Synthesis of Enantiomerically Pure Isoxazolidine Monomers for the Preparation of β^3-Oligopeptides by Iterative α-Keto Acid–Hydroxylamine (KAHA) Ligations

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Dedicated to Professor *Dieter Seebach* on the occasion of his 75th birthday

A versatile method for the synthesis of enantiomerically pure isoxazolidine monomers for the synthesis of β^3-oligopeptides *via* α-keto acid–hydroxylamine (KAHA) ligation is presented. This one-pot synthetic method utilizes *in situ* generated nitrones bearing gulose-derived chiral auxiliaries for the asymmetric 1,3-dipolar cycloaddition with methyl 2-methoxyacrylate. The resulting enantiomerically pure isoxazolidine monomers bearing diverse side chains (proteinogenic and non-proteinogenic) can be synthesized in either configuration (*like*- and *unlike*-configured). The scalable and enantioselective synthesis of the isoxazolidine monomers enables the use of the synthesis of β^3-oligopeptides *via* iterative α-keto acid–hydroxylamine (KAHA) ligation.

Introduction. – Peptides comprised of β-amino acids have attracted substantial interest for their synthesis, analysis, and application [1]. The advantages of β-peptides as functional mimics of natural peptides and therapeutic candidates derive from their resistance to peptidases [2] and their ability to form predictable structures, such as secondary structures [3–5], tertiary structures in the case of chimeric α/β-peptides [6], and quaternary structures [7]. Several biomedical applications of β-peptides have been studied, including antibacterial activity [8], cell penetration [9], inhibitors of protein–protein interaction [10][11], and inhibitors of virus–cell fusion [12]. Despite the potential biological activities of β-peptides, there are several synthetic limitations that hamper the development of β-peptide peptidomimetics. For example, the constituent monomers, β-amino acids, must be prepared from corresponding enantiomerically pure protected α-amino acids by *Arndt–Eistert* homologation [13]. While this is largely effective for most proteinogenic amino acids [13][14], which are now widely available at reasonable cost[1]), it restricts access to non-proteinogenic examples[2]). In

[1]) Fmoc-β^3hGly-, Ala-, Val-, Leu-, Ile-, Met-, Phe-, Trp, and Pro-OH without side-chain protection, Fmoc-β^3hSer-, Thr-, Asp-, Glu-, and Tyr-OH with ^{t}Bu protection, Fmoc-β^3hLys-OH with Boc protection, Fmoc-β^3hArg-OH with Pmc protection, and Fmoc β^3hAsn- and Gln-OH with trityl protection are commercially available. Fmoc-β^3hCys and His are not commercially available.

[2]) The examples of non-proteinogenic β-amino acids, including β^3-homoornithine (β^3-hOrn-OH) and β^3-homohomophenylalanine (β^3-hHop-OH), were shown in [15].

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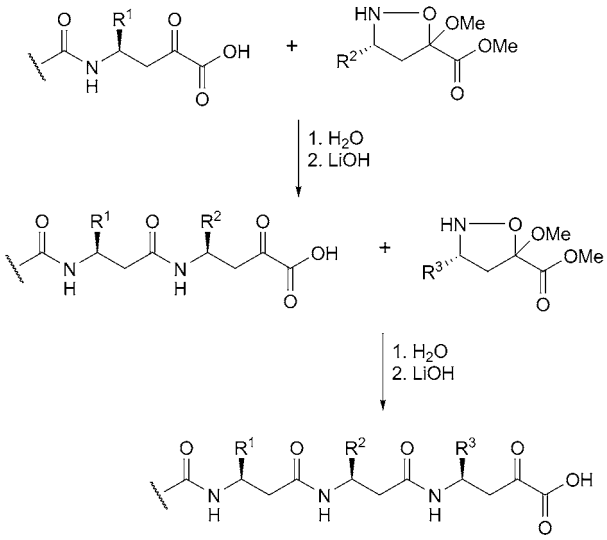
addition, although the synthesis of β-peptides by standard amide coupling is reliable [16], it is hampered by sluggish reactivity and the use of super-stoichiometric amounts of coupling reagents. The result is a generation of large amounts of waste and contributes to the high cost of synthesizing β-oligopeptides.

We have recently identified the α-keto acid–hydroxylamine (KAHA) ligation as an alternative amide-forming reaction that proceeds in the presence of unprotected functional groups and under aqueous conditions [17]. Our primary application to date has been the convergent ligation of unprotected peptide fragments or the cyclization of unprotected linear peptides [18], but we have also considered the utility of this reaction for iterative peptide synthesis. The advantages of this reaction, which do not require coupling reagents or side-chain protecting groups, must be weighed against the requirement of preparing the enantiomerically pure amino acid monomers. In the case of peptides comprised of proteinogenic α-amino acids, it is currently difficult to imagine how the need to prepare each individual monomer could offset the benefits of the KAHA amide formation. For unnatural peptides, for which the constituent monomers must be synthesized prior to assembly, the *de novo* preparation of enantiomerically pure monomers suitable for direct, coupling reagent-free coupling offers an appealing alternative. With these parameters in mind, we have recently demonstrated that the KAHA ligation can be used to assemble β^3-oligopeptides by iterative couplings of enantiomerically pure isoxazolidine monomers (*Scheme 1*) [19]. The amide formation between α-ketoacid and chiral isoxazolidine acetals results in N–O bond cleavage and regeneration of the α-keto ester. Following hydrolysis of α-keto ester provides the α-keto acid, which is ready for further peptide elongation. This amidation reaction proceeds in H_2O, without the need for coupling reagents or side-chain protecting groups, and without affording any non-volatile by-products. These advantages have the

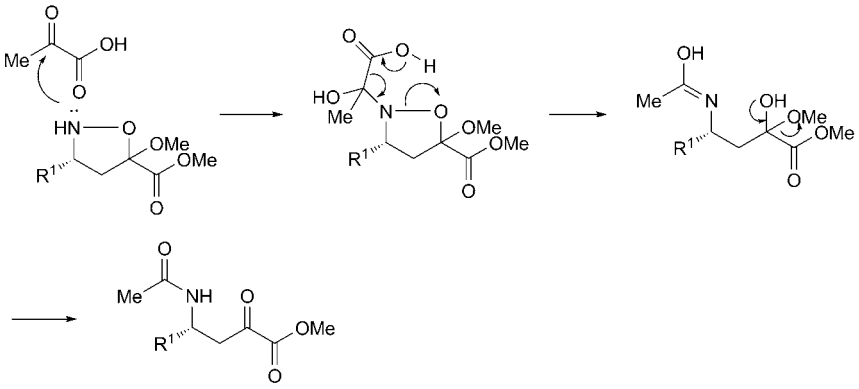
Scheme 1. *Iterative, Aqueous Synthesis of β^3-Oligopeptides* via *α-Keto Acid–Hydroxylamine Ligation*



potential to improve the synthesis of β^3-oligopeptides by avoiding issue of reactivity, solubility, and purification that hamper the traditional β-peptide synthesis.

A postulated mechanism for the decarboxylative condensation of α-keto acids and isoxazolidine acetals is shown in *Scheme 2*. Nucleophilic attack onto the α-ketone, followed by proton transfer, renders a hemianimal intermediate. Decarboxylation initiates a cascade of steps resulting in N–O bond cleavage, expelling MeOH and CO_2 as by-products. Tautomerization of enol intermediate gives rise to amide formation and formation of an α-keto ester.

Scheme 2. *Postulated Mechanism for Amide Formation between α-Keto Acids and Isoxazolidine Monomers*



The key to the widespread use of this synthetic method is the versatile and facile preparation of isoxazolidine monomers in eantiomerically pure forms. In addition, a broader scope of side-chain functionality, acquisition of both *like*- and *unlike*-configured monomers[3]), as well as increasing the ease of availability of starting material are also needed. In this report, we document our development of a general, reliable synthesis of both enantiomers of the isoxazolidine monomers bearing a broad scope of side chains.

Preparation of Enantiomerically Pure Isoxazolidine Monomers. – The study of chiral auxiliaries for the preparation of enantiomerically enriched isoxazolidines is a rich and long-studied area of organic asymmetric synthesis. *Vasella* introduced a chiral auxiliary derived from (+)-D-mannose for the diastereoselective 1,3-dipolar cycloaddition reactions between chiral nitrones and α,β-unsaturated esters [21]. Our early work took advantage of *Vasella*'s procedure to obtain a few enantiomerically pure isoxazolidine monomers [19][22]. Cycloadditions proceeded by refluxing a mixture of D-mannose-derived oxime, acrylate, and the corresponding aldehyde with a *Dean–Stark* trap in one pot. The D-mannose-derived oxime formed a nitrone *in situ* which underwent a 1,3-dipolar cycloaddition with the acrylate to form the isoxazolidine monomers with *ca.* 9:1 diastereoselectivity at the β-C-atom (*Scheme 3*).

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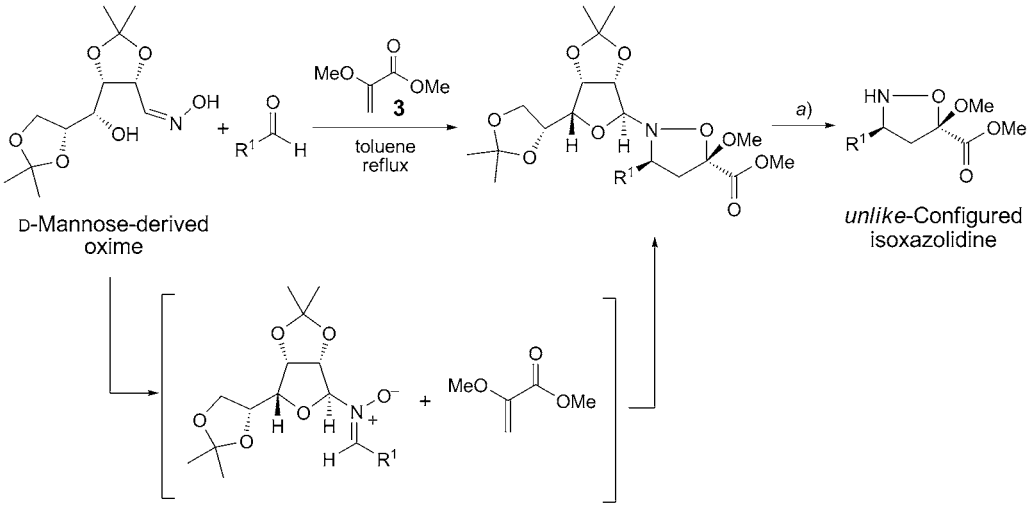
[3]) The stereochemical convention *like*/*unlike* was proposed in [20].

Scheme 3. *General Approach to the Synthesis of Enantiomerically Pure Isoxazolidine Synthesis* via *One-Pot Nitrone Cycloaddition with* D-*Mannose Oxime*



Although the synthesis of isozaxolidines was reliable, the D-mannose-derived auxiliary afforded the absolute configuration to the *unlike*-β^3-amino acids after ligation with α-keto acids, and the corresponding L-mannose is prohibitively expensive for use as a chiral auxiliary. Furthermore, in many cases the diastereoselectivites were lower, and the isoxazoline products were difficult to obtain as single stereoisomers by crystallization. We turned to the report of *Kibayashi* and co-workers about chiral auxiliaries derived from D-gulose and L-gulose as a convenient surrogate for mannose to synthesize (+)-negamycin and its epimer (−)-epinegamycin [23]. Both of D- and L-gulose are available at a reasonable price in the form of the gulonic acid-1,4-lactone[4]). More recently, we have developed and improved scalable synthesis of acetonide-protected D-gulose- and L-gulose-derived oximes [24–26]. We employed the acetonide-protected D-gulose- and L-gulose-derived oxime[5]) to synthesize *like*- and *unlike*-configured isoxazolidines, respectively, by the 1,3-dipolar cycloaddition (*Scheme 4*). These oximes not only show high selectivity but also enable easy handling as solids, and facile chromatography and recrystallization of the diastereoisomers.

Several enantiomerically pure isoxazolidine monomers **5a**–**5d**, **5f**, **5k**, and **5l**, containing common proteinogenic side chains, such as alanine, valine, leucine, phenylalanine, glutamate, tryptophan, and serine, respectively, have been readily synthesized by the two-step approach. By employing appropriate aldehyde, we can also obtain isoxazolidine monomers containing the non-proteinogenic side chain, such as **5g**, **5i**, and **5m**. The structures and synthetic yields of *like*-configured (*Scheme 5*) and *unlike*-configured (*Scheme 6*) monomers are shown.

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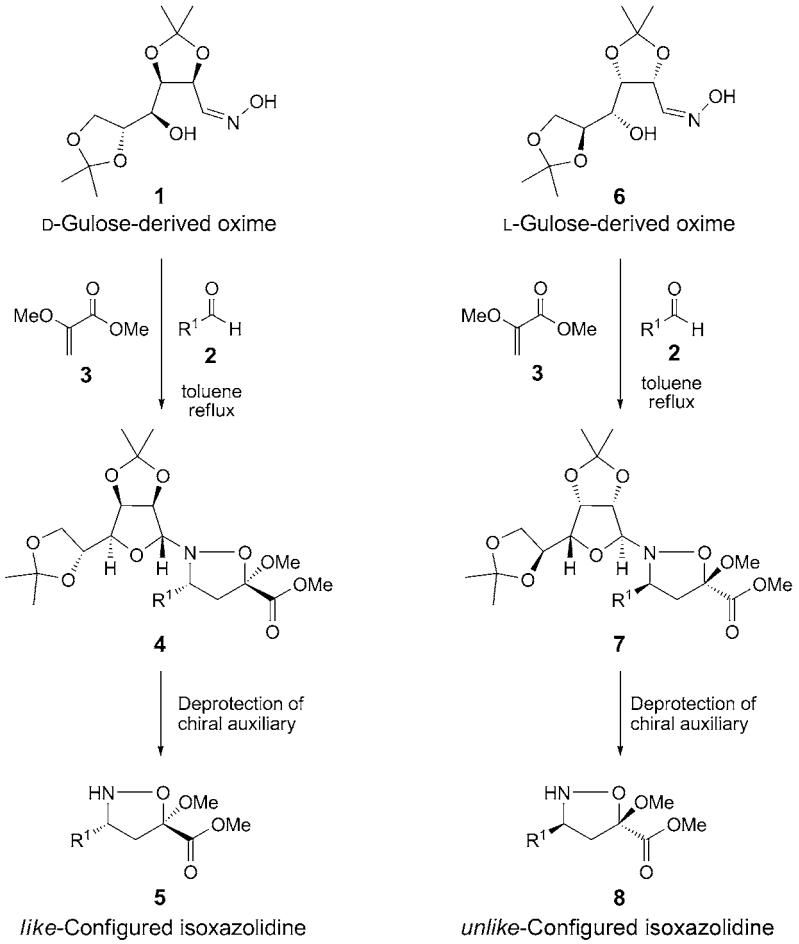
[4]) D- and L-Gulono lactones are derived from D-xylose and L-ascorbic acid, respectively. They are available from *Carbosynth*.

