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Synthesis of Unusual *N*-Acylated Aminosugar Fragments of *Mycobacterium Marinum* Lipooligosaccharide IV

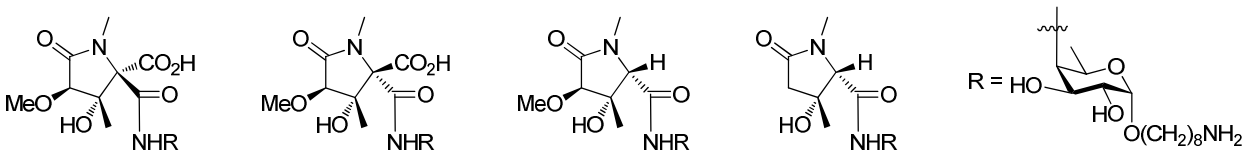
Lei Wang, Mengyao Dong, and Todd L. Lowary*

Alberta Glycomics Centre and Department of Chemistry, University of Alberta

Gunning–Lemieux Chemistry Centre, Edmonton, AB T6G 2G2, Canada

Email: tlowary@ualberta.ca

Graphical Abstract



Abstract

A convergent strategy was developed for the stereoselective synthesis of four unusual *N*-acylated monosaccharides (**5**–**8**), which are fragments of lipooligosaccharide IV (LOS-IV) from *Mycobacterium marinum*. A critical substrate-controlled asymmetric cyclization of an amino-acid derived oxazolidine provided a key lactam intermediate **11**, which was successfully converted to targets **5**–**7**. The key step in the synthesis of **8** was a one-pot cascade oxidation–cyclization–oxidation reaction of a Boc-protected amino alcohol, prepared from 3-butynol, which led to the formation of lactam **15**. The five member ring lactam intermediates in these synthetic routes were sensitive to elimination side reactions, but careful manipulation of the reaction sequence allowed for the stereoselective synthesis of the targets. This work represents the first synthesis of these unusual motifs, which have been shown to be essential to the bioactivity of LOS-IV.

Introduction

Lipooligosaccharides (LOSs) are antigenic cell surface glycolipids found in the cell wall complex of mycobacteria.[1] They are produced by a range of mycobacteria, including *Mycobacterium kansasii,*[2] *M. smegmatis*,[3] *M. gastri*,[4-6] *M. malmoense*,[7] *M. marinum*,[8-10] and the Canetti strain of *M. tuberculosis*.[11] Recent investigations[12] support a role for LOSs in important biological events including sliding motility, biofilm formation, and infection of host macrophages; however, their precise role in mycobacterial virulence remains unclear.[13]

M. marinum produces four LOSs (LOS-I–IV, Figure 1). Similar to all LOSs reported to date, these molecules contain an acylated trehalose core, which is functionalized with a species-specific glycan. The glycan in *M. marinum* LOS-IV is terminated with a family of *N*-acylated 4-amino-4,6-dideoxy-galactopyranose residues.[10] These unusual *N*-acylated monosaccharides share a common lactam core, differentiated by substitutions at C-2 (CO_2H or H) or C-4 (MeO or H). This heterogeneity generates two acidic (**1** and **2**, Figure 2) and two neutral (**3** and **4**) compounds. Compound **1** and **2**, substituted by both carboxy (C-2) and methoxy (C-4) groups, account for 95% of the total LOS-IV derivatives.[10] The absolute stereochemistry of the substituents in the lactam ring of **1**–**3** have been determined using ^{1}H NMR spectroscopy, in particular through NOE experiments. However, this was not possible for **4** and it was proposed that its lactam structure was either that shown in Figure 2, or its enantiomer.

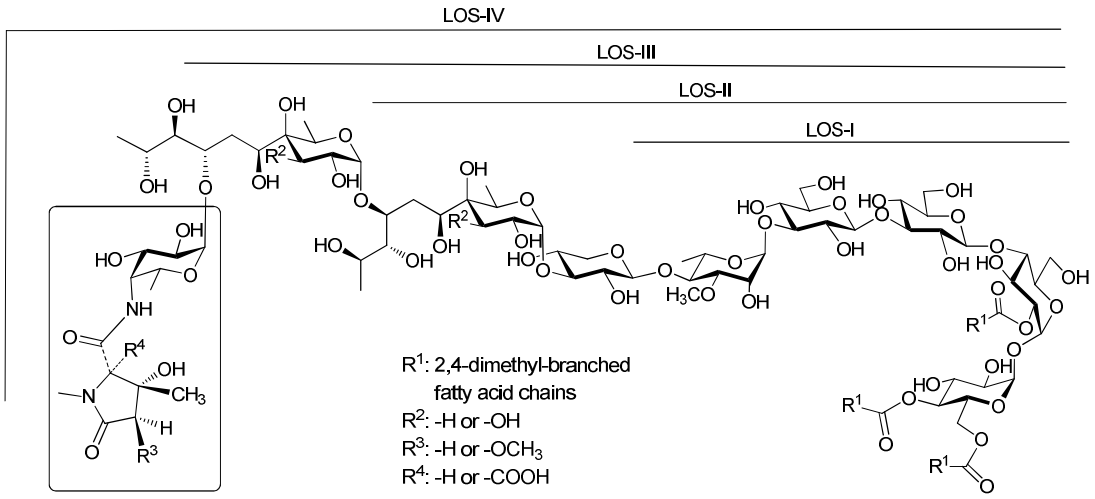


Figure 1. Structures of *M. marinum* LOSs.

