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Synthesis of Polyhydroxylated Piperidine and Pyrrolidine Peptidomimetics via One-Pot Sequential Lactam Reduction/Joullié–Ugi Reaction

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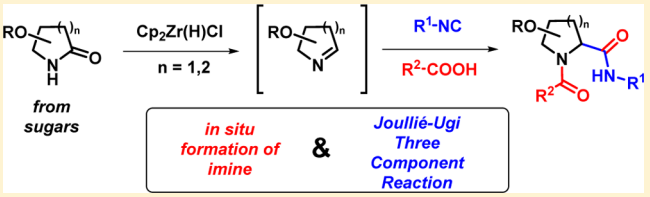
Supporting Information

ABSTRACT: A direct approach to the synthesis of polyhydroxylated piperidine and pyrrolidine peptidomimetics is described. The presented strategy is based on one-pot reduction of sugar-derived lactams with Schwartz's reagent followed by a multicomponent Ugi–Joullié reaction.



INTRODUCTION

Peptides and proteins play a key role in the biological functions of living organisms. Therefore, these molecules are excellent candidates for novel drugs. In recent decades, the investigation of peptide mimics (peptidomimetics) has received much attention.[1] In many cases, peptidomimetics have shown enhanced pharmacological properties over their natural peptide analogues. Particularly interesting examples of peptidomimetics are peptide analogues into which cyclic structural elements have been incorporated. By reducing their conformational flexibility, in many cases their affinity for certain receptors is enhanced. Another result of reduced flexibility is better defined secondary and tertiary peptide structure.[1]

Among various amino acids, proline and pipecolic acid as well as their derivatives have become particularly important structural elements responsible for constraining the structural and conformational features of biologically active peptides.[1,2] They have a tremendous effect on peptide folding and bioactive conformations.[3] As a result, these amino acids and their derivatives find application as β-turn mimetics[3c] and, therefore, as an element of several pharmaceutically relevant compounds.[2,3]

Proline and pipecolic acid themselves also display important bioactivity, as do their derivatives. In particular, polyhydroxylated pipecolic acid amides and proline amides, also known as iminosugar *C*-glycosides, have received much attention in recent decades.[2] Such aza-*C*-glycosides have become important targets in the quest for iminosugar-type glycosidase and glycosyltransferase inhibitors for the use in medical treatment.[4] Several piperidine and pyrrolidine amides (Figure 1) have been found to be potent inhibitors of α- and β-*N*-acetylhexosaminidases (HexNAcases). Their deficiencies in the human body can lead to lysosomal storage disorders (LSDs) such as Tay–Sachs and Sandhoff syndromes[5] and to Alzheimer's disease.[6] Moreover, some of them exhibit specific inhibition of α-*N*-acetylgalactosaminidases (α-GalNAcases) which are crucial targets in the treatment of the Schindler–Kanzaki LSD[7] and cancer by preventing the degradation of the macrophage-activating factor.[8]

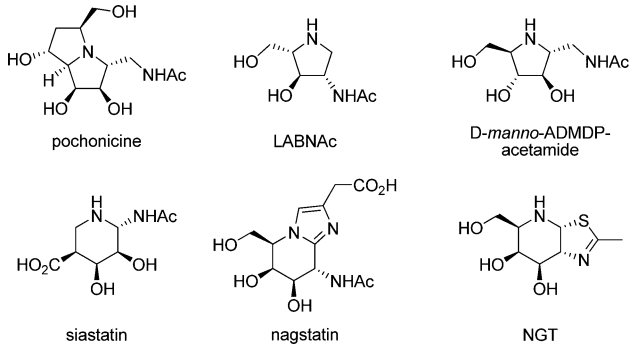


Figure 1. Potent inhibitors of α- and β-*N*-acetylhexosaminidases (HexNAcases).

Very recently, Ayers, Fleet, and Kato reported a series of polyhydroxylated proline amides (e.g., **1** or **2**, Figure 2) that

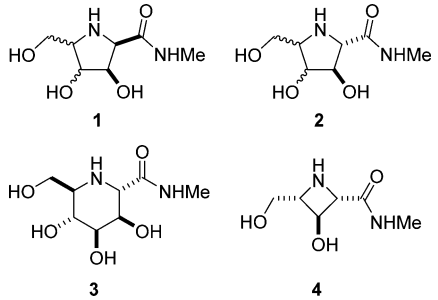


Figure 2. Examples of polyhydroxylated proline amides, pipecolic amide, and azetidine amide derivatives that display high bioactivity against hexosaminidases.

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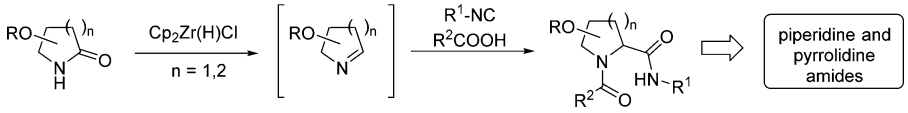
Scheme 1



displayed low to submicromolar inhibition of β-*N*-acetylhexosaminidases.[9] In addition, the same group has also reported that certain hydroxylated pipecolic amide (e.g., **3**)[10] and azetidine amide derivatives (e.g., **4**)[11] also display high bioactivity against hexosaminidases (Figure 2).

The reported bioactivity of compounds of types **1**−**3** as well as our long-term interest in the stereocontrolled synthesis of bioactive compounds, such as β-lactams,[12] iminosugars,[13] and alkaloids,[14] prompted us to search for an attractive method of the synthesis of such polyhydroxylated cyclic amino amides.

A particularly attractive pathway of the synthesis of such proline and pipecolic acid derivatives is the Joullié−Ugi reaction,[2,15] which involves the reaction of cyclic imines with isocyanides and carboxylic acids.[16,3b,c,17] Although the multicomponent Ugi reactions[15,18] enable preparation of broad libraries of peptides in a fast and efficient manner, it has rather limited applicability in the preparation of cyclic peptides due to the limited accessibility of cyclic imines. The reasons for that are the low stability of cyclic imines and difficulties in their synthesis. Typical methods of cyclic imine synthesis involve (1) *N*-chlorination/elimination of secondary amines,[19] (2) deoxygenation of cyclic nitrones,[20,21] or (3) cyclization of azidoaldehydes through Staudinger/aza-Wittig reaction.[16c,d,g,22] None of these methods is universal, and each of them has serious drawbacks, such as difficulties in regioselective formation of the C═N bond, long and multistep preparation of starting materials, or low stability.

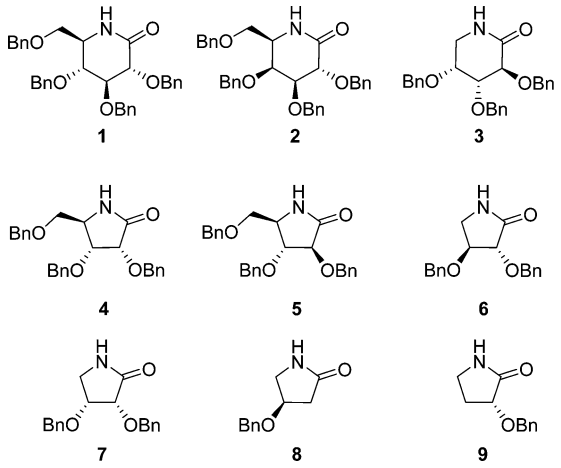
Recently, we demonstrated that upon treatment with $Cp_2Zr(H)Cl$ (Schwartz's reagent), five- and six-membered lactams, including sugar- and hydroxy acid-derived lactams,[20,23] can be easily converted into imines under mild conditions. In addition, as was also shown, in situ generated cyclic imines can be directly subjected to further reactions with nucleophilic reagents such as allyltributylstannane,[23] Grignard reagents,[23] enolates,[23] or Danishefsky's diene[20] to afford α-functionalized pyrrolidines and piperidines in a one-pot manner.

Excellent results of our recent studies on one-pot reduction/functionalization of lactams encouraged us to check whether under the same conditions the deoxygenative reduction of lactams and the Joullié−Ugi reaction sequence can be performed without isolation of the intermediate imine, as outlined in Scheme 1. In particular, we focused our attention on the synthesis of polyhydroxylated cyclic amides starting with carbohydrate-derived lactams.

RESULTS AND DISCUSSION

As in the previous studies, five- and six-membered polyhydroxylated lactams **1**−**9** were prepared starting with commercially available sugars and tartaric and malic acid following the previously reported methods.[20,23,24]

With the chiral lactams in hand, we began the investigation of the synthesis of pyrrolidine and piperidine derivatives via a sequential one-pot lactam reduction/Joullié−Ugi reaction. Treatment of *gluco*-lactam **1** with $Cp_2Zr(H)Cl$ (1.6 equiv) in THF provided the corresponding imine. As reported previously,[23] the progress of this step can be easily followed; the transition of



the reaction mixture from an initial white suspension into a clear solution indicates the end of the reduction (ca. 0.5−1.5 h). The resulting imine was directly subjected to the Joullié−Ugi reaction. Thus, TFA (4 equiv) and isocyanide (1.2 equiv) were added at −78 °C, and the reaction mixture was allowed to warm to room temperature. As shown in Table 1, the reaction proceeded smoothly either with aliphatic (ent 1, 2) or aromatic isocyanides (ent 3). In all three cases, the reaction proceeded diastereoselectively to provide predominantly products **10**−**12** (dr > 95:5 according to NMR) regardless of the isocyanide structure. The assignment of configuration of **10** by the analysis of NMR spectra was difficult due to the existence of this compound as a complex mixture of rotamers. Therefore, to simplify its spectra, compound **10** was hydrolyzed to afford amide **30**. Thus, the assignment of the absolute configuration at the newly formed stereogenic center did not present any difficulties and was unambiguously achieved by the analysis of coupling constants and NOE experiments. Following the same procedure, lactams **2**−**9** were converted into the corresponding cyclic trifluoroacetamides **11**−**29**. As presented in Table 1, their formation proceeded efficiently and in most cases stereoselectively. As in the case of compound **10**, amides **11**−**29** were hydrolyzed to provide compounds **31**−**49** (Table 2). The absolute configuration of obtained products was assigned by the analysis of NMR spectra and NOE experiments of *N*-deprotected products. In some cases, those assignments were confirmed by X-ray analysis (compounds **2-*epi*-23**, **24**, and **28**) (Figures 3−5).

As we have already shown, the course of the addition to five- and six-membered imines is not as straightforward and intuitive as one could expect.[20] The rationalization of the stereochemical outcome cannot be based only on steric effects but must also consider stereoelectronic effects and conformational preferences, as in the case of C-allylation of furanosyl- and pyranosyloxycarbenium ions investigated in detail by Woerpel and co-workers.[25]

The experimental data collected in Tables 1 and 2 indicates that, although the Ugi reaction is a complex process involving imine activation, addition of an isocyanate ion, carboxylate addition, and Mumm rearrangement,[2,26,18] its stereochemical

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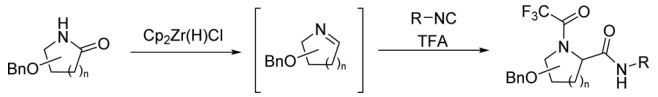
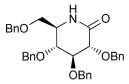
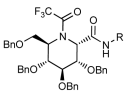
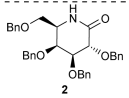
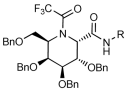
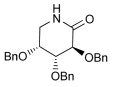
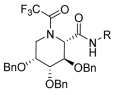
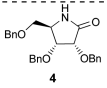
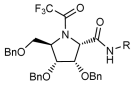
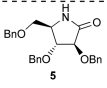
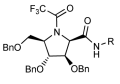
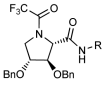
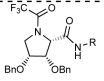
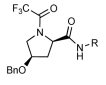
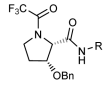
Table 1. Sequential Lactam Reduction/Joullié–Ugi Three-Component Reaction[a]



Entry	Lactam	Product (major isomer)	R	Yield[b] [%]	*dr*
1	 1		*t*-Bu (**10**)	69	>95:5
2			Cy (**11**)	74	>95:5
3			PMP (**12**)	86	>95:5
4	 2		*t*-Bu (**13**)	63[c]	86:14[d]
5			Cy (**14**)	67[c]	82:18[d]
6	 3		*t*-Bu (**15**)	76[c]	75:25[d]
7			Cy (**16**)	84[c]	80:20[d]
8			PMP (**17**)	68	59:41
9	 4		*t*-Bu (**18**)	72	84:16
10			Cy (**19**)	63	>95:5
11	 5		*t*-Bu (**20**)	83[c]	57:43[d]
12			Cy (**21**)	75[c]	63:37[d]
13	 6		*t*-Bu (**22**)	60	63:37
14			Cy (**23**)	60	57:43
15			PMP (**24**)	64	60:40
16	 7		*t*-Bu (**25**)	60[c]	>95:5[d]
17			PMP (**26**)	68[c]	>95:5[d]
18	 8		*t*-Bu (**27**)	58	77:23
19			Cy (**28**)	54[c]	74:26[d]
20	 9		*t*-Bu (**29**)	57	68:32

[a]Reaction conditions: (step 1) $Cp_2Zr(H)Cl$ (1.6 equiv) in THF for 30 min; (step 2) TFA (4.0 equiv), isocyanide (1.25 equiv) at −78 °C to rt for 24 h. [b]Isolated yield (overall after two steps). [c]Yield was assigned by ^1H NMR of crude reaction mixture. Isomeric products could not be separated by column chromatography; the crude mixture of products was subjected directly to hydrolysis. [d]Determined by ^1H NMR of the crude reaction mixture after hydrolysis of a mixture of isomeric trifluoroacetates.

course is determined by the isocyanide addition step and can be rationalized by Woerpel's model of allylation of oxycarbenium ions.[25]

In the case of allylation of furanosyloxycarbenium ions, Woerpel's model assumes that the relative stabilities of the oxycarbenium ion envelope conformers is dictated by the preferences of orientation of the substituents attached to the ring. Alkoxy groups at the C-3 and C-4 positions preferentially adopt the equatorial and axial position, respectively, and the nucleophile approaches the intermediate oxycarbenium ion from "inside", *syn* to the carbon atom which is located out of envelope plane (Figure 6). The effect of the C-5 group is minor.[25a−e,h]

The above rules explain the marked preference of formation of 2,3-*cis*-pyrrolidine derivatives in the case of lactam **9** (product **29**), D-*ribo*-lactam **4** (products **18** and **19**), and erythronolactam **7**, as well as the formation of 2,4-*cis* products **27** and **28** from lactam **8** (Scheme 2). The same high *cis*-selectivity was also observed by Codée and co-workers[16h] during the Ugi reaction involving D-*lyxo*-imine generated through the Staudinger/aza-Wittig reaction.