[5]) D- and L-Gulose oxime chiral auxiliaries are now commercially available from *BioBlocks, Inc.*

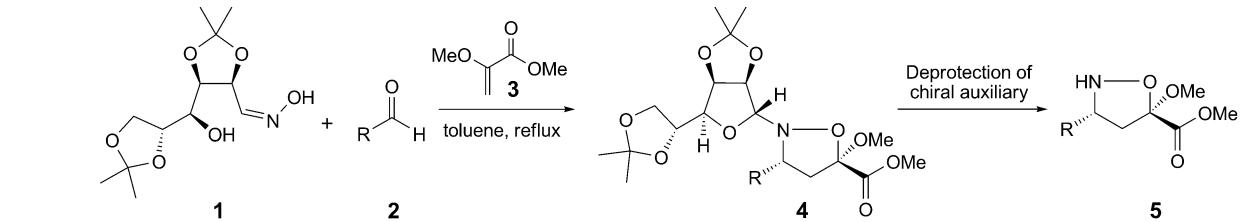
Scheme 4. *Diastereoselective Synthesis of* like- *and* unlike-*Isoxazolidine Monomers Controlled by* D-*Gulose- and* L-*Gulose-Derived Oxime, Respectively*

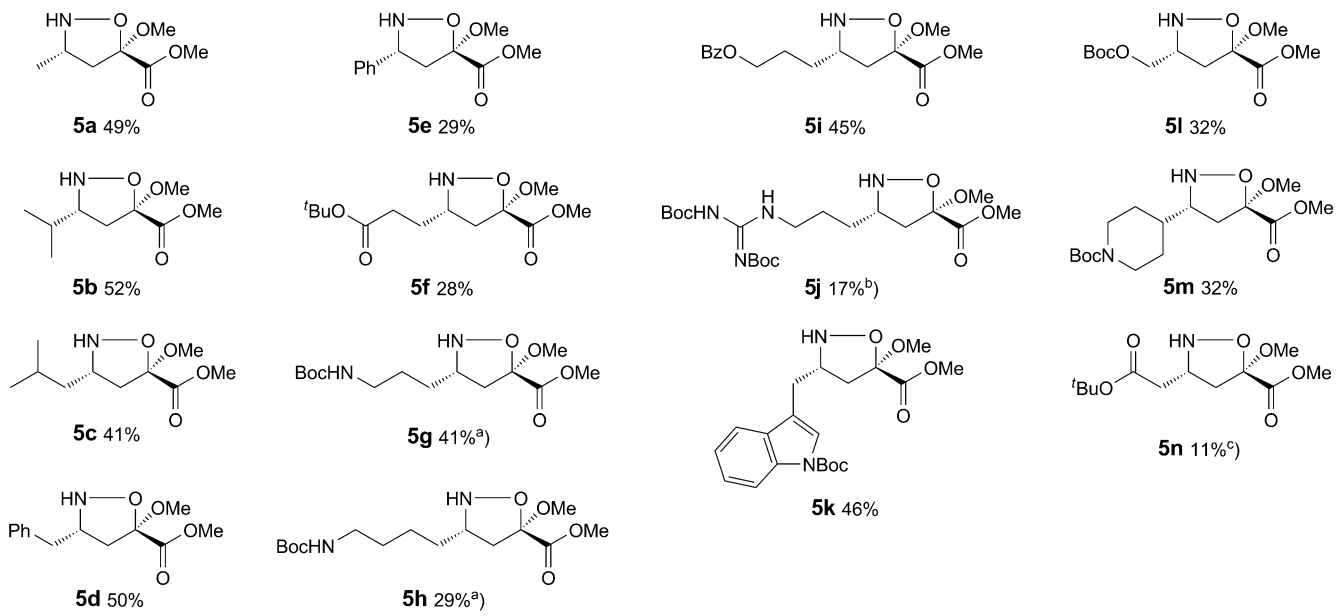


When attempting to synthesize monomers possessing nucleophilic N-atoms, such as lysine (**5h**), ornithine (**5g**), and arginine monomers (**5j**), we encountered a problematic self-condensation of nitrones by the side chain. For example, aldehyde **9** was synthesized as a suitable substrate for the one-pot synthesis to give the lysine monomer. Once nitrone **10** was formed, the amine was able to attack the nitrone functionality yielding **11**, rendering it useless for formation of the desired monomer (*Scheme 7*).

We considered several strategies to avoid the self-condensation of nitrones possessing N-atoms. First, a bis-protected amino aldehyde **12** was used in the synthesis of ornithine monomer **5g**. Bis-protected monomer **4g-1** was obtained in 53% isolated yield as the major diastereoisomer after chromatography and recrystallization. After

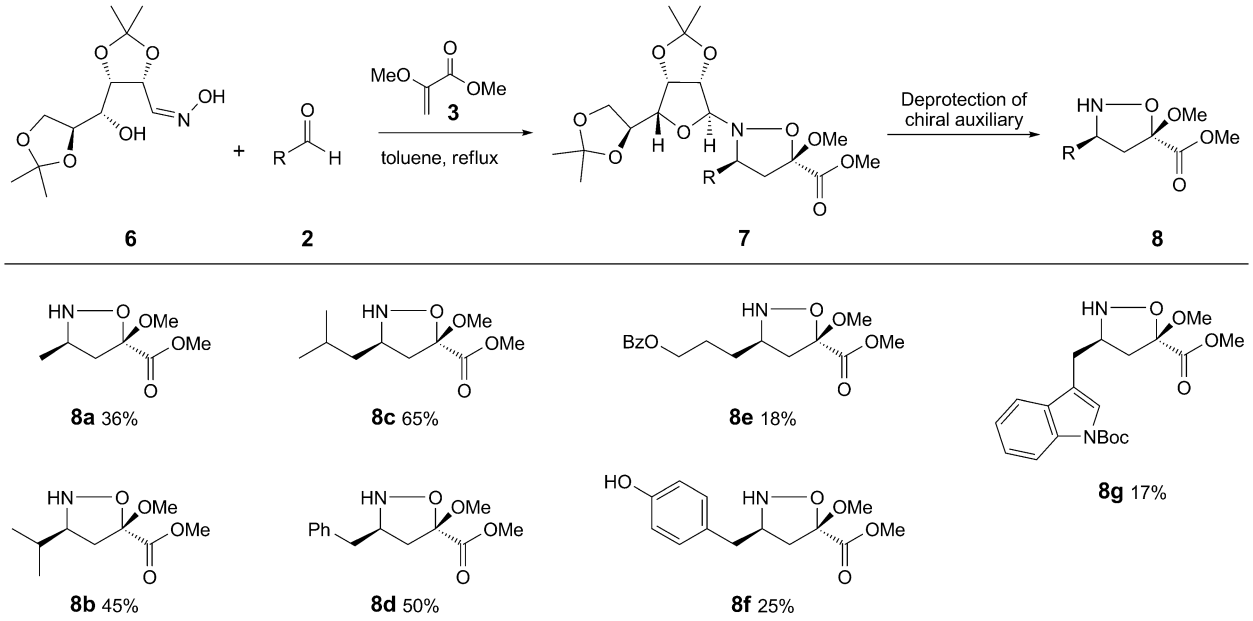
Scheme 5. *The Structures and Synthetic Yields of* like-*Configured Isoxazolidine Monomers*



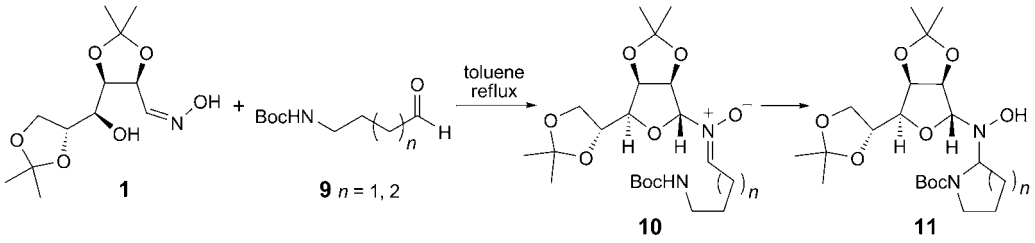


[a]) The yield was calculated from 3 steps. [b]) The yield was calculated from 5 steps. [c]) The yield was calculated from 6 steps.

Scheme 6. *The Structures and Synthetic Yields of* unlike-*Configured Isoxazolidine Monomers*

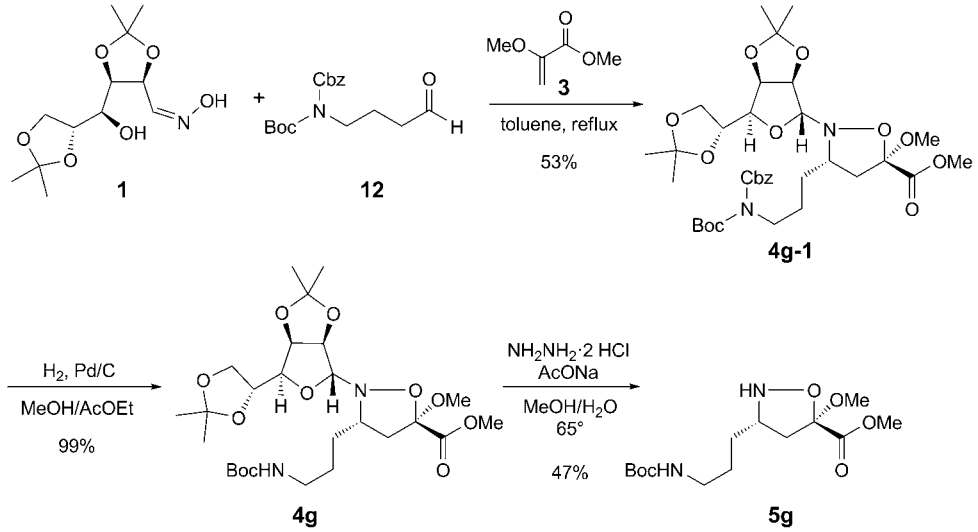


Scheme 7. *Intramolecular Cyclization with Nucleophilic Side Chains*



removal of the Cbz (=(benzyloxy)carbonyl) group by hydrogenation, a Boc-protected ornithine monomer **4g** was obtained (*Scheme 8*).

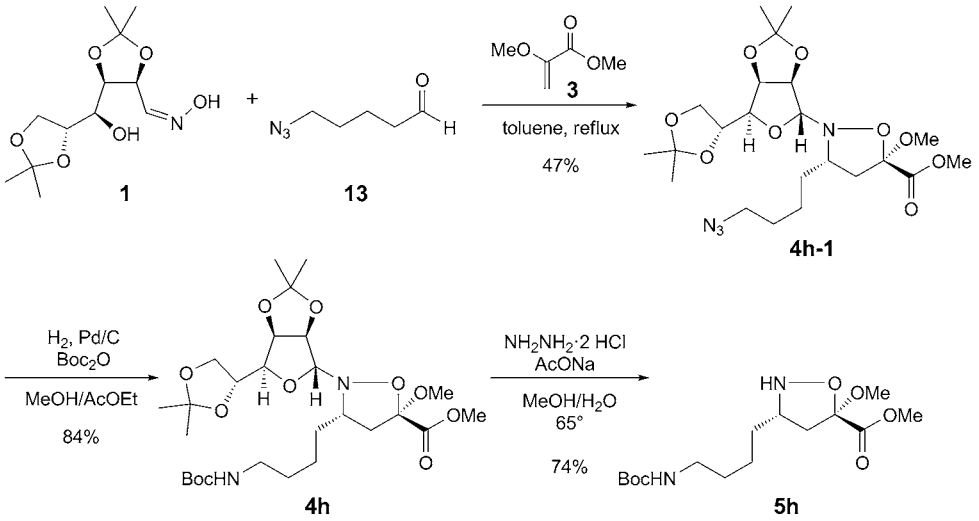
Scheme 8. *Synthesis of Isoxazolidine Monomers* **5g** *Bearing Ornithine Side Chain*



Alternatively, an azido aldehyde **13** can be used for the synthesis of lysine monomer **5h**. When an azide functionality was replaced with the protected amine (aldehyde **13**), no products similar to **11** were observed. Azide monomer **4h-1** was obtained in 31% isolated yield as the major diastereoisomer after chromatography and recrystallization. This required only one step to arrive at the sugar protected lysine monomer **4h**; reduction of the azide by hydrogenation and Boc protection (*Scheme 9*) in a one-pot reaction.

The synthesis of arginine monomer **5j** can be achieved from the azido monomers **4j-2**. To arrive at the sugar-protected bis-Boc-arginine isoxazolidine, simple use of the guanidino aldehyde resulted in very low yields presumably due to self-condensation of the generated nitrone. We used a Bz (= benzoyl)-protected alcohol that could serve as a modifiable functional group after cycloaddition. Aldehyde **14** was found to be suitable to give non-proteinogenic isoxazolidine **4i** in 48% yield. The Bz group was easily

Scheme 9. *Synthesis of Isoxazolidine Monomers* **5h** *Bearing Lysine Side Chain*

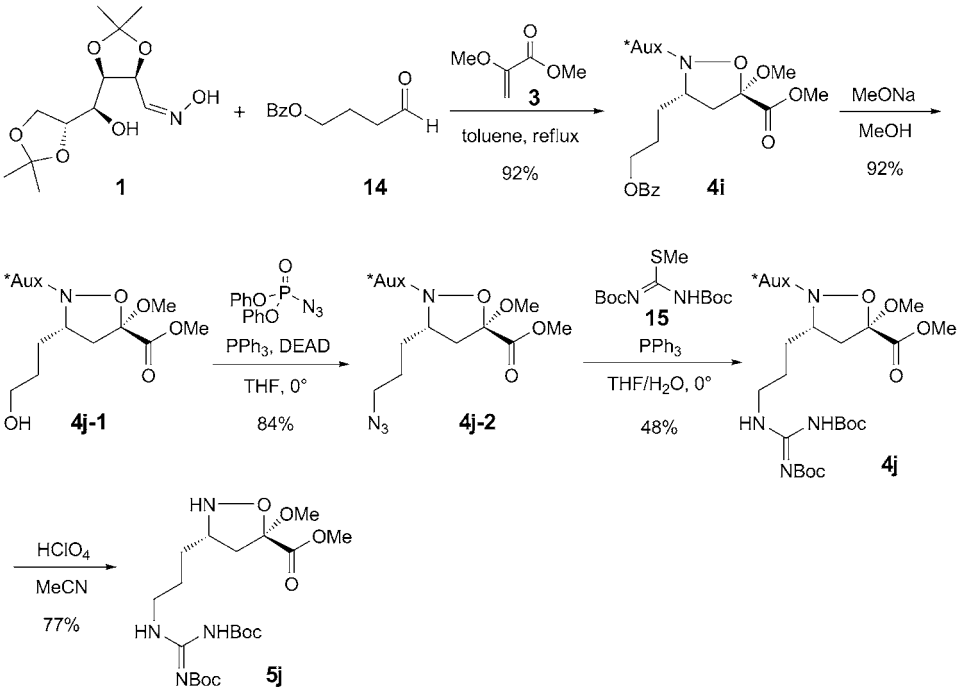


removed after the cycloaddition with MeONa, a reagent that did neither deprotect the sugar auxiliary nor disturb the integrity of the methyl ester functionality on the isoxazolidine ring, to afford free alcohol **4j-1** in 92% yield. Compound **4j-1** was converted to an azide with diphenylphosphoryl azide by *Mitsunobu* reaction in 84% yield. In a one-pot, two-step procedure, azide **4j-2** was reduced with Ph_3P and coupled with *N*,*N*′-bis[(*tert*-butoxy)carbonyl]-*S*-methylisothiourea (**15**) to give the sugar-protected bis-Boc arginine isoxazolidine monomer **4j** in 48% yield (*Scheme 10*).

The isoxazolidine monomer bearing aspartic acid side chain, **5n**, proved synthetically challenging and demanded an alternative route to its preparation. By using the established protocol for *unlike*-configured isoxazolidine monomer containing aspartic acid side chain with D-mannose-derived oxime [22], the synthesis of the *like*-configured monomer **5n** was achieved with D-gulose-derived oximes (*Scheme 11*). β-Sulfanyl aldehyde **16** proved to be a good surrogate of γ-protected formyl-ester and suitable for the use in the chiral auxiliary-directed cycloaddition. The cycoadduct **4n-1** can be obtained as a single diastereoisomer. Oxidation to the sulfoxide **4n-2**, followed by *Pummerer* oxidation, rendered the aldehyde **4n-3** in high yield. Subsequent *Pinnick* oxidation afforded the carboxylic acid **4n-4** in excellent yield. The free acid side chain was protected with ^{t}Bu group to afford ester **4n-5** for the purification purpose.

