*w*, 1051*w*, 1002*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.76 (*d*, $J = 6.8$, Me); 0.87 (*d*, $J = 7.0$, Me); 1.34–1.41 (*m*, CH_2); 1.53–1.62 (*m*, CH_2); 1.76–1.83 (*m*, CH_2); 1.94–2.02 (*m*, Me_2CH); 2.73–2.92 (*m*, CH_2CO); 3.34 (*t*, $J = 6.8$, CH_2Br); 5.36 (*t*, $J = 3.4$, CHN); 7.26–7.49 (*m*, 10 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.4, 21.8 (Me); 23.7, 27.4 (CH_2); 29.8 (CH); 32.4, 33.4, 34.9 (CH_2); 64.5 (CH); 89.4 (C); 125.6, 125.9, 127.9, 128.4, 128.6, 128.9 (CH); 138.1, 142.4, 153.0, 172.8 (C). MALDI-MS: 480.1 (100, $[M + Na]^+$), 416.1 (24). Anal. calc. for $C_{24}H_{28}BrNO_3$ (458.39): C 62.89, H 6.16, N 3.06, Br 17.43; found: C 63.11, H 6.13, N 3.30, Br 17.40.

*(4*R*)-3-[(2*S*)-2-({[(Benzyloxy)carbonyl]amino}methyl)-4-bromo-1-oxobutyl]-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* (**4**). Compound **1** (8.61 g, 20 mmol) was treated with $TiCl_4$ (2.30 ml, 21 mmol), Et_3N (3.07 ml, 22 mmol), $ZNHCH_2OMe$ (4.1 g, 21 mmol), and additional $TiCl_4$ (2.41 ml, 22 mmol) according to *GP 2*. FC (pentane/Et_2O 8:2 → 7:3) yielded, beside starting material **1** (1.57 g), **4** as a 89:11 mixture with its *C(2)*-epimer (7.79 g, 80%). For anal. purposes, a sample was recrystallized (pentane/Et_2O). Colorless solid. M.p. 51.5–53.5°. R_f (hexane/AcOEt 7:3) 0.32. $[\alpha]_D^{r.t.} = +96.1$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3442*w*, 3011*w*, 2968*w*, 1780*s*, 1719*s*, 1515*m*, 1450*m*, 1396*w*, 1364*m*, 1318*m*, 1122*w*, 1053*w*, 989*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.71 (*d*, $J = 6.8$, Me); 0.83 (*d*, $J = 7.0$, Me); 1.76–1.81, 2.01–2.09 (2*m*, CH_2); 1.96–2.01 (*m*, Me_2CH); 2.73–2.78, 2.92–2.96 (2*m*, CH_2Br); 3.37–3.42, 3.56–3.62 (2*m*, CH_2NH); 3.98–4.01 (*m*, CHCO); 5.01–5.12 (*m*, $PhCH_2$); 5.25 (*s*,

NH); 5.34 (*d*, *J* = 3.4, CHN); 7.27–7.50 (*m*, 15 arom. H). ^{13}C-NMR (125 MHz, $CDCl_3$): 16.2, 21.6 (Me); 21.6 (CH_2); 29.6 (CH); 32.2 (CH_2); 42.0 (CH); 43.0 (CH_2); 65.6 (CH); 66.8 (CH_2); 89.9 (C); 125.2, 125.5, 125.7, 128.1, 128.2, 128.5, 128.9, 129.0 (CH); 136.4, 137.5, 142.1, 153.2, 156.2, 173.4 (C). MALDI-MS: 615.2 (14, $[M + Na]^+$), 535.2 (100, $[M - Br + Na]^+$), 469.3 (8). Anal. calc. for $C_{31}H_{33}BrN_2O_5$ (593.52): C 62.73, H 5.60, N 4.72, Br 13.46; found: C 62.76, H 5.71, N 4.70, Br 13.28.

*(4*R*)-[(2*S*)-2-({[(Benzyloxy)carbonyl]amino}methyl)-5-bromo-1-oxopentyl]-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* (**5**). Compound **2** (20.44 g, 46 mmol) was treated with $TiCl_4$ (5.30 ml, 48.3 mmol), Et_3N (7.05 ml, 50.6 mmol), $ZNHCH_2OMe$ (9.43 g, 48.3 mmol), and additional $TiCl_4$ (5.55 ml, 50.6 mmol) according to *GP 2*. FC (pentane/Et_2O 9:1 → 7:3) yielded beside starting material **2** (1.63 g), **5** as a 93:7 mixture with its C(2)-epimer (22.1 g, 86%). Colorless glass. R_f (hexane/AcOEt 7:3) 0.31. $[\alpha]_D^{r.t.} = +102.2$ (*c* = 0.9, $CHCl_3$). IR ($CHCl_3$): 3448*w*, 3011*w*, 2967*w*, 1780*s*, 1719*s*, 1514*m*, 1450*m*, 1396*w*, 1364*m*, 1318*m*, 1092*w*, 1052*w*, 1001*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.71 (*d*, *J* = 6.8, Me); 0.83 (*d*, *J* = 7.0, Me); 1.24–1.30 (*m*, CH_2); 1.31–1.39, 1.45–1.49 (2*m*, CH_2); 1.95–2.01 (*m*, Me_2CH); 2.95–3.00 (*m*, CH_2Br); 3.35–3.40, 3.51–3.56 (2*m*, CH_2NH); 3.86 (br. *s*, CHCO); 5.04–5.10 (*m*, $PhCH_2$); 5.26 (*s*, NH); 5.32 (*d*, *J* = 3.5, CHN); 7.27–7.50 (*m*, 15 arom. H). ^{13}C-NMR (125 MHz, $CDCl_3$): 16.4, 21.6 (Me); 28.1, 29.3 (CH_2); 29.5 (CH); 32.7 (CH_2); 42.1 (CH); 42.7 (CH_2); 65.6 (CH); 66.7 (CH_2); 89.8 (C); 125.3, 125.7, 128.1, 128.2, 128.5, 128.8, 129.0 (CH); 136.5, 137.5, 142.2, 153.2, 156.2, 174.3 (C). MALDI-MS: 645.1 (14, $[M + K]^+$), 629.2 (91, $[M + Na]^+$), 565.0 (11, $[M - Br + K]^+$), 549.2 (38, $[M - Br + Na]^+$). Anal. calc. for $C_{32}H_{35}BrN_2O_5$ (607.54): C 63.26, H 5.81, N 4.61, Br 13.15; found: C 63.30, H 5.77, N 4.56, Br 13.04.