The low selectivity of isocyanide addition to the imines generated from lactams **5** and **6** can be explained in the same manner. In the case of *arabino*-imine **50**, obtained from lactam **5**, the adapting of the preferred pseudoaxial orientation by C-4 alkoxy group generates unfavorable *syn*-butanol interactions[27]

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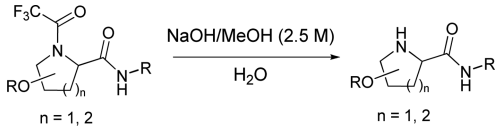
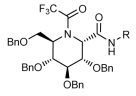
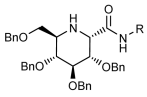
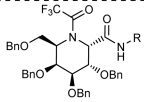
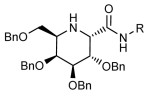
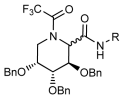
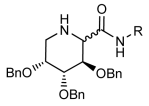
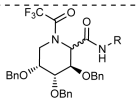
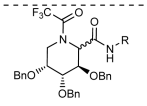
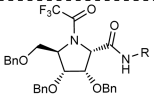
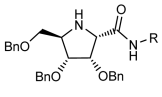
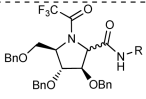
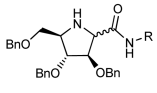
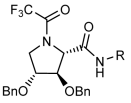
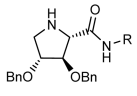
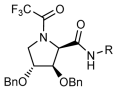
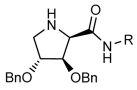
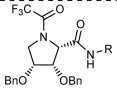
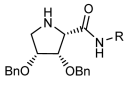
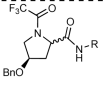
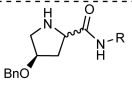
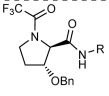
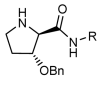
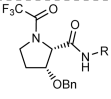
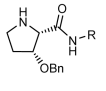
Table 2. Hydrolysis of Trifluoroacetamides 10−29[a]



Entry	Substrate		Product		Yield	*dr*[b]
	Structure	R	Structure	R	[%]	
1		*t*-Bu (**10**)		*t*-Bu (**30**)	59	-
2		Cy (**11**)		Cy (**31**)	61	-
3		PMP (**12**)		PMP (**32**)	58	-
4		*t*-Bu[c] (**13**)		*t*-Bu (**33**)	58[d]	86:14
5		Cy[c] (**14**)		Cy (**34**)	61[d]	82:18
6		*t*-Bu[c] (**15**)		*t*-Bu (**35**)	68[d]	75:25
7		Cy[c] (**16**)		Cy (**36**)	75[d]	80:20
8		PMP (**17**)		PMP (**37**)	88	-
9		PMP (**2-*epi*-17**)		PMP (**2-*epi*-37**)	69	-
10		*t*-Bu (**18**)		*t*-Bu (**38**)	74	-
11		Cy (**19**)		Cy (**39**)	58	-
12		*t*-Bu[c] (**20**)		*t*-Bu (**40**)	75[d]	57:43
13		Cy[c] (**21**)		Cy (**41**)	68[d]	63:37
14		*t*-Bu (**22**)		*t*-Bu (**42**)	79	-
15		Cy (**23**)		Cy (**43**)	78	-
16		PMP (**24**)		PMP (**44**)	95	-
17		Bu (**2-*epi*-22**)		Bu (**2-*epi*-42**)	84	-
18		Cy (**2-*epi*-23**)		Cy (**2-*epi*-43**)	75	-
19		PMP (**2-*epi*-24**)		PMP (**2-*epi*-44**)	95	-
20		*t*-Bu (**25**)		*t*-Bu (**45**)	75	-
21		PMP (**26**)		PMP (**46**)	79	-
24		*t*-Bu (**27**)		*t*-Bu (**47**)	65	77:23
25		Cy[c] (**28**)		Cy (**48**)	63[d]	74:26
26		*t*-Bu (**2-*epi*-29**)		*t*-Bu (**2-*epi*-49**)	71	-
27		*t*-Bu (**29**)		*t*-Bu (**49**)	69	-

[a]Reaction conditions: substrate (0.5 mmol), 2.5 M NaOH in MeOH (2 mL), H_2O (0.1 mL), rt. [b]Determined by ^{1}H NMR. [c]Mixture of isomers (crude reaction mixture from previous step) were subjected to hydrolysis. [d]Overall yield of both isomers; PMP = 4-methoxyphenyl, Cy = cyclohexyl.

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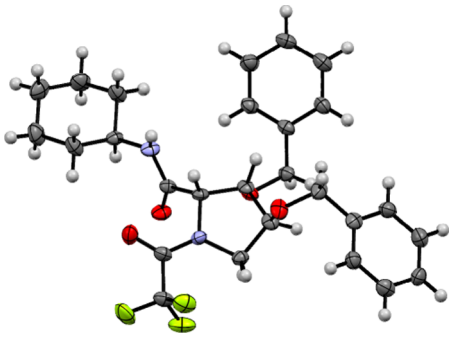


Figure 3. ORTEP plot of **2-*epi*-23** with 30% probability ellipsoids.

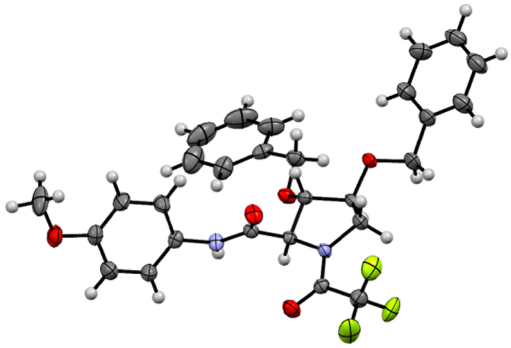


Figure 4. ORTEP plot of **24** with 30% probability ellipsoids.

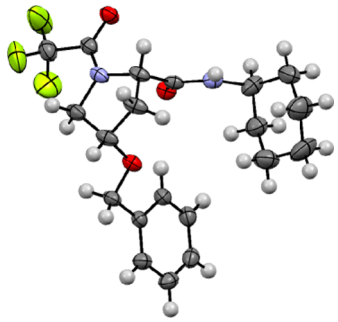


Figure 5. ORTEP plot of **28** with 30% probability ellipsoids.

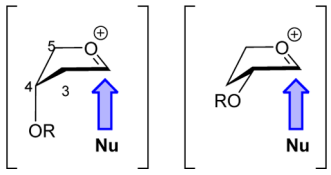
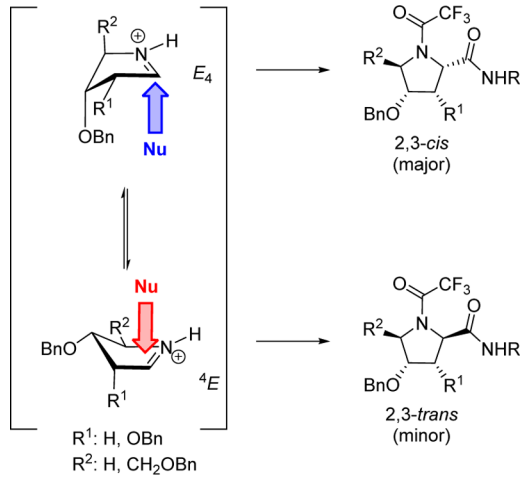


Figure 6. Stereochemical course of nucleophilic addition to furanyl oxycarbenium ions according to Woerpel's model.[23]

due to pseudoaxial arrangement of all substituents in E_4 conformer (Scheme 3). As a result, the alternative reaction course via the all-equatorially substituted conformer ^4E should also be possible and as a consequence lead to a poorly selective reaction. Such prediction is in agreement with our experimental observations (see Table 1, entries 12 and 13) as well as experimental results and computational predictions reported by others.[16h]

Following the analogous rules developed by Woerpel et al.[25b,f,g] for *C*-allylation of pyranosyl oxycarbenium ions (Figure 7), the course of the isocyanide addition to six-membered imines can be explained similarly.

Scheme 2



The formation of 2,3-*cis* product **10** results from an axial attack of the nucleophile to the all-equatorial $^4H_3$ conformer (Scheme 4). The $^3H_4$ conformer, which bears the stereoelectronically more preferred axially oriented C-3 and C-4 groups, is strongly destabilized by 1,3-diaxial interactions. The observed stereochemical outcome corresponds well with our previous studies of allylation[23] and tandem Mannich/Michael reaction[20] of in situ generated sugar-derived imines as well as allylation of *gluco*-oxycarbenium ion.[25b,c,f]

The same stereochemical outcome was observed in the case of isocyanide addition to *galacto*-imine obtained from lactam **2**. The same course of addition has been observed previously in the case of C-allylation of the same imine.[23] However, this stands in opposition to the result of the reaction of *galacto*-imine with Danishefsky's diene that led to the formation of 2,3-*trans* products predominantly.[20] This result again confirms our conclusion that the stereochemical outcome of nucleophilic addition to cyclic imines is governed not only by the imine's structure but also by the structure of the nucleophile.

The addition of isocyanides to D-*arabino*-imine obtained from lactam **3** resulted in the formation of 2,3-*trans*-substituted piperidine derivatives as the major products (**15**−**17**). The observed stereochemical course of the addition is similar to the outcome observed for the addition of Danishefsky's diene to the same imine[20] but is opposite to the result of its *C*-allylation with allyltributylstannane.[23] This result again confirms our previous assumptions that the course of the addition to cyclic imines is ruled not only by stereoelectronic and steric factors resulting from the structure of the imine but depends also on the structure of the nucleophile.[20]

CONCLUSIONS

In conclusion, an attractive method for the formation of polyhydroxylated piperidine and pyrrolidine peptidomimetic scaffolds was developed. The presented strategy is based on the one-pot, sugar-derived lactam reduction/Joullié−Ugi reaction. The key advantage of the presented approach is the simplicity and convenience of generation of sugar-derived imines from readily available starting materials: sugar-derived lactams. As demonstrated, the developed strategy enables not only the synthesis of proline amides but also pipecolic acid amides. The use of sugar-derived lactams as cyclic imine precursors is crucial to the efficiency of the described synthetic method. These compounds are more readily prepared, handled, and stored

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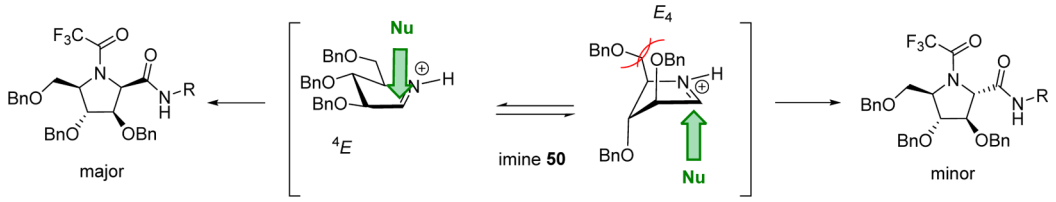
Scheme 3



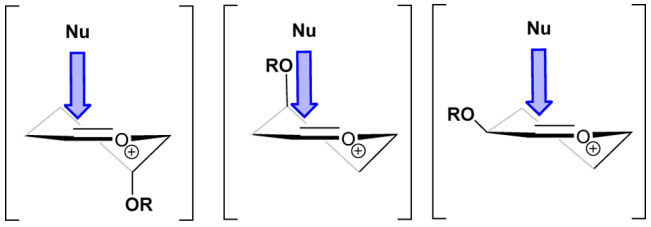
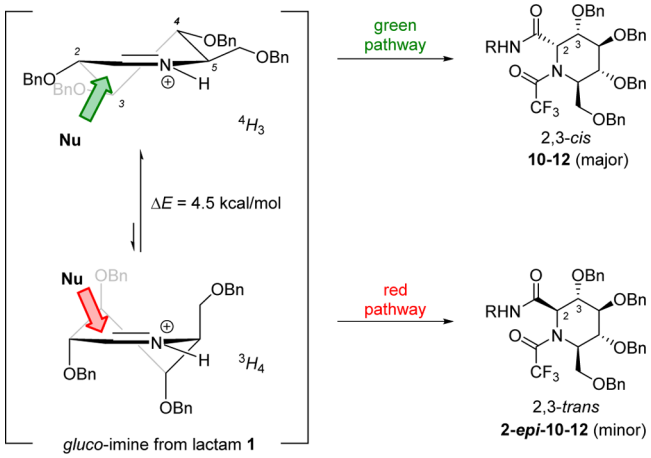


Figure 7. Stereochemical course of nucleophilic addition to pyranosyl oxycarbenium ions according to Woerpel's model.[23]

Scheme 4



than the alternative precursors of cyclic imines such as nitrones, *N*-chloroamines, or azido aldehydes. As demonstrated, there is no need to isolate the imines generated in situ as they can be directly used in the subsequent reaction with isocyanide and carboxylic acid.

EXPERIMENTAL SECTION

General Procedure for One-Pot Lactam Reduction/Ugi–Joullié Reaction. A solution of lactam (0.5 mmol) in THF (5 mL) was added to a solution of $Cp_2Zr(H)Cl$ (Schwartz's reagent; 1.6 equiv, 206 mg, 0.8 mmol) in THF (5 mL). The initially formed white suspension disappeared during the reaction progress; formation of a clear solution indicated the end of the reaction (ca. 1.5 h, TLC monitoring). The solution was then cooled to −78 °C, trifluoroacetic acid (4.0 equiv, 2.0 mmol, 228 mg, 155 μL) and isocyanide (1.25 equiv., 0.625 mmol) were successively added, and the reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched with saturated aqueous $NaHCO_3$ (5 mL) and diluted with Et_2O (5 mL). The organic layer was separated, and the aqueous layer was washed with Et_2O (3 × 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and the solvent was removed. The residue was purified by chromatography on silica gel to give the corresponding product. In cases when the isomeric products could not be separated by column chromatography, the crude mixture of trifluoroacetates was submitted directly to the next step.

(2S,3S,4S,5R,6R)-3,4,5-Tris(benzyloxy)-6-[(benzyloxy)methyl]]-N-tert-butyl-1-(2,2,2 trifluoroacetyl)piperidine-2-carboxamide ***(10):*** mixture of rotamers; colorless oil; isolated yield 173 mg (69%) starting from 187 mg (0.35 mmol) of compound **1**; dr > 95:5 (determined by ^{1}H NMR of crude reaction mixture after hydrolysis); TLC R_f 0.74 (2:3 AcOEt/hexanes); flash column chromatography (1:9 AcOEt/hexanes); $[\alpha]_D^{23}$ −11.1 (*c* 0.43, $CHCl_3$); ^{1}H NMR (600 MHz, toluene, 75 °C, mixture of rotamers) δ: 7.22−7.18 (m, 2H), 7.15−6.95 (m, 18H), 6.73 (s, 1H), 4.73 (d, *J* 6.0 Hz, 1H), 4.62 (dd, *J* 13.9, 6.9 Hz, 1H), 4.57 (d, *J* 11.5 Hz, 1H), 4.49−4.44 (m, 1H), 4.33−4.18 (m, 7H), 4.15−4.07 (m, 1H), 4.00 (d, *J* 6.8 Hz, 1H), 3.78 (d, *J* 5.9 Hz, 1H), 3.74−3.70 (m, 1H), 1.18 (s, 9H); ^{13}C NMR (151 MHz, toluene, 75 °C) δ 165.1, 158.4 (d, *J* 36.1 Hz), 137.9, 137.7 (2×), 137.6, 128.6−127.2 (aromatic overlap), 116.5 (q, *J* 290.0 Hz), 78.6, 76.7, 76.2, 73.9, 73.3, 71.6, 70.9, 67.8, 59.3, 56.1, 50.8, 28.3; HRMS (ESI-TOF) *m*/*z* calcd for $C_{41}H_{45}N_2O_6NaF_3$ [M + Na^+] 741.3127, found 741.3115; IR (film) ν 3369, 3032, 2965, 2927, 2869, 1708, 1680, 1534, 1454, 1200, 1149, 1091, 1074, 738, 698 cm^{-1}.

(2S,3S,4S,5R,6R)-3,4,5-Tris(benzyloxy)-6-[(benzyloxy)methyl]]-N-cyclohexyl-1-(2,2,2-trifluoroacetyl)piperidine-2-carboxamide ***(11:).*** mixture of rotamers; colorless oil; isolated yield 180 mg (74%) starting from 176 mg (0.33 mmol) of compound **1**; dr > 95:5 (determined by ^{1}H NMR of crude reaction mixture after hydrolysis); TLC R_f 0.72 (2:3 AcOEt/hexanes); flash column chromatography (1:9 AcOEt/hexanes); $[\alpha]_D^{23}$ −5.9 (*c* 0.42, $CHCl_3$); ^{1}H NMR (600 MHz, toluene, 75 °C) δ 7.23−7.19 (m, 2H), 7.16−6.96 (m, 18H), 6.78 (d, *J* 7.6 Hz, 1H), 4.84 (d, *J* 6.1 Hz, 1H), 4.66−4.59 (m, 2H), 4.50−4.44 (m, 1H), 4.36−4.21 (m, 6H), 4.19 (d, *J* 11.5 Hz, 1H), 4.03 (d, *J* 6.9 Hz, 1H), 3.80 (d, *J* 6.1 Hz, 1H), 3.79−3.72 (m, 3H), 1.71−1.65 (m, 1H), 1.64−1.58 (m, 1H), 1.43−1.34 (m, 2H), 1.33−1.24 (m, 1H), 1.13−1.01 (m, 2H), 0.93−0.71 (m, 3H); ^{13}C NMR (151 MHz, toluene, 75 °C) δ 164.9, 158.4 (d, *J* 35.8 Hz), 138.0, 137.66, 137.65, 137.6, 128.6−127.2 (aromatic overlap), 116.5 (q, *J* 289.5 Hz), 78.5, 76.7, 76.3, 73.9, 73.4, 71.7, 71.0, 68.0, 59.1, 56.2, 48.0, 32.5, 32.3, 25.3, 24.5, 24.4; HRMS (ESI-TOF) *m*/*z* calcd for $C_{43}H_{47}N_2O_6NaF_3$ [M + Na^+] 767.3284, found 767.3265; IR (film) ν 3364, 3031, 2930, 2855, 1705, 1676, 1534, 1454, 1202, 1149, 1092, 1075, 737, 698 cm^{-1}.