Deprotection and Recycling of the Chiral Auxiliary. – Several deprotection methods of carbohydrate-derived auxiliaries have been reported in the literature, such as with HCOOH [27], HCl [28], TsOH [29], or $HClO_4$ [30]. Early studies in our group showed that 2–3 equiv. of $HClO_4$ in MeOH served to deprotect the isoxazolidines cleanly and in good-to-high yields [19]. Hydrolysis of the sugar moiety allows for biphasic extraction to give relatively pure isoxazolidine in the organic layer, however, chromatography is still necessary. Although some epimerization occurs at the acetal,

Scheme 10. *Synthesis of Isoxazolidine Monomers* **5j** *Bearing Arginine Side Chain*

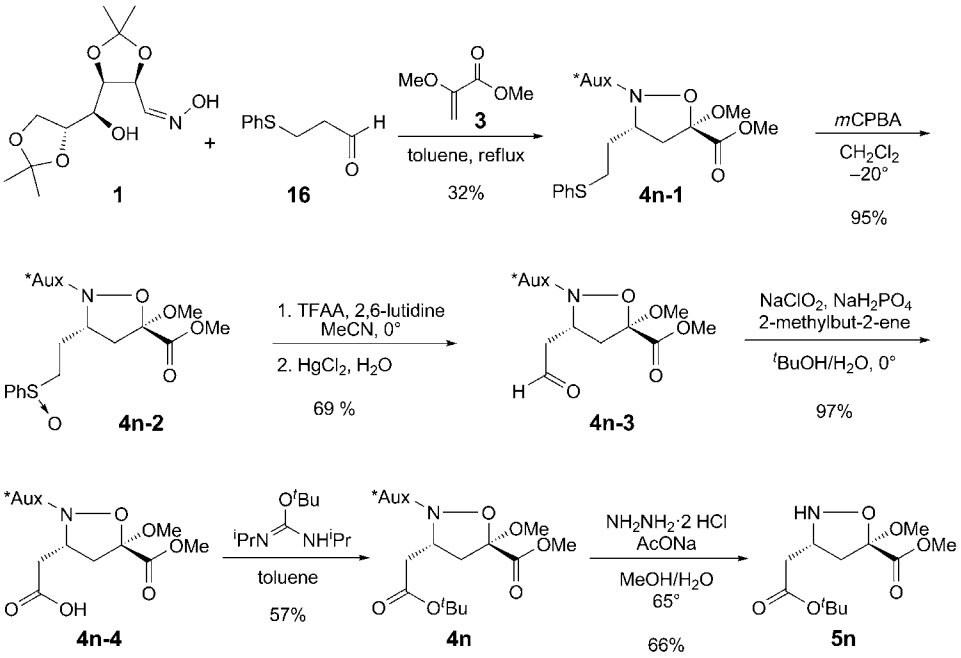


this is inconsequential, because the major diastereoisomer has already been isolated at this point, and the stereogenic center of acetal is lost in the subsequent ligation step. The procedure of acid hydrolysis works well when used in most cases where the amino acid side chain bears purely aliphatic or aromatic functionality. For acid-sensitive groups, alternative methods needed to be explored.

A milder deprotection method using hydroxylamine was adapted from work done by *Wittenberger* and co-workers [31], and later by *Carreira* and co-workers [32]. $NH_2OH \cdot HCl$ buffered with AcONa in aqueous MeOH provided the *N*-unsubstituted isoxazolidine and the gulose-derived oxime in good yields. This procedure was proved to be a good alternative cleavage method for the most isoxazolidine monomers bearing acid-sensitive group, such as *t*Bu- or Boc-protected side chains. A major advantage of NH_2OH-mediated cleavage is that the chiral auxiliary can be recovered and reused. Some substrates, however, did not survive well under the two conditions mentioned above, in particular, primary amine or alcohol with Boc protecting groups. *Carreira* and co-workers reported $NH_2NH_2 \cdot 2\,HCl$ buffered with AcONa can be another choice [32], albeit no recovery or recycling of the auxiliary was attempted. This cleavage method worked well to preserve Boc-protected side chains, such as ornithine, lysine, and serine, of the isoxazolidine monomers **5g**, **5h**, and **5l**, respectively.

With the arginine isoxazolidine monomer, none of the three methods mentioned above were successful. Removal of the auxiliary of **4j** using the $NH_2OH \cdot HCl$ method

Scheme 11. *Synthesis of Isoxazolidine Monomers* **5n** *Bearing Aspartic Acid Side Chain*



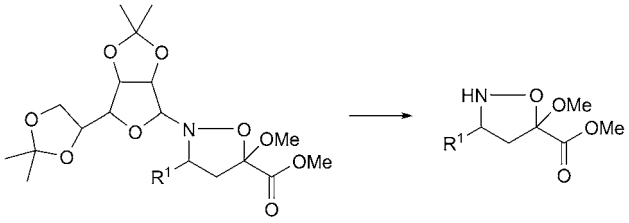
or $NH_2NH_2 \cdot 2\,HCl$ method led to hydrolysis of the guanidine group, actually giving a β^3-ornithine monomer instead. Interestingly, $HClO_4$ deprotection in MeCN proceeded first with deprotection of the auxiliary, so the reaction could be monitored and stopped to obtain the di-Boc-protected **5j** isoxazolidine monomer. The cleavage methods of chiral auxiliary are compiled in the *Table*.

Conclusions and Outlook. – We have developed and optimized the synthesis of isoxazolidine monomers as part of a larger program to establish the α-keto acid-hydroxylamine (KAHA) ligation as an alternative to traditional, coupling-reagent based approaches to β^3-oligopeptide synthesis. The production of these isoxazolidine monomers can be achieved on a reasonable scale and with good yields. We have optimized the synthesis of starting material, such as D-gulose- and L-gulose-derived oximes [26], and suitable aldehydes, so isoxazolidine monomers can be synthesized in a reasonable cost. In addition, the KAHA ligation proceeds in aqueous solution, requires no reagents or catalysts, and produces only MeOH and CO_2 as by-products. All of these advantages render our methodology more economic and environmentally friendly compared to the traditional approaches to β^3-oligopeptide synthesis.

Experimental Part

1. *General. Abbreviations:* Bn: benzyl, Boc: *tert*-butoxycarbonyl, Boc_2O: di(*tert*-butyl) dicarbonate, Bz: benzoyl, Cbz: (benzyloxy)carbonyl, DEAD: diethyl azodicarboxylate, DPPA: diphenylphosphoryl azide, *m*CPBA: *meta*-chloroperoxybenzoic acid, TFAA: trifluoroacetic anhydride, $(CF_3CO)_2O$.

Table. *Available Methods for Deprotection of Chiral Auxiliary*



Cleavage procedure	Reagents	Recovers of gulose oxime	Applicable isoxazolidine
GP B1	$HClO_4$, MeOH, 65°	no	Aliphatic or aromatic side chain: **5a**–**5e**, **8a**–**8d**
GP B2	$NH_2OH \cdot HCl$, AcONa, MeOH/H_2O 3 : 1, 65°	yes	Acid-sensitive side chain: **5f**, **5i**, **5k**, **5m**, **8e**–**8g**
GP B3	$NH_2NH_2 \cdot 2$ HCl, AcONa, MeOH/H_2O 3 : 1, 65°	no	Acid-sensitive side chain[a]): **5g**, **5h**, **5l**, **5n**
GP B4	$HClO_4$, MeCN, r.t.	no	Arg[b]) (**5j**)

[a]) In particular, primary amine or alcohol with Boc protecting groups. [b]) This procedure could also be applied to most isoxazolidines with aliphatic or aromatic side chains.

All reactions utilizing air- or moisture-sensitive reagents were performed in dried glassware under dry N_2. CH_2Cl_2 were distilled from CaH_2. THF was distilled from Na. *N*,*N*-Diisopropylethylamine (EtN^iPr_2) were distilled from KOH. TLC: EMD precoated plates (silica gel *60* F_{254}, Art 5715, 0.25 mm); visualization by fluorescence quenching under UV and by staining with phosphomolybdic acid or $KMnO_4$. Prep. thin-layer chromatography (PTLC): plates prepared from EMD silica gel *60* PF_{254} (Art. 7749). Column chromatography (CC): EMD silica gel *60* (230–400 mesh) using a forced flow of 0.5–1.0 bar. Optical rotations: *Jasco DIP-1000* polarimeter operating at the sodium D-line with a 100-mm path length cell; as $[\alpha]_D^T$ (concentration (g/100 ml), solvent). IR Spectra: *Jasco FT/IR-4100* spectrophotometer as a thin film; in cm^{-1}. ^{1}H- (500 MHz) and ^{13}C-NMR (125 MHz): *Bruker Avance AVII-500* spectrometer; ^{1}H- (400 MHz) and ^{13}C-NMR (100 MHz): *Varian Unity 400* spectrometer in $CDCl_3$; chemical shifts in ppm downfield from residual of protonated deuterium solvent peaks for ^{1}H-NMR and deuterium solvent peaks for ^{13}C-NMR, coupling constants *J* in Hz.

2. *General Procedures A, B1, B2, B3, and B4. General Procedure A* (*GP A*): *Nitrone Cycloadditions with the Gulose-Derived Chiral Auxiliary.* A 0.3M soln. of D-gulose oxime or L-gulose oxime (32.6 mmol, 1.00 equiv.), aldehyde (1.00–1.50 equiv.), and methyl 2-methoxyacrylate (2.50–5.00 equiv.) in toluene (0.3M) was heated to reflux and stirred in a round-bottom flask with a *Dean–Stark* trap fitted with a reflux condenser. The reaction was monitored by TLC until the absence of a UV-active nitrone spot. After cooling to r.t., the solvent was concentrated under reduced pressure. The crude product was purified by flash chromatography (FC) with the following conditions: *1*) The column was packed with hexanes/AcOEt 9 : 1 and the crude mixture loaded with a minimal amount of toluene. *2*) The excess *methyl 2-methoxyacrylate* (**3**) was eluted with the same solvent mixture as was packed with (monitored by TLC, UV-active spot R_f 0.7 in hexanes/AcOEt 9 : 1). *3*) Fractions were collected eluting all four possible diastereoisomers (*Note:* the diastereoisomers with the highest R_f and the lowest R_f are always the undesired diastereoisomers, the middle two diastereoisomers are always the desired diastereoisomers. The separation on the column should be so that most of the undesired diastereoisomers are not present in the collected fractions). *4*) The collected fractions of the desired diastereoisomers were combined, the solvent was evaporated and further dried under vacuum. The crude solid (or sometimes thick oil) was recrystallized from heptanes (50 ml/g) to give a single diastereoisomer.

General Procedure B1 (*GP B1*): *Auxillary Cleavage with $HClO_4$ in MeOH.* To a 0.1M soln. of the gulose-isoxazolidine (5.27 mmol, 1.00 equiv.) in MeOH was slowly added $HClO_4$ (70% (*w*/*w*), 10.6 mmol, 2.00 equiv.) and refluxed for 4 h. After cooling to r.t., the reaction was quenched by the addition of a sat. Na_2CO_3 soln., and the mixture was extracted with AcOEt (3×). The org. layers were combined, washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The resulting residue was purified by FC.

General Procedure B2 (*GP B2*): *Auxiliary Cleavage with $NH_2OH \cdot HCl$.* To a 0.1M soln. of the gulose-isoxazolidine (2.28 mmol, 1.00 equiv.) in MeOH/H_2O 3:1 was added $NH_2OH \cdot HCl$ (9.60 equiv.) and AcONa (9.00 equiv.) in one portion and heated at 65° for 12 h. Another portion of $NH_2OH \cdot HCl$ and AcONa was added until starting material was consumed (TLC). The mixture was cooled to r.t. and further cooled in an ice bath. The reaction was quenched with sat. aq. $NaHCO_3$, and the mixture was extracted with AcOEt (3×). The org. layers were combined, washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The resulting residue was purified by FC to the afford the *N*-unsubstituted isoxazolidine and the gulose oxime.

General Procedure B3 (*GP B3*): *Auxiliary Cleavage with $NH_2NH_2 \cdot 2\,HCl$.* To a 0.10M soln. of the gulose-isoxazolidine (9.90 mmol, 1.00 equiv.) in MeOH/H_2O (3:1) was added $NH_2NH_2 \cdot 2\,HCl$ (9.00 equiv.) and AcONa (8.60 equiv.). The mixture was stirred at 60° for 9 h, then treated with ice, neutralized with $NaHCO_3$, and extracted with AcOEt (3×). The org. layers were separated, washed with brine, dried ($NaSO_4$), filtered, and concentrated *in vacuo*. The resulting material was purified by FC to afford the *N*-unsubstituted isoxazolidine.

General Procedure B4 (*GP B4*): *Auxillary Cleavage with $HClO_4$ in MeCN.* To a 0.1M soln. of the gulose-isoxazolidine (0.05 mmol, 1.00 equiv.) in MeCN was slowly added $HClO_4$ (70% (*w*/*w*), 0.125 mmol, 2.50 equiv.) and stirred for 2 h. The reaction was quenched by the addition of a sat. $NaHCO_3$ soln., and the mixture was extracted with AcOEt (3×). The org. layers were combined, washed with brine, dried (Na_2SO_4O), filtered, and concentrated under reduced pressure. The resulting residue was purified by FC.

3. *Preparation of Isoxazolidine Monomers.* 3.1. *Preparation of Enantiomerically Pure Isoxazolidine Monomers with* like-*Configured Residues* (*Scheme 5*). *Methyl (3*S,5R*)*-N-*(2,3:5,6-Di*-O-*isopropylidene-β*-D-*gulofuranosyl)-5-methoxy-3-methylisoxazolidine-5-carboxylate* (**4a**). Prepared according to *GP A*. Yield: 54%. White crystalline solid. M.p. 105°. $[\alpha]_D^{20} = +28.3$ ($c = 1.00$, $CHCl_3$). IR: 2991, 2939, 1748, 1452, 1374, 1270, 1227, 1069, 852. ^{1}H-NMR (400 MHz): 5.00 (*d*, *J* = 6.0, 1 H); 4.70 (*dd*, *J* = 6.0, 4.0, 1 H); 4.67 (*s*, 1 H); 4.39–4.33 (*m*, 1 H); 4.19 (*dd*, *J* = 8.8, 6.8, 1 H); 4.10 (*dd*, *J* = 8.4, 3.6, 1 H); 3.80 (*s*, 3 H); 3.72 (*dd*, *J* = 8.8, 6.8, 1 H); 3.53–3.48 (*m*, 1 H); 3.36 (*s*, 3 H); 2.72 (*dd*, *J* = 13.2, 7.6, 1 H); 2.19 (*dd*, *J* = 13.6, 6.0, 1 H); 1.46 (*s*, 3 H); 1.40 (*s*, 3 H); 1.37 (*s*, 3 H); 1.31 (*d*, *J* = 6.4, 3 H); 1.30 (*s*, 3 H). ^{13}C-NMR (100 MHz): 169.2; 112.9; 109.9; 105.2; 98.9; 84.4; 84.0; 80.5; 75.9; 66.2; 58.8; 53.1; 52.1; 47.2; 27.0; 26.3; 25.6; 25.1; 19.1. HR-ESI-MS: 440.1892 ($[M+Na]^+$, $C_{19}H_{31}NO_9^+$; calc. 440.1891).

*Methyl (3*S,5R*)-5-Methoxy-3-methylisoxazolidine-5-carboxylate* (**5a**). Prepared according to *GP B1*. Yield: 90%. Clear oil. $[\alpha]_D^{20} = +78.5$ ($c = 1.00$, $CHCl_3$). IR: 3214, 2955, 2838, 1749, 1438, 1069. ^{1}H-NMR (400 MHz): 5.46 (*s*, 1 H); 3.78 (*s*, 3 H); 3.56–3.46 (*m*, 1 H); 3.29 (*s*, 3 H); 2.64 (*dd*, *J* = 13.2, 8.4, 1 H); 1.91 (*dd*, *J* = 13.2, 8.0, 1 H); 1.20 (*d*, *J* = 6.4, 3 H). ^{13}C-NMR (100 MHz): 168.5; 108.6; 56.3; 52.9; 52.0; 49.5; 16.2. HR-ESI-MS: 198.0750 ($[M+Na]^+$, $C_7H_{13}NNaO_4^+$; calc. 198.0742).