*(4*R*)-3-[(2*S*)-2-({[(Benzyloxy)carbonyl]amino}methyl)-6-bromo-1-oxohexyl]-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* (**6**). Compound **3** (6.87 g, 15 mmol) was treated with $TiCl_4$ (1.73 ml, 15.7 mmol), Et_3N (2.30 ml, 16.5 mmol), $ZNHCH_2OMe$ (3.06 g, 15.7 mmol), and additional $TiCl_4$ (1.81 ml, 16.5 mmol) according to *GP 2*. FC (pentane/Et_2O 8:2 → 7:3) yielded beside starting material **3** (774 mg), **6** as a 94:6 mixture with its C(2)-epimer (6.41 g, 77%). For anal. purposes, a sample was recrystallized (pentane/Et_2O). Colorless needles. M.p. 95–98°. R_f (hexane/AcOEt 7:3) 0.31. $[\alpha]_D^{r.t.} = +96.5$ (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): 3450*w*, 3026*w*, 2967*w*, 1780*s*, 1719*s*, 1514*m*, 1450*m*, 1395*w*, 1364*m*, 1318*m*, 1153*w*, 1093*w*, 1052*w*, 1002*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.71 (*d*, *J* = 6.7, Me); 0.83 (*d*, *J* = 7.0, Me); 0.88–0.92 (*m*, CH_2); 1.18–1.27, 1.35–1.47 (2*m*, CH_2); 1.48–1.54 (*m*, CH_2); 1.95–2.00 (*m*, Me_2CH); 3.08 (*t*, *J* = 6.8, CH_2Br); 3.35–3.38, 3.48–3.54 (2*m*, CH_2NH); 3.82–3.86 (*m*, CHCO); 5.07 (*s*, $PhCH_2$); 5.19 (br. *s*, NH); 5.32 (*d*, *J* = 3.5, CHN); 7.26–7.51 (*m*, 15 arom. H). ^{13}C-NMR (125 MHz, $CDCl_3$): 16.4, 21.7 (Me); 25.0, 28.6 (CH_2); 29.6 (CH); 32.4, 32.8 (CH_2); 42.7 (CH); 43.3 (CH_2); 65.5 (CH); 66.7 (CH_2); 89.7 (C); 125.4, 125.7, 128.1, 128.2, 128.4, 128.5, 129.0 (CH); 136.5, 137.6, 142.3, 153.2, 156.2, 174.6 (C). MALDI-MS: 659.2 (7, $[M + K]^+$), 643.2 (96, $[M + Na]^+$), 599.2 (81), 577.2 (9). Anal. calc. for $C_{33}H_{37}BrN_2O_5$ (621.57): C 63.77, H 6.00, N 4.51, Br 12.86; found: C 63.56, H 5.87, N 4.48, Br 12.75.

*(4*R*)-3-({3-[(*tert*-Butoxy)carbonyl]amino}-1-oxopropyl)-4-isopropyl-5,5-diphenyloxazolidin-2-one* (**7**). (*R*)-DIOZ (11.3 g, 40 mmol) was treated with pivaloyl chloride (5.7 g, 42 mmol), 3-{[(*tert*-butoxy)carbonyl]-amino}propanoic acid (7.6 g, 40 mmol), Et_3N (14.5 ml, 104 mmol) and dry LiCl (1.95 g, 46 mmol) according to *GP 3*. FC (pentane/Et_2O 9:1 → 8:2) yielded **7** (13.06 g, 84%). Colorless needles. M.p. 109–110°. R_f (pentane/Et_2O 1:1) 0.25. $[\alpha]_D^{r.t.} = +173.3$ (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): 3457*w*, 3005*w*, 2975*w*, 2933*w*, 1783*s*, 1708*s*, 1505*m*, 1450*m*, 1393*m*, 1368*m*, 1319*w*, 1051*w*, 1002*w*. ^{1}H-NMR (500 MHz,$CDCl_3$): 0.75 (*d*, *J* = 6.8, Me); 0.88 (*d*, *J* = 7.0, Me); 1.41 (*s*, *t*-Bu); 1.95–2.01 (*m*, Me_2CH); 2.85–2.91 (*m*, CH_2); 3.12–3.18 (*m*, CH_2); 3.36–3.39 (*m*, CH_2); 4.85 (br. *s*, NH); 5.36 (*d*, *J* = 3.5, CHN); 7.27–7.48 (*m*, 10 arom. H). ^{13}C-NMR (125 MHz, $CDCl_3$): 16.4; 21.8; 28.4; 29.9; 35.8; 36.0; 64.6; 79.3; 89.6; 125.2; 125.9; 128.0; 128.4; 128.7; 129.0; 138.0; 142.2; 152.9; 155.7; 171.9. MALDI-MS: 475.22 (42, $[M + Na]^+$), 412.2 (37), 375.2 (100, $[M - Boc + Na]^+$), 353.2 (6), 331.2 (21), 309.2 (8). Anal. calc. for $C_{26}H_{32}N_2O_5$ (452.55): C 69.01, H 7.13, N 6.19; found: C 69.08, H 7.28, N 6.25.

*(4*R*)-[(2*R*,3*S*)-2-({[(*tert*-Butoxy)carbonyl]amino}methyl)-3-hydroxy-1-oxopropyl]-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* (**8**). According to *GP 4*, **7** (15.0 g, 33.1 mmol) was treated with Bu_2BOTf (72.9 ml, 72.9 mmol), and the formed enolate reacted with acetaldehyde (3.74 ml, 66.2 mmol) at −78° for 1 h and at 0° for 4 h. FC (hexane/AcOEt 9:1 → 7:3) yielded **8** (11.15 g, 68%). Colorless needles. M.p. 137–138°. R_f (hexane/AcOEt 7:3) 0.16. $[\alpha]_D^{r.t.} = +105.2$ (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): 3453*w*, 2980*w*, 2934*w*, 1781*s*, 1693*s*, 1513*m*, 1450*m*, 1392*m*, 1368*m*, 1317*m*, 1289*m*, 1175*s*, 1122*w*, 1102*w*, 1052*w*, 990*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.72 (*d*, *J* = 5.9, Me; 0.78 (*d*, *J* = 6.8, Me); 0.87 (*d*, *J* = 7.0, Me); 1.42 (*s*, *t*-Bu); 1.98–2.04 (*m*, Me_2CH); 3.44–3.49 (*m*, CH_2); 3.77–3.83 (*m*, 2 CH); 3.71 (br. *s*, OH); 5.06 (br. *s*, NH); 5.36 (*d*, *J* = 3.5, CHN); 7.26–7.50 (*m*, 10 arom. H). ^{13}C-NMR (125 MHz, $CDCl_3$): 16.4; 19.7; 21.8; 28.3; 29.7; 39.1; 49.7; 65.1; 66.1; 80.0; 89.7; 125.4; 125.8; 128.1; 128.5; 128.8; 128.9; 137.7; 142.2; 152.9; 156.8; 174.0. MALDI-MS: 535.2 (8, $[M + K]^+$), 519.3 (100, $[M + Na]^+$), 463.2 (11), 419.2 (70, $[M - Boc + Na]^+$), 397.2 (83, $[M - Boc + H]^+$), 358.1 (52). Anal. calc. for $C_{28}H_{36}N_2O_6$ (496.60): C 67.72, H 7.31, N 5.64; found: C 67.82, H 7.22, N 5.60.