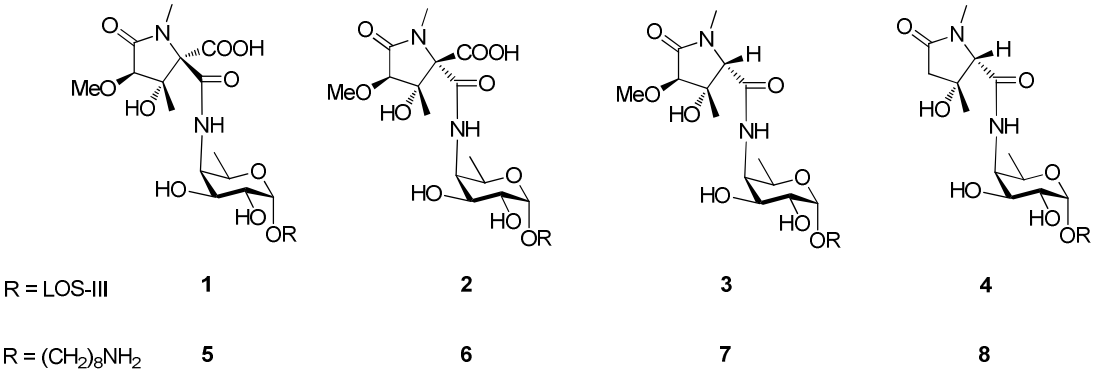


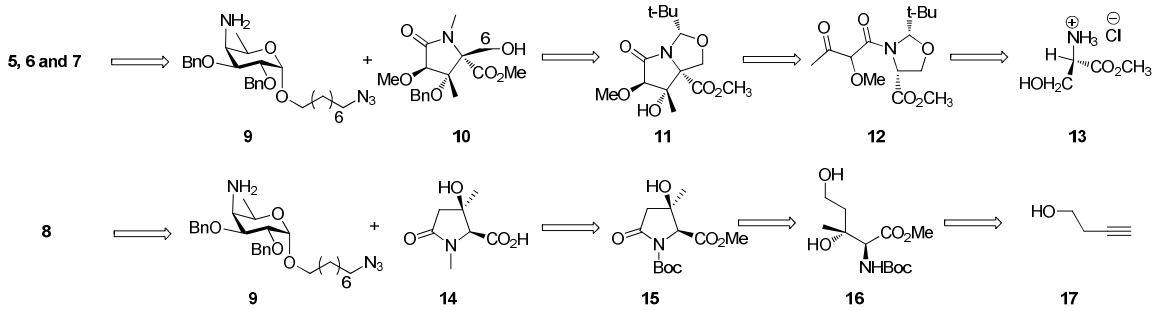
Figure 2. Structures of unusual *N*-acylated monosaccharides present in *M. marinum* LOS-IV (**1**–**4**) and synthetic targets (**5**–**8**).

Recent studies by Guérardel and co-workers showed that LOS-IV induces the expression of both Intercellular Adhesion Molecule 1(ICAM-1) and CD40 on macrophages. In addition, LOS-IV stimulates Interleukin-8 (IL-8) secretion from THP-1 cells. However, LOS-III did not show these activities,[10] thus indicating that these terminal *N*-acylated monosaccharides confer important biological functions to LOS-IV. The biological activity of these motifs, in conjunction with their intriguing structure, motivated us to develop a synthetic route that would provide these compounds in a form that could be used for future investigations of their function. In this paper,

we describe the first stereoselective synthesis of these unusual *N*-acylated monosaccharides (**5**–**8**). These molecules were synthesized bearing an aminooctyl aglycone, a group that provides a convenient handle for conjugation, for example, to proteins for the generation of monoclonal antibodies.

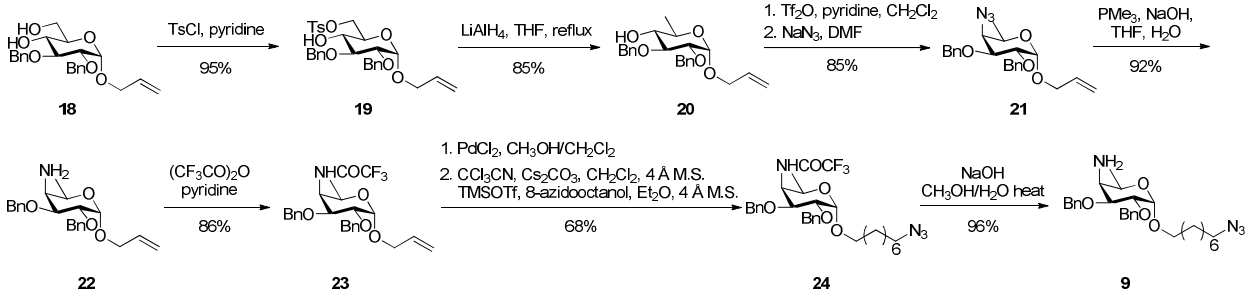
Results and discussion

The targets feature a structure consisting of a highly substituted γ-lactam connected through an amide bond to a 4-amino-4,6-dideoxy-α-D-galactopyranoside moiety. Retrosynthetic analysis of **5**–**8** is outlined in Scheme 1. The disconnection of the amide bond in **5**–**7** affords protected 4-amino-4,6-dideoxy-galactose derivative **9** and three γ-lactams, which could be accessed from the same key intermediate **10**. Compound **10** could be produced from the fused bicyclic oxazolidine–pyrrolinone **11** through a series of functional group transformations. In turn, **11** could be accessed by stereoselective cyclization of **12**, which is accessible from D-serine (**13**). With regard to the synthesis of **8**, disconnection of the amide bond leads to amine **9** and *N*-methyl lactam **14**. Following a series of functional group manipulations, Boc protected lactam **15** could be converted to *N*-methyl lactam **14**. The key step is the conversion of the highly functionalized α-amino acid ester **16**[14] to lactam **15**.