*Methyl (3*R,5R*)*-N-*(2,3:5,6-Di*-O-*isopropylidene-β*-D-*gulofuranosyl)-3-isopropyl-5-methoxyisoxazolidine-5-carboxylate* (**4b**). Prepared according to *GP A*. Yield: 55%. White crystalline solid. M.p. 114–116°. $[\alpha]_D^{20} = +7.8$ ($c = 1.00$, $CHCl_3$). IR: 2983, 2873, 1751, 1455, 1371, 1210, 1068, 895, 733. ^{1}H-NMR (400 MHz): 5.04 (*d*, *J* = 6.0, 1 H); 4.71 (*dd*, *J* = 6.0, 4.0, 1 H); 4.65 (*s*, 1 H); 4.39–4.33 (*m*, 1 H); 4.21 (*dd*, *J* = 8.4, 6.8, 1 H); 4.12 (*dd*, *J* = 8.4, 4.0, 1 H); 3.82 (*s*, 3 H); 3.74 (*dd*, *J* = 8.4, 6.4, 1 H); 3.33 (*s*, 3 H); 3.28–3.23 (*m*, 1 H); 2.54–2.42 (*m*, 2 H); 2.01–1.92 (*m*, 1 H); 1.46 (*s*, 3 H); 1.40 (*s*, 3 H); 1.38 (*s*, 3 H); 1.31 (*s*, 3 H); 0.96 (*d*, *J* = 6.4, 3 H); 0.90 (*d*, *J* = 6.8, 3 H). ^{13}C-NMR (100 MHz): 170.0; 112.8; 110.0; 106.9; 97.9; 84.5; 84.2; 80.5; 75.9; 68.1; 66.2; 53.2; 52.2; 40.6; 29.7; 26.8; 26.3; 25.5; 25.2; 21.4; 19.3. HR-ESI-MS: 468.2225 ($[M+Na]^+$, $C_{21}H_{35}NNaO_9^+$; calc. 468.2204).

*Methyl (3*R,5R*)-3-Isopropyl-5-methoxyisoxazolidine-5-carboxylate* (**5b**). Prepared according to *GP B1*. Yield: 94%. Clear oil. $[\alpha]_D^{20} = +101.8$ ($c = 1.00$, $CHCl_3$). IR: 3213, 2959, 1752, 1466, 1438, 1267, 1219, 1070, 1047. ^{1}H-NMR (400 MHz): 5.61 (br. *s*, 1 H); 3.78 (*s*, 3 H); 3.29 (*s*, 3 H); 3.23–3.10 (*m*, 1 H);

2.54 (*dd*, *J* = 8.3, 13.4, 1 H); 2.06–1.96 (*m*, 1 H); 1.72–1.61 (*m*, 1 H); 0.96 (*d*, *J* = 6.8, 1 H); 0.90 (*d*, *J* = 6.4, 1 H). ^{13}C-NMR (100 MHz): 168.8; 108.53; 67.6; 53.2; 52.2; 51.9; 46.8; 45.4; 30.9; 21.1; 20.4. HR-ESI-MS: 204.1230 ($[M+Na]^+$, $C_9H_{17}NNaO_4^+$; calc. 204.1230).

*Methyl (3*S,5R*)*-N-*(2,3:5,6-Di*-O-*isopropylidene-β*-D-*gulofuranosyl)-5-methoxy-3-(2-methylpropyl)-isoxazolidine-5-carboxylate* (**4c**). Prepared according to *GP A*. Yield: 47%. White crystalline solid. M.p. 122–123°. $[\alpha]_D^{20} = +10.4$ (*c* = 1.00, $CHCl_3$). IR: 2986, 254, 1755, 1449, 1380, 1275, 1221, 1092, 872, 721, 598. ^{1}H-NMR (400 MHz): 5.04 (*d*, *J* = 6.0, 1 H); 4.70 (*dd*, *J* = 6.0, 3.6, 1 H); 4.66 (*s*, 1 H); 4.40–4.35 (*m*, 1 H); 4.21 (*dd*, *J* = 8.4, 6.8, 1 H); 4.08 (*dd*, *J* = 8.4, 4.0, 1 H); 3.82 (*s*, 3 H); 3.73–3.69 (*m*, 1 H); 3.37 (*s*, 3 H); 2.70 (*dd*, *J* = 13.6, 8.0, 1 H); 2.19 (*dd*, *J* = 13.6, 2.8, 1 H); 1.85–1.78 (*m*, 1 H); 1.70–1.60 (*m*, 1 H); 1.46 (*s*, 3 H); 1.41 (*s*, 3 H); 1.37 (*s*, 3 H); 1.31 (*s*, 3 H); 1.24–1.17 (*m*, 1 H); 0.92 (*dd*, *J* = 6.4, 5.6, 6 H). ^{13}C-NMR (100 MHz): 169.6; 112.9; 109.9; 107.2; 97.9; 84.5; 84.3; 80.5; 75.8; 66.2; 60.0; 53.2; 52.3; 44.8; 42.9; 26.8; 26.3; 25.9; 25.4; 25.2; 23.3; 22.2. HR-ESI-MS: 482.2342 ($[M+Na]^+$, $C_{22}H_{37}NNaO_9^+$; calc. 482.2360).

*Methyl (3*S,5R*)-5-Methoxy-3-(2-methylpropyl)isoxazolidine-5-carboxylate* (**5c**). Prepared according to *GP B1*. Yield: 87%. Colorless oil. $[\alpha]_D^{20} = +93.3$ (*c* = 1.00, $CHCl_3$). IR: 3215, 2955, 2872, 2842, 1752, 1439, 1387, 1267, 1070, 810. ^{1}H-NMR (400 MHz)[6]): 6.15 (*s*, 1 H*); 5.46 (*s*, 1 H#); 3.79 (*s*, 3 H#); 3.77 (*s*, 3 H*); 3.59–3.52 (*m*, 1 H*); 3.52–3.42 (*m*, 1 H#); 3.30 (*s*, 3 H#); 3.27 (*s*, 3 H*); 2.62 (*dd*, *J* = 13.2, 8.0, 1 H#); 2.50 (*dd*, *J* = 13.2, 7.2, 1 H*); 2.04 (*m*, 1 H*); 1.91 (*m*, 1 H#); 1.68–1.58 (*m*, 1 H#); 1.48–1.42 (*m*, 1 H#); 1.37–1.30 (*m*, 1 H#); 0.89 (*dd*, *J* = 10, 6.4, 6 H#). ^{13}C-NMR (100 MHz): 168.6; 108.2; 59.4; 53.0; 52.9; 52.0; 51.9; 48.6; 47.9; 40.7; 26.7; 23.0; 22.9; 22.8. HR-ESI-MS: 240.1212 ($[M+Na]^+$, $C_{10}H_{19}NNaO_4^+$; calc. 240.1206).

*Methyl (3*S,5R*)-3-Benzyl*-N-*(2,3:5,6-di*-O-*isopropylidene-β*-D-*gulofuranosyl)-5-methoxyisoxazolidine-5-carboxylate* (**4d**). Prepared according to *GP A*. Yield: 57%. White crystalline solid. M.p. 121°. $[\alpha]_D^{20} = -19.1$ (*c* = 1.00, $CHCl_3$). IR: 3217, 3027, 2951, 1749, 1454, 1438, 1067. ^{1}H-NMR (400 MHz): 7.30–7.18 (*m*, 5 H); 5.02 (*d*, *J* = 6.0, 1 H); 4.71 (*s*, 1 H); 4.66 (*dd*, *J* = 5.6, 4.0, 1 H); 4.35–4.30 (*m*, 1 H); 4.16 (*dd*, *J* = 8.4, 6.8, 1 H); 3.90–3.81 (*m*, 1 H); 3.80 (*s*, 3 H); 3.62 (*dd*, *J* = 8.4, 6.8, 1 H); 3.43 (*s*, 3 H); 3.12 (*dd*, *J* = 13.6, 6.8, 1 H); 2.83 (*dd*, *J* = 13.6, 8.8, 1 H); 2.51 (*dd*, *J* = 13.6, 8.0, 1 H); 2.32 (*dd*, *J* = 14.0, 3.2, 1 H); 1.45 (*s*, 3 H); 1.42 (*s*, 3 H); 1.37 (*s*, 3 H); 1.31 (*s*, 3 H). ^{13}C-NMR (100 MHz): 169.5; 138.8; 129.7; 128.6; 126.5; 112.9; 109.9; 106.6; 97.8; 84.4; 84.2; 80.4; 75.8; 66.2; 63.0; 53.2; 52.2; 43.5; 39.9; 27.1; 26.3; 25.6; 25.1. HR-ESI-MS: 516.2216 ($[M+Na]^+$, $C_{25}H_{35}NNaO_9^+$; calc. 516.2204).

*Methyl (3*S,5R*)-3-Benzyl-5-methoxyisoxazolidine-5-carboxylate* (**5d**). Prepared according to *GP B1*. Yield: 88%. Clear oil. $[\alpha]_D^{20} = +90.1$ (*c* = 1.00, $CHCl_3$). IR: 3214, 3028, 2952, 1750, 1497, 1439, 1310, 1209, 1067, 702. ^{1}H-NMR (400 MHz)[6]): 7.31–7.18 (*m*, 5 H#); 6.21 (*s*, 1 H*); 5.68 (*s*, 1 H#); 3.78 (*s*, 3 H#); 3.78 (*s*, 3 H*); 3.34 (*s*, 3 H#); 3.33 (*s*, 3 H*); 3.04 (*dd*, *J* = 13.6, 5.6, 1 H#); 3.03–2.98 (*m*, 1 H*); 2.79–2.71 (*m*, 1 H*); 2.72–2.67 (*m*, 1 H#); 2.55–2.48 (*m*, 1 H#); 2.47–2.42 (*m*, 1 H*); 2.26 (*m*, 1 H*); 2.10 (*m*, 1 H#). ^{13}C-NMR (100 MHz): 168.5; 137.7; 129.5; 129.1; 128.9; 128.7; 126.9; 126.7; 108.3; 107.9; 62.0; 61.1; 53.1; 53.0; 52.1; 51.9; 47.4; 47.0; 37.6. HR-ESI-MS: 247.1050 ($[M+Na]^+$, $C_{13}H_{17}NNaO_4^+$; calc. 274.1049).

*Methyl (3*R,5R*)*-N-*(2,3:5,6-Di*-O-*isopropylidene-β*-D-*gulofuranosyl)-5-methoxy-3-phenylisoxazolidine-5-carboxylate* (**4e**). Prepared according to *GP A*. Yield: 32%. White crystalline solid. M.p. 110–113°. $[\alpha]_D^{20} = +47.8$ (*c* = 1.00, $CHCl_3$). IR: 3062, 2986, 2938, 1753, 1496, 1455, 1381, 1211, 1089, 1068, 891, 850, 701. ^{1}H-NMR (400 MHz): 7.45–7.38 (*m*, 2 H); 7.32–7.21 (*m*, 3 H); 5.08 (*d*, *J* = 6.4, 1 H); 4.75 (*s*, 1 H); 4.67 (*dd*, *J* = 6.0, 4.0, 1 H); 4.39 (*t*, *J* = 8.4, 1 H); 4.23 (*dd*, *J* = 14.8, 6.8, 1 H); 4.11 (*dd*, *J* = 8.4, 6.8, 1 H); 3.83 (*s*, 3 H); 3.86–3.80 (*m*, 1 H); 3.58 (*dd*, *J* = 8.4, 7.2, 1 H); 3.40 (*s*, 3 H); 2.98 (*dd*, *J* = 12513.6, 8.4, 1 H); 2.58 (*dd*, *J* = 13.6, 7.6, 1 H); 1.42 (*s*, 3 H); 1.31 (*s*, 3 H); 1.29 (*s*, 3 H); 1.26 (*s*, 3 H). ^{13}C-NMR (100 MHz): 168.9; 138.7; 128.8; 128.1; 127.8; 112.9; 109.8; 104.7; 98.5; 84.6; 82.8; 80.8; 76.0; 66.8; 66.1; 53.2; 52.0; 48.9; 26.9; 26.3; 25.5; 25.0. HR-ESI-MS: 502.2064 ($[M+Na]^+$, $C_{24}H_{33}NNaO_9^+$; calc. 502.2047).

*Methyl (3*R,5R*)-5-Methoxy-3-phenylisoxazolidine-5-carboxylate* (**5e**). Prepared according to *GP B1*. Yield: 91%. Clear oil. $[\alpha]_D^{20} = +21.2$ (*c* = 1.00, $CHCl_3$). IR: 2952, 1749, 1496, 1437, 1265, 1069. ^{1}H-NMR (400 MHz)[6]): 7.42–7.25 (*m*, 5 H#); 5.78 (*s*, 1 H#); 4.66 (*m*, 1 H*); 4.56 (*m*, 1 H#); 3.85 (*s*, 3 H#); 3.80 (*s*, 3 H*); 3.40 (*s*, 3 H#); 2.93 (*dd*, *J* = 13.2, 9.2, 1 H#); 2.54 (*dd*, *J* = 13.2, 7.2, 1 H#). ^{13}C-NMR

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[6]) #: Major diastereoisomer, *: minor diastereoisomer.

(100 MHz): 168.5; 137.0; 129.5; 129.0; 128.3; 108.9; 64.7; 53.4; 52.3; 49.1. HR-ESI-MS: 260.0895 ($[M+Na]^+$, $C_{12}H_{15}NNaO_4^+$; calc. 260.0899).

*Methyl (3*S*,5*R*)-3-[3-(*tert*-Butoxy)-3-oxopropyl]-*N*-(2,3:5,6-di-*O*-isopropylidene-β-*D*-gulofuranosyl)-5-methoxyisoxazolidine-5-carboxylate* (**4f**). Prepared according to *GP A*. Yield: 61%. Colorless oil. $[\alpha]_D^{26} = +3.9$ ($c = 0.60$, CH_2Cl_2). IR: 2981, 2937, 1752, 1729, 1455, 1381, 1370, 1209. ^{1}H-NMR (400 MHz): 5.03 (*d*, *J* = 6.1, 1 H); 4.72 (*dd*, *J* = 6.0, 3.9, 1 H); 4.65 (*s*, 1 H); 4.41–4.36 (*m*, 1 H); 4.24 (*dd*, *J* = 8.5, 6.8, 1 H); 4.14 (*dd*, *J* = 8.5, 3.9, 1 H); 3.84 (*s*, 3 H); 3.78 (*dd*, *J* = 8.5, 6.8, 1 H); 3.64–3.59 (*m*, 1 H); 3.39 (*s*, 3 H); 2.71 (*dd*, *J* = 13.5, 8.2, 1 H); 2.36 (*dd*, *J* = 9.9, 5.8, 1 H); 2.29–2.25 (*m*, 2 H); 2.18–2.11 (*m*, 1 H); 1.77–1.71 (*m*, 1 H); 1.48 (*s*, 3 H); 1.47 (*s*, 3 H); 1.45 (*s*, 9 H); 1.41 (*s*, 3 H); 1.33 (*s*, 3 H). ^{13}C-NMR (100 MHz): 172.4; 169.5; 112.7; 109.8; 106.6; 97.7; 84.4; 83.9; 80.3; 80.1; 75.7; 66.0; 61.3; 53.0; 52.0; 43.9; 33.4; 28.8; 28.1; 28.1; 26.7; 26.1; 25.5; 24.9. HR-ESI-MS: 532.2751 ($[M+H]^+$, $C_{25}H_{42}NO_{11}^+$; calc. 532.2752).