*(4*R*)-3-(3-{[(Benzyloxy)carbonyl]amino}-1-oxopropyl)-4-(1-methylethyl)oxazolidin-2-one* (**9**). (*R*)-4-(1-Methylethyl)oxazolidin-2-one (2.47 g, 19.12 mmol) was treated with pivaloyl chloride (3.56 ml, 28.94 mmol), 3-{[(benzyloxy)carbonyl]amino}propanoic acid (6.4 g, 28.94 mmol), Et_3N (7.4 ml, 53.53 mmol), and dry LiCl (0.9 g, 21.98 mmol) according to *GP 3*. FC (AcOEt/hexane 1:2 → 1:1) yielded **9** (3.50 g, 82%). White foam. R_f (AcOEt/hexane 1:1) 0.58. IR ($CHCl_3$): 3351*w*, 3016*w*, 2954*w*, 1771*s*, 1742*s*, 1723*s*, 1625*m*, 1503*m*, 1430*m*, 1395*m*, 1354*m*, 1328*m*, 1149*w*, 1118*m*, 1051*w*, 992*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.84 (*d*, *J* = 6.8, Me); 0.89 (*d*, *J* = 7.1, Me); 2.22–2.31 (*m*, Me_2CH); 3.09 (*t*, CH_2N); 3.41–3.47 (*m*, CH_2); 4.27 (*m*, CHN); 5.05 (*s*, CH_2O); 7.29–7.33 (*m*, 5 arom. H). ^{13}C-NMR (125 MHz, $CDCl_3$): 15.3; 21.5; 25.4; 29.5; 41.6; 43.2; 64.7; 66.8; 75.6; 88.7; 95.4; 115.3; 118.8; 119.1; 122.3; 125.6; 125.8; 127.6; 128.3; 128.8; 136.5; 140.4; 155.1; 172.1. MALDI-MS: 335.1 (100, $[M + H]^+$), 357.2 (70, $[M + Na]^+$).

*(4*R*)-3-[(2*S*)-2-({[(Benzyloxy)carbonyl]amino}methyl)-3-hydroxy-3-{1-[(2,2,2-trichloroethoxy)carbonyl]-indol-3-yl}-1-oxopropyl]-4-(1-methylethyl)oxazolidin-2-one* (**10**). According to *GP 4*, **9** (4.14 g, 12.40 mmol) in CH_2Cl_2 (30 ml) at − 78° was treated with Bu_2BOTf (27.28 ml, 27.28 mmol) and Et_3N (4.14 ml, 29.76 mmol) for 1 h, and then with 1-Troc-(1*H*-indole-3-carbaldehyde (9.88 g, 31 mmol) at − 78° for 3 h. FC (hexane/AcOEt 7:3) yielded **10** (5.42 g, 67%). White foam. R_f (hexane/AcOEt 7:3) 0.36. IR ($CHCl_3$): 3442*w*, 3010*w*, 2978*w*, 1777*s*, 1703*s*, 1525*m*, 1452*m*, 1388*w*, 1354*m*, 1320*w*, 1281*w*, 1106*w*, 1007*w*, 994*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.73 (*d*, *J* = 6.8, Me); 0.75 (*d*, *J* = 6.2, Me); 0.79 (*d*, *J* = 6.8, Me); 2.16–2.22 (*m*, Me_2CH); 3.17 (*m*, CH); 3.56–3.59 (*m*, CH); 3.71 (*t*, *J* = 8.2, CH_2N); 4.05–4.12 (*m*, 2 CH); 4.69–4.76 (m, CHO); 7.25–7.38 (*m*, 8 arom. H); 7.78 (d, *J* = 7.7, 1 arom. H); 8.20 (d, *J* = 8.4, 1 arom. H). HR-MALDI-MS: 653.1081 ($C_{29}H_{31}Cl_3N_3O_8^+$; calc. 653.1098).

*(4*R*)-3-[(2*S*)-2-({[(Benzyloxy)carbonyl]amino}methyl)-4-(methylsulfanyl)-1-oxobutyl]-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* (**11**). Compound **4** (594 mg, 1 mmol) was treated with MeSNa (70 mg, 1 mmol), according to *GP 5*. FC (pentane/AcOEt 9:1 → 8:2) yielded **11** (302 mg, 54%). For anal. purposes, a sample was recrystallized (hexane/AcOEt). Colorless needles. M.p. 131–133°. R_f (hexane/AcOEt 8:2) 0.13. $[\alpha]_D^{rt}$ = + 101.6 (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): 3443*w*, 3008*w*, 2968*w*, 2923*w*, 1779*s*, 1720*s*, 1514*m*, 1450*m*, 1395*w*, 1364*m*, 1318*m*, 1145*w*, 1092*w*, 1052*w*, 1002*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.71 (*d*, *J* = 6.7, Me); 0.83 (*d*, *J* = 7.1, Me); 1.49–1.55, 1.73–1.77 (2*m*, CH_2); 1.78 (*s*, Me); 1.94–2.02 (*m*, Me_2CH, CH_2SMe); 3.36–3.42, 3.52–3.59 (2*m*, CH_2NH); 3.92–3.96 (*m*, CHCO); 5.04–5.10 (*m*, $PhCH_2$); 5.24 (br. *s*, NH); 5.35 (*d*, *J* = 3.4, CHN); 7.26–7.50 (*m*, 15 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 15.1, 16.3, 21.6 (Me); 28.8 (CH_2); 29.6 (CH); 31.0 (CH_2); 42.3 (CH); 43.0 (CH_2); 65.4 (CH); 66.8 (CH_2); 89.7 (C); 125.3, 125.7, 128.1, 128.2, 128.5, 128.8, 128.9 (CH); 136.5, 137.7, 142.3, 153.2, 156.2, 174.1 (C). MALDI-MS: 583.2 (100, $[M + Na]^+$), 539.2 (59), 144.7 (23). Anal. calc. for $C_{32}H_{36}N_2O_5S$ (560.71): C 68.55, H 6.47, N 5.00, S 5.72; found: C 68.50, H 6.62, N 4.99, S 5.62.

*(4*R*)-3-({(3*S*)-1-[(Benzyloxy)carbonyl]pyrrolidin-3-yl}carbonyl)-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* (**12**). To a soln. of **4** (2.37 g, 4.0 mmol) in DMF (20 ml), 55 wt-% NaH (210 mg, 4.8 mmol) and Bu_4NI (15 mg, 0.04 mmol) were added at r.t. The mixture was warmed to 70°, stirred for 2 h, cooled again to r.t., diluted with Et_2O (100 ml), washed successively with 1M HCl (2 × 50 ml), sat. $NaHCO_3$ soln. (50 ml), and brine (50 ml). The org. phase was dried ($MgSO_4$) and evaporated. FC (pentane/Et_2O 8:2 → 7:3) yielded **12** (1.21 g, 59%). For anal. purposes, a sample was recrystallized (pentane/Et_2O). Colorless solid. M.p. 59–60°. R_f (pentane/Et_2O 1:1) 0.25. $[\alpha]_D^{rt}$ = + 148.6 (*c* = 0.9, $CHCl_3$). IR ($CHCl_3$): 3008*w*, 2969*w*, 2933*w*, 2881*w*, 1781*s*, 1699*s*, 1495*w*, 1450*m*, 1426*m*, 1362*m*, 1346*m*, 1119*m*, 1052*w*, 1001*w*. ^{1}H-NMR (500 MHz, $CDCl_3$, mixture of rotamers): 0.76 (*d*, *J* = 6.7, Me); 0.86 (*d*, *J* = 7.0, Me); 1.63–1.91, 2.10–2.38 (2*m*, CH_2); 1.97–2.02 (*m*, Me_2CH); 3.35–3.77 (*m*, 2 CH_2); 4.03–4.11 (*m*, CHCO); 5.08–5.12 (*m*, $PhCH_2$); 5.34–5.39 (*m*, CHN); 7.26–7.48 (*m*, 15 arom. H). ^{13}C-NMR (125 MHz, $CDCl_3$): 16.4, 21.6 (Me); 27.5, 28.3, 28.8 (CH_2); 29.8, 41.7, 42.7 (CH); 45.0, 45.1, 45.4, 45.6, 47.2, 47.7, 48.2, 48.8 (CH_2); 64.7, 64.8 (CH); 66.8 (CH_2); 89.7 (C); 125.5, 125.8, 127.9, 128.1, 128.4, 128.5, 128.9, 129.0 (CH); 136.8, 136.9, 137.7, 141.9, 142.0, 152.7, 152.9, 154.5, 172.5 (C). MALDI-MS: 535.2 (100, $[M + Na]^+$), 491.2 (42), 469.3 (45), 425.3 (18). Anal. calc. for $C_{31}H_{32}N_2O_5$ (512.60): C 72.64, H 6.29, N 5.46; found: C 72.73, H 6.44, N 5.37.