(2S,3S,4S,5R,6R)-3,4,5-Tris(benzyloxy)-6-[(benzyloxy)methyl]]-N-(4-methoxyphenyl)-1-(2,2,2-trifluoroacetyl)piperidine-2-carboxamide ***(12):*** mixture of rotamers; coloress oil; isolated yield 175 mg (86%) starting from 142 mg (0.26 mmol) of compound **1**; TLC R_f 0.38 (1:4 AcOEt/hexanes); flash column chromatography (1:9 than 1:4 AcOEt/hexanes); $[\alpha]_D^{23}$ −4.7 (*c* 0.19, $CHCl_3$); ^{1}H NMR (600 MHz, PhMe-d_7, at 75 °C) δ 8.71 (s, 1H), 7.32−7.25 (m, 2H), 7.20−6.95 (m, 20H), 6.60−6.56 (m, 2H), 4.96 (d, *J* 6.2 Hz, 1H), 4.74 (dd, *J* 13.4, 6.8 Hz, 1H), 4.61 (d, *J* 11.5 Hz, 1H), 4.49 (d, *J* 11.4 Hz, 1H), 4.32 (d, *J* 11.4 Hz, 1H), 4.30−4.23 (m, 5H), 4.18 (d, *J* 11.5 Hz, 1H), 4.14−4.03 (m, 2H), 3.84 (d, *J* 6.1 Hz, 1H), 3.77−3.70 (m, 1H), 3.35 (s, 3H); ^{13}C NMR (151 MHz, PhMe-d_7, at 75 °C) δ 164.0, 158.5 (d, *J* 36.2 Hz), 156.5, 138.0−136.7 (aromatic overlap), 131.6, 128.7−127.2 (aromatic overlap), 121.2, 116.5 (q, *J* 289.2 Hz), 114.0, 79.1, 77.1, 75.9, 74.0, 73.4, 71.9, 71.0, 67.9, 59.1, 55.9, 54.5; HRMS (ESI-TOF) *m*/*z* calcd for $C_{44}H_{43}N_2O_7NaF_3$ [M + Na^+] 791.2920, found 791.2914; IR (film) ν 3334, 3031, 2931, 2869, 2837, 1705, 1687, 1538, 1511, 1454, 1245, 1202, 1148, 1089, 1074, 1030, 738, 698 cm^{-1}.

(3S,4S,5S,6R)-3,4,5-Tris(benzyloxy)-6-[(benzyloxy)methyl]]-N-tert-butyl-1-(2,2,2-trifluoroacetyl)piperidine-2-carboxamide ***(13/2-epi-13):*** mixture of rotamers 4:1 and diastereoisomers; colorless oil; isolated yield 161 mg (63%) starting from 191 mg (0.36 mmol) of compound **2**; dr 86:14 (determined by ^{1}H NMR of crude reaction mixture after

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hydrolysis); TLC R_f 0.75 (1:2 AcOEt/hexanes); HRMS (ESI-TOF) m/z calcd for $C_{41}H_{45}N_2O_6NaF_3$ [M + Na^+] 741.3127, found 741.3107. Products were not isolated but directly submitted to the hydrolysis step.

*(3S,4S,5S,6R)-3,4,5-Tris(benzyloxy)-6-[(benzyloxy)methyl)]-N-cyclohexyl-1-(2,2,2-trifluoroacetyl)piperidine-2-carboxamide (**14/2-epi-14**):* mixture of rotamers and diastereoisomers; colorless oil; isolated yield 147 mg (67%) starting from 158 mg (0.29 mmol) of compound **2**; dr 82:18 (determined by ^{1}H NMR of crude reaction mixture after hydrolysis); TLC R_f 0.74 (1:2 AcOEt/hexanes); HRMS (ESI-TOF) m/z calcd for $C_{43}H_{47}N_2O_6NaF_3$ [M + Na^+] 767.3284, found 767.3257. Products were not isolated but directly submitted to the hydrolysis step.

*(3R,4R,5R)-3,4,5-Tris(benzyloxy)-N-tert-butyl-1-(2,2,2-trifluoroacetyl)piperidine-2-carboxamide (**15/2-epi-15**):* mixture of rotamers 2.5:1 and diastereoisomers; colorless oil; isolated yield 132 mg (76%) starting from 121 mg (0.29 mmol) of compound **3**; dr 75:25 (determined by ^{1}H NMR of crude reaction mixture after hydrolysis); TLC R_f 0.85 (1:2 AcOEt/hexanes); HRMS (ESI-TOF) m/z calcd for $C_{33}H_{37}N_2O_5NaF_3$ [M + Na^+] 621.2552, found 621.2544. Products were not isolated but directly submitted to the hydrolysis step.

*(2S,3R,4R,5R)-3,4,5-Tris(benzyloxy)-N-cyclohexyl-1-(2,2,2-trifluoroacetyl)piperidine-2-carboxamide (**16/2-epi-16**:).* mixture of rotamers and diastereoisomers; colorless oil; isolated yield 161 mg (84%) starting from 128 mg (0.31 mmol) of compound **3**; dr 80:20 (determined by ^{1}H NMR of crude reaction mixture after hydrolysis); TLC R_f 0.85 (1:2 AcOEt/hexanes); HRMS (ESI-TOF) m/z calcd for $C_{35}H_{39}N_2O_5NaF_3$ [M + Na^+] 647.2709, found 647.2708. Products were not isolated but directly submitted to the hydrolysis step.

*(2S,3R,4R,5R)-3,4,5-Tris(benzyloxy)-N-(4-methoxyphenyl)-1-(2,2,2-trifluoroacetyl)piperidine-2-carboxamide (**17**):* mixture of rotamers; colorless oil; isolated yield 78 mg (40%) starting from 125 mg (0.30 mmol) of compound **3**; TLC R_f 0.42 (1:4 hexanes/AcOEt); column chromatography (1:9 AcOEt/hexanes); $[\alpha]_D^{23}$ −65.3 (c 0.34, $CHCl_3$); ^{1}H NMR (600 MHz, pyridine-d_5) δ 11.36 (s, 1H), 7.84−7.80 (m, 2H), 7.56−7.53 (m, 2H), 7.50−7.43 (m, 4H), 7.37−7.23 (m, 9H), 6.96−6.92 (m, 2H), 6.04 (d, J 6.9 Hz, 1H), 4.97 (d, J 11.6 Hz, 2H), 4.92 (d, J 11.6 Hz, 2H), 4.87 (s, 2H), 4.78−4.71 (m, 3H), 4.58 (dd, J 10.0, 6.9 Hz, 1H), 4.50 (d, J 13.6 Hz, 1H), 4.36 (d, J 14.1 Hz, 1H), 4.26 (s, 1H), 3.60 (s, 3H); ^{13}C NMR (151 MHz, pyridine-d_5) δ 168.1, 158.9 (d, J 35.5 Hz), 158.1, 140.6, 140.2, 140.1, 133.7, 130.1−128.8 (aromatic overlap), 123.6, 118.5 (q, J 288.2 Hz), 115.7, 80.8, 76.5, 75.4, 74.6, 74.1, 74.0, 58.4, 56.5, 47.8; HRMS (ESI-TOF) m/z calcd for $C_{36}H_{35}N_2O_6NaF_3$ [M + Na^+] 671.2345, found 671.2344; IR (film) ν 3438, 2935, 1677, 1511, 1455, 1203, 1097, 1027, 735, 698 cm^{-1}.

*(2S,3R,4R,5R)-3,4,5-Tris(benzyloxy)-N-(4-methoxyphenyl)-1-(2,2,2-trifluoroacetyl)piperidine-2-carboxamide (**2-epi-17**):* mixture of rotamers (1:0.7); colorless oil; isolated yield 54 mg (28%) starting from 125 mg (0.30 mmol) of compound **3**; TLC R_f 0.38 (1:4 AcOEt/hexanes); column chromatography (1:9 AcOEt/hexanes); $[\alpha]_D^{23}$ −38.3 (c 0.21, $CHCl_3$); ^{1}H NMR (600 MHz, pyridine-d_5) δ 10.04 (s, 0.7H), 10.00* (s, 1H), 6.89−6.83* (m, 3.4H), 6.80−6.45* (m, 25.5H), 6.16−6.09* (m, 3.4H), 5.27* (s, 1H), 4.47 (s, 0.7H), 4.42−4.39 (m, 0.7H), 4.32−4.29* (m, 1H), 4.23−4.11* (m, 3.4H), 4.07* (d, J 12.0 Hz, 1H), 3.96−3.77* (m, 6.5H), 3.72* (d, J 11.4 Hz, 1H), 3.63−3.59* (m, 1H), 3.56 (d, J 3.4 Hz, 0.7H), 3.52* (ddd, J 11.3, 4.5, 2.4 Hz, 1H), 3.47−3.42 (m, 0.7H), 3.41−3.39* (m, 1.7H), 2.83 (s, 2.1H), 2.82* (s, 3H); *major rotamer; ^{13}C NMR** (151 MHz, pyridine-d_5) δ 166.7, 158.4, 158.0, 140.13, 140.08, 140.04, 140.01, 139.44, 139.42, 133.5, 133.2, 130.2−129.1 (aromatic overlap), 125.3, 124.7, 116.6 (q, J 269.9 Hz), 115.6, 115.5, 78.2, 77.7, 75.8, 75.5, 74.6, 74.4, 74.3, 73.6, 73.5, 73.3, 72.6, 72.4, 61.1, 58.2, 56.54, 56.52, 44.1, 41.4; **both rotamers; HRMS (ESI-TOF) m/z calcd for $C_{36}H_{35}N_2O_6NaF_3$ [M + Na^+] 671.2345, found 671.2339; IR (film) ν 3320, 3032, 2933, 2870, 1698, 1512, 1455, 1200, 1145, 1029, 738, 698 cm^{-1}.

*(2S,3S,4R,5R)-3,4-Bis(benzyloxy)-5-[(benzyloxy)methyl)]-N-tert-butyl-1-(2,2,2-trifluoroacetyl)pyrrolidine-2-carboxamide (**18**):* mixture of rotamers 5:1; colorless oil; isolated yield 116 mg (60%) starting from 135 mg (0.32 mmol) of compound **4**; TLC R_f 0.53 (1:4 AcOEt/hexanes); flash column chromatography (12% AcOEt in hexanes); $[\alpha]_D^{23}$ +3.9 (c 2.6, $CHCl_3$); major rotamer ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.23 (m, 13H), 7.23−7.17 (m, 2H), 6.39 (s, 1H), 4.66−4.49 (m, 7H), 4.46−4.42 (m, 2H), 4.05 (d, J 4.1 Hz, 1H), 3.69 (dd, J 10.2, 4.7 Hz, 1H), 3.55 (dd, J 10.2, 2.6 Hz, 1H), 1.11 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 137.6, 137.3, 136.9, 128.51, 128.49, 128.38, 128.2, 128.1, 128.0, 127.9, 127.5, 78.9, 76.5, 73.5, 72.8, 72.1, 67.0, 64.0, 51.2, 28.2; HRMS (ESI-TOF) m/z calcd for $C_{33}H_{37}N_2O_5NaF_3$ [M + Na^+] 621.2552, found 621.2540; IR (film) ν 3376, 3063, 3032, 2965, 2921, 2868, 1691, 1514, 1453, 1363, 1197, 1145, 1023, 958, 738, 699 cm^{-1}.

*(2R,3S,4R,5R)-3,4-Bis(benzyloxy)-5-[(benzyloxy)methyl)]-N-tert-butyl-1-(2,2,2-trifluoroacetyl)pyrrolidine-2-carboxamide (**2-epi-18**):* mixture of rotamers; colorless oil; isolated yield 23 mg (12%) starting from 135 mg (0.32 mmol) of compound **4**; TLC R_f 0.56 (1:4 AcOEt/hexanes); flash column chromatography (10% AcOEt in hexanes); $[\alpha]_D^{23}$ −7.1 (c 0.5, $CHCl_3$); major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 1H), 4.61−4.58 (m, 2H), 4.54−4.50 (m, 2H), 4.43−4.40 (m, 2H), 4.29 (s, 1H), 4.27−4.21 (m, 1H), 4.12−4.08 (m, 1H), 3.82−3.75 (m, 1H), 3.55 (dd, J 10.1, 2.5 Hz, 1H), 1.26 (s, 1H); HRMS (ESI-TOF) m/z calcd for $C_{33}H_{37}N_2O_5NaF_3$ [M + Na^+] 621.2552, found 621.2552; IR (film) ν 3335, 3064, 2926, 28671694, 1454, 1204, 1146, 1027, 737, 698 cm^{-1}.

*(2S,3S,4R,5R)-3,4-Bis(benzyloxy)-5-[(benzyloxy)methyl)]-N-cyclohexyl-1-(2,2,2-trifluoroacetyl)pyrrolidine-2-carboxamide (**19**:).* mixture of rotamers 3:1; colorless oil; isolated yield 143 mg (63%) starting from 152 mg (0.36 mmol) of compound **4**; dr > 95:5 (determined by ^{1}H NMR of crude reaction mixture after hydrolysis); TLC R_f 0.78 (1:4 AcOEt/hexanes); flash column chromatography (12% AcOEt in hexanes); $[\alpha]_D^{23}$ −9.4 (c 4.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.14 (m, 15H), 4.76−4.72 (m, 1H), 4.67−4.54 (m, 4H), 4.53−4.48 (m, 2H), 4.45−4.40 (m, 2H), 4.03 (d, J 4.2 Hz, 1H), 3.69 (dd, J 10.2, 4.7 Hz, 2H), 3.67−3.62 (m, 1H), 3.55 (dd, J 10.2, 2.6 Hz, 1H), 1.70−1.57 (m, 2H), 1.53−1.41 (m, 3H), 1.28−1.13 (m, 2H), 1.05−0.95 (m, 1H), 0.91−0.78 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 137.5, 137.1, 136.8, 128.5, 128.5, 128.4, 128.2, 128.0, 127.5, 78.8, 76.3, 73.4, 72.9, 71.9, 66.9, 63.9, 61.81, 61.79, 48.5, 32.3, 32.2, 25.5, 24.4; HRMS (ESI-TOF) m/z calcd for $C_{35}H_{39}N_2O_5NaF_3$ [M + Na^+] 647.2709, found 647.2703; IR (film) ν 3361, 2930, 2855, 1686, 1538, 1452, 1198, 1146, 735, 698 cm^{-1}.

*(2R,3R,4R,5R)-3,4-Bis(benzyloxy)-5-[(benzyloxy)methyl)]-N-tert-butyl-1-(2,2,2-trifluoroacetyl)pyrrolidine-2-carboxamide (**20**):* mixture of rotamers and diastereoisomers; colorless oil; isolated yield 149 mg (83%) starting from 125 mg (0.30 mmol) of compound **5**; dr 57:43 (determined by ^{1}H NMR of crude reaction mixture after hydrolysis); TLC R_f 0.55 (1:4 AcOEt/hexanes); HRMS (ESI-TOF) m/z calcd for $C_{33}H_{37}N_2O_5NaF_3$ [M + Na^+] 621.2552, found 621.2543, found 647.2708. Products were not isolated but directly submitted to the hydrolysis step.