*Methyl (3*S*,5*R*)-3-[3-(*tert*-Butoxy)-3-oxopropyl]-5-methoxyisoxazolidine-5-carboxylate* (**5f**). Prepared according to *GP B2*. Yield: 46%. Clear oil. $[\alpha]_D^{27} = +22.3$ ($c = 0.37$, CH_2Cl_2). IR: 2979, 2952, 1749, 1730, 1437, 1367. ^{1}H-NMR (400 MHz)[6]): 3.85 (*s*, 3 H*); 3.84 (*s*, 3 H#); 3.57–3.44 (*m*, 1 H); 3.37 (*s*, 3 H#); 3.36 (*s*, 3 H*); 2.68 (*dd*, *J* = 13.3, 8.4, 1 H#); 2.59 (*dd*, *J* = 13.3, 7.7, 1 H*); 2.36 (*t*, *J* = 7.5, 2 H); 2.17 (*dd*, *J* = 13.3, 4.4, 1 H*); 2.04 (*dd*, *J* = 13.0, 7.1, 1 H#); 1.88 (*m*, 2 H); 1.47 (*s*, 9 H). ^{13}C-NMR (100 MHz): 172.5; 172.0; 168.3; 108.0; 107.6; 80.6; 80.3; 60.3; 52.8; 52.7; 51.9; 51.6; 47.7; 33.0; 32.6; 28.1; 26.8. HR-ESI-MS: 290.1600 ($[M+H]^+$, $C_{13}H_{24}NO_6^+$; calc. 290.1598).

*Methyl (3*S*,5*R*)-3-{3-[(*tert*-Butoxycarbonyl)amino]propyl}-*N*-(2,3:5,6-di-*O*-isopropylidene-β-*D*-gulofuranosyl)-5-methoxyisoxazolidine-5-carboxylate* (**4g**). Compound **4g-1** was prepared according to *GP A* (yield: 53%). Compound **4g-1** (10.0 g, 14.4 mmol) was dissolved in AcOEt/MeOH (140 ml/14 ml), and 10% Pd/C (1.0 g) was added. The resulting black suspension was stirred vigorously under H_2 for 2 h. The mixture was filtered through *Celite*, and the filtrate was concentrated *in vacuo*. The crude compound was purified by FC (hexanes/AcOEt 70:30) to give **4g** (8.0 g 99%). White crystalline solid. M.p. 93–95°. $[\alpha]_D^{20} = -4.28$ ($c = 0.27$, $CHCl_3$). IR: 3382, 2980, 2937, 1752, 1713, 1519, 1454, 1369, 1252, 1210, 1168, 1088, 1065. ^{1}H-NMR (500 MHz): 5.02 (*d*, *J* = 6.0, 1 H); 4.70 (*dd*, *J* = 4.0, 6.0, 1 H); 4.68 (br., 1 H); 4.64 (*s*, 1 H); 4.22 (*dd*, *J* = 7.0, 9.0, 1 H); 4.10 (*dd*, *J* = 4.0, 8.5, 1 H); 3.81 (*s*, 3 H); 3.72 (*dd*, *J* = 7.0, 8.5, 1 H); 3.36 (*s*, 3 H); 3.13–3.12 (*m*, 2 H); 2.70 (*dd*, *J* = 8.0, 13.5, 1 H); 2.22 (*dd*, *J* = 2.5, 13.5, 1 H); 1.89–1.81 (*m*, 1 H); 1.58 (br., 1 H); 1.52–1.47 (*m*, 2 H); 1.46 (*s*, 3 H); 1.43 (*s*, 12 H); 1.39 (*s*, 3 H); 1.31 (*s*, 3 H). ^{13}C-NMR (125 MHz): 169.5; 156.0; 112.9; 109.9; 106.4; 98.2; 84.5; 84.0; 80.4; 79.1; 75.9; 66.2; 62.0; 53.1; 52.2; 44.5; 40.4; 31.0; 28.6; 27.7; 26.9; 26.3; 25.5; 25.1. HR-ESI-MS: 583.2872 ($[M+Na]^+$, $C_{26}H_{44}N_2NaO_{11}^+$; calc. 583.2837).

*Methyl (3*S*,5*R*)-3-{3-[(*tert*-Butoxycarbonyl)amino]propyl}-5-methoxyisoxazolidine-5-carboxylate* (**5g**). Prepared according to *GP B3*. Yield: 78%. Yellow oil. $[\alpha]_D^{20} = +30.9$ ($c = 1.06$, $CHCl_3$). IR: 3392, 2976, 2936, 2868, 1752, 1710, 1522, 1454, 1391, 1366, 1269, 1252, 1172, 1070. ^{1}H-NMR (500 MHz)[6]): 6.15 (br., 1 H*); 5.54 (br., 1 H#); 4.59 (br., 1 H#); 4.35 (br., 1 H*); 3.81 (*s*, 3 H); 3.43 (br., 1 H); 3.33 (*s*, 3 H); 3.12 (br., 2 H); 2.64 (*dd*, *J* = 8.5, 13, 1 H#); 2.55 (*dd*, *J* = 7.5, 13.5, 1 H*); 2.10 (br., 1 H*); 1.96 (br., 1 H#); 1.55–1.52 (*m*, 4 H); 1.42 (*s*, 9 H). ^{13}C-NMR (125 MHz): 156.0; 108.1; 107.7; 79.3; 60.7; 52.9; 52.8; 51.9; 51.7; 48.0; 40.3; 29.8; 28.5; 28.0. HR-ESI-MS: 341.1723 ($[M+Na]^+$, $C_{14}H_{26}N_2NaO_6^+$; calc. 341.1683).

*Methyl (3*S*,5*R*)-3-{4-[(*tert*-Butoxycarbonyl)amino]butyl}-*N*-(2,3:5,6-di-*O*-isopropylidene-β-*D*-gulofuranosyl)-5-methoxyisoxazolidine-5-carboxylate* (**4h**). Compound **4h-1** was prepared according to *GP A* (yield: 47%). Compound **4h-1** (4.4 g, 8.8 mmol) and Boc_2O (2.85 g, 13.2 mmol) were dissolved in AcOEt/MeOH (90 ml/9 ml), and 10% Pd/C (0.44 g) was added. The resulting black suspension was stirred vigorously under H_2 for 48 h. The mixture was filtered through *Celite*, and the filtrate was concentrated *in vacuo*. The crude compound was purified *via* FC (hexanes/AcOEt 7:3) to give **4h** (4.25 g, 84%). White solid. M.p. 95–97°. $[\alpha]_D^{24} = +8.8$ ($c = 1.00$, $CHCl_3$). IR: 3370, 2979, 2936, 1750, 1455, 1368, 1210, 1065, 848, 774. ^{1}H-NMR (400 MHz): 5.02 (*d*, *J* = 6.0, 1 H); 4.73–4.65 (*m*, 1 H); 4.63 (*s*, 1 H); 4.60–4.50 (*m*, 1 H); 4.40–4.01 (*m*, 3 H); 3.81 (*s*, 3 H); 3.74–3.6 (*m*, 1 H); 3.40–3.60 (*m*, 1 H); 3.33 (*s*, 3 H); 3.15–3.01 (*m*, 2 H); 2.67 (*dd*, *J* = 13.2, 4.8, 1 H); 2.15–2.25 (*m*, 1 H); 1.60–1.20 (*m*, 2 H). ^{13}C-NMR (100 MHz): 169.5; 156.1; 112.8; 109.9; 106.3; 98.3; 84.4; 84.1; 80.5; 79.2; 75.9; 66.2; 62.2; 53.1; 52.2; 44.6; 33.3; 29.8; 28.6; 26.3; 25.5; 25.1; 24.4. HR-ESI-MS: 575.3206 ($[M+H]^+$, $C_{27}H_{47}N_2O_{11}^+$; calc. 575.3174).

*Methyl (3*S*,5*R*)-3-{4-[(*tert*-Butoxycarbonyl)amino]butyl}-5-methoxyisoxazolidine-5-carboxylate* (**5h**). Prepared according to *GP B3*. Yield: 74%. Yellow oil. $[\alpha]_D^{24} = +39.6$ ($c = 1.13$, $CHCl_3$). IR: 3374, 2976, 2935, 1751, 1707, 1520, 1455. ^{1}H-NMR (400 MHz): 4.55 (br., 1 H); 3.83 (*s*, 3 H); 3.51–3.39 (*m*, 1 H); 3.35 (*s*, 3 H); 3.19–3.05 (*m*, 2 H); 2.66 (*dd*, $J = 13.3$, 8.4, 1 H); 1.99 (*dd*, $J = 13.3$, 7.5, 1 H); 1.71–1.58 (*m*, 1 H); 1.58–1.48 (*m*, 3 H); 1.45 (*s*, 9 H); 1.42–1.39 (*m*, 2 H). ^{13}C-NMR (100 MHz): 168.4; 156.0; 108.0; 60.7; 52.7; 51.8; 47.9; 40.2; 31.2; 30.0; 28.4; 26.7; 24.4. HR-ESI-MS: 333.2029 ($[M+H]^+$, $C_{15}H_{29}N_2O_6^+$; calc. 333.2020).

*Methyl (3*S*,5*R*)-3-[3-(Benzoyloxy)propyl]-*N*-(2,3:5,6-di-*O*-isopropylidene-β-*D*-gulofuranosyl)-5-methoxyisoxazolidine-5-carboxylate* (**4i**). Prepared according to *GP A*. Yield: 49%. White solid. M.p. 104.5°. $[\alpha]_D^{20} = +5.5$ ($c = 1.00$, $CHCl_3$). IR: 2985, 1750, 1718, 1452, 1372, 1276, 1209, 1069, 715. ^{1}H-NMR (400 MHz): 8.10–7.39 (*m*, 5 H); 5.01 (*d*, $J = 6.0$, 1 H); 4.76–4.68 (*m*, 1 H); 4.62 (*s*, 1 H); 4.40–4.22 (*m*, 3 H); 4.21–4.19 (*m*, 1 H); 4.16–4.06 (*m*, 1 H); 3.83 (*s*, 3 H); 3.36 (*s*, 3 H); 2.76–2.65 (*m*, 1 H); 2.29–2.13 (*m*, 1 H); 1.98–1.57 (*m*, 6 H); 1.43 (*s*, 3 H); 1.29–1.25 (*m*, 6 H); 1.21 (*s*, 3 H). ^{13}C-NMR (100 MHz): 213.1; 169.9; 166.3; 133.1; 130.2; 129.1; 128.6; 112.6; 109.5; 106.2; 97.9; 82.8; 82.5; 80.3; 75.5; 65.8; 64.3; 61.8; 52.7; 52.0; 44.2; 30.2; 26.8; 26.3; 25.0; 24.5. HR-ESI-MS: 588.2415 ($[M+Na]^+$, $C_{32}H_{54}N_4NaO_{13}^+$; calc. 588.2415).

*Methyl (3*S*,5*R*)-3-[3-(Benzoyloxy)propyl]-5-methoxyisoxazolidine-5-carboxylate* (**5i**). Prepared according to *GP B2*. Yield: 92%. Clear oil. IR: 2985, 1750, 1718, 1452, 1372, 1276, 1209, 1069, 715. ^{1}H-NMR (400 MHz): 8.10–7.39 (*m*, 5 H); 5.5–5.59 (br. *s*, 1 H); 4.31 (*t*, 2 H); 3.81 (*s*, 3 H); 3.56–3.49 (*m*, 1 H); 3.36 (*s*, 3 H); 2.71–2.62 (*m*, 1 H); 2.06–1.92 (*m*, 1 H); 1.83–1.62 (*m*, 6 H). ^{13}C-NMR (100 MHz): 166.5; 133.3; 130.2; 129.9; 128.5; 107.8; 64.3; 60.6; 53.0; 52.1; 48.1; 28.1; 26.8.

*Methyl (3*S*,5*R*)-3-{3-[*N*′,*N*″-Bis(*tert*-butoxycarbonyl)carbamimidamido]propyl}-*N*-(2,3:5,6-di-*O*-isopropylidene-β-*D*-gulofuranosyl)-5-methoxyisoxazolidine-5-carboxylate* (**4j**). A soln. of **4i** (2.54 g, 4.50 mmol, 1.00 equiv.) in 45 ml of MeOH (0.1M) was added a freshly prepared soln. of 340 mg of Na in 6.8 ml of MeOH (2.2M Na in MeOH) at 0° for 1 h. The reaction was quenched by the addition of dry ice, and the mixture was allowed to slowly warm to r.t. The soln. was poured into aq. NH_4Cl and extracted with AcOEt (2 × 30 ml). The crude product was purified by FC (hexanes/AcOEt 1:1 to 7:3; R_f 0.15) to give **4j-1** (1.904 g, 92%). To a soln. of **4j-1** (4.11 mmol) in anh. THF (0.1M), cooled at 0°, was added Ph_3P (4.5 mmol, 1.1 equiv.). The mixture was stirred for 5 min at 0°, and then DEAD (4.5 mmol, 1.1 equiv.) and DPPA (4.5 mmol, 1.1 equiv.) were added dropwise. The mixture was allowed to warm slowly to r.t. under stirring for 12 h, and the soln. was concentrated *in vacuo*. The crude residue was purified by FC (hexanes/AcOEt 7:3) to afford **4j-2** (1.62 g, 4.8 mmol, 84%). To a soln. of **4j-2** (1.40 g, 2.87 mmol, 1.00 equiv.) in 14.3 ml of THF (0.20M) were added Ph_3P (2.26 g, 8.62 mmol, 3.00 equiv.), H_2O (10.0 equiv.), and isothiourea **16** (916 mg, 3.16 mmol, 1.10 equiv.), and the mixture was heated to 65° while stirring for 1 h. EtN^iPr_2 (1.00 equiv.) was added, and the mixture was stirred for 90 min. The mixture was poured into 25.0 ml of aq. NH_4Cl and extracted with CH_2Cl_2 (3 × 30 ml), and the org. layers were combined, dried (Na_2SO_4), filtered, and evaporated. The crude product was purified by FC (hexanes/AcOEt 3:1) to give **4j** (951 mg, 48%). White solid. IR: 3335, 2980, 2936, 1750, 1417, 1369, 1210, 1054. ^{1}H-NMR (400 MHz): 11.47 (*s*, 1 H); 8.40–8.25 (*m*, 1 H); 5.02 (*d*, $J = 6.0$, 1 H); 4.71 (*dd*, $J = 5.6$, 3.6, 1 H); 4.63 (*s*, 1 H); 4.33 (*dd*, $J = 15.2$, 6.8, 1 H); 4.19 (*dd*, $J = 8.4$, 6.8, 1 H); 4.07 (*dd*, $J = 8.4$, 4.0, 1 H); 3.80 (*s*, 3 H); 3.71 (*dd*, $J = 8.4$, 6.8, 1 H); 3.63–3.58 (*m*, 1 H); 3.49–3.41 (*m*, 1 H); 3.35 (*s*, 3 H); 2.67 (*dd*, $J = 13.2$, 4.44, 1 H); 2.22 (*dd*, $J = 13.2$, 2.0, 1 H); 1.89–1.51 (*m*, 4 H); 1.49 (*s*, 9 H); 1.47 (*s*, 9 H); 1.46 (*s*, 3 H); 1.38 (*s*, 3 H); 1.36 (*s*, 3 H); 1.30 (*s*, 3 H). ^{13}C-NMR (100 MHz): 169.7; 163.8; 156.3; 153.4; 112.9; 109.9; 106.6; 97.8; 84.6; 84.2; 83.2; 80.4; 79.4; 75.9; 66.2; 61.7; 53.2; 52.2; 44.3; 40.9; 31.1; 28.5; 28.2; 27.1; 26.9; 26.3; 25.7; 25.1. HR-ESI-MS: 703.3779 ($[M+H]^+$, $C_{32}H_{55}N_4ON_{13}^+$; calc. 703.3766).