*(4*R*)-3-({(3*S*)-1-[(Benzyloxy)carbonyl]piperidin-3-yl}carbonyl)-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* (**13**). To a soln. of **5** (3.43 g, 5.65 mmol) in DMF (30 ml), 55 wt-% NaH (296 mg, 6.78 mmol) and Bu_4NI (21 mg, 0.057 mmol) were added at r.t. The mixture was warmed to 70°, stirred for 3 h, cooled again to r.t., diluted with Et_2O (130 ml), washed successively with 1M HCl (2 × 30 ml), sat. $NaHCO_3$ (30 ml), and brine (30 ml). The org. phase was dried ($MgSO_4$) and evaporated. FC (AcOEt/*n*-hexane 2:1) yielded **13** (2.38 g, 80%). Colorless solid. M.p. 58–62°. R_f (pentane/Et_2O 1:1) 0.38. $[\alpha]_D^{rt}$ = + 119.3 (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): 3008*w*, 2959*w*, 2933*w*, 2862*w*, 1780*s*, 1693*s*, 1496*w*, 1470*m*, 1450*m*, 1436*m*, 1391*w*, 1363*m*, 1348*m*, 1321*w*, 1140*m*, 1077*w*, 1052*w*. ^{1}H-NMR (500 MHz, $CDCl_3$, mixture of rotamers): 0.74 (*d*, *J* = 6.7, Me); 0.85 (*d*, *J* = 7.0, Me); 1.21–1.28, 1.43–1.49 (2*m*, CH_2); 1.54–1.71 (*m*, CH_2); 1.94–2.00 (*m*, Me_2CH); 2.80–2.84, 3.95–3.99 (2*m*, CH_2);

3.12–3.16 and 4.18–4.22 (2*m*, CH_2); 3.44–3.48, 3.59–3.63 (2*m*, CHCO); 5.08–5.13 (*m*, PhCH_2); 5.31 (*d*, *J* = 3.5, CHN); 7.26–7.46 (*m*, 15 arom. H). ^{13}C-NMR (125 MHz, $CDCl_3$): 16.2, 16.4, 21.6, 21.8 (Me); 23.9, 24.2, 26.9, 27.3 (CH_2); 29.7, 29.9, 40.0, 40.7 (CH); 44.1, 45.8 (CH_2); 64.8 (CH); 67.2 (CH_2); 89.4 (C); 125.5, 125.6, 125.9, 127.9, 128.0, 128.4, 128.6, 128.9 (CH); 136.8, 137.9, 142.3, 152.7, 155.1, 173.6 (C). MALDI-MS: 565.2 (10, $[M + K]^+$), 549.2 (100, $[M + Na]^+$), 505.3 (62), 483.3 (22), 439.3 (9). Anal. calc. for $C_{32}H_{34}N_2O_5$ (526.63): C 72.98, H 6.51, N 5.32; found: C 72.88, H 6.70, N 5.30.

*(*S*)-1-[(Benzyloxy)carbonyl]piperidine-3-carboxylic Acid* (**14a**). To a soln. of **13** (2.32 g, 4.41 mmol) in THF/H_2O (20 ml/5 ml) at 0°, H_2O_2 (30%, 1.99 g, 17.6 mmol) and LiOH · H_2O (296 mg, 7.05 mmol) were added, and the resulting mixture was stirred for 4 h at 0°. The mixture was diluted with H_2O, and the preticipated chiral auxiliary was removed by filtration. After adjusting the pH of the soln. to 1–2 with 1N HCl, the aq. phase was extracted with AcOEt (1 × 80 ml, 2 × 40 ml). The combined org. layers were washed with brine (40 ml), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by FC (AcOEt/hexane/AcOH 50:50:2) to obtain 984 mg (85%) of **14a**. White solid. M.p. 100–101°. R_f (AcOEt/hexane/AcOH 50:50:2) 0.32. $[\alpha]_D^{r.t.} = +43.7$ (*c* = 1.1, $CHCl_3$). IR ($CHCl_3$): 3020*s*, 1695*s*, 1520*w*, 1472*m*, 1435*m*, 1220*s*, 1145*m*, 1080*w*, 1040*m*, 930*m*, 800*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.43–1.56 (*m*, 1 H–C(5)); 1,60–1.79 (*m*, 1 H–C(4), 1 H–C(5)); 2.05–2.14 (*m*, 1 H–C(4)); 2.51 (br. *s*, H–C(3)); 2.94 (*ddd*, *J* = 3.0, 10.8, 13.4, 1 H–C(6)); 3.13 (br. *s*, 1 H–C(6)); 3.93–4.00 (*m*, 1 H–C(6)); 4.19 (br. *s*, 1 H–C(2)); *AB* system (δ_A = 5.11, δ_B = 5.16, J_{AB} = 12.4, 1 H each, PhCH_2); 7.28–7.37 (*m*, 5 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 24.1; 27.0; 41.0; 44.2; 45.4; 67.3; 127.9; 128.0; 128.5; 136.6; 155.2; 178.6. HR-ESI-MS: 286.1046 ($C_{14}H_{17}NO_4Na^+$; calc. 286.1050). Anal. calc. for $C_{14}H_{17}NO_4$ (263.30): C 63.87, H 6.51, N 5.32; found: C 63.72, H 6.49, N 5.42.