*(2R,3R,4R,5R)-3,4-Bis(benzyloxy)-5-[(benzyloxy)methyl)]-N-cyclohexyl-1-(2,2,2-trifluoroacetyl)pyrrolidine-2-carboxamide (**21**:).* mixture of rotamers and diastereoisomers; colorless oil; isolated yield 135 mg (75%) starting from 120 mg (0.29 mmol) of compound **5**; dr > 63:37 (determined by ^{1}H NMR of crude reaction mixture after hydrolysis); TLC R_f 0.55 (1:4 AcOEt/hexanes); HRMS (ESI-TOF) m/z calcd for $C_{35}H_{39}N_2O_5NaF_3$ [M + Na^+] 647.2709, found 647.2706. Products were not isolated but directly submitted to the hydrolysis step.

*(2S,3R,4R)-3,4-Bis(benzyloxy)-N-tert-butyl-1-(2,2,2-trifluoroacetyl)-pyrrolidine-2-carboxamide (**22**):* mixture of rotamers 3:1; colorless oil; isolated yield 95 mg (38%) starting from 156 mg (0.52 mmol) of compound **6**; TLC R_f 0.72 (1:2 AcOEt/hexanes); flash column chromatography (18% AcOEt in hexanes); $[\alpha]_D^{23}$ +29.8 (c 2.7, $CHCl_3$); major rotamer: ^{1}H NMR (500 MHz, pyridine-d_5) δ 7.79−7.62 (m, 1H), 5.35−4.89 (m, 7H), 4.68 (dd, J 10.2, 5.8 Hz, 1H), 4.52 (dd, J 10.3, 6.1 Hz, 1H), 4.29 (dd, J 11.1, 5.6 Hz, 1H), 1.71 (s, 9H); major rotamer: ^{13}C NMR (126 MHz, pyridine-d_5) δ 168.0, 138.3, 138.3, 128.9, 128.4, 128.4, 84.0, 81.3, 72.5, 72.3, 67.2, 51.5, 28.7; HRMS (ESI-TOF) m/z calcd for $C_{25}H_{29}N_2O_4NaF_3$ [M + Na^+] 501.1977, found 501.1969; IR (film) ν 3333, 3064, 3030, 2968, 2929, 2873, 1697, 1531, 1455, 1365, 1207, 1207, 1179, 1146, 1098, 739, 698 cm^{-1}.

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*(2R,3R,4R)-3,4-Bis(benzyloxy)-N-tert-butyl-1-(2,2,2-trifluoroacetyl)-pyrrolidine-2-carboxamide (**2-epi-22**):* mixture of rotamers; colorless oil; isolated yield 55 mg (22%) starting from 156 mg (0.52 mmol) of compound **6**; TLC R_f 0.68 (1:2 AcOEt/hexanes); flash column chromatography (21% AcOEt in hexanes); $[\alpha]_D^{23}$ +3.2 (*c* 1.2, $CHCl_3$); major rotamer ^{1}H NMR (500 MHz, pyridine-d_5) δ 6.14−6.10 (m, 2H), 6.00−5.94 (m, 2H), 5.93−5.83 (m, 6H), 3.77 (d, *J* 7.1 Hz, 1H), 3.51 (d, *J* 11.9 Hz, 1H), 3.41 (d, *J* 11.8 Hz, 1H), 3.30 (dd, *J* 11.2, 5.4 Hz, 1H), 3.19 (d, *J* 11.8 Hz, 1H), 3.13 (d, *J* 11.8 Hz, 1H), 3.00 (dd, *J* 7.1, 5.5 Hz, 1H), 2.86 (dd, *J* 11.2, 6.1 Hz, 1H), 2.33 (dd, *J* 10.8, 4.4 Hz, 1H), 0.00 (s, 9H); major rotamer ^{13}C NMR (126 MHz, pyridine-d_5) δ 164.9, 137.1, 137.0, 127.4, 127.3, 126.75, 126.6, 79.6, 78.8, 71.7, 70.9, 62.2, 50.1, 27.4; HRMS (ESI-TOF) *m*/*z* calcd for $C_{25}H_{29}N_2O_4NaF_3$ [M + Na$^+$] 501.1977, found 501.1974; IR (film) ν 3322, 2969, 2929, 2870, 1690, 1551, 1455, 1147, 1105, 738, 698 cm^{-1}.

*(2S,3R,4R)-3,4-Bis(benzyloxy)-N-cyclohexyl-1-(2,2,2-trifluoroacetyl)-pyrrolidine-2-carboxamide (**23**:).* mixture of rotamers 2:1; white crystals; mp 143−144 °C; isolated yield 89 mg (34%) starting from 155 mg (0.52 mmol) of compound **6**; TLC R_f 0.80 (1:2 AcOEt/hexanes); flash column chromatography (15% AcOEt in hexanes); $[\alpha]_D^{23}$ +29.5 (*c* 2.8, $CHCl_3$); major rotamer ^{1}H NMR (500 MHz, pyridine-d_5) δ 6.67−6.45 (m, 10H), 4.20 (d, *J* 3.1 Hz, 1H), 4.08 (s, 1H), 3.98 (d, *J* 6.1 Hz, 1H), 3.95 (t, *J* 3.5 Hz, 1H), 3.91−3.88 (m, 1H), 3.80 (d, *J* 11.5 Hz, 1H), 3.55 (dd, *J* 9.5, 5.0 Hz, 1H), 3.38 (dd, *J* 11.0, 5.8 Hz, 1H), 3.21−3.12 (m, 3H), 1.15−1.08 (m, 1H), 1.02 (d, *J* 10.4 Hz, 1H), 0.74−0.60 (m, 2H), 0.58−0.49 (m, 1H), 0.37−0.17 (m, 4H), 0.08−0.04 (m, 1H); major rotamer ^{13}C NMR (126 MHz, pyridine-d_5) δ 166.0, 136.8, 127.41, 127.39, 127.0, 126.82, 126.80, 82.3, 79.7, 70.9, 70.7, 65.7, 47.6, 31.6, 31.5, 24.3, 23.9, 23.9; HRMS (ESI-TOF) *m*/*z* calcd for $C_{27}H_{31}N_2O_4NaF_3$ [M + Na$^+$] 527.2134, found 527.2123; IR (film) ν 3285, 2931, 2854, 1700, 1659, 1591, 1453, 1145, 732, 696 cm^{-1}.

*(2R,3R,4R)-3,4-Bis(benzyloxy)-N-cyclohexyl-1-(2,2,2-trifluoroacetyl)-pyrrolidine-2-carboxamide (**2-epi-23**):* mixture of rotamers 2:1; white crystal; mp 128−129 °C; isolated yield 68 mg (26%) starting from 155 mg (0.52 mmol) of compound **6**; TLC R_f 0.73 (1:2 AcOEt/hexanes); flash column chromatography (19% AcOEt in hexanes); $[\alpha]_D^{23}$ +13.9 (*c* 2.4, $CHCl_3$); major rotamer ^{1}H NMR (500 MHz, pyridine-d_5) δ 7.57−7.50 (m, 2H), 7.43−7.26 (m, 8H), 5.22 (d, *J* 7.0 Hz, 1H), 5.00−4.93 (m, 1H), 4.85 (d, *J* 11.9 Hz, 1H), 4.77 (dd, *J* 10.8, 5.3 Hz, 1H), 4.66 (d, *J* 11.8 Hz, 1H), 4.61 (d, *J* 11.8 Hz, 1H), 4.49 (dd, *J* 6.9, 5.3 Hz, 1H), 4.32 (dd, *J* 11.4, 5.9 Hz, 1H), 4.11−4.02 (m, 1H), 3.80 (dd, *J* 11.3, 4.5 Hz, 1H), 2.06−1.94 (m, 1H), 1.60−1.45 (m, 2H), 1.43−1.33 (m, 1H), 1.32−1.06 (m, 4H), 0.98−0.86 (m, 1H); major rotamer ^{13}C NMR (126 MHz, pyridine-d_5) δ 164.7, 137.1, 137.0, 127.4, 126.7, 126.6, 79.5, 78.7, 71.7, 70.8, 62.2, 47.6, 31.9, 31.9, 24.3, 23.9, 23.9; HRMS (ESI-TOF) *m*/*z* calcd for $C_{27}H_{31}N_2O_4NaF_3$ [M + Na$^+$] 527.2134., found 527.2128; IR (film) ν 3292, 3064, 3032, 2932, 2856, 1698, 1660, 1551, 1453, 1181, 1146, 1103, 737, 698 cm^{-1}.

*(2R,3S,4S)-3,4-Bis(benzyloxy)-N-(4-methoxyphenyl)-1-(2,2,2-trifluoroacetyl)pyrrolidine-2-carboxamide (**24**):* mixture of rotamers; white crystals; mp 139−140 °C; isolated yield 105 mg (38%) starting from 156 mg (0.52 mmol) of compound **6**; TLC R_f 0.71 (2:3 AcOEt/hexanes); flash column chromatography (1:9 AcOEt/hexanes); $[\alpha]_D^{23}$ +49.6 (*c* 0.19, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.8 (s, 1H), 7.39−7.32 (m, 5H), 7.30−7.25 (m, 3H), 7.23−7.19 (m, 2H), 7.17−7.13 (m, 2H), 6.79−6.74 (m, 2H), 4.77 (s, 1H), 4.72 (d, *J* 11.8 Hz, 1H), 4.63−4.56 (m, 3H), 4.43 (d, *J* 11.2 Hz, 1H), 4.16−4.14 (m, 1H), 4.03 (dd, *J* 11.5, 4.3 Hz, 1H), 3.96 (d, *J* 11.3 Hz, 1H), 3.77 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.1, 157.5 (d, *J* 37.8 Hz), 156.6, 136.7, 136.4, 130.1, 128.7, 128.6, 128.28, 128.27, 128.2, 128.0, 122.0, 116.0 (q, *J* 287.4 Hz), 114.0, 80.7, 80.3, 72.0, 71.8, 67.7, 55.5, 52.1; HRMS (ESI-TOF) *m*/*z* calcd for $C_{28}H_{27}N_2O_5NaF_3$ [M + Na$^+$] 551.1770, found 551.1761; IR (film, CH_2Cl_2) ν 3299, 3032, 2910, 2836, 1703, 1673, 1512, 1455, 1238, 1147, 1030, 733, 697 cm^{-1}.

*(2S,3S,4S)-3,4-Bis(benzyloxy)-N-(4-methoxyphenyl)-1-(2,2,2-trifluoroacetyl)pyrrolidine-2-carboxamide (**2-epi-24**).* mixture of rotamers; white crystals; mp 116−117 °C; isolated yield 71 mg (26%) starting from 156 mg (0.52 mmol) of compound **6**; TLC R_f 0.60 (2:3 AcOEt/hexanes); Column chromatography (3:7 AcOEt/hexanes); $[\alpha]_D^{23}$ +15.9 (*c* 0.63, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.4 (s, 1H), 7.39−7.22 (m, 12H), 6.80−6.76 (m, 2H), 4.74−4.71 (m, 1H), 4.67 (d, *J* 11.9 Hz, 1H), 4.63−4.56 (m, 2H), 4.52 (d, *J* 11.9 Hz, 1H), 4.35 (dd, *J* 9.7, 4.5 Hz, 1H), 4.32−4.29 (m, 1H), 4.08 (dd, *J* 11.3, 5.5 Hz, 1H), 3.77 (s, 3H), 3.75−3.72 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 160.0 (d, *J* 37.8 Hz), 159.3, 139.7, 139.6, 132.8, 131.3, 131.2, 130.90, 130.85, 130.7, 130.4, 124.7, 118.6 (q, *J* 287.6 Hz), 116.7, 82.8, 82.1, 76.1, 75.0, 66.7, 58.1, 53.2; HRMS (ESI-TOF) *m*/*z* calcd for $C_{28}H_{27}N_2O_5NaF_3$ [M + Na$^+$] 551.1770, found 551.1762; IR (film, CH_2Cl_2) ν 3278, 3033, 2935, 2838, 1693, 1512, 1454, 1243, 1146, 1031, 740, 699 cm^{-1}.

*(2S,3S,4R)-3,4-Bis(benzyloxy)-N-tert-butyl-1-(2,2,2-trifluoroacetyl)-pyrrolidine-2-carboxamide (**25**:).* mixture of rotamers; yellowish oil; isolated yield 60%; R_f 0.3 (3:2 hexanes/AcOEt); HRMS (ESI-TOF) *m*/*z* calcd for $C_{25}H_{29}N_2O_4NaF_3$ [M + Na$^+$] 501.1977, found 501.1979. Products were not isolated but used directly in the hydrolysis step.

*(2S,3S,4R)-3,4-Bis(benzyloxy)-N-(4-methoxyphenyl)-1-(2,2,2-trifluoroacetyl)pyrrolidine-2-carboxamide (**26**:).* mixture of two rotamers; colorless oil; isolated yield 68%; TLC R_f 0.28 (3:2 hexanes/AcOEt); HRMS (ESI-TOF) *m*/*z* calcd for $C_{28}H_{27}N_2O_5NaF_3$ [M + Na$^+$] 551.1770, found 551.1775. Products were not isolated but used directly in the hydrolysis step.

*(2R,4R)-4-(Benzyloxy)-N-tert-butyl-1-(2,2,2-trifluoroacetyl)-pyrrolidine-2-carboxamide (**27**).* mixture of rotamers and diastereosiomers; colorless oil; isolated yield 165 mg (58%) starting from 146 mg (0.76 mmol) of compound **8**; dr 77:23 (determined by ^{1}H NMR of crude reaction mixture after hydrolysis); TLC R_f 0.3 (2:3 AcOEt/hexanes); HRMS (ESI-TOF) *m*/*z* calcd for $C_{18}H_{23}N_2O_3NaF_3$ [M + Na$^+$]: 395.1558; found 395.1555; Products were not isolated but used directly in the hydrolysis step.

*(2R,4R)-4-(Benzyloxy)-N-cyclohexyl-1-(2,2,2-trifluoroacetyl)-pyrrolidine-2-carboxamide (**28**):* mixture of rotamers; colorless crystals; mp 115−116 °C; isolated yield 162 mg (54%) starting from 144 mg (0.75 mmol) of compound **8**; dr 74:26 (determined by ^{1}H NMR of crude reaction mixture after hydrolysis); TLC R_f 0.26 (2:3 AcOEt/hexanes); column chromatography (1:4 than 3:7 AcOEt/hexanes); $[\alpha]_D^{23}$ −37.0 (*c* 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.26 (m, 6.75H), 6.02* (d, *J* 6.9 Hz, 1H), 5.76 (d, *J* 8.0 Hz, 0.35H), 4.66 (d, *J* 9.4 Hz, 0.35H), 4.60−4.54* (m, 2H), 4.50 (d, *J* 11.4 Hz, 0.35H), 4.44−4.38* (m, 1.35H), 4.25−4.21* (m, 1H), 4.20−4.17 (m, 0.35H), 3.91−3.78* (m, 2.7H), 3.70−3.58* (m, 1.35H), 2.74 (d, *J* 14.1 Hz, 0.35H), 2.67* (d, *J* 14.0 Hz, 1H), 2.32−2.22 (m, 0.35H), 2.17* (ddd, *J* 14.1, 9.7, 4.7 Hz, 1H), 1.96−1.89 (m, 0.35H), 1.84−1.76* (m, 1H), 1.74−1.68 (m, 0.35H), 1.68−1.57* (m, 2H), 1.57−1.49* (m, 2H), 1.48−1.38 (m, 0.7H), 1.35−1.14* (m, 3.05H), 1.13−0.93* (m, 2.7H), 0.93−0.83* (m, 1H), 0.76 (ddd, *J* 15.0, 11.7, 3.0 Hz, 0.35H); * major rotamer ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.2, 168.2*, 157.2 (d, *J* 37.4 Hz), 156.7* (d, *J* 37.5 Hz), 136.91*, 136.85, 128.5−128.0 (aromatic overlap), 116.3* (q, *J* 286.6 Hz), 115.5 (q, *J* 288.0 Hz), 76.6*, 74.2, 71.0*, 70.8, 61.4*, 60.8, 55.4, 53.4*, 48.5, 48.2*, 36.5, 32.60, 32.55*, 32.5*, 32.3*, 32.1, 25.4*, 25.3, 24.79, 24.75, 24.5* (2×); * major rotamer; HRMS (ESI-TOF) *m*/*z* calcd for $C_{20}H_{25}N_2O_3NaF_3$ [M + Na$^+$] 421.1715, found 421.1707; IR (film) ν 3308, 2932, 2855, 1696, 1544, 1452, 1249, 1208, 1147, 1004, 732, 698 cm^{-1}.