*Methyl (3*S*,5*R*)-3-{3-[*N*′,*N*″-Bis(*tert*-butoxycarbonyl)carbamimidamido]propyl}-5-methoxyisoxazolidine-5-carboxylate* (**5j**). Prepared according to *GP B4*. Yield: 77%. Yellow oil. $[\alpha]_D^{22} = +26.3$ ($c = 0.89$, $CHCl_3$). IR: 3334, 2930, 1753, 1721, 1414, 1367. ^{1}H-NMR (400 MHz)[6]: 11.48 (br. *s*, 1 H); 8.33 (br. *s*, 1 H); 5.55 (br. *s*, 1 H); 3.82 (*s*, 3 H); 3.54–3.39 (*m*, 3 H); 3.34 (*s*, 3 H); 2.66 (*dd*, $J = 13.3$, 8.4, 1 H#); 2.55 (*dd*, $J = 13.3$, 7.6, 1 H*); 1.99 (br., 1 H); 1.76–1.57 (*m*, 4 H); 1.49 (*s*, 9 H); 1.49 (*s*, 9 H); 1.33–1.18 (*m*, 2 H); 0.97–0.73 (*m*, 2 H). ^{13}C-NMR (100 MHz): 163.6; 156.2; 153.3; 130.9; 128.8; 108.0; 83.2; 79.3; 60.5; 52.8; 51.9; 47.8; 40.5; 29.7; 28.3; 28.1; 26.9. HR-ESI-MS: 461.2611 ($[M+H]^+$, $C_{20}H_{37}N_4O_8^+$; calc. 461.2611).

tert-*Butyl 3-{[(3*S*,5*R*)*-N-*(2,3 :5,6-Di-*O*-*isopropylidene-β-*D*-*gulofuranosyl)-5-methoxy-5-(methoxycarbonyl)isoxazolidin-3-yl]methyl}-1*H*-indole-1-carboxylate* (**4k**). Prepared according to *GP A*. Yield: 57%. White crystalline solid. M.p. 104°. $[\alpha]_D^{20} = +24.3$ ($c = 1.00$, $CHCl_3$). IR: 2982, 2936, 1733, 1454, 1370, 1309, 1257, 1159, 1088. ^{1}H-NMR (400 MHz): 8.09 (br. *s*, 1 H); 7.65 (*d*, *J* = 7.6, 1 H); 7.40 (*s*, 1 H); 7.28 (*t*, *J* = 7.2, 1 H); 7.21 (*t*, *J* = 7.2, 1 H); 5.02 (*d*, *J* = 6.0, 1 H); 4.68 (*s*, 1 H); 4.65–4.62 (*m*, 1 H); 4.34–4.28 (*m*, 1 H); 4.16–4.12 (*m*, 1 H); 3.98–3.90 (*m*, 1 H); 3.87 (*dd*, *J* = 8.8, 4.0, 1 H); 3.78 (*s*, 3 H); 3.59–3.54 (*m*, 1 H); 3.44 (*s*, 3 H); 3.14 (*dd*, *J* = 14.0, 5.6, 1 H); 2.96 (*dd*, *J* = 14.0, 9.6, 1 H); 2.51 (*dd*, *J* = 13.2, 8.0, 1 H); 2.37 (*dd*, *J* = 13.6, 2.4, 1 H); 1.64 (*s*, 9 H); 1.44 (*s*, 3 H); 1.35 (*s*, 3 H); 1.32 (*s*, 3 H); 1.30 (*s*, 3 H). ^{13}C-NMR (100 MHz): 169.2; 149.8; 135.7; 131.4; 130.7; 124.5; 123.9; 122.6; 119.9; 117.8; 115.3; 112.9; 109.8; 106.6; 97.8; 84.4; 83.7; 80.4; 75.7; 66.1; 61.2; 53.2; 52.3; 43.7; 29.8; 28.3; 26.9; 26.3; 25.7; 25.1. HR-ESI-MS: 655.2822 ($[M+Na]^+$, $C_{32}H_{44}N_2NaO_{11}^+$; calc. 655.2843).

tert-*Butyl 3-{[(3*S*,5*R*)-5-Methoxy-5-(methoxycarbonyl)isoxazolidin-3-yl]methyl}-1*H*-indole-1-carboxylate* (**5k**). Prepared according to *GP B2*. Yield: 80%. Clear oil. $[\alpha]_D^{20} = +44.4$ ($c = 1.00$, $CHCl_3$). IR: 2960, 1734, 1452, 1372, 1309, 1259, 1157, 1083, 768. ^{1}H-NMR (400 MHz): 8.12 (br. *s*, 1 H); 7.52 (*d*, *J* = 7.6, 1 H); 7.46 (*s*, 1 H), 7.32 (*t*, *J* = 7.2, 1 H); 7.24 (*t*, *J* = 7.2, 1 H); 3.98–3.86 (*m*, 1 H); 3.80 (*s*, 3 H); 3.57 (*s*, 3 H); 3.10 (*dd*, *J* = 9.2, 5.6, 1 H); 2.89 (*dd*, *J* = 8.0, 6.8, 1 H); 2.62 (*dd*, *J* = 8.4, 4.8, 1 H); 2.19 (*dd*, *J* = 6.8, 6.4, 1 H); 1.67 (*s*, 9 H). ^{13}C-NMR (100 MHz): 168.5; 149.9; 135.7; 130.4; 124.9; 123.8. 122.8; 119.0; 116.6; 115.6; 108.3; 83.9; 60.3; 53.1; 52.2; 47.7; 29.9; 28.5; 27.3. HR-ESI-MS: 413.1687 ($[M+Na]^+$, $C_{32}H_{44}N_2NaO_{11}^+$; calc. 413.1691).

*Methyl (3*R*,5*R*)-3-{[(*tert*-Butoxycarbonyl)oxy]methyl}-*N*-(2,3 :5,6-di-*O*-isopropylidene-β-*D*-gulofuranosyl)-5-methoxyisoxazolidine-5-carboxylate* (**4l**). Prepared according to *GP A*. Yield: 36%. White crystalline solid. ^{1}H-NMR (400 MHz): 5.01 (*d*, *J* = 6.0, 1 H); 4.76–4.68 (*m*, 2 H); 4.40–4.35 (*m*, 1 H); 4.30–4.18 (*m*, 2 H); 4.16–4.01 (*m*, 1 H); 4.06–3.95 (*m*, 2 H); 3.83 (*s*, 3 H); 3.76–3.7 (*m*, 1 H); 3.38 (*s*, 3 H); 2.69 (*dd*, *J* = 13.6, 5.6, 1 H); 2.38 (*dd*, *J* = 13.6, 1.6, 1 H); 1.47–1.44 (*m*, 15 H); 1.39 (*s*, 3 H); 1.32 (*s*, 3 H).

*Methyl (3*R*,5*R*)-3-{[(*tert*-Butoxycarbonyl)oxy]methyl}-5-methoxyisoxazolidine-5-carboxylate* (**5l**). Prepared according to *GP B3*. Yield: 61%. Clear oil. ^{1}H-NMR (400 MHz): 6.19–5.95 (br. *s*, 1 H); 4.30–4.15 (*m*, 1 H); 3.83 (*s*, 3 H); 3.82–3.76 (*m*, 1 H); 3.37 (*s*, 3 H); 2.61 (*dd*, *J* = 13.6, 5.6, 1 H); 2.27 (*m*, 1 H); 1.49 (*s*, 9 H).

tert-*Butyl 4-[(3*R*,5*R*)-*N*-(2,3 :5,6-Di-*O*-isopropylidene-β-*D*-gulofuranosyl)-5-Methoxy-5-(methoxycarbonyl)isoxazolidin-3-yl]piperidine-1-carboxylate* (**4m**). Prepared according to *GP A*. Yield: 39%. White crystalline solid. M.p. 113–114°. $[\alpha]_D^{20} = +5.1$ ($c = 1.00$, $CHCl_3$). IR: 3489, 2982, 2973, 1751, 1692, 1427, 1369, 1282, 1213, 1166, 1087, 1066, 848, 755. ^{1}H-NMR (400 MHz): 5.01 (*d*, *J* = 6.0, 1 H); 4.68 (*dd*, *J* = 6.0, 3.6, 1 H); 4.61 (*s*, 1 H); 4.37–4.32 (*m*, 1 H); 4.21 (*dd*, *J* = 8.4, 6.8, 1 H); 4.11–4.02 (*m*, 2 H); 4.05 (*dd*, *J* = 8.4, 4.0, 1 H); 3.81 (*s*, 3 H); 3.75–3.71 (*m*, 1 H); 3.38–3.33 (*m*, 1 H); 3.33 (*s*, 3 H); 2.70–2.60 (*m*, 2 H); 2.50 (*dd*, *J* = 14.0, 8.0, 1 H); 2.42 (*dd*, *J* = 13.6, 2.0, 1 H); 1.90–1.87 (*m*, 1 H); 1.80–1.77 (*m*, 1 H); 1.67–1.62 (*m*, 1 H); 1.44 (*s*, 3 H); 1.42 (*s*, 3 H); 1.42 (*s*, 9 H); 1.37 (*s*, 3 H); 1.30 (*s*, 3 H); 1.15–1.04 (*m*, 2 H). ^{13}C-NMR (125 MHz): 169.7; 154.8; 112.9; 110.1; 107.0; 97.9; 84.7; 84.2; 80.4; 79.4; 75.8; 66.2; 53.2; 52.2; 40.0; 37.7; 28.9; 28.6; 26.9; 26.3; 25.4; 25.18. HR-ESI-MS: 609.2971 ($[M+Na]^+$, $C_{28}H_{46}N_2NaO_{11}^+$; calc. 609.3002).

tert-*Butyl 4-[(3*R*,5*R*)-5-Methoxy-5-(methoxycarbonyl)isoxazolidin-3-yl]piperidine-1-carboxylate* (**5m**). Prepared according to *GP B2*. Yield: 83%. Clear oil. $[\alpha]_D^{20} = +44.6$ ($c = 1.00$, $CHCl_3$). IR: 3484, 3207, 2976, 2937, 2854, 1751, 1689, 1426, 1366, 1275, 1242, 1161, 1073, 732. ^{1}H-NMR (400 MHz): 4.13–4.02 (*m*, 2 H); 3.81 (*s*, 3 H); 3.33 (*s*, 3 H); 3.27–3.22 (*m*, 1 H); 2.70–2.60 (*m*, 2 H); 2.58 (*dd*, *J* = 13.2, 8.4, 1 H); 2.06 (*dd*, *J* = 13.2, 7.6, 1 H); 1.82–1.77 (*m*, 1 H); 1.60–1.56 (*m*, 1 H); 1.55–1.53 (*m*, 1 H); 1.44 (*s*, 9 H); 1.28–1.21 (*m*, 2 H). ^{13}C-NMR (125 MHz): 168.5; 15439; 108.1; 79.8; 65.4; 53.0; 52.1; 46.1; 38.9; 30.4; 29.6; 28.6. HR-ESI-MS: 367.1829 ($[M+Na]^+$, $C_{16}H_{28}N_2NaO_6^+$; calc. 367.1847).

*Methyl (3*R*,5*R*)-3-[2-(*tert*-Butoxy)-2-oxoethyl]-*N*-(2,3 :5,6-di-*O*-isopropylidene-β-*D*-gulofuranosyl)-5-methoxyisoxazolidine-5-carboxylate* (**4n**). Compound **4n-1** was prepared according to *GP A* using β-sulfanylaldehyde **16** (white solid, yield: 32%). To a soln. of **4n-1** (0.93 mmol) in CH_2Cl_2 (0.10M) was added 0.29M *m*CPBA in CH_2Cl_2 (0.93 mmol, 1.0 equiv.) dropwise at −20°. The soln. was stirred for 30 min. The reaction was quenched by the addition of sat. $NaHCO_3$ soln., and the mixture was extracted with CH_2Cl_2 (3×). The org. layers were combined, washed with brine, dried (Na_2SO_4), and concentrated

in vacuo to give **4n-2** as a mixture of diastereoisomers (490 mg, 95%). To a soln. of **4n-2** (0.88 mmol) and 2,6-lutidine (2.29 mmol, 2.6 equiv.) in MeCN (0.17M) was added 0.50M TFAA in MeCN (1.76 mmol, 2.0 equiv.) dropwise at 0°. After 10 min, further TFAA (0.5 equiv.) was added, stirring was continued for 10 min., and sat. $NaHCO_3$ soln. and $HgCl_2$ (1.94 mmol, 2.2 equiv.) were added, and the soln. was stirred at r.t. for 2 h. The resulting mixture was filtered through a pad of *Celite* and extracted with AcOEt (3×). The org. layers were combined, washed with brine, dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was purified by FC (hexanes/AcOEt 3:1) to give **4n-3** as a pale yellow oil (272 mg, 69%). To a soln. of **4n-3** (0.61 mmol) and 2-methylbut-2-ene (6.1 mmol, 10 equiv.) in ^{t}BuOH/H_2O (3:1, 0.09M) were added $NaClO_2$ (3.00 mmol, 4.9 equiv.) and NaH_2PO_4 (3.30 mmol, 5.4 equiv.) at 0°. After 20 min, the soln. was treated with ice and extracted with AcOEt (3×). The org. layers were combined, washed with brine, dried (Na_2SO_4), and concentrated *in vacuo* to give **4n-4** as a pale yellow oil (270 mg, 97%). To a soln. of **4n-4** (0.59 mmol) in toluene (0.1M) was added 2-(*tert*-butyl)-1,3-diisopropylisourea (1.17 mmol, 2.0 equiv.), and the mixture was stirred at r.t. for 10 h. Further 2-(*tert*-butyl)-1,3-diisopropylisourea (1.0 equiv.) was added, and stirring was continued for 6 h. The solvent was concentrated under reduced pressure, and the residue was purified by FC (hexanes/AcOEt 5:1) to give **4n** (182 mg, 57%). Pale yellow oil. $[\alpha]_D^{20} = +21.9$ ($c = 1.02$, $CHCl_3$). IR: 2983, 2937, 1751, 1733, 1370, 1259. ^{1}H-NMR (500 MHz): 4.98 (*d*, *J* = 6.5, 1 H); 4.69–4.66 (*m*, 1 H); 4.39–4.35 (*m*, 1 H); 4.21–4.18 (*m*, 1 H); 4.11 (*dd*, *J* = 4.0, 8.5, 1 H); 3.90–3.85 (*m*, 1 H); 3.80 (*s*, 3 H); 3.74–3.71 (*m*, 1 H); 3.35 (*s*, 3 H); 2.85–2.79 (*m*, 1 H); 2.50 (*dd*, *J* = 8.5, 16.5, 1 H); 2.29 (*dd*, *J* = 4.0, 13.5, 1 H); 1.45 (*s*, 3 H); 1.44 (*s*, 3 H); 1.42 (*s*, 9 H); 1.38 (*s*, 3 H); 1.30 (*s*, 3 H). ^{13}C-NMR (125 MHz): 170.3; 169.0; 112.8; 109.9; 105.6; 98.5; 84.3; 84.0; 75.8; 66.2; 58.9; 53.1; 52.1; 45.0; 39.5; 28.2; 26.9; 26.2; 25.5; 24.0. HR-ESI-MS: 540.2430 ($[M+Na]^+$, $C_{24}H_{39}NNaO_{11}^+$; calc. 540.2421).