*(*S*)-1-{[(*9H*-Fluoren-9-yl)methoxy]carbonyl}piperidine-3-carboxylic Acid* (**14b**). Compound **14a** (263 mg, 1.00 mmol) was dissolved in MeOH (10 ml) under N_2, and Pd/C (10%, 26 mg, 0.02 mmol) was added. The apparatus was evacuated and flushed with H_2 (3 ×), and the soln. was stirred under H_2 (balloon) for 1.5 h. Subsequent filtration through *Celite*, washing with MeOH, and concentration under reduced pressure yielded the crude product (148 mg). This material was dissolved in dioxane/H_2O (5 ml/5 ml), and Na_2CO_3 (265 mg, 2.5 mmol) and FmocOSu (371 mg, 1,10 mmol) were added. The mixture was stirred for 2 h at r.t., diluted with H_2O (10 ml), and the pH of the soln. was adjusted to 1–2 with 1N HCl. The aq. phase was extracted with AcOEt (3 × 20 ml), and the combined org. layers were dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by FC (AcOEt/hexane/AcOH 50:50:2) to give 324 mg (92%) of **14b**. White solid. M.p. 160–161°. R_f (AcOEt/hexane/AcOH 50:50:2) 0.46. $[\alpha]_D^{r.t.} = +38.1$ (*c* = 1.2, $CHCl_3$). IR ($CHCl_3$): 3010*w*, 2950*w*, 1695*s*, 1475*w*, 1450*m*, 1260*m*, 1150*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.46 (br. *s*, 1 H–C(5)); 1,61–1.77 (*m*, 1 H–C(4), 1 H–C(5)); 2.02–2.12 (*m*, 1 H–C(4)); 2.43 (br. *s*, 1 H–C(3)); 2.92 (*ddd*, *J* = 2.9, 10.9, 13.4, 1 H–C(6)); 3.11 (br. *s*, 1 H–C(2)); 3.90 (br. *s*, 1 H–C(6)); 4.09 (br. *s*, 1 H–C(2)); 4.24 (*t*, *J* = 6.7, 1 H–C(9′)), 4.44 (*d*, *J* = 6.7, CH_2O); 7.31–7.75 (*m*, 8 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 24.0; 27.0; 40.9; 44.2; 45.6; 47.4; 67.4; 120.0; 125.0; 127.0; 127.7; 141.4; 144.0; 155.2; 178.3. HR-ESI-MS: 374.1361 ($C_{21}H_{21}NO_4Na^+$; calc. 374.1363). Anal. calc. for $C_{21}H_{21}NO_4$ (351.41): C 71.78, H 6.02, N 3.99; found: C 71.54, H 6.14, N 4.13.

*(*S*)-1-[(*tert*-Butoxy)carbonyl]piperidine-3-carboxylic Acid* (**14c**). Compound **14a** (132 mg, 0.50 mmol) was dissolved in MeOH (5 ml) under N_2, and Pd/C (10%, 20 mg, 0.02 mmol) and Boc_2O (133 mg, 0.61 mmol) were added. The apparatus was evacuated and flushed with H_2 (3 ×), and the soln. was stirred under H_2 (balloon) for 2 h. The mixture was filtered through *Celite*, washed with AcOEt, and concentrated under reduced pressure. The crude product was purified by FC (AcOEt/hexane/AcOH 50:50:2) to obtain 108 mg (94%) of **14c**. White solid. M.p. 160–161°. R_f (AcOEt/hexane/AcOH 50:50:2) 0.55. $[\alpha]_D^{r.t.} = +44.2$ (*c* = 0.9, $CHCl_3$). IR ($CHCl_3$): 2980*w*, 2945*w*, 2865*w*, 1710*m*, 1685*s*, 1425*m*, 1365*m*, 1270*m*, 1170*m*, 1150*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.46 (*s*, *t*-Bu); 1.55–1.41 (*m*, 1 H–C(5)); 1.59–1.76 (*m*, 1 H–C(4), 1 H–C(5)); 2.02–2.11 (*m*, 1 H–C(4)); 2.44–2.54 (*m*, 1 H–C(3)); 2.86 (*ddd*, *J* = 2.8, 10.8, 13.4, 1 H–C(6)); 3.05 (br. *s*, 1 H–C(2)); 3.88 (br. *td*, *J* = 4.0, 13.4, 1 H–C(6)); 4.11 (br. *s*, 1 H–C(2)). ^{13}C-NMR (100 MHz, $CDCl_3$): 24.1; 27.2; 28.4; 41.1; 43.9; 45.5; 79.9; 154.7, 178.8. HR-ESI-MS: 252.1202 ($C_{11}H_{19}NO_4Na^+$; calc. 252.1206). Anal. calc. for $C_{11}H_{19}NO_4$ (229.28): C 57.63, H 8.35, N 6.11; found: C 57.50, H 8.23, N 6.02.

*Ethyl (*S*)-1-(2,4-dinitrophenyl)piperidine-3-carboxylate* (**14d**). Compound **14a** was dissolved in EtOH (5 ml), and racemic camphersulfonic acid was added. After heating at reflux for 15 h sat. $NaHCO_3$ soln. (20 ml) was added. The soln. was extracted with AcOEt (3 × 20 ml), dried (Na_2SO_4), and evaporated. The crude material was dissolved in EtOH (5 ml) under N_2, and Pd/C (10%, 20 mg, 0.02 mmol) and AcOH (57 µl) were added. The apparatus was evacuated and flushed with H_2 (3 ×), and the solution was stirred under H_2 (balloon) for 3 h. The mixture was filtered through *Celite*, washed with AcOEt, and concentrated under reduced pressure. To a soln. of this material in H_2O (2 ml) was added $NaHCO_3$ (100 mg, 1.20 mmol) under N_2 at 0°. Then 2,4-dinitrofluorobenzene in EtOH (2 ml) was added. The mixture was stirred at 0° under N_2 for 7 h. After addition

of H_2O (20 ml), the aq. phase was extracted with AcOEt (3 × 20 ml), and the combined org. layers were dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by FC (AcOEt/hexane 3:1) to give 85 mg (69%) of **14d**. Orange oil. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.22 (*t*, *J* = 7.1, Me); 1.65–1.88 (*m*, 3 CH); 2.06–2.17 (*m*, CH); 2.67–2.77 (*m*, COCH); 3.03–3.13 (*m*, NCH); 3.26–3.39 (*m*, 2 NCH), 3.53–3.61 (*m*, NCH); 4.12 (*q*, *J* = 7.1, CH_2O); 7.18 (*d*, *J* = 9.3, 1 arom. H); 8.21 (*dd*, *J* = 9.3, 2.8, 1 arom. H); 8.65 (*d*, *J* = 2.8, 1 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 14.1; 23.8; 26.2; 40.8; 51.4; 52.4; 60.9; 119.8; 123.6; 128.1; 137.9; 138.1; 149.6; 172.5[18]).

*(4*R*)-3-[(2*S*)-6-Azido-2-({[(benzyloxy)carbonyl]amino}methyl)-1-oxohexyl]-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* (**15**). Compound **6** (3.91 g, 6.3 mmol) was treated with NaN_3 (0.49 g, 7.6 mmol) according to *GP 5*. FC (pentane/Et_2O 95:5 → 7:3) yielded **15** (3.51 g, 95%). Colorless needles. M.p. 88–89°. R_f (hexane/AcOEt 7:3) 0.25. $[\alpha]_D^{r.t.} = +108.4$ (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): 3449*w*, 3011*w*, 2940*w*, 2099*s*, 1780*s*, 1720*s*, 1514*m*, 1451*m*, 1396*w*, 1364*m*, 1318*m*, 1148*w*, 1093*w*, 1052*w*, 1002*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.71 (*d*, *J* = 6.7, Me); 0.83 (*d*, *J* = 7.0, Me); 0.82–0.87 (*m*, CH_2); 1.19–1.26, 1.33–1.36 (2*m*, 2 CH_2); 1.94–2.01 (*m*, Me_2CH); 2.95 (*t*, *J* = 6.9, CH_2N_3); 3.35–3.39, 3.48–3.54 (2*m*, CH_2NH); 3.85 (br. *s*, CHCO); 5.07 (*s*, PhCH_2); 5.19 (br. *s*, NH); 5.32 (*d*, *J* = 3.5, CHN); 7.26–7.50 (*m*, 15 arom. H). ^{13}C-NMR (125 MHz, $CDCl_3$): 16.4, 21.7 (Me); 23.5, 28.4, 29.0 (CH_2); 29.6 (CH); 42.7 (CH_2); 43.4 (CH); 50.8 (CH_2); 65.5 (CH); 66.7 (CH_2); 89.7 (C); 125.4, 125.7, 128.1, 128.2, 128.5, 128.7, 128.9 (CH); 136.5, 137.6, 142.4, 153.1, 156.2, 174.7 (C). MALDI-MS: 606.3 (97, [*M* + Na]$^+$), 558.3 (100, [*M* − N_2 + H]$^+$). Anal. calc. for $C_{33}H_{37}N_5O_5$ (583.69): C 67.91, H 6.39, N 12.00; found: C 67.79, H 6.53, N 11.95.