Scheme 1. Retrosynthetic analysis of **5**–**8**.

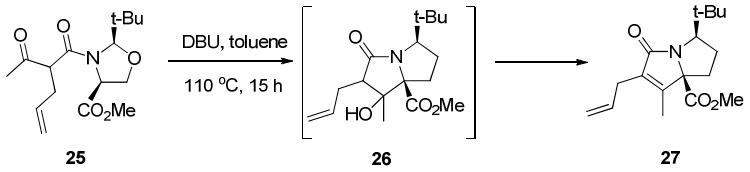
Synthesis of Monosaccharide 9. With a plan in place, the synthesis began with the preparation of galactopyranoside derivative **9** (Scheme 2). Glucopyranoside **18**[15] was treated with tosyl chloride, leading to regioselective tosylation of the C-6 hydroxyl group to form **19** in 95% yield. Subsequent reduction of **19** by $LiAlH_4$ provided 6-deoxysugar **20** in 85% yield. Triflation of **20** followed by azide substitution at room temperature provided, in 85% overall yield, azide **21**. Azide reduction by the Staudinger reaction and trifluoroacetylation of the resulting amine gave the corresponding trifluoroacetamide derivative **23** in 79% yield over the two steps. The anomeric allyl group in **23** was then removed by treatment with a catalytic amount of $PdCl_2$ in a solution of methanol and CH_2Cl_2 to afford the hemiacetal, which upon exposure to trichloroacetonitrile, Cs_2CO_3 and 4 Å molecular sieves in anhydrous CH_2Cl_2 gave the desired trichloroacetimidate donor. Glycosylation of the trichloroacetimidate donor with 8-azido-octanol in the presence of TMSOTf was α-selective affording **24** in 68% overall yield from **23**. Finally, the trifluroacetyl protecting group was removed under basic conditions to afford 8-azidooctyl 4-amino-4,6-dideoxy-galactopyranoside (**9**) in 96% yield.



Scheme 2. Synthesis of 8-azidooctyl 4-amino-4,6-dideoxy-α-D-galactopyranoside (**9**).

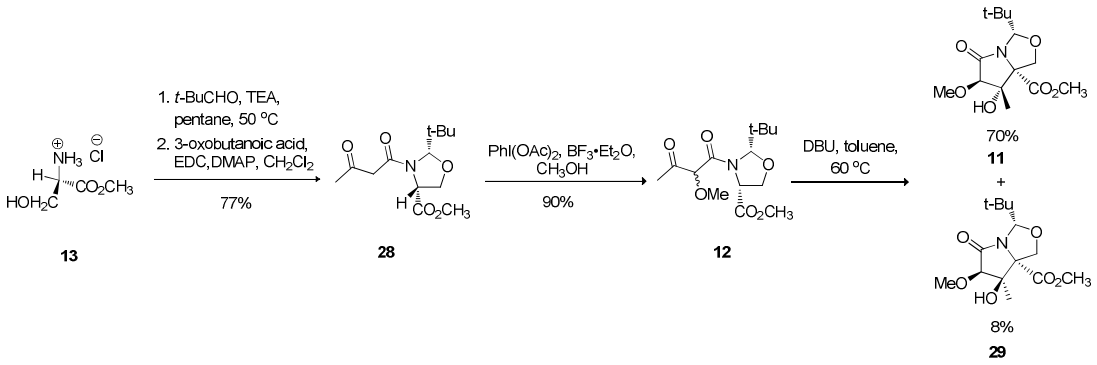
Synthesis of key lactam precursor 11. After the successful synthesis of **9**, we turned our attention to the preparation of the protected lactam derivative **11**. The key issue was to introduce stereocenters at α and β positions of the lactam. In previous work, Ling and co-workers (Scheme

3)[16] treated α-alkyl-β-keto amide **25** with DBU at 110 °C, which led to a cyclization–dehydration sequence forming α, β-unsaturated lactam **27**.