*(2S,3R)-3-(Benzyloxy)-N-isopropyl-1-(2,2,2-trifluoroacetyl)-pyrrolidine-2-carboxamide (**29**):* mixture of rotamers 3:1; colorless oil; isolated yield 112 mg (39%) starting from 148 mg (0.77 mmol) of compound **9**; TLC R_f 0.35 (1:4 AcOEt/hexanes); column chromatography (22% AcOEt in hexanes); $[\alpha]_D^{23}$ +13.4 (*c* 1.9, $CHCl_3$); major rotamer ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.29 (m, 1H), 5.46 (s, 1H), 4.64−4.53 (m, 1H), 4.39 (d, *J* 6.9 Hz, 1H), 4.27 (dd, *J* 13.6, 6.6 Hz, 1H), 4.02−3.94 (m, 1H), 3.71 (dd, *J* 17.6, 7.6 Hz, 1H), 2.34 (dq, *J* 12.5, 7.9 Hz, 1H), 2.19−2.11 (m, 1H), 1.30 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6, 137.3, 128.5, 128.0, 127.7, 72.4, 64.3, 51.7, 28.6; HRMS (ESI-TOF) *m*/*z* calcd for $C_{18}H_{23}N_2O_3NaF_3$ [M + Na$^+$] 395.1558, found 395.1560; IR (film) ν 3333, 2969, 1687, 1546, 1454, 1364, 1244, 1206, 1146, 756, 736, 698 cm^{-1}.

*(2R,3R)-3-(Benzyloxy)-N-isopropyl-1-(2,2,2-trifluoroacetyl)-pyrrolidine-2-carboxamide (**2-epi-29**):* mixture of rotamers 8:1; colorless oil; isolated yield 52 mg (18%) starting from 148 mg (0.77 mmol) of

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compound **9**; R_f 0.42 (1:4 AcOEt/hexanes); column chromatography (15% AcOEt in hexanes); $[\alpha]_D^{23}$ −13.4 (*c* 0.9, $CHCl_3$); major rotamer ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.28 (m, 1H), 6.07 (s, 1H), 4.57−4.54 (m, 1H), 4.44−4.42 (m, *J* 5.7 Hz, 1H), 4.31 (dd, *J* 2.7, 1.3 Hz, 1H), 3.85 (dd, *J* 9.6, 4.8 Hz, 2H), 2.41−2.30 (m, 1H), 2.22−2.15 (m, 1H), 1.31 (s, 9H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 137.3, 128.6, 128.1, 127.8, 79.0, 71.4, 67.8, 51.7, 28.6; HRMS (ESI-TOF) *m*/*z* calcd for $C_{18}H_{23}N_2O_3NaF_3$ [M + Na^+] 395.1558, found 395.1555; IR (film) ν 3357, 2967, 1680, 1547, 1455, 1364, 1245, 1205, 1147, 756, 734, 698 cm^{-1}.

Hydrolysis of Trifluoroacetates 10−29. General Procedure. The product (or crude postreaction mixture) of Ugi−Joullié reaction (0.5 mmol) was dissolved in 2 mL of (2.5 M NaOH solution in MeOH), and H_2O (100 μL) was added. The reaction mixture was stirred at room temperature for (ca. 0.5 h, TLC monitoring). When hydrolysis was completed, the reaction mixture was diluted with H_2O (3 mL) and Et_2O (3 mL). The organic layer was separated, and the aqueous layer was washed with Et_2O (3 × 3 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and the solvent was removed. The residue was purified by chromatography on silica gel to give the corresponding product.

*(2S,3S,4S,5R,6R)-3,4,5-Tris(benzyloxy)-6-[(benzyloxy)methyl)]-N-tert-butylpiperidine-2-carboxamide (**30**):* yellow oil; isolated yield 88 mg (59%) starting from 172 mg (0.24 mmol) of compound **10**: TLC R_f 0.30 (2:3 AcOEt/hexanes); column chromatography (3:7 to 2:3 AcOEt/hexanes); $[\alpha]_D^{23}$ +54.5 (*c* 0.33, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49 (s, 1H, CONH), 7.35−7.26 (m, 18H), 7.19−7.17 (m, 2H), 4.83 (d, *J* 11.2 Hz, 1H, OCHHPh), 4.79−4.73 (m, 3H, 3 × OCHHPh), 4.68 (d, *J* 11.2 Hz, 1H, OCHHPh), 4.58 (d, *J* 12.1 Hz, 1H, OCHHPh), 4.48 (d, *J* 11.1 Hz, 1H, OCHHPh), 4.46 (d, *J* 12.4 Hz, 1H, OCHHPh), 4.03 (dd, *J* 8.6, 5.1 Hz, 1H, H-3), 3.64 (t, *J* 8.2 Hz, 1H, H-2), 3.62 (dd, *J* 9.6, 2.8 Hz, 1H, C(6)−CHHOBn), 3.60 (d, *J* 5.1 Hz, 1H, H-2), 3.51 (dd, *J* 9.6, 5.9 Hz, 1H, C(6)−CHHOBn), 3.43 (dd, *J* 9.4, 7.7 Hz, 1H, H-5), 3.02 (ddd, *J* 9.4, 5.9, 2.8 Hz, 1H, H-6), 1.28 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.4, 141.0, 140.9, 140.8, 140.1, 131.2, 131.1, 131.02, 130.98, 130.8, 130.74, 130.73, 130.6 (2×), 130.4, 130.3, 130.2, 85.1, 82.3 (2×), 77.3, 77.2, 76.7, 75.8, 72.6, 59.0, 57.7, 53.6, 31.5; HRMS (ESI-TOF) *m*/*z* calcd for $C_{39}H_{47}N_2O_5$ [M + H^+] 623.3485, found 623.3475; IR (film) ν 3341, 3030, 2961, 2904, 2867, 1671, 1535, 1454, 1363, 1114, 1087, 1070, 737, 697 cm^{-1}.

*(2S,3S,4S,5R,6R)-3,4,5-Tris(benzyloxy)-6-[(benzyloxy)methyl)]-N-cyclohexylpiperidine-2-carboxamide (**31**):* yellow oil; isolated yield 81 mg (61%) starting from 152 mg (0.20 mmol) of compound **11**; TLC R_f 0.25 (2:3 AcOEt/hexanes); column chromatography on silica gel (1:4 AcOEt/hexanes); yellow oil; $[\alpha]_D^{23}$ +33.7 (*c* 0.47, $CHCl_3$); ^{1}H NMR (600 MHz, CD_3OD) δ 7.34−7.23 (m, 18H), 7.18−7.15 (m, 2H), 4.84−4.82 (m, 2H), 4.73−4.69 (m, 3H), 4.51 (d, *J* 11.9 Hz, 1H), 4.46 (d, *J* 11.2 Hz, 1H), 4.40 (d, *J* 11.9 Hz, 1H), 3.97 (t, *J* 8.1 Hz, 1H), 3.84 (dd, *J* 8.5, 5.6 Hz, 1H), 3.76 (d, *J* 5.5 Hz, 1H), 3.67 (ddd, *J* 13.9, 10.1, 3.8 Hz, 1H), 3.60 (dd, *J* 9.5, 2.8 Hz, 1H), 3.46 (dd, *J* 9.5, 6.1 Hz, 1H), 3.34 (dd, *J* 9.6, 7.7 Hz, 1H), 3.27−3.23 (m, 1H), 1.80−1.74 (m, 2H), 1.67−1.59 (m, 2H), 1.59−1.52 (m, 1H), 1.37−1.26 (m, 3H), 1.21−1.09 (m, 3H); ^{13}C NMR (151 MHz, CD_3OD) δ 170.9, 138.5, 138.3, 138.0, 137.9, 128.98, 127.95, 127.91, 127.87, 127.77, 127.70, 127.63, 127.60, 127.5, 127.3, 127.2, 81.6, 79.6, 79.1, 74.3, 73.9, 73.02, 72.7, 69.4, 56.0, 54.4, 32.3, 32.1, 25.2, 24.2; HRMS (ESI-TOF) *m*/*z* calcd for $C_{41}H_{49}N_2O_5$ [M + H^+] 649.3641, found 649.3633; IR (film) ν 3341, 3030, 2928, 2854, 1663, 1453, 1091, 1069, 736, 697 cm^{-1}.

*(2S,3S,4S,5R,6R)-3,4,5-Tris(benzyloxy)-6-[(benzyloxy)methyl)]-N-(4-methoxyphenyl)piperidine-2-carboxamide (**32**).* waxy solid; isolated yield 75 mg (58%) starting from 148 mg (0.19 mmol) of compound **12**; TLC R_f 0.36 (2:3 AcOEt/hexanes); column chromatography on silica gel (1:9 than 3:7 AcOEt/hexanes); $[\alpha]_D^{23}$ +72.9 (*c* 0.24, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.44 (s, 1H, CONH), 7.37−7.22 (m, 20H, 4 × Ph), 7.19−7.13 (m, 2H, PMP), 6.84−6.79 (m, 2H, PMP), 4.82 (d, *J* 11.2 Hz, 1H, OCHHPh), 4.80 (d, *J* 11.2 Hz, 1H, OCHHPh), 4.76−4.69 (m, 3H, 3 × OCHHPh), 4.59 (d, *J* 12.0 Hz, 1H, OCHHPh), 4.48−4.44 (m, 2H, 2 × OCHHPh), 4.12 (dd, *J* 8.2, 5.0 Hz, 1H, H-3), 3.79 (d, *J* 5.0 Hz, 1H, H-2), 3.77 (s, 3H, OCH_3), 3.74 (dd, *J* 8.2, 7.0 Hz, 1H, H-4), 3.65 (dd, *J* 9.6, 2.8 Hz, 1H, C(6)-CHHOBn), 3.54 (dd, *J* 9.6, 5.8 Hz, 1H, C(6)-CHHOBn), 3.45 (dd, *J* 9.4, 7.0 Hz, 1H, H-5), 3.11 (ddd, *J* 9.4, 5.8, 2.8 Hz, 1H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 156.2, 138.3, 138.2, 138.1, 137.3, 131.2, 128.7, 128.5, 128.39, 128.37, 128.3, 128.2, 128.1, 128.0, 127.82, 127.80, 127.68, 127.67, 121.3, 114.1, 82.4, 79.6, 79.4, 74.6, 74.28, 74.26, 73.1, 69.9, 56.7, 55.5, 54.8; HRMS (ESI-TOF) *m*/*z* calcd for $C_{42}H_{45}N_2O_6$ [M + H^+] 673.3278, found 673.3272; IR (film) ν 3311, 3061, 3030, 2908, 2864, 1678, 1512, 1435, 1244, 1069, 829, 738, 698 cm^{-1}.

*(2S,3S,4S,5S,6R)-3,4,5-Tris(benzyloxy)-6-[(benzyloxy)methyl)]-N-tert-butylpiperidine-2-carboxamide (**33**):* major isomer; yellow oil; isolated yield 67 mg (50%) starting from 155 mg (0.22 mmol) of mixture of **13**/**2-*epi*-13**; TLC R_f 0.53 (1:2 AcOEt/hexanes); column chromatography (1:5 AcOEt/hexanes); $[\alpha]_D^{23}$ −45.7 (*c* 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.21 (m, 18H), 7.15−7.12 (m, 2H), 4.67 (dd, *J* 3.7, 1.5 Hz, 1H), 4.63 (d, *J* 13.0 Hz, 1H), 4.58 (d, *J* 12.2 Hz, 1H), 4.55−4.47 (m, 2H), 4.43 (d, *J* 12.2 Hz, 1H), 4.38 (d, *J* 13.0 Hz, 1H), 4.28 (d, *J* 11.5 Hz, 1H), 4.21 (d, *J* 11.5 Hz, 1H), 3.88−3.75 (m, 3H), 3.54 (dd, *J* 9.1, 2.5 Hz, 1H), 3.40 (d, *J* 1.2 Hz, 1H), 3.26 (dt, *J* 9.9, 2.6 Hz, 1H), 1.28 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 156.2, 138.3, 138.1, 137.3, 128.7, 128.5, 128.4, 128.4, 128.2, 128.0, 127.8, 127.7, 127.7, 121.3, 114.1, 79.6, 74.6, 74.3, 74.3, 73.1, 69.9, 56.7, 55.5, 54.8; HRMS (ESI-TOF) *m*/*z* calcd for $C_{39}H_{47}N_2O_5$ [M + H^+] 623.3485, found 623.3478; IR (film) ν 3347, 3030, 2961, 2924, 2865, 1673, 1514, 1454, 1364, 1103, 1028, 736, 698 cm^{-1}.

*(2R,3S,4S,5S,6R)-3,4,5-Tris(benzyloxy)-6-[(benzyloxy)methyl)]-N-tert-butylpiperidine-2-carboxamide (**2-epi-33**):* minor isomer; yellow oil; isolated yield 11 mg (8%) starting from 155 mg (0.22 mmol) of mixture of **13**/**2-*epi*-13**; TLC R_f 0.39 (1:2 AcOEt/hexanes); flash column chromatography (1:5 AcOEt: hexanes); $[\alpha]_D^{23}$ +30.9 (*c* 0.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.17 (m, 20H), 4.67−4.46 (m, 8H), 4.23 (dd, *J* 6.8, 3.6 Hz, 1H), 3.90 (dd, *J* 4.1, 2.9 Hz, 1H), 3.76−3.68 (m, 1H), 3.62−3.59 (m, 2H), 3.56 (dd, *J* 9.8, 4.3 Hz, 1H), 3.27 (dt, *J* 8.3, 4.0 Hz, 1H), 1.26 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 138.5, 138.4, 138.3, 138.0, 128.4, 128.3, 128.2, 128.0, 127.9, 127.62, 127.56, 127.53, 74.5, 74.0, 73.2, 72.5, 54.7 50.9, 28.7; HRMS (ESI-TOF) *m*/*z* calcd for $C_{39}H_{47}N_2O_5$ [M + H^+] 623.3485, found 623.3476; IR (film) ν 3348, 2925, 2868, 1672, 1519, 1454, 1364, 1095, 1028, 737, 697 cm^{-1}.

*(2S,3S,4S,5S,6R)-3,4,5-Tris(benzyloxy)-6-[(benzyloxy)methyl)]-N-cyclohexylpiperidine-2-carboxamide (**34**):* major isomer; colorless oil; isolated yield 62 mg (50%) starting from 142 mg (0.19 mmol) of mixture of **14**/**2-*epi*-14**; TLC R_f 0.55 (1:2 AcOEt/hexanes); flash column chromatography (25% AcOEt in hexanes); $[\alpha]_D^{23}$ −32.3 (*c* 2.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.22 (m, 18H), 7.21−7.13 (m, 2H), 4.71 (dd, *J* 3.5, 1.5 Hz, 1H), 4.63 (d, *J* 12.3 Hz, 1H), 4.60 (d, *J* 12.2 Hz, 1H), 4.56−4.44 (m, 3H), 4.37 (d, *J* 12.3 Hz, 1H), 4.33 (d, *J* 11.7 Hz, 1H), 4.26 (d, *J* 11.6 Hz, 1H), 3.87−3.81 (m, 3H), 3.73−3.63 (m, 1H), 3.56 (dd, *J* 9.2, 2.6 Hz, 1H), 3.45 (s, 1H), 3.24 (d, *J* 9.8 Hz, 1H), 1.89−1.77 (m, 1H), 1.75−1.48 (m, 5H), 1.40−1.01 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 138.44, 138.42, 138.37, 138.36, 128.4, 128.3, 128.24, 128.19, 128.09, 128.02, 127.6, 127.54, 127.50, 127.3, 74.7, 73.3, 72.8, 72.2, 71.7, 71.3, 70.9, 69.2, 57.1, 50.5, 47.4, 32.9, 32.8, 25.6, 24.7, 24.6; HRMS (ESI-TOF) *m*/*z* calcd for $C_{41}H_{49}N_2O_5$ [M + H^+] 649.3641, found 649.3637; IR (film) ν 3349, 3030, 2927, 2854, 1666, 1513, 1452, 1103, 1027, 736, 698 cm^{-1}.