*(4*R*)-3-[(2*S*)-2-({[(Benzyloxy)carbonyl]amino}methyl)-6-{[(*tert*-butoxy)carbonyl]amino}-1-oxohexyl]-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* (**16**). According to the procedure described in [5], *Lindlar* catalyst (220 mg, 10 wt-%) and Boc_2O (890 mg, 4.1 mmol) were added to a soln. of **15** (2.15 g, 3.7 mmol) in MeOH (37 ml). The apparatus was evacuated and flushed with H_2 (3 ×), then the mixture was stirred at r.t. for 4 h, filtered through a *Celite* pad, and concentrated under reduced pressure. FC (pentane/AcOEt 8:2 → 7:3) yielded **16** (2.24 g, 92%). Colorless glass. R_f (hexane/AcOEt 6:4) 0.29. $[\alpha]_D^{r.t.} = +104.0$ (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): 3451*w*, 3008*w*, 2970*w*, 2935*w*, 1780*s*, 1710*s*, 1511*s*, 1451*m*, 1394*m*, 1366*m*, 1318*m*, 1052*w*, 1002*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.71 (*d*, *J* = 6.7, Me); 0.70–0.75 (*m*, CH_2); 0.83 (*d*, *J* = 7.0, Me); 1.09–1.26, 1.34–1.43 (2*m*, 2CH_2); 1.45 (*s*, *t*-Bu); 1.94–2.01 (*m*, Me_2CH); 2.83 (br. *s*, CH_2); 3.32–3.38, 3.48–3.54 (2*m*, CH_2); 3.80–3.84 (*m*, CHCO); 4.37 (br. *s*, NHBoc); 5.04–5.09 (*m*, PhCH_2); 5.24 (*s*, NHZ); 5.32 (*d*, *J* = 3.5, CHN); 7.26–7.51 (*m*, 15 arom. H). ^{13}C-NMR (125 MHz, $CDCl_3$): 16.3, 21.7 (CH_3); 23.4 (CH_2); 28.5 (CH); 29.0 (CH_2); 29.5 (CH); 29.6, 39.9, 42.7 (CH_2); 42.8, 58.4, 65.5 (CH); 66.7, 72.2 (CH_2); 79.0, 89.6 (C); 125.4, 125.7, 128.1, 128.5, 128.7, 128.9 (CH); 136.5, 137.6, 142.3, 153.2, 155.8, 156.2, 174.7 (C). MALDI-MS: 696.3 (20, [*M* + K]$^+$), 680.3 (100, [*M* + Na]$^+$), 624.3 (100), 595.3 (11, [*M* − Boc + K]$^+$), 680.3 (14, [*M* − Boc + Na]$^+$), 558.3 (76, [*M* − Boc + H]$^+$). Anal. calc. for $C_{38}H_{47}N_3O_7$ (657.81): C 69.38, H 7.20, N 6.39; found: C 69.48, H 7.09, N 6.11.

*(4*R*)-[(2*R*,3*S*)-2-({[(Benzyloxy)carbonyl]amino}methyl)-3-hydroxy-1-oxopropyl]-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* (**17**). A soln. of **8** (8.13 g, 16.4 mmol) in CH_2Cl_2 (30 ml) and TFA (30 ml) was stirred at 0° for 1 h and evaporated under reduced pressure. To a soln. of the resulting crude product in CH_2Cl_2 (50 ml), sat. $NaHCO_3$ soln. (50 ml) and Z–Cl (2.53 ml, 18 mmol) were added at r.t. The biphasic mixture was vigorously stirred for 1 h, decanted, and the aq. phase was extracted with CH_2Cl_2 (2 ×). The combined org. fractions were dried ($MgSO_4$) and evaporated. FC (hexane/AcOEt 9:1 → 6:4) yielded **17** (7.52 g, 86%). Colorless solid. M.p. 64–68°. R_f (hexane/AcOEt 6:4) 0.26. $[\alpha]_D^{r.t.} = +111.4$ (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): 3448*w*, 3008*w*, 2971*w*, 1781*s*, 1700*s*, 1520*m*, 1450*m*, 1390*w*, 1364*m*, 1318*w*, 1283*w*, 1149*w*, 1102*w*, 1052*w*, 1002*w*, 985*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.73 (*d*, *J* = 6.8, Me); 0.75 (*d*, *J* = 6.2, Me); 0.82 (*d*, *J* = 7.0, Me); 1.95–2.01 (*m*, Me_2CH); 3.17 (*m*, CH); 3.56–3.59 (*m*, CH); 3.72 (br. *s*, CHN); 3.82–3.86 (*m*, CH_2); 5.08 (*q*, *J* = 12.2, PhCH_2); 5.35 (br. *s*, NH); 7.26–7.49 (*m*, 15 arom. H). ^{13}C-NMR (125 MHz, $CDCl_3$): 16.2; 19.8; 21.6; 29.6; 39.5; 49.4; 65.1; 66.3; 67.0; 89.7; 125.4; 125.7; 128.1; 128.2; 128.5; 128.7; 128.9; 136.3; 137.6; 142.1; 152.9; 157.0; 173.8. MALDI-MS: 569.2 (5, [*M* + K]$^+$), 553.2 (100, [*M* + Na]$^+$), 509.2 (14), 487.3 (17). Anal. calc. for $C_{31}H_{34}N_2O_6$ (530.62): C 70.17, H 6.46, N 5.28; found: C 69.97, H 6.54, N 5.23.

*(4*R*)-[(2*R*,3*S*)-2-({[(Benzyloxy)carbonyl]amino}methyl)-3-(*tert*-butoxy)-1-oxopropyl]-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* (**18**). In a *Schott* flask, a soln. of **17** (6.90 g, 13 mmol) in CH_2Cl_2 (50 ml) was cooled to −78°, conc. H_2SO_4 (0.65 ml) was added, and isobutylene (*ca.* 50 ml) condensed. The flask was hermetically closed, the mixture was stirred 4 d at r.t., partially evaporated, diluted with CH_2Cl_2, and washed with sat. K_2CO_3. The org. phase was dried ($MgSO_4$) and evaporated. FC (pentane/AcOEt 9:1 → 7:3) yielded **18** (5.73 g, 78%).

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[18]) Anal. data are in accordance with those in [26].