Scheme 3. Reference method for synthesis of α, β-unsaturated lactam **27.**

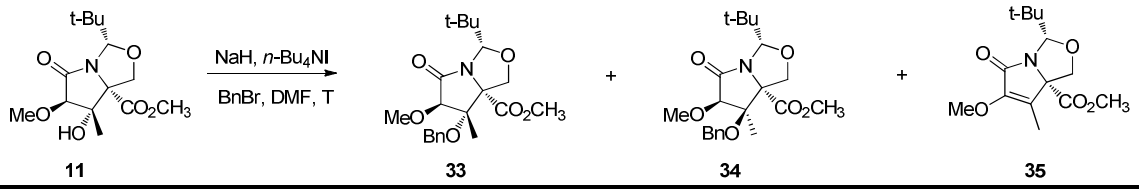
Inspired by this reaction, we hypothesized that if α-methoxy-β-keto amide **12** (Scheme 4) was reacted with DBU, a product with the hydroxyl group *cis* to ester would be formed because of H-bonding with the carbonyl group. In addition, we anticipated that the methoxy group would be *trans* to the hydroxy group due to a dipole effect. With this plan in mind, we started our synthetic work from D-serine methylester hydrochloride (**13**). This α-amino ester was condensed with pivaldehyde to afford an oxazolidine intermediate that was directly coupled with acetoacetic acid in the presence of EDC and DMAP giving β-keto amide **28** in 77% overall yield. Iodosobenzenediacetate-mediated oxidation of **28** in methanol provided the α-methoxy-β-keto amide **12** in 90% yield. DBU-promoted cyclization of **12** was carried out as reported by Ling and coworkers; however, in our hands, it was necessary to use a lower temperature (60 °C) to avoid the dehydration following cyclization. After 12 hours, two diastereomeric cyclized products were formed (ratio 9:1 from the ^{1}H NMR spectrum of the crude product), which could be separated by chromatography. Pleasingly, NOESY experiments (see Supporting Information) showed that the major product (70% isolated yield) was the desired intermediate **11** and the minor product (8% isolated yield) was the undesired stereoisomer (**29**) where the hydroxyl and methoxy groups are *cis*. X-ray crystallographic analysis of **11** further confirmed the structure of major product (see Figure S1 and Tables S1 and S2 in the Supporting Information).



Scheme 4. Synthesis of oxazolidine **11**.

The next step was to protect the tertiary alcohol in **11** as a benzyl ether. Mindful of the anticipated base-sensitivity of **11**, initial attempts to benzylate this tertiary alcohol were carried out under acidic conditions (TMSOTf and benzyl trichloroacetimidate). However, these attempts were unsuccessful and so we turned out attention to base-promoted alkylation. Treatment of alcohol **11** with NaH and benzyl bromide (2 equiv) led to the formation of two benzylated compounds (ratio 24:71) and a trace amount of elimination by-product **35** (Table 1). Disappointingly, NOESY experiments (see Supporting Information) confirmed that the major product was **34**, in which the substituents α and β to carbonyl group were *cis*. Presumably, upon deprotonation of alcohol with base, the resulting anion undergoes a reversible retro-aldol reaction (Scheme 5).[17] Although, upon recyclization both stereoisomers can be formed in this process, the *cis* intermediate **32** would be expected to react faster with benzyl bromide given dipolar effects, leading to a majority of **34**. We imagined that using a higher concentration of benzyl bromide would allow the trapping of alkoxide **30** before ring opening. Gratifyingly, as outlined in Table 1, increasing the ratio of BnBr to DMF to 1:2, led to a 3:2 ratio of the desired (**33**) to undesired (**34**) stereoisomers. Further increasing the ratio of BnBr to DMF to 3:1 and decreasing the temperature to –15 °C gave a 9:1 mixture of **33** and **34**.

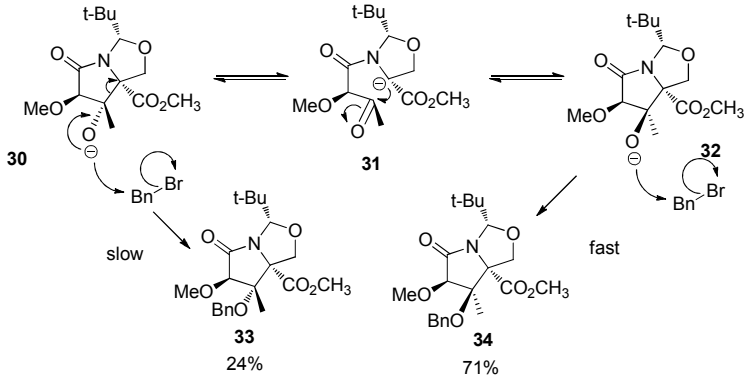
Table 1. Protection of tertiary alcohol in bicyclic intermediate **11**[a]



11 **33** **34** **35**

Entry	T (°C)	BnBr:DMF	Products distribution (NMR yield[b])		
			33	**34**	**35**
1	0	2 equiv of BnBr	24%	71%	5%
2	0	1:2	60%	40%	–
3	0	3:1	80%	20%	–
4	−15	3:1	90%	10%	–