*(2R,3S,4S,5S,6R)-3,4,5-Tris(benzyloxy)-6-[(benzyloxy)methyl)]-N-cyclohexylpiperidine-2-carboxamide (**2-epi-34**):* minor isomer; compound was not isolated in pure form; colorless oil; isolated yield 14 mg (11%) starting from 142 mg (0.19 mmol) of mixture of **14**/**2-*epi*-14**; TLC R_f 0.38 (1:2 AcOEt/hexanes); HRMS (ESI-TOF) *m*/*z* calcd for $C_{41}H_{49}N_2O_5$ [M + H^+] 649.3641, found 649.3639

*(2S,3R,4R,5R)-3,4,5-Tris(benzyloxy)-N-tert-butylpiperidine-2-carboxamide (**35**):* major isomer; colorless oil; isolated yield 54 mg (51%) starting from 125 mg (0.21 mmol) of mixture of **15**/**2-*epi*-15**; TLC R_f 0.35 (1:1 AcOEt/hexanes); flash column chromatography (35% AcOEt in hexanes); colorless oil; $[\alpha]_D^{23}$ −2.24 (*c* 0.7, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41−7.17 (m, 15H, 3 × Ph), 6.77 (s, 1H, CONH), 4.66 (d, *J* 12.0 Hz, 1H, CHHOBn), 4.63 (d, *J* 12.0 Hz, 1H, CHHOBn), 4.60 (d, *J* 11.3 Hz, 1H, CHHOBn), 4.45−4.42 (m, 3H,

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3 × CHHOBn), 4.28 (dd, *J* 4.2, 1.8 Hz, 1H, H-3), 3.81 (dd, *J* 4.2, 2.8 Hz, 1H, H-4), 3.66 (ddd, *J* 9.3, 6.8, 2.8 Hz, 1H, H-5), 3.56 (d, *J* 1.8 Hz, 1H, H-2), 3.00−2.92 (m, 2H, H-6′ and H-6″), 1.33 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 138.50, 138.45, 138.42, 128.36, 128.29, 128.28, 128.0, 127.8, 127.7, 127.60, 127.56, 127.55, 75.5, 74.4, 73.6, 73.2, 72.6, 70.7, 58.7, 50.7, 44.6, 28.7; HRMS (ESI-TOF) *m*/*z* calcd for $C_{31}H_{39}N_2O_4$ [M + H$^+$] 503.2910, found 503.2910; IR (film) ν 3370, 3031, 2963, 2929, 2871, 1673, 1518, 1454, 1364, 1227, 1116, 1092, 1064, 736, 698 cm^{-1}.

*(2R,3R,4R,5R)-3,4,5-Tris(benzyloxy)-N-tert-butylpiperidine-2-carboxamide (**2-epi-35**):* minor isomer; colorless oil; isolated yield 18 mg (17%) starting from 125 mg (0.21 mmol) of compound **15**; TLC R_f 0.12 (1:1 AcOEt/hexanes); flash column chromatography (25% hexanes in AcOEt); colorless oil; $[\alpha]_D^{23}$ −18.4 (*c* 1.6, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.36−7.22 (m, 15H, 3 × Ph), 6.34 (s, 1H, CONH), 4.77 (d, *J* 11.1 Hz, 1H, CHHOBn), 4.65−4.51 (m, 5H, 5 × CHHOBn), 4.25 (m, 1H, H-3), 3.72 (dt, *J* 5.8, 2.7 Hz, 1H, H-5), 3.61 (dd, *J* 7.3, 2.2 Hz, 1H, H-4), 3.13 (dd, *J* 14.0, 6.1 Hz, 1H, H-6′), 3.05 (d, *J* 6.5 Hz, 1H, H-2), 2.58 (dd, *J* 14.0, 1.9 Hz, 1H, H-6″), 1.29 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4, 138.5, 138.4, 128.4, 128.3, 128.3, 127.8, 127.69, 127.66, 127.65, 127.57, 127.5, 73.1, 71.4, 71.0, 50.9, 28.6; HRMS (ESI-TOF) *m*/*z* calcd for $C_{31}H_{39}N_2O_4$ [M + H$^+$] 503.2910. Found 503.2910; IR (film) ν 3321, 3030, 2964, 2924, 2869, 1669, 1452, 1363, 1226, 1093, 1027, 737, 698 cm^{-1}.

*(2S,3R,4R,5R)-3,4,5-Tris(benzyloxy)-N-cyclohexylpiperidine-2-carboxamide (**36**):* major isomer; white crystals; mp 67−68 °C; isolated yield 74 mg (60%) starting from 145 mg (0.23 mmol) of compound **16**; TLC R_f 0.53 (100% AcOEt); flash column chromatography (40% AcOEt in hexanes); $[\alpha]_D^{23}$ −3.85 (*c* 2.8, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.38−7.27 (m, 13H), 7.24−7.19 (m, 2H), 6.82 (d, *J* 7.9 Hz, 1H), 4.65 (d, *J* 12.1 Hz, 1H), 4.62−4.58 (m, 2H), 3.80−3.73 (m, 3H), 3.68 (ddd, *J* 9.1, 6.2, 2.8 Hz, 1H), 3.64 (d, *J* 1.3 Hz, 1H), 3.00−2.95 (m, 2H), 1.91−1.81 (m, 2H), 1.74−1.63 (m, 2H), 1.59 (dd, *J* 9.0, 4.0 Hz, 1H), 1.41−1.24 (m, 2H), 1.21−1.07 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 138.50, 138.45, 138.4, 128.4, 128.31, 128.28, 128.0, 127.82, 127.75, 127.61, 127.57, 127.55, 75.5, 74.4, 73.6, 73.4, 72.7, 70.7, 58.3, 47.8, 44.6, 33.1, 32.9, 25.6, 24.8; HRMS (ESI-TOF) *m*/*z* calcd for $C_{33}H_{41}N_2O_4$ [M + H$^+$] 529.3066, found 529.3062; IR (film) ν 3377, 3030, 2928, 2853, 1668, 1514, 1452, 1092, 1063, 736, 698 cm^{-1}.

*(2R,3R,4R,5R)-3,4,5-Tris(benzyloxy)-N-cyclohexylpiperidine-2-carboxamide (**2-epi-36**):* minor isomer; white crystals; mp 72−73 °C; isolated yield 18 mg (15%) starting from 145 mg (0.23 mmol) of compound **16**; TLC R_f 0.35 (100% AcOEt); flash column chromatography (50% AcOEt in hexanes); $[\alpha]_D^{23}$ −11.1 (*c* 0.9, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.35−7.23 (m, 13H), 6.48 (s, 1H), 4.78 (d, *J* 11.2 Hz, 1H), 4.61−4.57 (m, 3H), 4.53 (d, *J* 12.0 Hz, 1H), 4.32−4.24 (m, 1H), 3.79−3.76 (m, 1H), 3.75−3.67 (m, 1H), 3.62 (d, *J* 5.5 Hz, 1H), 3.23 (d, *J* 6.7 Hz, 1H), 3.18 (dd, *J* 14.0, 5.6 Hz, 1H), 2.68 (d, *J* 12.3 Hz, 1H), 1.85−1.78 (m, 2H), 1.65−1.58 (m, 2H), 1.58−1.52 (m, 1H), 1.33−1.22 (m, 2H), 1.15−0.99 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 138.5, 138.4, 128.4, 128.2, 127.8, 127.72, 127.67, 127.66, 127.58, 127.5, 73.1, 71.5, 70.9, 48.0, 32.9, 25.5, 24.7; HRMS (ESI-TOF) *m*/*z* calcd for $C_{33}H_{41}N_2O_4$ [M + H$^+$] 529.3066, found 529.3062; IR (film) ν 3424, 3316, 3053, 2931, 2855, 1666, 1519, 1453, 1265, 1093, 1075, 738, 700 cm^{-1}.

*(2S,3R,4R,5R)-3,4,5-Tris(benzyloxy)-N-(4-methoxyphenyl)piperidine-2-carboxamide (**37**):* colorless oil; isolated yield 56 mg (88%) starting from 75 mg (0.12 mmol) of compound **17**; TLC R_f 0.29 (3:2 AcOEt/hexanes); flash column chromatography (30% AcOEt in hexanes); $[\alpha]_D^{23}$ +7.7 (*c* 0.22, $CHCl_3$); ^1H NMR (600 MHz, C_6D_6) δ 8.56 (s, 1H), 7.59−7.49 (m, 2H), 7.3−7.21 (m, 4H), 7.19−6.98 (m, 11H), 6.73−6.67 (m, 2H), 4.63 (d, *J* 11.3 Hz, 1H), 4.58 (d, *J* 12.0 Hz, 1H), 4.52−4.48 (m, 2H), 4.44 (d, *J* 11.3 Hz, 1H), 4.28−4.22 (m, 2H), 3.81 (s, 1H), 3.69 (d, *J* 1.3 Hz, 1H), 3.61−3.55 (m, 1H), 3.22 (s, 3H), 3.03−2.95 (m, 1H), 2.77 (dd, *J* 12.5, 4.7 Hz, 1H); ^{13}C NMR (151 MHz, C_6D_6) δ 168.4, 156.1, 138.9, 138.8, 138.7, 131.8, 128.3−127.3 (aromatic overlap), 120.5, 114.0, 75.6, 74.7, 73.6, 73.5, 72.7, 70.4, 58.9, 54.5, 44.6; HRMS (ESI-TOF) *m*/*z* calcd for $C_{34}H_{37}N_2O_5$ [M + H$^+$] 553.2702, found 553.2693; IR (film) ν 3333, 3030, 2931, 2870, 1682, 1514, 1454, 1245, 1091, 1029, 829, 739, 698 cm^{-1}.

*(2R,3R,4R,5R)-3,4,5-Tris(benzyloxy)-N-(4-methoxyphenyl)piperidine-2-carboxamide (**2-epi-37**):* white crystals; mp 152−153 °C; isolated yield 30 mg (69%) starting from 51 mg (0.08 mmol) of compound **2-*epi*-17**; TLC R_f 0.64 (100% AcOEt); flash column chromatography (60% AcOEt in hexanes); $[\alpha]_D^{23}$ −5.9 (*c* 0.13, $CHCl_3$); ^1H NMR (600 MHz, C_6D_6) δ 8.31 (s, 1H), 7.21−7.16 (m, 2H), 7.13−7.06 (m, 2H), 7.05−6.99 (m, 2H), 6.95−6.72 (m, 11H), 6.47−6.40 (m, 2H), 4.43−4.38 (m, 2H), 4.24−4.19 (m, 2H), 4.11 (d, *J* 11.4 Hz, 1H), 4.07 (d, *J* 12.3 Hz, 1H), 4.04 (d, *J* 12.3 Hz, 1H), 3.45 (d, *J* 4.1 Hz, 1H), 3.30 (dd, *J* 5.0, 2.9 Hz, 1H), 2.98 (s, 3H), 2.89 (dd, *J* 13.6, 8.3 Hz, 1H), 2.85 (d, *J* 4.4 Hz, 1H), 2.13 (dd, *J* 13.6, 3.3 Hz, 1H); ^{13}C NMR (151 MHz, C_6D_6) δ 167.7, 156.1, 139.0, 138.8, 138.6, 131.8, 128.8−126.7 (aromatic overlap), 120.9, 113.9, 77.0, 76.3, 72.9 (2×), 71.6, 70.2, 59.5, 54.5, 42.6; HRMS (ESI-TOF) *m*/*z* calcd for $C_{34}H_{37}N_2O_5$ [M + H$^+$] 553.2702, found 553.2702; IR (film) ν 3298, 3033, 2907, 2859, 1654, 1512, 1453, 1244, 1100, 1031, 828, 736, 697 cm^{-1}.

*(2S,3S,4R,5R)-3,4-Bis(benzyloxy)-5-[(benzyloxy)methyl)]-N-tert-butylpyrrolidine-2-carboxamide **38**.* colorless oil; isolated yield 65 mg (74%) starting from 105 mg (0.18 mmol) of compound **18**; TLC R_f 0.38 (1:1 AcOEt/hexanes); flash column chromatography (35% AcOEt in hexanes); colorless oil; $[\alpha]_D^{23}$ +41.9 (*c* 1.6, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.21 (m, 15H), 4.72 (d, *J* 11.6 Hz, 1H, OCHHPh), 4.67 (d, *J* 11.6 Hz, 1H, OCHHPh), 4.47 (d, *J* 9.9 Hz, 1H, OCHHPh), 4.45 (d, *J* 9.9 Hz, 1H, OCHHPh), 4.41 (d, *J* 12.0 Hz, 1H, OCHHPh), 4.37 (t, *J* 4.0 Hz, 1H, H-3), 4.29 (d, *J* 12.0 Hz, 1H, OCHHPh), 3.79 (dd, *J* 9.2, 3.7 Hz, 1H, H-4), 3.77 (d, *J* 4.2 Hz, 1H, H-2), 3.63 (dd, *J* 10.0, 3.1 Hz, 1H, C(5)-CHHOBn), 3.54 (dd, *J* 10.0, 3.3 Hz, 1H, C(5)-CHHOBn), 3.46 (dt, *J* 9.2, 3.2 Hz, 1H, H-5), 1.31 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 138.7, 138.03, 137.96, 128.4, 128.3, 128.1, 128.0, 127.8, 127.73, 127.70, 127.67, 127.4, 80.4, 78.1, 73.9, 73.2, 72.1, 68.1, 63.5, 59.9, 50.4, 28.7; HRMS (ESI-TOF) *m*/*z* calcd for $C_{31}H_{39}N_2O_4$ [M + H$^+$] 503.2910, found 503.2910; IR (film) ν 3333, 3030, 2964, 2914, 2866, 1669, 1521, 1453, 1362, 1130, 1065, 737, 697 cm^{-1}.

*(2S,3S,4R,5R)-3,4-Bis(benzyloxy)-5-[(benzyloxy)methyl)]-N-cyclohexylpyrrolidine-2-carboxamide (**39**):* colorless oil; isolated yield 66 mg (58%) starting from 135 mg (0.22 mmol) of compound **19**; TLC R_f 0.60 (100% AcOEt); flash column chromatography (50% AcOEt in hexanes); $[\alpha]_D^{23}$ +50.3 (*c* 1.8, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.51 (d, *J* 8.2 Hz, 1H, CONH), 7.36−7.20 (m, 15H, 3 × Ph), 4.68 (d, *J* 11.5 Hz, 1H, OCHHPh), 4.65 (d, *J* 11.5 Hz, 1H, OCHHPh), 4.49 (d, *J* 11.9 Hz, 1H, OCHHPh), 4.46 (d, *J* 11.9 Hz, 1H, OCHHPh), 4.44−4.40 (m, 2H, OCHHPh, H-3), 4.30 (d, *J* 11.9 Hz, 1H, OCHHPh), 3.87 (d, *J* 4.1 Hz, 1H, H-2), 3.80 (dd, *J* 9.2, 3.7 Hz, 1H, H-4), 3.77−3.70 (m, 1H), 3.63 (dd, *J* 10.0, 3.0 Hz, 1H, C(5)-CHHOBn), 3.53 (dd, *J* 10.0, 3.5 Hz, 1H, C(5)-CHHOBn), 3.47 (dt, *J* 9.0, 3.2 Hz, 1H, H-5), 1.86−1.50 (m, 6H), 1.37−1.24 (m, 2H), 1.18−1.02 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 138.6, 138.0, 137.9, 128.42, 128.35, 128.04, 128.00, 127.79, 127.76, 127.74, 127.69, 127.4, 80.4, 78.2, 73.9, 73.2, 72.1, 68.2, 63.1, 59.9, 47.6, 33.00, 32.97, 25.58, 24.85, 24.76; HRMS (ESI-TOF) *m*/*z* calcd for $C_{33}H_{41}N_2O_4$ [M + H$^+$] 529.3066, found 529.3062; IR (film) ν 3343, 3030, 2929, 2854, 1667, 1520, 1453, 1363, 1209, 1133, 1065, 1028, 736, 698 cm^{-1}.