Colorless glass. R_f (hexane/AcOEt 7:3) 0.35. $[\alpha]_D^{r.t.} = +95.8$ ($c = 0.6$, $CHCl_3$). IR ($CHCl_3$): 2975*m*, 1779*s*, 1718*s*, 1513*m*, 1450*m*, 1365*m*, 1319*w*, 1178*m*, 1092*w*, 1052*m*, 991*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.64 (*d*, $J = 6.0$, Me); 0.67 (*d*, $J = 6.7$, Me); 0.84 (*d*, $J = 7.0$, Me); 0.97 (*s*, *t*-Bu); 1.95–2.01 (*m*, Me_2CH); 3.48–3.89 (*m*, CH_2, 2 CH); 5.02–5.08 (*m*, $PhCH_2$); 5.28 (br. *s*, NH); 5.32 (*d*, $J = 3.4$, CHN); 7.22–7.53 (*m*, 15 arom. H). ^{13}C-NMR (125 MHz, $CDCl_3$): 16.2; 21.3; 21.7; 21.8; 29.8; 41.2; 49.9; 65.9; 66.5; 67.3; 73.9; 89.3; 125.3; 125.7; 128.0; 128.1; 128.4; 128.5; 128.6; 128.9; 136.7; 137.8; 142.5; 153.1; 156.1; 173.3. MALDI-MS: 625.3 (2, $[M + K]^+$), 609.3 (100, $[M + Na]^+$), 587.3 (21, $[M + H]^+$), 565.3 (56), 487.3 (33), 397.2 (8), 350.2 (12). Anal. calc. for $C_{35}H_{42}N_2O_6$ (586.73): C 71.65, H 7.21, N 4.77; found: C 71.38, H 7.30, N 4.74.

*(2*R*,3*S*)-2-({[(Benzyloxy)carbonyl]amino}methyl)-3-(*tert*-butoxy)butanoic Acid* (**19**). To a soln. of **18** (2.21 g, 3.77 mmol) in THF/H_2O (3:1, 40 ml), H_2O_2 (1.5 ml, 37.7 mmol, 30% soln. in H_2O) was added at 0°. After stirring for 5 min, a soln. of $Bu_4NOH \cdot 30\ H_2O$ (6.02 g, 7.54 mmol) in THF (10 ml) was slowly added, and the mixture was stirred at 0° for 1 h and at r.t. for 12 h. Sat. NH_4Cl soln. (20 ml) and Et_2O (20 ml) were added, and the resulting suspension was vigorously stirred for an additional 15 min and filtered. The residue was washed successively with H_2O, cold Et_2O, and pentane, and dried under h.v. to yield the chiral auxiliary. The filtrate was diluted with Et_2O, the aq. phase was separated, and the pH was adjusted to pH 2–3 by the addition of 1M HCl. The mixture was extracted with Et_2O (2 × 20 ml), and the org. phases were combined, washed with 1M HCl and brine, dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt/AcOH 2:1:0.01 → 1:1:0.01) yielded **19** (0.987 g, 81%). Colorless oil. R_f (AcOEt/hexane/AcOH 1:1:0.01) 0.42. $[\alpha]_D^{r.t.} = -2.0$ ($c = 0.5$, $CHCl_3$). IR ($CHCl_3$): 3446*w*; 2974*m*, 3008*s*, 1749*s*, 1713*s*, 1513*s*, 1369*m*, 1133*w*, 1067*w*, 979*w*. ^{1}H-NMR (400 MHz, CD_3OD): 1.12 (*s*, *t*-Bu); 1.14 (*d*, $J = 6.2$, MeCH); 2.53–2.59 (*m*, $CHCO_2H$); 3.27–3.32 (*m*, 1 H, NCH_2); 3.37 (*dd*, $J = 6.2$, 12.2, 1 H, NCH_2); 3.92 (*dt*, $J = 6.2$, 12.0, $MeCH$); 5.03 (*s*, $PhCH_2$); 6.83–6.81 (*m*, ZHN); 7.30–7.20 (*m*, 5 arom. H). ^{13}C-NMR (100 MHz, CD_3OD): 21.6; 28.9; 40.8; 54.2; 67.4; 68.5; 75.3; 128.8; 129.0; 129.5; 138.5; 158.8; 176.6. MALDI-MS: 441.2 (11), 428.2 (7), 368.1 (22), 346.2 (100, $[M + Na]^+$), 290.1 (29), 224.1 (21). Anal. calc. for $C_{17}H_{25}NO_5$ (323.39): C 63.14, H 7.79, N 4.33; found: C 63.27, H 7.91, N 4.27.

*(4*R*)-3-[(2*S*)-2-({[(Benzyloxy)carbonyl]amino}methyl)-3-{1-[(2,2,2-trichloroethoxy)carbonyl]indol-3-yl}-1-oxopropyl]-4-(1-methylethyl)oxazolidin-2-one* (**20**). To a soln. of **10** (2.66 g, 4.07 mmol) in CH_2Cl_2 (50 ml), Et_3SiH (6.4 ml, 40.7 mmol) and $BF_3 \cdot Et_2O$ (5.0 ml, 40.7 mmol) were added at 0°. The mixture was stirred 1 h at 0°, treated with a sat. $NaHCO_3$ soln., and extracted with Et_2O. The org. phase was washed with brine, dried ($MgSO_4$), and evaporated. The crude product was purified by FC (AcOEt/hexane 2:8) to give **20** (1.94 g, 75%). White foam. R_f (AcOEt/hexane 7:3) 0.51. IR ($CHCl_3$): 3351*w*, 3021*w*, 2951*w*, 1768*s*, 1734*s*, 1615*m*, 1511*m*, 1449*m*, 1390*m*, 1351*m*, 1322*m*, 1144*w*, 1102*m*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.73 (*d*, $J = 6.8$, Me); 0.81 (*d*, $J = 7.1$, Me); 2.16–2.23 (*m*, Me_2CH); 2.85–3.12 (*m*, CH_2); 3.48 (*d*, $J = 6.5$, CH_2); 3.89 (*t*, $J = 8.7$, CH); 4.07–4.14 (*m*, CH_2); 4.50–4.55 (*m*, CH); 5.03 (*q*, $J = 8.4$, $PhCH_2$); 5.10 (*s*, CH_2CCl_3); 5.30 (*d*, $J = 3.5$, CHN); 7.22–7.50 (*m*, 8 arom. H); 7.61 (*d*, $J = 7.7$, 1 arom. H); 8.14 (*d*, $J = 7.7$, 1 arom. H). ^{13}C-NMR (125 MHz, $CDCl_3$): 15.4; 22.3; 25.2; 28.9; 43.1; 65.2; 67.1; 75.2; 91.1; 93.2; 112.2; 117.9; 118.7; 123.3; 125.4; 128.7; 135.8; 137.3; 141.5; 151.3; 155.2. HR-MALDI-MS: 638.1151 ($C_{29}H_{31}Cl_3N_3O_7^+$; calc. 638.1149).