*Methyl (3*R*,5*R*)-3-[2-(*tert*-Butoxy)-2-oxoethyl]-5-methoxyisoxazolidine-5-carboxylate* (**5n**). Prepared according to *GP B3*. Yield: 66%. Yellow oil. $[\alpha]_D^{27} = +64.3$ ($c = 0.825$, $CHCl_3$). IR: 2979, 2952, 1751, 1728, 1437, 1369. ^{1}H-NMR (500 MHz): 3.78 (*s*, 3 H); 3.73 (br. *s*, 1 H); 3.30 (*s*, 3 H); 2.67 (*dd*, *J* = 8.5, 13.5, 1 H); 2.55 (*dd*, *J* = 6.0, 16.0, 1 H); 2.43 (*dd*, *J* = 9.0, 15.5, 1 H); 2.07 (br. *s*, 1 H); 1.40 (*s*, 9 H). ^{13}C-NMR (125 MHz): 169.7; 168.3; 112.6; 108.2; 81.6; 57.0; 52.9; 52.0; 47.0; 36.7; 28.2. HR-ESI-MS: 298.1275 ($[M+Na]^+$, $C_{12}H_{21}NNaO_6^+$; calc. 298.1267).

3.2. *Preparation of Enantiomerically Pure Isoxazolidine Monomers with* unlike-*Configured Residues* (*Scheme 6*). *Methyl (3*R*,5*S*)-*N*-(2,3:5,6-Di-*O*-isopropylidene-β-*L*-gulofuranosyl)-5-methoxy-3-methylisoxazolidine-5-carboxylate* (**7a**). Prepared according to *GP A*. Yield: 46%. White crystalline solid. M.p. 103–104°. $[\alpha]_D^{20} = -55.4$ ($c = 1.00$, $CHCl_3$). IR: 2986, 1751, 1455, 1372, 1254, 1210, 1066, 894. ^{1}H-NMR (400 MHz): 5.01 (*d*, *J* = 6.0, 1 H); 4.71 (*dd*, *J* = 6.0, 4.0, 1 H); 4.68 (*s*, 1 H); 4.40–4.35 (*m*, 1 H); 4.20 (*dd*, *J* = 8.4, 6.4, 1 H); 4.11 (*dd*, *J* = 8.4, 4.0, 1 H); 3.81 (*s*, 3 H); 3.73 (*dd*, *J* = 8.4, 6.4, 1 H); 3.55–3.48 (*m*, 1 H); 3.37 (*s*, 3 H); 2.73 (*dd*, *J* = 13.2, 7.6, 1 H); 2.20 (*dd*, *J* = 13.6, 6.0, 1 H); 1.47 (*s*, 3 H); 1.42 (*s*, 3 H); 1.38 (*s*, 1 H); 1.32 (*d*, *J* = 6.0, 3 H); 1.31 (*s*, 3 H). ^{13}C-NMR (100 MHz): 169.3; 112.9,109.9; 105.2; 98.9; 84.4; 84.0; 80.5; 75.9; 66.2; 58.7; 53.1; 52.2; 47.2; 26.9; 26.3; 25.6; 25.0; 19.1. HR-ESI-MS: 440.1911 ($[M+Na]^+$, $C_{19}H_{31}NNaO_9^+$; calc. 440.1891).

*Methyl (3*R*,5*S*)-5-Methoxy-3-methylisoxazolidine-5-carboxylate* (**8a**). Prepared according to *GP B1*. Yield: 79%. Clear oil. $[\alpha]_D^{20} = -74.1$ ($c = 1.00$, $CHCl_3$). IR: 3214, 2955, 2838, 1749, 1438, 1068. ^{1}H-NMR (400 MHz)[6]): 5.46 (*s*, 1 H#); 3.74 (*s*, 3 H#); 3.60–3.51 (*m*, 1 H*); 3.50–3.43 (*m*, 1 H#); 3.25 (*s*, 3 H#); 2.60 (*dd*, *J* = 13.2, 8.4, 1 H#); 2.47 (*dd*, *J* = 13.2, 7.2, 1 H*); 2.05 (*dd*, *J* = 13.2, 8.0, 1 H*); 1.87 (*dd*, *J* = 13.2, 8.0, 1 H#); 1.16 (*d*, *J* = 6.4, 3 H#); 1.14 (*d*, *J* = 6.4, 3 H*). ^{13}C-NMR (100 MHz)[6]): 168.5; 108.6#; 108.0*; 56.3#; 55.28*; 53.0#; 52.9*; 52.0#; 51.8*; 49.5#; 49.1*; 16.1#. HR-EI-MS: 175.0839 ($[M+Na]^+$, $C_7H_{13}NNaO_4^+$; calc. 175.0844).

*Methyl (3*S*,5*S*)-*N*-(2,3:5,6-Di-*O*-isopropylidene-β-*L*-gulofuranosyl)-3-isopropyl-5-methoxyisoxazolidine-5-carboxylate* (**7b**). Prepared according to *GP A*. Yield: 52%. White crystalline solid. M.p. 111–112°. $[\alpha]_D^{20} = -6.8$ ($c = 1.00$, $CHCl_3$). IR: 2983, 2873, 1751, 1455, 1371, 1210, 1068, 895, 733. ^{1}H-NMR (400 MHz): 5.04 (*d*, *J* = 6.0, 1 H); 4.71 (*dd*, *J* = 6.0, 4.0, 1 H); 4.65 (*s*, 1 H); 4.39–4.33 (*m*, 1 H); 4.21 (*dd*, *J* = 8.4, 6.8, 1 H); 4.12 (*dd*, *J* = 8.4, 4.0, 1 H); 3.82 (*s*, 3 H); 3.74 (*dd*, *J* = 8.4, 6.4, 1 H); 3.33 (*s*, 3 H); 3.28–3.23 (*m*, 1 H); 2.54–2.42 (*m*, 2 H); 2.01–1.92 (*m*, 1 H); 1.46 (*s*, 3 H); 1.40 (*s*, 3 H); 1.38 (*s*, 3 H); 1.31 (*s*, 3 H); 0.96 (*d*, *J* = 6.4, 3 H); 0.90 (*d*, *J* = 6.8, 3 H). ^{13}C-NMR (100 MHz): 170.0; 112.8; 110.0; 106.9; 97.9; 84.5; 84.2; 80.5; 75.9; 68.1; 66.2; 53.2; 52.2; 40.6; 29.7; 26.8; 26.3; 25.5; 25.2; 21.4; 19.3. HR-ESI-MS: 468.2225 ($[M+Na]^+$, $C_{21}H_{35}NNaO_9^+$; calc. 468.2204).

*Methyl (3*S*,5*S*)-3-Isopropyl-5-methoxyisoxazolidine-5-carboxylate* (**8b**). Prepared according to *GP B1*. Yield: 86%. Clear oil. $[\alpha]_D^{20} = -98.8$ ($c = 1.00$, $CHCl_3$). IR: 3213, 2959, 1752, 1466, 1438, 1267, 1219, 1070, 1047. ^{1}H-NMR (400 MHz): 5.61 (br. *s*, 1 H); 3.78 (*s*, 3 H); 3.29 (*s*, 3 H); 3.23–3.10 (*m*, 3 H); 2.54 (*dd*, $J = 8.3, 13.4$, 1 H); 2.06–1.96 (*m*, 1 H); 1.72–1.61 (*m*, 1 H); 0.96 (*d*, $J = 6.8$, 1 H); 0.90 (*d*, $J = 6.4$, 1 H). ^{13}C-NMR (100 MHz): 168.8; 108.53; 67.6; 53.2; 52.2; 51.9; 46.8; 45.4; 30.9; 21.1; 20.4. HR-ESI-MS: 204.1230 ($[M+Na]^+$, $C_9H_{17}NNaO_4^+$; calc. 204.1230).

*Methyl (3*R*,5*S*)-*N*-(2,3:5,6-Di-*O*-isopropylidene-β-*L*-gulofuranosyl)-5-methoxy-3-(2-methylpropyl)-isoxazolidine-5-carboxylate* (**7c**). Prepared according to *GP A*. Yield: 81%. White crystalline solid. M.p. 119–121°. $[\alpha]_D^{20} = -3.2$ ($c = 1.00$, $CHCl_3$). IR: 2987, 2954, 1756, 1454, 1381, 1372, 1219, 1178, 1086, 873, 741. ^{1}H-NMR (400 MHz): 5.03 (*d*, $J = 6.0$, 1 H); 4.69 (*dd*, $J = 6.0, 4.0$, 1 H); 4.65 (*s*, 1 H); 4.39–4.34 (*m*, 1 H); 4.20 (*dd*, $J = 8.4, 6.8$, 1 H); 4.06 (*dd*, $J = 8.4, 3.6$, 1 H); 3.81 (*s*, 3 H); 3.72–3.66 (*m*, 1 H); 3.35 (*s*, 3 H); 2.69 (*dd*, $J = 13.6, 8.0$, 1 H); 2.18 (*dd*, $J = 13.2, 2.4$, 1 H); 1.83–1.76 (*m*, 1 H); 1.69–1.61 (*m*, 1 H); 1.45 (*s*, 3 H); 1.40 (*s*, 3 H); 1.36 (*s*, 3 H) 1.30 (*s*, 3 H); 1.22–1.17 (*m*, 1 H); 0.93 (*dd*, $J = 6.4, 5.6$, 6 H). ^{13}C-NMR (100 MHz): 170.0; 112.8; 109.9; 106.8; 97.8; 84.5; 84.3; 80.4; 75.7; 66.2; 59.9; 53.2; 52.3; 44.8; 42.9; 26.8; 26.3; 25.9; 25.4; 25.1; 23.3; 22.2. HR-ESI-MS: 482.2383 ($[M+Na]^+$, $C_{22}H_{37}NNaO_9^+$; calc. 482.2361).

*Methyl (3*R*,5*S*)-5-Methoxy-3-(2-methylpropyl)isoxazolidine-5-carboxylate* (**8c**). Prepared according to *GP B1*. Yield: 80%. Clear oil. $[\alpha]_D^{20} = -76.3$ ($c = 1.00$, $CHCl_3$). IR: 3215, 2955, 2872, 2842, 1752, 1439, 1387, 1267, 1070, 810. ^{1}H-NMR (400 MHz)[6]: 6.15 (*s*, 1 H*); 5.46 (*s*, 1 H#); 3.79 (*s*, 3 H#); 3.77 (*s*, 3 H*); 3.59–3.52 (*m*, 1 H*); 3.52–3.42 (*m*, 1 H#); 3.30 (*s*, 3 H#); 3.27 (*s*, 3 H*); 2.62 (*dd*, $J = 13.2, 8.0$, 1 H#); 2.50 (*dd*, $J = 13.2, 7.2$, 1 H*); 2.04 (*m*, 1 H*); 1.91 (*m*, 1 H#); 1.68–1.58 (*m*, 1 H#); 1.48–1.42 (*m*, 1 H#); 1.37–1.30 (*m*, 1 H#); 0.89 (*dd*, $J = 10, 6.4$, 6 H#). ^{13}C-NMR (100 MHz): 168.6; 108.2; 59.4; 53.0; 52.9; 52.0; 51.9; 48.6; 47.9; 40.7; 26.7; 23.0; 22.9; 22.8. HR-ESI-MS: 240.1212 ($[M+Na]^+$, $C_{10}H_{19}NNaO_4^+$; calc. 240.1206).

*Methyl (3*R*,5*S*)-3-Benzyl-*N*-(2,3:5,6-di-*O*-isopropylidene-β-*L*-gulofuranosyl)-5-methoxyisoxazolidine-5-carboxylate* (**7d**). Prepared according to *GP A*. Yield: 53%. White crystalline solid. M.p. 116–118°. $[\alpha]_D^{20} = +15.8$ ($c = 1.00$, $CHCl_3$). IR: 3217, 3027, 2951, 1749, 1454, 1438, 1067. ^{1}H-NMR (400 MHz): 7.29–7.17 (*m*, 5 H); 5.01 (*d*, $J = 6.4$, 1 H); 4.70 (*s*, 1 H); 4.65 (*dd*, $J = 6.0, 4.0$, 1 H); 4.33–4.29 (*m*, 1 H); 4.15 (*dd*, $J = 8.0, 6.8$, 1 H); 3.88–3.77 (*m*, 1 H); 3.79 (*s*, 3 H); 3.61 (*dd*, $J = 8.4, 6.8$, 1 H); 3.42 (*s*, 3 H); 3.11 (*dd*, $J = 13.6, 8.0$, 1 H); 2.82 (*dd*, $J = 13.2, 8.8$, 1 H); 2.51 (*dd*, $J = 13.6, 8.0$, 1 H); 2.31 (*dd*, $J = 13.6, 2.8$, 1 H); 1.45 (*s*, 3 H); 1.41 (*s*, 3 H); 1.36 (*s*, 3 H); 1.30 (*s*, 3 H). ^{13}C-NMR (100 MHz): 169.5; 138.8; 129.7; 128.6; 126.5; 112.9; 109.9; 106.6; 97.8; 84.4; 84.2; 80.4; 75.8; 66.2; 63.0; 53.2; 52.2; 43.5; 39.9; 27.1; 26.3; 25.6; 25.1. HR-ESI-MS: 516.2229 ($[M+Na]^+$, $C_{25}H_{35}NNaO_9^+$; calc. 516.2204).

*Methyl (3*R*,5*S*)-3-Benzyl-5-methoxyisoxazolidine-5-carboxylate* (**8d**). Prepared according to *GP B1*. Yield: 94%. Clear oil. $[\alpha]_D^{20} = -89.2$ ($c = 1.00$, $CHCl_3$). IR: 3028, 2952, 1749, 1604, 1498, 1439, 1268, 1209, 1153, 932, 702. ^{1}H-NMR (400 MHz)[6]: 7.31–7.18 (*m*, 5 H#); 6.21 (*s*, 1 H*); 5.69 (*s*, 1 H#); 3.84 (*s*, 3 H*); 3.78 (*s*, 3 H#); 3.34 (*s*, 3 H#); 3.33 (*s*, 3 H*); 3.03 (*dd*, $J = 13.2, 5.6$, 1 H#); 3.03–2.98 (*m*, 1 H*); 2.79–2.71 (*m*, 1 H*); 2.72–2.67 (*m*, 1 H#); 2.55–2.48 (*m*, 1 H#); 2.46–2.42 (*m*, 1 H*); 2.26 (*m*, 1 H*); 2.10 (*m*, 1 H#). ^{13}C-NMR (100 MHz): 168.2; 137.6; 129.5; 129.1; 128.9; 128.7; 126.9; 108.3; 107.9; 62.0; 61.1; 53.1; 53.0; 52.1; 51.9; 47.5; 37.4. HR-ESI-MS: 247.1050 ($[M+Na]^+$, $C_{13}H_{17}NNaO_4^+$; calc. 274.1049).

*Methyl (3*R*,5*S*)-3-[3-(Benzoyloxy)propyl]-*N*-(2,3:5,6-di-*O*-isopropylidene-β-*L*-gulofuranosyl)-5-methoxyisoxazolidine-5-carboxylate* (**7e**). Prepared according to *GP A*. Yield: 20%. White crystalline solid. M.p. 104.5°. $[\alpha]_D^{20} = -5.0$ ($c = 1.00$, $CHCl_3$). IR: 2985, 1752, 1719, 1452, 1372, 1275, 1210, 1070, 847, 714. ^{1}H-NMR (400 MHz): 8.10–7.39 (*m*, 5 H); 5.01 (*d*, $J = 6.0$, 1 H); 4.76–4.68 (*m*, 1 H); 4.62 (*s*, 1 H); 4.40–4.22 (*m*, 3 H); 4.21–4.19 (*m*, 1 H); 4.16–4.06 (*m*, 1 H); 3.83 (*s*, 3 H); 3.36 (*s*, 3 H); 2.76–2.65 (*m*, 1 H); 2.29–2.13 (*m*, 1 H); 1.98–1.57 (*m*, 6 H); 1.43 (*s*, 3 H); 1.29–1.25 (*m*, 6 H); 1.21 (*s*, 3 H). ^{13}C-NMR (100 MHz): 213.1; 169.9; 166.3; 133.1; 130.2; 129.1; 128.6; 112.6; 109.5; 106.2; 97.9; 82.8; 82.5; 80.3; 75.5; 65.8; 64.3; 61.8; 52.7; 52.0; 44.2; 30.2; 26.8; 26.3; 25.0; 24.5. HR-ESI-MS: 588.2424 ($[M+Na]^+$, $C_{32}H_{54}N_4NaO_{13}^+$; calc. 588.2415).