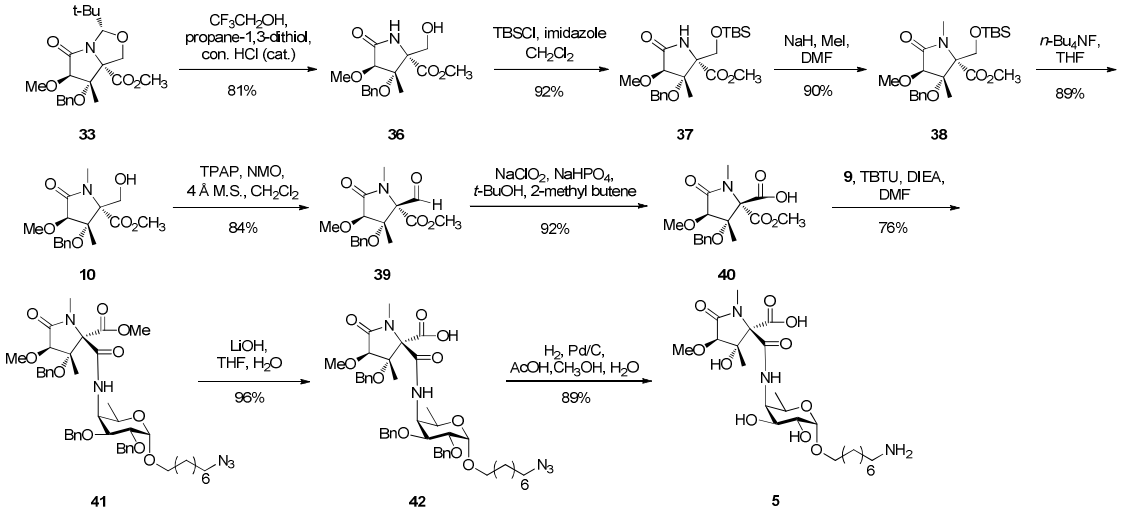
[a]Reaction conditions: **11** (1 equiv), NaH (1.5equiv), *n*-Bu_4NI (1.2 equiv)
[b]Yields were obtained by integration of CO_2CH_3 protons of the products observed in the crude ^1H NMR spectrum.



Scheme 5. Proposed mechanism for the formation of by-product **34**.

Synthesis of target 5. After the successful alkylation of the tertiary alcohol, a series of functional group manipulations converted **33** into the key intermediate **10** (Scheme 6). Acidic conditions were used to cleave the oxazolidine ring in 81% yield. The primary alcohol product of this reaction, **36**, was then converted to TBS ether **37** and then *N*-methyl amide **38** in 83% yield over the two steps. Finally, *n*-Bu_4NF deprotection of the TBS ether provided **10** in 89% yield. With **10** in hand, we examined a number of different oxidation conditions (Jones, PDC in wet DMF, $RuCl_3$ and $NaIO_4$, TEMPO and $NaClO/NaClO_2$) in an attempt to oxidize the primary

alcohol to the corresponding carboxylic acid. Unfortunately, none of these methods afforded the desired product and therefore a two-step approach was explored. Ley oxidation (TPAP/NMO) afforded aldehyde **39** in 84% yield; subsequent Pinnick oxidation easily oxidized **39** to carboxylic acid **40** in 92% yield. With the acid **40** in hand, amidation with the amine **9** led to **41** in 76% yield. The methyl ester was then hydrolyzed by treatment with LiOH in THF and water to furnish **42** (96% yield). Global debenzylation and reduction of **42** was achieved in a mixture of methanol, water and acetic acid (10:1:0.1) under a H_2 atmosphere with 10% Pd/C as the catalyst to give an 89% yield of **5**.

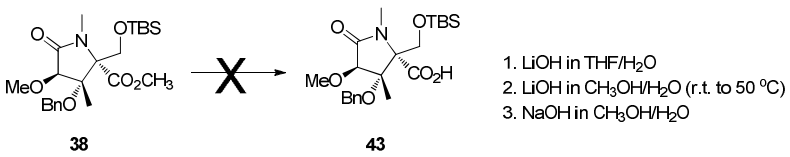


Scheme 6. Synthesis of target **5**.

When **5**, which was homogenous based on HRMS analysis, was dissolved in CD_3OD, the ^1H NMR spectrum showed a mixture of two species in a 4:3 ratio. When the solvent was changed to DMSO-d_6, the ratio for these two isomers was still 4:3; however, it changed to 10:1 after two days. Finally, when AcOH-d_4 was used as solvent, the ratio changed to 2:3 after one day and did not change further (see Supporting Information). Recovery of the samples dissolved in DMSO-d_6 and AcOH-d_4 and redissolution in CD_3OD, resulted in a 4:3 mixture of isomers. These experiments suggest that following deprotection, *N*-acylated monosaccharide **5** exists as a

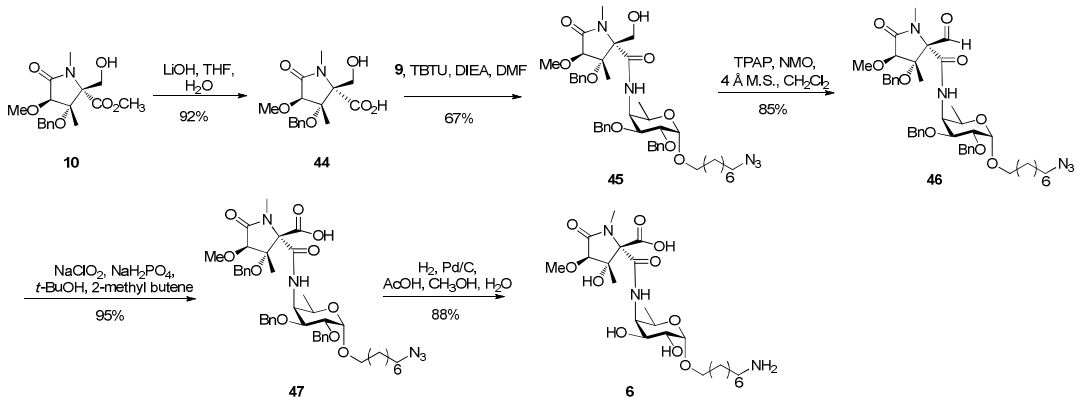
mixture of two atropisomers about the C-4 amide bond, with solvent-dependent populations. Attempts to resolve the atropisomers into a single species using elevated temperature (60 °C) NMR experiments in CD_3OD did not result in significant changes in the distributions of the two species. Interestingly, in the report[10] detailing the structure of these LOSs from *M. marinum*, atropoisomerism was not reported. In these synthetic compounds, restricted rotation about this bond may arise from the presence of the aminooctyl aglyone, which would lead to these compounds existing at zwitterions at neutral pH. We note, however, that the use of AcOH-d_4, which would be expected to protonate the molecule, did not lead to a single species in the ^{1}H NMR spectrum. Unfortunately, direct comparison of the NMR data from **5** with those reported for the natural product was not possible. The NMR spectra of the natural glycolipids were measured in D_2O, a solvent in which **5** (as well as **6**–**8**) is insoluble.