*(4*R*)-3-[(2*S*)-2-({[(Benzyl)oxycarbonyl]amino}methyl)-3-{1-[(*tert*-butoxy)carbonyl]indol-3-yl}-1-oxopropyl]-4-(1-methylethyl)oxazolidin-2-one* (**21**). To a soln. of **20** (1.90 g, 3.04 mmol) in AcOH (15 ml) was added Zn powder (0.5 g), and the soln. was stirred for 1 h at r.t. The mixture was then filtered through *Celite.* AcOH was then co-evaporated with toluene under reduced pressure to yield the crude product, which was used in the next step without purification. The residue was dissolved in MeCN (15 ml) and treated with Boc_2O (1.1 g, 4.6 mmol) and DMAP (24 mg, 0.2 mmol). The mixture was stirred 30 min, and diluted with Et_2O (15 ml) and sat. NH_4Cl soln. (10 ml). The org. phase was separated, washed with 1M HCl (5 ml) and brine (5 ml), dried ($MgSO_4$), and evaporated. FC (AcOEt/hexane 2:8 → 3:7) yielded **21** (1.11 g, 65% over 2 steps). Colorless oil. R_f (AcOEt/hexane 3:7) 0.51. $[\alpha]_D^{r.t.} = -45.6$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3449*w*, 3032*w*, 2975*m*, 1778*s*, 1724*s*, 1608*w*, 1514*s*, 1453*m*, 1386*s*, 1302*s*, 1157*w*, 1087*m*. ^{1}H-NMR (400 MHz, CD3OD): 0.79 (*d*, $J = 6.9$, Me); 0.86 (*d*, $J = 7.0$, Me); 1.66 (*s*, *t*-Bu); 2.25–2.33 (*m*, Me_2CH); 2.87–2.95 (*m*, CH_2); 3.14 (*dd*, $J = 8.1$, 14.3, CH_2); 3.50–3.62 (*m*, CH); 3.91–3.95 (*m*, CH_2CHO); 4.09 (*dd*, $J = 2.4$, 9.0, CH_2CHO); 4.23–4.26 (*m*, CHN); 4.43–4.46 (*m*, CHCO); 5.11–5.15 (*m*, NH); 7.20–7.32 (*m*, 7 arom. H); 7.42 (*s*, 1 arom. H); 7.55 (*d*, $J = 7.6$, 1 arom. H); 8.11 (*d*, $J = 7.4$, 1 arom. H). ^{13}C-NMR (100 MHz, CD_3OD): 14.6; 18.0; 25.2; 28.2; 28.5; 43.0; 43.5; 58.9; 63.4; 66.8; 83.6; 115.2; 116.5; 119.0; 122.6; 124.1; 124.5; 128.1; 128.5; 130.2; 135.4; 136.5; 149.6; 153.8; 156.3; 174.3. HR-MALDI-MS: 586.2525 ($C_{31}H_{37}N_3O_7Na^+$; calc. 586.2524).

*(2*S*)-2-({[(Benzyl)oxycarbonyl]amino}methyl)-3-{1-[(*tert*-butoxy)carbonyl]indol-3-yl}propanoic Acid* (**22**). To a soln. of **21** (3.64 g, 6.46 mmol) in THF/H_2O 4:1 (50 ml) at 0°, H_2O_2 (30% aq., 20 ml) and LiOH · H_2O (0.4 g) were added, and the resulting mixture stirred at 0° for 2 h before addition of a sat. aq. Na_2SO_3 soln. (15 ml). The mixture was diluted with H_2O, and the THF was evaporated at 25° under reduced pressure. The aq.

soln. was cooled to 0°, and the pH was adjusted to 1–2 by addition of 1M HCl. The aq. phase was extracted with AcOEt (3 ×), and the combined org. layers were dried ($MgSO_4$) and concentrated under reduced pressure. FC (pentane/AcOEt/ AcOH 100:100:1) yielded **22** (2.07 g, 71%). White foam. $[\alpha]_D^{r.t.} = -0.57$ ($c = 0.6$, $CHCl_3$). IR ($CHCl_3$): 3448*w*, 2982*w*, 1724*s*, 1514*m*, 1453*m*, 1371*m*, 1157*m*, 1092*w*, 1040*w*, 1020*w*, 855*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.66 (*s*, *t*-Bu); 2.90–2.94 (*m*, CH_2); 3.01–3.15 (*m*, CH_2, CHNH); 3.41–3.55 (*m*, 1 H, CH_2); 3.56–3.64 (*m*, 1 H, CH_2); 5.04–5.11 (*m*, PhCH_2); 5.22–5.30 (*m*, NH); 7.13–7.52 (*m*, 9 arom. H); 8.12 (br., 1 arom. H). ^{13}C-NMR (125 MHz, $CDCl_3$)): 24.9; 25.2; 28.2; 41.8; 42.3; 45.3; 45.6; 66.9; 67.3; 83.7; 115.4; 116.7; 118,7; 122.6; 123.7; 123.9; 124.5; 127.8; 128.2; 128.5; 130.2; 135.5; 136.3; 149.7; 156.5; 157.4; 157.8; 177.5; 178.4. HR-MALDI-MS: 475.1845 ($C_{25}H_{28}N_2O_6Na^+$; calc. 475.1840).

*(*S*)-4-[*N*-[(*tert*-Butoxy)carbonyl]-2-({[(9*H*-fluoren-9-yl)methoxy]carbonyl}amino)-1*H*-indol-3-yl}butanoic Acid* (**23**). Compound **22** (1.90 g, 3.97 mmol) was dissolved in EtOH (40 ml), and the soln. was stirred under H_2 (1 atm, balloon) with 10% Pd/C (19 mg) for 2 h at r.t. The mixture was filtered through *Celite*, and the filtrate was concentrated *in vacuo* to yield the crude amino acid. The crude amino acid was suspended in 0.15M aq. Na_2CO_3 (65 ml, 9.92 mmol) and treated with a soln. of Fmoc-OSu (2.1 g, 5.95 mmol) in acetone (30 ml). If necessary, the pH was re-adjusted to 9–10 with additional aq. Na_2CO_3 soln., and the mixture was stirred for 4 h. The aq. mixture was then extracted with Et_2O (2 × 20 ml). The aq. phase was cooled to 0°, and the pH was adjusted to 2–3 with slow addition of 1M HCl. The aq. phase was then extracted with AcOEt (3 × 40 ml), and the combined org. layers were dried ($MgSO_4$) and concentrated under reduced pressure. Recrystallization (cyclohexane/AcOEt) yielded **23** (1.92 g, 88%). Colorless solid. $[\alpha]_D^{r.t.} = +5.0$ ($c = 1.4$, $CHCl_3$). IR ($CHCl_3$): 3451*w*, 3008*w*, 1725*s*, 1522*m*, 1451*m*, 1369*w*, 1142*w*, 1108*w*, 1032*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.63 (*s*, *t*-Bu); 2.85–3.05 (*m*, CH_2, CHC(O)); 4.19 (*t*, $J = 6.8$, CH); 4.32–4.38 (*m*, CH_2); 7.17–7.40 (*m*, 6 arom. H); 7.48 (*s*, 1 arom. H); 7.56 (*d*, $J = 7.7$, 1 arom. H); 7.64 (*d*, $J = 7.7$, 1 arom. H). ^{13}C–NMR (125 MHz, $CDCl_3$): 26.1; 28.3; 43.5; 46.9; 66.7; 84.5; 116.3; 119.5; 121.2; 123.8; 125.4; 127.2; 128.8; 130.9; 135.4; 142.5; 145.2; 150.9; 160.1. HR-MALDI-MS: 563.2465 ($C_{32}H_{32}N_2O_6Na^+$; calc. 563.2153).

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