*(2R,3R,4R,5R)-3,4-Bis(benzyloxy)-5-[(benzyloxy)methyl)]-N-tert-butylpyrrolidine-2-carboxamide (**40**):* major isomer; colorless oil; isolated yield 49 mg (43%) starting from 137 mg (0.23 mmol) of mixture of **20**/**2-*epi*-20**; TLC R_f 0.36 (1:1 AcOEt/hexanes); flash column chromatography (35% AcOEt in hexanes); $[\alpha]_D^{23}$ +30.5 (*c* 0.8, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.35−7.21 (m, 15H, 3 × Ph), 4.60 (d, *J* 11.8 Hz, 1H, OCHHPh), 4.53 (d, *J* 12.1 Hz, OCHHPh), 4.49 (d, *J* 12.1 Hz, OCHHPh), 4.47 (d, *J* 5.8 Hz, OCHHPh), 4.44 (d, *J* 5.8 Hz, 1H, OCHHPh), 4.39 (d, *J* 11.8 Hz, 1H, OCHHPh), 4.24 (dd, *J* 5.5, 1.7 Hz, 1H, H-3), 4.01 (d, *J* 5.5 Hz, 1H, H-2), 3.83 (br s, 1H, H-4), 3.55−3.45 (m, 3H, H-5, C(5)-CH_2OBn), 1.30 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 138.3, 138.2, 137.9, 128.4, 128.4, 128.2, 127.8, 127.72, 127.66, 127.62, 127.6, 127.5, 83.8, 83.2, 73.2, 72.9, 72.5, 71.4, 65.3, 62.5, 50.5, 28.7;

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HRMS (ESI-TOF) m/z calcd for $C_{31}H_{39}N_2O_4$ [M + H$^+$] 503.2910, found 503.2915; IR (film) ν 3425, 3352, 3031, 2965, 2925, 2864, 1668, 1523, 1454, 1362, 1227, 1093, 1072, 737, 697 cm^{-1}.

(2S,3R,4R,5R)-3,4-Bis(benzyloxy)-5-[(benzyloxy)methyl)]-N-tert-butylpyrrolidine-2-carboxamide (**2-epi-40**): colorless oil; isolated yield 37 mg (32%) starting from 137 mg (0.23 mmol) of mixture of **20**/**2-epi-20**; TLC R_f 0.45 (1:1 AcOEt/hexanes); flash column chromatography on silica gel (20% AcOEt in hexanes); $[\alpha]_D^{23}$ +8.6 (c 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.22 (m, 15H, 3 × Ph), 4.76 (d, J 11.8 Hz, 1H, OCH*H*Ph), 4.61 (d, J 11.8 Hz, 1H, OCH*H*Ph), 4.55 (d, J 11.7 Hz, 1H, OCH*H*Ph), 4.51 (d, J 11.9 Hz, OCH*H*Ph), 4.48 (d, J 11.9 Hz, OCH*H*Ph), 4.44 (d, J 11.7 Hz, 1H, OCH*H*Ph), 4.34 (t, J 3.0 Hz, 1H, H-3), 3.88 (dd, J 5.5, 3.1 Hz, 1H, H-4), 3.65 (d, J 2.6 Hz, 1H, H-2), 3.60−3.51 (m, 2H, C(5)-C*H*$_2$OBn), 3.24 (m, 1H, H-5), 1.32 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 138.3, 138.0, 137.9, 128.4, 128.34, 128.29, 127.87, 127.85, 127.76, 127.7, 127.62, 127.55, 87.4, 85.0, 73.2, 71.8, 71.6, 69.1, 66.1, 62.4, 50.3, 28.7; HRMS (ESI-TOF) m/z calcd for $C_{31}H_{39}N_2O_4$ [M + H$^+$] 503.2910, found 503.2921; IR (film) ν 3330, 3062, 3031, 2964, 2920, 2866, 1671, 1516, 1454, 1363, 1092, 1074, 736, 698 cm^{-1}.

(2R,3R,4R,5R)-3,4-Bis(benzyloxy)-5-[(benzyloxy)methyl)]-N-cyclohexylpyrrolidine-2-carboxamide (**41**). major isomer; white crystals; mp 72−73 °C; isolated yield 44 mg (43%) starting from 122 mg (0.20 mmol) of mixture of **21**/**2-epi-21**; TLC R_f 0.43 (1:1 AcOEt/hexanes); flash column chromatography on silica gel (40% AcOEt in hexanes); $[\alpha]_D^{23}$ +18.7 (c 2.3, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39−7.16 (m, 15H), 4.58 (d, J 11.7 Hz, 1H), 4.53−4.46 (m, 3H), 4.44 (d, J 11.7 Hz, 1H), 4.40 (d, J 11.8 Hz, 1H), 4.27 (d, J 4.7 Hz, 1H), 4.11 (d, J 4.7 Hz, 1H), 3.84 (mi, 1H), 3.79−3.72 (m, 1H), 3.55−3.45 (m, 3H), 1.83 (d, J 9.5 Hz, 1H), 1.74 (d, J 10.1 Hz, 1H), 1.69−1.63 (m, 1H), 1.61−1.52 (m, 2H), 1.40−1.24 (m, 2H), 1.17−1.10 (m, 2H), 1.08−1.00 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.9, 138.3, 138.1, 137.9, 128.41, 128.39, 128.2, 127.8, 127.73, 127.67, 127.64, 127.5, 83.5, 83.2, 73.2, 72.9, 72.4, 71.4, 64.7, 62.5, 47.5, 33.0, 32.9, 25.6, 24.8, 24.6; HRMS (ESI-TOF) m/z calcd for $C_{33}H_{41}N_2O_4$ [M + H$^+$] 529.3066, found 529.3071; IR (film) ν 3332, 2928, 2854, 1663, 1523, 1452, 1093, 1027, 737, 698 cm^{-1}.

(2S,3R,4R,5R)-3,4-Bis(benzyloxy)-5-[(benzyloxy)methyl)]-N-cyclohexylpyrrolidine-2-carboxamide (**2-epi-41**). minor isomer; white crystals; mp 78−79 °C; isolated yield 34 mg (32%) starting from 122 mg (0.20 mmol) of mixture of **21**/**2-epi-21**; TLC R_f 0.55 (1:1 AcOEt/hexanes); flash column chromatography on silica gel (25% AcOEt in hexanes); $[\alpha]_D^{23}$ +8.4 (c 0.8, $CHCl_3$); ^{1}H NMR (600 MHz, C_6D_6) δ 7.15−6.99 (m, 15H), 4.66 (d, J 11.9 Hz, 1H), 4.52 (d, J 11.9 Hz, 1H), 4.41 (t, J 2.5 Hz, 1H), 4.36 (d, J 11.6 Hz, 1H), 4.23 (d, J 11.8 Hz, 1H), 4.19 (d, J 3.5 Hz, 2H), 3.78 (dd, J 4.9, 2.9 Hz, 1H), 3.71 (dt, J 14.9, 7.0 Hz, 1H), 3.56 (s, 1H), 3.34−3.28 (m, 2H), 3.21 (dd, J 9.0, 4.4 Hz, 1H), 1.75 (dd, J 12.6, 3.2 Hz, 1H), 1.61 (dd, J 12.5, 3.3 Hz, 1H), 1.50−1.37 (m, 2H), 1.37−1.29 (m, 1H), 1.24−1.04 (m, 2H), 0.99−0.82 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 138.2, 138.0, 137.9, 128.43, 128.35, 128.26, 128.0, 127.9, 127., 127.76, 127.62, 127.60, 87.2, 84.9, 73.2, 71.8, 71.6, 69.0, 65.7, 62.4, 47.7, 33.0, 25.6, 24.8; HRMS (ESI-TOF) m/z calcd for $C_{33}H_{41}N_2O_4$ [M + H$^+$] 529.3066, found 529.3067; IR (film) ν 3334, 3062, 3031, 2928, 2854, 1665, 1516, 1452, 1094, 1074, 737, 698 cm^{-1}.

(2S,3R,4R)-3,4-Bis(benzyloxy)-N-tert-butylpyrrolidine-2-carboxamide (**42**): colorless oil; isolated yield 55 mg (79%) starting from 87 mg (0.18 mmol) of compound **22**; TLC R_f 0.24 (1:1 AcOEt/hexanes); flash column chromatography (35% AcOEt in hexanes); colorless oil; $[\alpha]_D^{23}$ +9.38 (c 1.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (s, 1H, NH), 7.37−7.23 (m, 10H, 2 × Ph), 4.71 (d, J 11.8 Hz, 1H, CH*H*OBn), 4.60 (d, J 11.8 Hz, 1H, CH*H*OBn), 4.51 (d, J 11.9 Hz, 1H, CH*H*OBn), 4.40 (d, J 11.9 Hz, 1H, CH*H*OBn), 4.36 (s, 1H, H-3), 3.99−3.94 (m, 1H, H-4), 3.68 (d, J 1.1 Hz, 1H, H-2), 3.31 (dd, J 11.5, 5.2 Hz, 1H, H-5′), 3.03 (dd, J 11.5, 2.6 Hz, 1H, H-5″), 1.28 (s, 9H, $(CH_3)_3$C); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 138.0, 137.9, 128.4, 128.3, 127.82, 127.76, 127.71, 127.6, 85.7, 82.8, 71.4, 71.2, 66.5, 50.9, 50.3, 28.6; HRMS (ESI-TOF) m/z calcd for $C_{23}H_{31}N_2O_3$ [M + H$^+$] 383.2335, found 383.2330; IR (film) ν 3321, 2964, 2926, 2869, 1667, 1520, 1454, 1363, 1227, 1096, 736, 697 cm^{-1}.

(2R,3R,4R)-3,4-Bis(benzyloxy)-N-tert-butylpyrrolidine-2-carboxamide (**2-epi-42**): isolated yield 32 mg (84%) starting from 47 mg (0.10 mmol) of compound **2-epi-22**; TLC R_f 0.12 (1:1 AcOEt/hexanes); column chromatography (50% AcOEt in hexanes); colorless oil; $[\alpha]_D^{23}$ −13.1 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (s, 1H, NH), 7.34−7.21 (m, 10H, 2 × Ph), 4.65 (d, J 11.9 Hz, 1H, CH*H*OBn), 4.52 (d, J 11.9 Hz, 1H, CH*H*OBn), 4.44 (d, J 11.9 Hz, 1H, CH*H*OBn), 4.37−4.29 (m, 2H, CH*H*OBn, H-3), 3.99 (d, J 5.0 Hz, 1H, H-2), 3.91−3.86 (m, 1H, H-4), 3.18 (dd, J 12.2, 3.6 Hz, 1H, H-5′), 3.04 (d, J 12.2 Hz, 1H, H-5″), 1.34 (s, 9H, $(CH_3)_3$C); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 138.2, 137.9, 128.5, 128.2, 127.9, 127.8, 127.6, 82.8, 82.3, 73.3, 71.0, 65.1, 50.8, 50.4, 28.8; HRMS (ESI-TOF) m/z calcd for $C_{23}H_{31}N_2O_3$ [M + H$^+$] 383.2335, found 383.2331; IR (film) ν 3425, 3352, 3031, 2965, 2925, 2864, 1668, 1523, 1454, 1362, 1227, 1093, 1072, 737, 697 cm^{-1}.

(2S,3R,4R)-3,4-Bis(benzyloxy)-N-cyclohexylpyrrolidine-2-carboxamide (**43**): white crystals; mp 67−68 °C; isolated yield 47 mg (78%) starting from 75 mg (0.15 mmol) of compound **23**; TLC R_f 0.26 (1:1 AcOEt/hexanes); column chromatography (35% AcOEt in hexanes); $[\alpha]_D^{23}$ +0.48 (c 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (d, J 7.5 Hz, 1H), 7.39−7.22 (m, 10H, 2 × Ph), 4.72 (d, J 11.8 Hz, 1H, CH*H*OBn), 4.60 (d, J 11.8 Hz, 1H, CH*H*OBn), 4.46 (d, J 11.6 Hz, 1H, CH*H*OBn), 4.39−4.35 (m, 2H, CH*H*OBn, H-3), 3.97−3.94 (m, 1H, H-4), 3.78 (s, 1H, H-2), 3.69−3.63 (m, 1H), 3.32 (dd, J 11.5, 5.1 Hz, 1H, H-5′), 3.03 (dd, J 11.5, 2.3 Hz, 1H, H-5″), 1.85−182 (m, 1H), 1.70−1.62 (m, 2H), 1.61−1.52 (m, 2H), 1.37−1.22 (m, 2H), 1.18−1.08 (m, 2H), 1.05−0.96 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 138.0, 137.9, 128.43, 128.42, 128.3, 127.92, 127.85, 127.74, 127.6, 85.6, 82.7, 71.4, 71.2, 66.1, 50.9, 47.6, 32.9, 32.8, 25.6, 24.8, 24.7; HRMS (ESI-TOF) m/z calcd for $C_{25}H_{33}N_2O_3$ [M + H$^+$] 409.2491, found 409.2498; IR (film) ν 3329, 3062, 3031, 2929, 2853, 1664, 1518, 1453, 1098, 737, 698 cm^{-1}.

(2R,3R,4R)-3,4-Bis(benzyloxy)-N-cyclohexylpyrrolidine-2-carboxamide (**2-epi-43**): isolated yield 35 mg (75%) starting from 57 mg (0.11 mmol) of compound **2-epi-23**; TLC R_f 0.17 (100% AcOEt); flash column chromatography (60% AcOEt in hexanes); white crystals; mp 71−72 °C; $[\alpha]_D^{23}$ −1.0 (c 0.7, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 (s, 1H, NH), 7.36−7.19 (m, 10H, 2 × Ph), 4.63 (d, J 11.8 Hz, 1H, CH*H*OBn), 4.50 (d, J 11.8 Hz, 1H, CH*H*OBn), 4.45 (d, J 11.9 Hz, 1H, CH*H*OBn), 4.39 (br s, 1H, H-3), 4.35 (d, J 11.8 Hz, 1H, CH*H*OBn), 4.12 (d, J 3.9 Hz, 1H, H-4), 3.88 (d, J 3.2 Hz, 1H, H-2), 3.80−3.73 (m, 1H), 3.19 (dd, J 12.2, 3.6 Hz, 1H, H-5′), 3.08 (d, J 12.2 Hz, 1H, H-5′), 1.90−1.77 (m, 2H), 1.72−1.60 (m, 2H), 1.60−1.53 (m, 1H), 1.39−1.27 (m, 2H), 1.22−1.07 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 138.2, 137.8, 128.5, 128.2, 127.81, 127.80, 127.6, 82.8, 82.3, 73.3, 71.0, 64.7, 50.8, 47.5, 33.2, 32.9, 25.6, 24.8, 24.7; HRMS (ESI-TOF) m/z calcd for $C_{25}H_{33}N_2O_3$ [M + H$^+$] 409.2491, found 409.2504; IR (film) ν 3302, 3062, 3031, 2930, 2854, 1651, 1526, 1453, 1098, 737, 698 cm^{-1}.