Synthesis of target 6. To synthesize **6**, an inverted order for the oxidation and amidation sequence was used. The initial plan was to hydrolyze the ester in **38** to afford an acid **43** that could be coupled to amine **9** (Scheme 7). Unfortunately, presumably due to steric effects arising from the TBS protecting group, a number of different conditions (e.g., LiOH in THF/H_2O, LiOH in CH_3OH/H_2O (r.t. to 50 °C), NaOH in CH_3OH/H_2O) only afforded trace amounts of desired product. Thus, we decided to hydrolyze the key intermediate **10**, which possesses a free hydroxyl group (Scheme 8). Compound **10** was easily hydrolyzed by treatment with LiOH in THF and water at room temperature to afford acid **44** in 92% yield. TBTU-promoted amidation of **44** with amine **9** led to a 67% yield of **45**. Late-stage Ley oxidation (TPAP/NMO) and then Pinnick oxidation straightforwardly afforded acid precursor **47** in 80% yield over two steps. Finally, global debenzylation and azide reduction provided **6** in 88% yield. Like **5**, compound **6** demonstrated atropisomerism in CD_3OD with a ratio about 5:1 (see Supporting Information).



38 43

Scheme 7. Attempts to hydrolyze the ester in **38**.

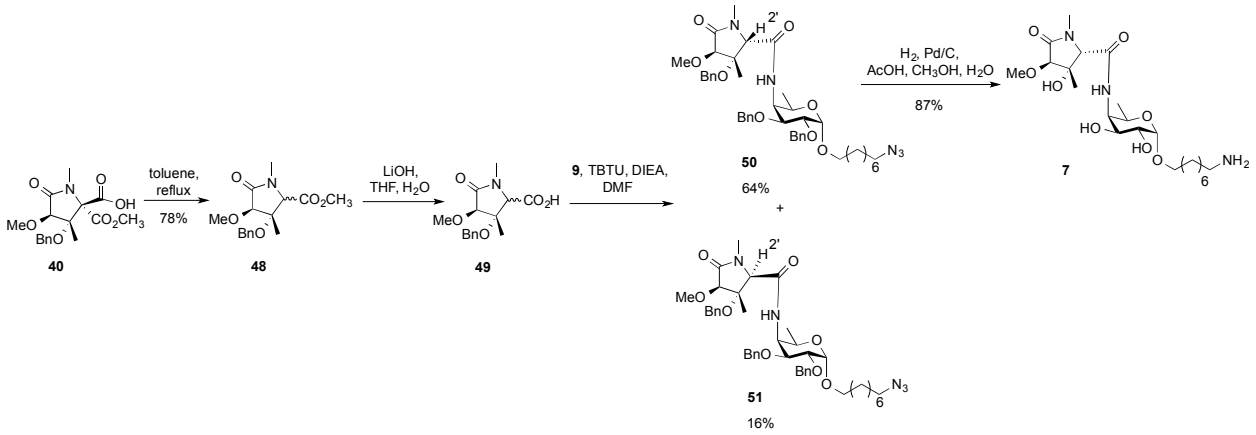


10 44 45 46 47 6

Scheme 8. Synthesis of target **6**.

Synthesis of target 7. To synthesize **7**, dicarboxylic acid monoester **40** (Scheme 9) was used as the starting material. Decarboxylation of **40** in toluene at reflux afforded ester **48** as a 1:1 mixture of diasteroisomers in 78% yield. These compounds were inseparable using silica gel column chromatography and were therefore carried forward as a mixture. Hydroylsis of **48** by treatment with LiOH in THF and water afforded the corresponding carboxylic acids **49** (also as an inseparable mixture of diastereomers), which were coupled with amine **9**. The resulting two amidation products, **50** and **51**, were separated by column chromatography to give major and minor products in a 4:1 ratio. NOESY experiments (see Supporting Information) showed that the interaction between the CH_3 (δ1.52 ppm) and H-2′(δ3.90 ppm) in the major product was stronger than the interaction between the CH_3 (δ1.38 ppm) and H-2′ (δ4.03 ppm) in the minor product. These results suggest that **50**, with a *cis* relationship between the benzyl ether and amide groups was formed as the major product (64% yield calculated based on amine **9**). Compound **51** was

formed as minor product in 16% yield. Unreacted **49** was also isolated at the end of the reaction. These yields presumably arise from differences in reactivities between the two stereoisomeric acids in the amidation reaction. After deprotection in a mixture of methanol, water and acetic acid (10:1:0.1) under a H_2 atmosphere with 10% Pd/C as the catalyst, **7** was obtained in 87% yield. Unlike the **5** and **6**, *N*-acylated monosaccharide **7** did not show any atropisomeric effects in CD_3OD, which we attribute to more efficient amide bond rotation due to the lack of an adjacent carboxylic acid group.