*Methyl (3*R*,5*S*)-3-[3-(Benzoyloxy)propyl]-5-methoxyisoxazolidine-5-carboxylate* (**8e**). Prepared according to *GP B2*. Yield: 92%. Clear oil. IR: 2985, 1750, 1718, 1452, 1372, 1276, 1209, 1069, 715. ^{1}H-NMR (400 MHz): 8.10–7.39 (*m*, 5 H); 5.5–5.59 (br. *s*, 1 H); 4.31 (*t*, 2 H); 3.81 (*s*, 3 H); 3.56–3.49 (*m*, 1 H); 3.36 (*s*, 3 H); 2.71–2.62 (*m*, 1 H); 2.06–1.92 (*m*, 1 H); 1.83–1.62 (*m*, 6 H). ^{13}C-NMR (100 MHz): 166.5; 133.3; 130.2; 129.9; 128.5; 107.8; 64.3; 60.6; 53.0; 52.1; 48.1; 28.1; 26.8.

*Methyl (3*R,5S*)*-N-*(2,3:5,6-Di*-O-*isopropylidene-β*-L-*gulofuranosyl)-3-(4-hydroxybenzyl)-5-methoxyisoxazolidine-5-carboxylate* (**7f**). Bn-Protected **7f-1** was prepared according to *GP A* (yield: 27%). To a soln. of **7f-1** (5.08 g, 8.50 mmol, 1.00 equiv.) in 3.0 ml of MeOH was added Pd/C (5.0 wt-%, 1.80 g, 0.10 equiv.), followed by dry MeOH (85.0 ml, 0.10M). The resulting black suspension was stirred vigorously under H_2 overnight. The soln. was filtered through *Celite*, and the solvent was evaporated. The crude solid was recrystallized by dissolving in a minimal amount of hot AcOEt, followed by slowly layering hexanes on top. Upon standing, white crystals formed which were filtered and dried *in vacuo* to give **7f** (3.50 g, 81.0 %). M.p. 136°. $[\alpha]_D^{20} = +17.0$ ($c = 1.00$, $CHCl_3$). IR: 3408, 2988, 2938, 1750, 1516, 1440, 1373, 1264, 1211, 1087, 846, 756. ^{1}H-NMR (400 MHz): 7.01 (*d*, *J* = 8.4, 2 H); 6.72 (*d*, *J* = 8.4, 2 H); 6.19 (*s*, 1 H); 4.99 (*d*, *J* = 6.0, 1 H); 4.68 (*s*, 1 H); 4.65–4.62 (*m*, 1 H); 4.34–4.28 (*m*, 1 H); 4.16–4.12 (*m*, 1 H); 3.86 (*dd*, *J* = 8.4, 4.0, 1 H); 3.77–3.60 (*m*, 1 H); 3.76 (*s*, 3 H); 3.67–3.61 (*m*, 1 H); 3.39 (*s*, 3 H); 2.98 (*dd*, *J* = 13.2, 6.4, 1 H); 2.72 (*dd*, *J* = 13.6, 9.2, 1 H); 2.44 (*dd*, *J* = 14.0, 8.0, 1 H); 2.26 (*dd*, *J* = 14.0, 2.8, 1 H); 1.43 (*s*, 3 H); 1.41 (*s*, 3 H); 1.35 (*s*, 3 H); 1.28 (*s*, 3 H). ^{13}C-NMR (100 MHz): 169.6; 154.7; 130.8; 130.4; 115.6; 112.9; 110.0; 106.6; 97.7; 84.3; 84.1; 80.4; 75.8; 66.2; 63.2; 53.3; 52.2; 43.3; 38.8; 27.0; 26.2; 25.5; 25.0. HR-ESI-MS: 532.2137 ($[M+Na]^+$, $C_{25}H_{35}NNaO_{10}^+$; calc. 532.2159).

*Methyl (3*R,5S*)-3-(4-Hydroxybenzyl)-5-methoxyisoxazolidine-5-carboxylate* (**8f**). Prepared according to *GP B2*. Yield: 93%. Clear oil. $[\alpha]_D^{20} = -33.0$ ($c = 1.00$, $CHCl_3$). IR: 3500–3300 (br.), 3208, 2953, 1750, 1516, 1269. ^{1}H-NMR (400 MHz): 7.01 (*d*, *J* = 8.4, 2 H); 6.72 (*d*, *J* = 8.4, 2 H); 6.00–5.80 (br. *s*, 1 H); 3.81 (*s*, 3 H); 3.76–3.69 (*m*, 1 H); 3.36 (*s*, 3 H); 2.91 (*dd*, *J* = 13.6, 6.0, 1 H); 2.71 (*dd*, 14.0, 8.0, 1 H); 2.56 (*dd*, *J* = 13.6, 8.8, 1 H); 2.14 (*dd*, 13.2, 7.2, 1 H). ^{13}C-NMR (100 MHz): 168.9; 155.1; 130.0; 128.9; 115.9; 108.2; 62.0; 53.1; 52.2; 47.1; 36.5. HR-ESI-MS: 290.1010 ($[M+Na]^+$, $C_{13}H_{17}NNaO_5^+$; calc. 290.0998).

tert-*Butyl 3-{[(3*R,5S*)*-N-*(2,3:5,6-Di*-O-*isopropylidene-β*-L-*gulofuranosyl)-5-methoxy-5-(methoxycarbonyl)isoxazolidin-3-yl]methyl}-1*H*-indole-1-carboxylate* (**7g**). Prepared according to *GP A*. Yield: 41%. White crystalline solid. M.p. 102°. $[\alpha]_D^{20} = -20.1$ ($c = 1.00$, $CHCl_3$). ^{1}H-NMR (400 MHz): 8.09 (br. *s*, 1 H); 7.66 (*d*, *J* = 7.6, 1 H); 7.41 (*s*, 1 H); 7.29 (*t*, *J* = 7.2, 1 H); 7.22 (*t*, *J* = 7.2, 1 H); 5.02 (*d*, *J* = 6.0, 1 H); 4.69 (*s*, 1 H); 4.65–4.62 (*m*, 1 H); 4.34–4.28 (*m*, 1 H); 4.16–4.12 (*m*, 1 H); 3.98–3.90 (*m*, 1 H); 3.87 (*dd*, *J* = 8.8, 4.0, 1 H); 3.79 (*s*, 3 H); 3.59–3.54 (*m*, 1 H); 3.45 (*s*, 3 H); 3.15 (*dd*, *J* = 14.0, 5.6, 1 H); 2.97 (*dd*, *J* = 14.0, 9.6, 1 H); 2.52 (*dd*, *J* = 13.2, 8.0, 1 H); 2.37 (*dd*, *J* = 13.6, 2.4, 1 H); 1.65 (*s*, 9 H); 1.45 (*s*, 3 H); 1.36 (*s*, 3 H); 1.33 (*s*, 3 H); 1.31 (*s*, 3 H). ^{13}C-NMR (100 MHz): 169.3; 149.8; 135.7; 131.4; 130.7; 124.5; 123.9; 122.6; 119.9; 117.8; 115.3; 112.9; 109.8; 106.6; 97.8; 84.4; 83.7; 80.4; 75.7; 66.1; 61.2; 53.2; 52.3; 43.7; 29.8; 28.3; 26.9; 26.3; 25.7; 25.1. HR-ESI-MS: 655.2821 ($[M+Na]^+$, $C_{32}H_{44}N_2NaO_{11}^+$; calc. 655.2843).

tert-*Butyl 3-{[(3*R,5S*)-5-Methoxy-5-(methoxycarbonyl)isoxazolidin-3-yl]methyl}-1*H*-indole-1-carboxylate* (**8g**). Prepared according to *GP B2*. Yield: 42%. Clear oil. $[\alpha]_D^{20} = -47.7$ ($c = 1.00$, $CHCl_3$). IR: 2957, 1730, 1454, 1372, 1309, 1259, 1157, 1085, 749. ^{1}H-NMR (400 MHz): 8.12 (br. *s*, 1 H); 7.52 (*d*, *J* = 7.6, 1 H); 7.46 (*s*, 1 H); 7.32 (*t*, *J* = 7.2, 1 H); 7.24 (*t*, *J* = 7.2, 1 H); 3.98–3.86 (*m*, 1 H); 3.80 (*s*, 3 H); 3.57 (*s*, 3 H); 3.10 (*dd*, *J* = 9.2, 5.6, 1 H); 2.89 (*dd*, *J* = 8.0, 6.8, 1 H); 2.62 (*dd*, *J* = 8.4, 4.8, 1 H); 2.19 (*dd*, *J* = 6.8, 6.4, 1 H); 1.67 (*s*, 9 H). ^{13}C-NMR (100 MHz): 168.4; 149.9; 135.7; 130.4; 124.9; 123.9. 122.9; 119.0; 116.6; 115.6; 108.3; 83.9; 60.3; 53.1; 52.2; 47.6; 29.9; 28.5; 27.3. HR-ESI-MS: 413.1684 ($[M+Na]^+$, $C_{32}H_{44}N_2NaO_{11}^+$; calc. 413.1691).

REFERENCES

[1] D. Seebach, A. K. Beck, D. J. Bierbaum, *Chem. Biodiversity* **2004**, *1*, 1111.

[2] D. Seebach, M. Rueping, P. I. Arvidsson, T. Kimmerlin, P. Micuch, C. Noti, D. Langenegger, D. Hoyer, *Helv. Chim. Acta* **2001**, *84*, 3503.

[3] D. Seebach, M. Overhand, F. N. M. Kühnle, B. Martinoni, L. Oberer, U. Hommel, H. Widmer, *Helv. Chim. Acta* **1996**, *79*, 913; D. Seebach, P. E. Ciceri, M. Overhand, B. Jaun, D. Rigo, L. Oberer, U. Hommel, R. Amstutz, H. Widmer, *Helv. Chim. Acta* **1996**, *79*, 2043; D. Seebach, J. V. Schreiber, S. Abele, X. Daura, W. F. van Gunsteren, *Helv. Chim. Acta* **2000**, *83*, 34.

[4] D. H. Appella, L. A. Christianson, I. L. Karle, D. R. Powell, S. H. Gellman, *J. Am. Chem. Soc.* **1996**, *118*, 13071.

[5] S. A. Hart, A. B. F. Bahadoor, E. E. Matthews, X. Y. J. Qiu, A. Schepartz, *J. Am. Chem. Soc.* **2003**, *125*, 4022.
[6] R. David, R. Günther, L. Baumann, T. Luhmann, D. Seebach, H.-J. Hofmann, A. G. Beck-Sickinger, *J. Am. Chem. Soc.* **2008**, *130*, 15311.
[7] J. X. Qiu, E. J. Petersson, E. E. Matthews, A. Schepartz, *J. Am. Chem. Soc.* **2006**, *128*, 11338; D. S. Daniels, E. J. Petersson, J. X. Qiu, A. Schepartz, *J. Am. Chem. Soc.* **2007**, *129*, 1532; J. L. Goodman, E. J. Petersson, D. S. Daniels, J. X. Qiu, A. Schepartz, *J. Am. Chem. Soc.* **2007**, *129*, 14746; E. J. Petersson, C. J. Craig, D. S. Daniels, J. X. Qiu, A. Schepartz, *J. Am. Chem. Soc.* **2007**, *129*, 5344; E. J. Petersson, A. Schepartz, *J. Am. Chem. Soc.* **2008**, *130*, 821.
[8] Y. Hamuro, J. P. Schneider, W. F. DeGrado, *J. Am. Chem. Soc.* **1999**, *121*, 12200.
[9] M. Rueping, Y. Mahajan, M. Sauer, D. Seebach, *ChemBioChem* **2002**, *3*, 257.
[10] J. A. Kritzer, J. D. Lear, M. E. Hodsdon, A. Schepartz, *J. Am. Chem. Soc.* **2004**, *126*, 9468.
[11] M. Werder, H. Hauser, S. Abele, D. Seebach, *Helv. Chim. Acta* **1999**, *82*, 1774.
[12] O. M. Stephens, S. Kim, B. D. Welch, M. E. Hodsdon, M. S. Kay, A. Schepartz, *J. Am. Chem. Soc.* **2005**, *127*, 13126.
[13] D. Seebach, S. Abele, K. Gademann, G. Guichard, T. Hintermann, B. Jaun, J. L. Matthews, J. V. Schreiber, *Helv. Chim. Acta* **1998**, *81*, 932.
[14] G. Lelais, P. Micuch, D. Josien-Lefebvre, F. Rossi, D. Seebach, *Helv. Chim. Acta* **2004**, *87*, 3131.
[15] S. Abele, G. Guichard, D. Seebach, *Helv. Chim. Acta* **1998**, *81*, 2141.
[16] P. I. Arvidsson, J. Frackenpohl, D. Seebach, *Helv. Chim. Acta* **2003**, *86*, 1522.
[17] J. W. Bode, R. M. Fox, K. D. Baucom, *Angew. Chem., Int. Ed.* **2006**, *45*, 1248.
[18] J. Wu, J. Ruiz-Rodríguez, J. M. Comstock, J. Z. Dong, J. W. Bode, *Chem. Sci.* **2011**, *2*, 1976; V. R. Pattabiraman, A. O. Ogunkoya, J. W. Bode, *Angew. Chem., Int. Ed.* **2012**, *51*, 5114; T. Fukuzumi, L. Ju, J. W. Bode, *Org. Biomol. Chem.* **2012**, *10*, 5837; Y.-L. Huang, R. Frey, M. E. Juarez-Garcia, J. W. Bode, *Heterocycles* **2012**, *84*, 1179.
[19] N. Carrillo, E. A. Davalos, J. A. Russak, J. W. Bode, *J. Am. Chem. Soc.* **2006**, *128*, 1452.
[20] D. Seebach, V. Prelog, *Angew. Chem., Int. Ed.* **1982**, *21*, 654.
[21] A. Vasella, *Helv. Chim. Acta* **1977**, *60*, 1273.
[22] H. Ishida, N. Carrillo, J. W. Bode, *Tetrahedron Lett.* **2009**, *50*, 3258.
[23] K. Kasahara, H. Iida, C. Kibayashi, *J. Org. Chem.* **1989**, *54*, 2225.
[24] S. Y. Yu, H. Ishida, M. E. Juarez-Garcia, J. W. Bode, *Chem. Sci.* **2010**, *1*, 637.
[25] M. E. Juarez-Garcia, S. Y. Yu, J. W. Bode, *Tetrahedron* **2010**, *66*, 4841.
[26] T. Gerfaud, Y. L. Chiang, I. Kreituss, J. A. Russak, J. W. Bode, *Org. Process Res. Dev.* **2012**, *16*, 687.
[27] S. Mzengeza, R. A. Whitney, *J. Org. Chem.* **1988**, *53*, 4074.
[28] S. Cicchi, M. Marradi, M. Corsi, C. Faggi, A. Goti, *Eur. J. Org. Chem.* **2003**, 4152.
[29] U. Chiacchio, M. G. Saita, L. Crispino, G. Gumina, S. Mangiafico, V. Pistarà, G. Romeo, A. Piperno, E. De Clercq, *Tetrahedron* **2006**, *62*, 1171.
[30] S. Mzengeza, C. M. Yang, R. A. Whitney, *J. Am. Chem. Soc.* **1987**, *109*, 276.
[31] A. Basha, R. Henry, M. A. Mclaughlin, J. D. Ratajczyk, S. J. Wittenberger, *J. Org. Chem.* **1994**, *59*, 6103.
[32] R. Fässler, D. E. Frantz, J. Oetiker, E. M. Carreira, *Angew. Chem., Int. Ed.* **2002**, *41*, 3054.

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