(2R,3S,4S)-3,4-Bis(benzyloxy)-N-(4-methoxyphenyl)pyrrolidine-2-carboxamide (**44**): isolated yield 67 mg (95%) starting from 86 mg (0.16 mmol) of compound **24**; TLC R_f 0.27 (3:2 AcOEt/hexane); column chromatography (30% AcOEt in hexanes); white crystals; mp 55−56 °C; $[\alpha]_D^{23}$ −2.1 (c 0.22, $CHCl_3$); ^{1}H NMR (600 MHz, C_6D_6) δ 9.43 (s, 1H), 7.60−7.55 (m, 2H), 7.33−7.29 (m, 2H), 7.18−7.13 (m, 2H), 7.08−7.05 (m, 3H), 7.01−6.93 (m, 3H), 6.70−6.66 (m, 2H), 4.60 (d, J 11.9 Hz, 1H), 4.56 (s, 1H), 4.46 (d, J 11.9 Hz, 1H), 4.23 (d, J 11.5 Hz, 1H), 4.03 (d, J 11.5 Hz, 1H), 3.73−3.70 (m, 1H), 3.60 (s, 1H), 3.22 (s, 3H), 2.88 (dd, J 11.0, 4.5 Hz, 1H), 2.84 (dd, J 11.0, 1.8 Hz, 1H); ^{13}C NMR (151 MHz, C_6D_6) δ 169.2, 156.0, 138.4, 138.0, 132.0, 128.3−127.2 (aromatic overlap), 120.3, 114.0, 85.1, 82.2, 71.0, 70.9, 66.2, 54.5, 50.7; HRMS (ESI-TOF) m/z calcd for $C_{26}H_{29}N_2O_4$ [M + H$^+$] 433.2127, found 433.2125; IR (film) ν 3280, 3031, 2931, 2868, 1675, 1523, 1455, 1245, 1098, 1032, 830, 739, 698 cm^{-1}.

(2S,3S,4S)-3,4-Bis(benzyloxy)-N-(4-methoxyphenyl)pyrrolidine-2-carboxamide (**2-epi-44**): isolated yield 50 mg (95%) starting from 64 mg (0.12 mmol) of compound **2-epi-24**; TLC R_f 0.14 (3:2 AcOEt/hexane); flash column chromatography on silica gel (30% AcOEt in hexanes); colorless oil; $[\alpha]_D^{23}$ −35.4 (c 0.26, $CHCl_3$); ^{1}H NMR (600 MHz, C_6D_6) δ 9.34 (s, 1H), 7.70−7.61 (m, 2H), 7.26−6.88 (m, 12H),

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6.79−6.66 (m, 2H), 4.55 (d, *J* 11.7 Hz, 1H), 4.38−4.33 (m, 2H), 4.12 (d, *J* 12.0 Hz, 1H), 4.03−3.99 (m, 2H), 3.62 (d, *J* 3.0 Hz, 1H), 3.21 (s, 3H), 3.00 (dd, *J* 12.1, 3.4 Hz, 1H), 2.65 (d, *J* 12.1 Hz, 1H); ^{13}C NMR (151 MHz, C_6D_6) δ 168.3, 156.0, 138.29, 138.27, 132.1, 128.3−127.2 (aromatic overlap), 120.4, 114.0, 82.6, 82.5, 73.2, 70.4, 65.5, 54.5, 50.4; HRMS (ESI-TOF) *m*/*z* calcd for $C_{26}H_{29}N_2O_4$ [M + H$^+$] 433.2127, found 433.2118; IR (film) ν 3288, 3030, 2931, 2869, 1674, 1514, 1454, 1244, 1096, 1032, 829, 738, 698 cm^{-1}.

(2S,3S,4R)-3,4-Bis(benzyloxy)-N-tert-butylpyrrolidine-2-carboxamide ***(45)****:* isolated yield 14 mg (75%) starting from 24 mg (0.05 mmol) of compound **25**; TLC R_f 0.09 (100% AcOEt); column chromatography (60−100% AcOEt in hexanes); $[\alpha]_D$ +4.4 (*c* 1.31, $CHCl_3$); ^{1}H NMR (600 MHz, C_6D_6) δ 7.49−7.42 (m, 2H), 7.33 (s, 1H), 7.22−7.00 (m, 8H), 4.81 (d, *J* 11.5 Hz, 1H, CH*H*OBn), 4.77 (d, *J* 11.5 Hz, 1H, CH*H*OBn), 4.25 (d, *J* 12.2 Hz, 1H, CH*H*OBn), 4.15 (dd, *J* 4.7, 3.6 Hz, 1H, H-3), 4.10 (d, *J* 12.2 Hz, 1H, CH*H*OBn), 3.42 (d, *J* 4.7 Hz, 1H, H-2), 3.30 (ddd, *J* 9.4, 7.1, 3.6 Hz, 1H, H-4), 3.06 (t, *J* 9.8 Hz, 1H, H-5′), 2.57 (dd, *J* 10.2, 7.1 Hz, 1H, H-5″), 1.28 (s, 9H, *t*-Bu); ^{13}C NMR (151 MHz, C_6D_6) δ 169.4, 139.2, 138.6, 128.2, 128.0, 128.0, 127.4, 127.2, 127.2, 80.8, 78.5, 73.9, 71.6, 63.9, 49.8, 48.0, 28.5; HRMS (ESI-TOF) *m*/*z* calcd for $C_{23}H_{31}N_2O_3$ [M + H$^+$] 383.2335, found 383.2328; IR (film) ν 3298, 3033, 2907, 2859, 1654, 1512, 1453, 1244, 1100, 1031, 828, 736, 697 cm^{-1}.

(2S,3S,4R)-3,4-Bis(benzyloxy)-N-(4-methoxyphenyl)pyrrolidine-2-carboxamide ***(46)****:* isolated yield 59 mg (79%) starting from 92 mg (0.18 mmol) of compound **27**: white crystals; R_f 0.2 (100% AcOEt); column chromatography (50% AcOEt in hexanes); $[\alpha]_D^{25}$ −12.4 (*c* 1.57, $CHCl_3$); ^{1}H NMR (600 MHz, C_6D_6) δ 9.24 (s, 1H, NH), 7.45−7.41 (m, 2H), 7.30−7.16 (m, 7H), 7.14−7.06 (m, 3H), 6.80−6.74 (m, 2H), 4.71 (d, *J* 11.5 Hz, 1H, CH*H*OBn), 4.67 (d, *J* 11.5 Hz, 1H, CH*H*OBn), 4.45 (d, *J* 12.0 Hz, 1H, CH*H*OBn), 4.34 (d, *J* 12.0 Hz, 1H, CH*H*OBn), 4.26 (dd, *J* 5.0, 3.7 Hz, 1H, H-3), 3.72 (d, *J* 5.0 Hz, 1H, H-2), 3.70−3.66 (ddd, *J* 8.8, 7.0, 3.7 Hz, 1H, H-4), 3.57 (s, 3H, OCH_3), 3.06 (dd, *J* 10.4, 8.8 Hz, 1H, H-5′), 2.90 (dd, *J* 10.4, 7.0 Hz, 1H, H-5″); ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.1, 156.1, 138.3, 138.0, 131.1, 128.4, 128.1, 127.8, 127.7, 127.5, 127.4, 121.2, 114.0, 80.2, 79.0, 74.0, 72.1, 63.8, 55.5, 48.1; HRMS (ESI-TOF) *m*/*z* calcd for $C_{26}H_{29}N_2O_4$ [M + H$^+$] 433.2127, found 433.2128; IR (film) ν 3288, 3030, 2931, 2881, 2836, 1674, 1514, 1454, 1246, 1140, 1090, 1031, 829, 739, 698 cm^{-1}.

(2R,4R)-4-(Benzyloxy)-N-tert-butylpyrrolidine-2-carboxamide ***(47)****:* isolated yield 72 mg (65%) starting from 148 mg (0.4 mmol) of compound **27**; TLC R_f 0.36 (1:1 acetone/hexanes); flash column chromatography (3:7 then 3:2 acetone/hexanes); colorless oil; $[\alpha]_D^{23}$ −8.2 (*c* 0.27, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 (s, 1H), 7.34−7.22 (m, 5H, Ph), 4.50 (d, *J* 11.8 Hz, 1H, C*H*HOBn), 4.39 (d, *J* 11.8 Hz, 1H, CH*H*OBn), 4.04 (ddd, *J* 8.6, 5.1, 3.8 Hz, 1H, H-4), 3.63 (dd, *J* 8.8, 5.6 Hz, 1H, H-2), 3.11 (dd, *J* 11.1, 5.1 Hz, 1H, H-5′), 3.05 (dd, *J* 11.1, 3.0 Hz, 1H, H-5″), 2.23−2.19 (m, 2H, H-3′/H-3″), 1.27 (s, 9H, $(CH_3)_3$C); ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.4, 140.9, 130.9, 130.3, 130.2, 81.3, 73.5, 62.6, 55.0, 52.7, 38.5, 31.3; HRMS (ESI-TOF) *m*/*z* calcd for $C_{16}H_{25}N_2O_2$ [M + H$^+$] 277.1916. Found 277.1913; IR (film) ν 3316, 2966, 2929, 2868, 1658, 1522, 1453, 1362, 1227, 1111, 1094, 1071, 737, 698 cm^{-1}.

(2R,4R)-4-(Benzyloxy)-N-cyclohexylpyrrolidine-2-carboxamide ***(48)****:* major isomer; compound was not isolated in pure form; yield 47 mg (40%) starting from 155 mg (0.39 mmol) of mixture **28**/**2-*epi*-28**; R_f 0.13 (100% AcOEt); flash column chromatography (2:3 acetone/hexanes); colorless oil; ^{1}H NMR (600 MHz, C_6D_6) δ 7.36 (d, *J* 7.3 Hz, 1H, NH), 7.27−7.13 (m, 5H, Ph), 4.39 (d, *J* 11.6 Hz, 1H, CH*H*OBn), 4.29 (d, *J* 11.6 Hz, 1H, CH*H*OBn), 3.98−3.94 (m, 1H, H-4), 3.63 (t, *J* 7.1 Hz, 1H, H-2), 3.61−3.54 (m, 1H), 3.02 (dd, *J* 11.0, 5.0 Hz, 1H, H-5′), 2.97 (dd, *J* 11.0, 2.9 Hz, 1H, H-5″), 2.16−2.13 (m, 2H, H-3′/H-3″), 1.76−1.70 (m, 1H), 1.64−1.54 (m, 2H), 1.52−1.43 (m, 2H), 1.26−1.13 (m, 2H), 1.06−0.97 (m, 2H), 0.96−0.87 (m, 1H); ^{13}C NMR (151 MHz, C_6D_6) δ 176.2, 140.7, 130.8, 130.3, 130.1, 81.2, 73.4, 62.0, 54.9, 49.9, 38.5, 35.6, 35.4, 28.1, 27.4, 27.3; HRMS (ESI-TOF) *m*/*z* calcd for $C_{18}H_{27}N_2O_2$ [M + H$^+$] 303.2073, found 303.2070; IR (film) ν 3316, 2928, 2853, 1652, 1523, 1451, 1349, 1108, 1068, 737, 698 cm^{-1}.

*(2S,4R)-4-(Benzyloxy)-N-cyclohexylpyrrolidine-2-carboxamide (2-*epi*-48):* minor isomer; compound was not isolated in pure form; yield 17 mg (14%) starting from 155 mg (0.39 mmol) of the mixture **28**/**2-*epi*-28**; TLC R_f 0.11 (100% AcOEt); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* 7.6 Hz, 1H, NH), 7.38−7.27 (m, 5H, Ph), 4.56 (d, *J* 11.7 Hz, 1H, CH*H*OBn), 4.50 (d, *J* 11.3 Hz, 1H, CH*H*OBn), 4.35 (ddd, *J* 10.4, 7.0, 3.7 Hz, 1H, H-4), 4.16−4.09 (m, 1H, H-2), 4.03−3.96 (m, 1H), 3.61 (dd, *J* 10.4, 6.4 Hz, 1H, H-5′), 3.44 (dd, *J* 10.4, 3.0 Hz, 1H, H-5″), 2.57 (dd, *J* 17.3, 6.9 Hz, 1H, H-3′), 2.46 (dd, *J* 17.3, 4.0 Hz, 1H, H-3″), 1.87−1.51 (m, 5H), 1.39−1.05 (m, 5H); selected signals ^{13}C NMR (151 MHz, C_6D_6) δ 178.2, 140.0, 131.1, 130.5, 130.3, 76.4, 73.6, 51.1, 39.6; HRMS (ESI-TOF) *m*/*z* calcd for $C_{18}H_{27}N_2O_2$ [M + H$^+$] 303.2073, found 303.2070; IR (film) ν 3266, 2929, 2854, 1675, 1530, 1451, 1348, 1096, 1071, 737, 698 cm^{-1}.

(2S,3R)-3-(Benzyloxy)-N-tert-butylpyrrolidine-2-carboxamide ***(49)****:* isolated yield 52 mg (71%) starting from 98 mg (0.26 mmol) of compound **29**; colorless oil; TLC R_f 0.15 (100% acetone); flash column chromatography (100% acetone); $[\alpha]_D^{23}$ +49.1 (*c* 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.25 (m, 5H, Ph), 4.58 (d, *J* 12.0 Hz, 1H, CH*H*OBn), 4.54 (d, *J* 12.0 Hz, 1H, CH*H*OBn), 4.35 (td, *J* 4.9, 2.1 Hz, 1H, H-3), 3.71 (d, *J* 5.1 Hz, 1H, H-2), 3.19−3.11 (m, 1H, H-5′), 3.06−3.02 (m, 1H, H-5″), 2.02−1.96 (m, 1H, H-4′), 1.85−1.75 (m, 1H, H-4″), 1.33 (s, 9H, $(CH_3)_3$C); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 138.6, 128.1, 127.6, 127.3, 80.5, 72.2, 66.9, 50.4, 44.7, 33.0, 28.8; HRMS (ESI-TOF) *m*/*z* calcd for $C_{16}H_{25}N_2O_2$ [M + H$^+$] 277.1916, found 277.1910; IR (film) ν 3332, 2962, 2926, 2872, 1659, 1523, 1454, 1362, 1228, 1118, 1065, 1026, 737, 698 cm^{-1}.

*(2R,3R)-3-(Benzyloxy)-N-tert-butylpyrrolidine-2-carboxamide (2-*epi*-49):* isolated yield 22 mg (69%) starting from 43 mg (0.12 mmol) of compound **2-*epi*-29**; colorless oil; TLC R_f 0.23 (100% AcOEt); Flash column chromatography (75% AcOEt in hexanes); $[\alpha]_D^{23}$ −19.8 (*c* 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.23 (m, 5H, Ph), 4.65 (d, *J* 11.8 Hz, 1H, CH*H*OBn), 4.57 (d, *J* 11.9 Hz, 1H, CH*H*OBn), 4.29 (d, *J* 5.3 Hz, 1H, H-3), 3.69 (m, 1H, H-2), 3.20 (td, *J* 9.7, 6.9 Hz, 1H, H-5′), 2.95 (ddd, *J* 9.8, 7.9, 3.4 Hz, 1H, H-5″), 1.95−1.87 (m, 1H, H-4′), 1.79−1.73 (m, 1H, H-4″), 1.33 (s, 9H, $(CH_3)_3$C); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 138.6, 128.4, 127.7, 127.3, 80.5, 72.1, 79.0, 51.2, 45.3, 33.5, 28.7; HRMS (ESI-TOF) *m*/*z* calcd for $C_{16}H_{25}N_2O_2$ [M + H$^+$] 277.1916, found 277.1915; IR (film) ν 3322, 2964, 2928, 2869, 1667, 1520, 1454, 1363, 1228, 1097, 736, 697 cm^{-1}.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra, stereochemical proofs and X-ray crystallographic data (CIF file) for compounds **2-*epi*-23**, **24** and **28**. This material is available free of charge via the Internet at http://pubs.acs.org

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Notes

The authors declare no competing financial interest.

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