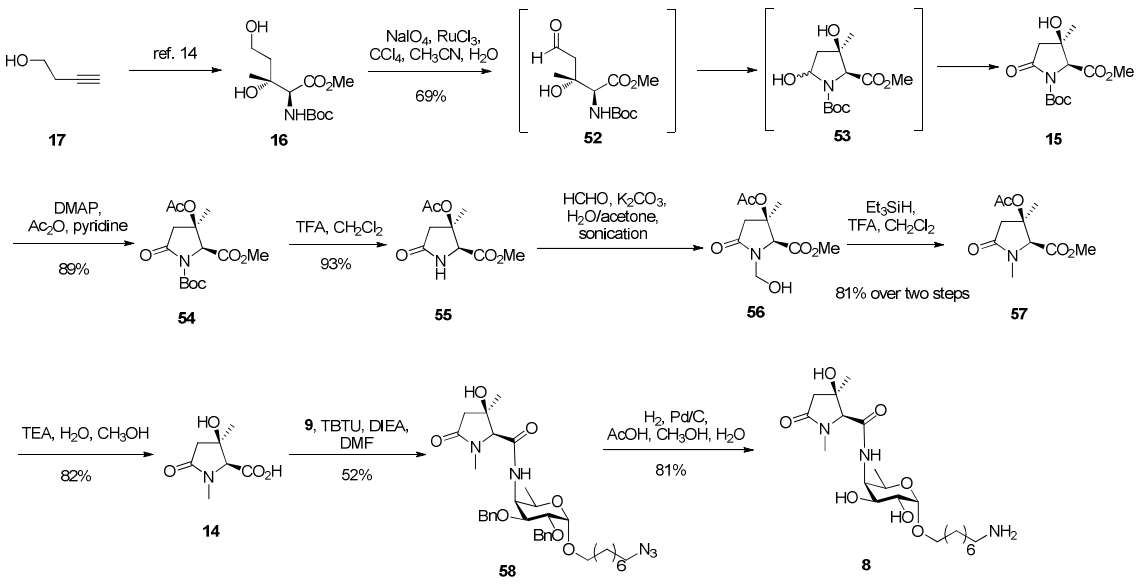


Scheme 9. Synthesis of target **7**.

Synthesis of target 8. The synthesis of **8** (Scheme 10) began with 3-butynol (**17**), which was converted to α-amino acid ester **16** following the route reported by Qin and co-workers.[14] Treatment of **16** with $NaIO_4$ and $RuCl_3$ led to a cascade oxidation–cyclization–oxidation sequence, which produced *N*-Boc protected lactam **15** in 69% yield. Protecting the tertiary alcohol of **15** with an acetyl group and removing the Boc group afforded lactam **55** in 82% yield over two steps. Because lactam **55** was anticipated to be unstable in basic solution, milder conditions were chosen for the *N*-methylation step. Thus, *N*-hydroxymethylation of lactam **55** was achieved using paraformaldehyde in acetone in the presence of K_2CO_3 and water with sonication. To reduce the hemiaminal **56** to an *N*-methyl group (i.e., compound **57**), we initially

explored the use of Pd/C catalyzed hydrogenation at atmospheric pressure in the presence of trifluoroacetic acid. However, this reaction was very slow and only a trace amount of product was formed. We found, however, that the hemiaminal **56** could be converted to **57** by treatment with triethylsilane and trifluoroacetic acid at room temperature. *N*-Methylamide **57** was obtained in 81% yield over two steps from **55**. Hydrolysis of methyl and acetate esters in **57** failed when LiOH was used in THF and water; the major product formed was elimination of the acetate to give the α,β unsaturated carboxylic acid. Fortunately, the use of milder conditions (1:2:2 TEA–H_2O–CH_3OH), led to the desired compound **14** in 82% yield. Amidation of the carboxylic acid **14** with the amine **9** was sluggish and led to **58** in modest 52% yield. Given the ease with which the amidations leading to **5**–**7** were carried out, the relatively low yield and sluggishness of the reaction were surprising. However, attempts to improve the yield of the product by changing the reaction conditions (e.g., use of EDC and DIEA) were unsuccessful. Debenzylation and reduction of **58** was achieved in a mixture of methanol, water and acetic acid (10:1:0.1) under a H_2 atmosphere with 10% Pd/C as the catalyst to afford **8**. The ^{1}H NMR spectrum of **8**, similar to that obtained for **7**, did not show evidence of atropisomerism.

As was the case for **5**, comparison of the NMR data for **8** with that reported for the polysaccharide was prohibited by the insolubility of **8** in D_2O, the solvent used for NMR studies of the naturally-occurring glycan. In this context it should be noted that the synthesis of the enantiomer of **16**, which could also be prepared from 3-butynol using the route described previously,[14] would enable the production of a lactam that could be used to prepare a derivative **8** with the opposable stereochemistry in this side-chain appendage.



Scheme 10. Synthesis of target **8**.

Conclusion

In summary, an efficient convergent strategy was developed for the synthesis of four unusual *N*-acylated monosaccharides (**5**–**8**) fragments present in LOS-IV from *M. marinum*. The general approach to the targets involved the formation of a lactam intermediates (**40**, **44**, **49** and **14**), which were coupled to aminosugar **9** and then deprotection of the resulting product. Monosaccharide **9** was prepared via a conventional route. The lactam moieties required for the targets were assembled via two approaches. A key feature of the sequence leading to the lactam precursors needed for the synthesis of **5**–**7** was the construction of highly substituted oxazolidine–pyrrolinone bicyclic ring system **11** through a substrate controlled stereoselective cyclization of α-methoxy-β-keto amide **12**. This reaction installed the two key stereocenters of the lactam moiety in a single step. A different approach was developed to synthesize the lactam needed for the preparation of target **8**. A cascade oxidation–cyclization–oxidation sequence of amino acid **16** was used to construct the core lactam **15**. Due to the decomposition under strongly basic conditions, a milder approach (hemiaminal formation with paraformaldehyde and K_2CO_3

followed by reaction with triethylsilane and trifluoroacetic acid) was used to furnish the *N*-methyl lactam **14**. The routes developed here will be useful in preparation of building blocks needed for the synthesis of the complete LOS-IV molecule. In addition, **5**–**8** have been synthesized in a form for conjugation to appropriate proteins and/or probes and hence represent useful biochemical tools.

Experimental section

General experimental methods: All reagents were purchased from commercial sources and were used without further purification unless noted. All reactions were monitored by TLC on silica gel 60-F_{254} (0.25 mm). Visualization of the reaction components was achieved using UV fluorescence (254 nm) and/or by charring with acidified anisaldehyde solution in ethanol or $KMnO_4$ in water or cerium ammonium molybdate stain. Organic solvents were evaporated under reduced pressure and the products were purified by column chromatography on silica gel (230–400 mesh). Optical rotations were measured in a microcell (1 cm, 1 mL) at ambient temperature and are in units of degree·mL/(g·dm). ^{1}H NMR spectra were recorded at 400 MHz, 500 MHz, 600 MHz or 700 Mz and chemical shifts are referenced to residual $CHCl_3$ (7.26 ppm, $CDCl_3$), CHD_2OD (3.30 ppm, CD_3OD) or DMSO-d_5 (2.50 ppm, DMSO-d_6). ^{13}C NMR spectra were recorded at 125 MHz and chemical shifts are referenced to $CDCl_3$ (77.0 ppm) or CD_3OD (49.3 ppm). Reported splitting patterns are abbreviated as s = singlet, d = doublet, t = triplet, m = multiplet, br = broad, app = apparent. Assignments of NMR spectra were based on two-dimensional experiments (^{1}H–^{1}H COSY, HSQC and HMBC) and stereochemistry of the anomeric centers of the pyranose rings were confirmed by measuring $^1J_{C\text{-}1,H\text{-}1}$ via coupled HSQC

experiments. ESI/TOF-HRMS spectra were recorded on samples suspended in THF or CH_3OH and added NaCl.

8-Azidooctyl 4-[(2′*R*,3′*S*,4′*R*)-3′-(hydroxy)-4′-methoxy-2′-carboxyl-1′,3′-dimethyl-5′-oxopyrrolidine-2′-carboxamido]-4,6-dideoxy-α-D-galactopyranoside (**5**) To a solution of **42** (30 mg, 0.037 mmol) in CH_3OH (5 mL), water (0.5 mL) and acetic acid (0.1 mL) was treated with palladium on charcoal (10%, 10 mg) and subjected to hydrogen atmosphere for 20 h. The mixture was filtered through Celite and the filtrate was concentrated. The residue was subjected to flash chromatography (C18 column, gradient 0→50% CH_3OH–H_2O) to yield **5** (17 mg, 89% yield) as a white amorphous solid. $[\alpha]_D$ = +28.6 (*c* 0.3, CH_3OH); The NMR data showed that there were two atropisomers in CD_3OD in a 4:3 ratio. ^{1}H NMR (500 MHz, CD_3OD, δ_H) 4.80 (d, 1 H, *J* = 3.5 Hz, H-1 (major)), 4.78 (d, 1 H, *J* = 3.5 Hz, H-1 (minor)), 4.22–4.13 (m, 2H, H-4 and H-5), 3.95 (s, 1 H, CH_3OCH (major)), 3.96–3.90 (m, 1 H, H-3), 3.85 (s, 1 H, CH_3OCH (minor)), 3.69–3.66 (m, 2 H, octyl OCH_2 and H-2), 3.66 (s, 3 H, OCH_3 (minor)), 3.55–3.59 (m, 1 H, H-2), 3.49–3.44 (m, 1 H, octyl OCH_2), 2.91–2.88 (m, 2 H, CH_2NH_2), 2.90 (s, 3 H, NCH_3 (major)), 2.80 (s, 3 H, NCH_3 (minor)), 1.68–1.60 (m, 4 H, CH_2 x 2), 1.55 (s, 3 H, CCH_3 (minor)), 1.44–1.32 (m, 8 H, CH_2 x 4), 1.21 (d, 3 H, *J* = 6.5 Hz, H-6 (major)), 1.18 (d, 3 H, *J* = 6.5 Hz, H-6 (minor)), 1.17 (s, 3 H, CCH_3 (major)); ^{13}C NMR (125 MHz, CD_3OD, δ_C) for major atropisomer 173.3 (CH_3NC=O), 167.9 (HNC=O), 99.0 (C-1), 85.2 (CH_3OCH), 78.9 (CH_3COH), 72.5 (CCO_2H), 70.1 (C-3), 69.1 (C-2), 68.0 (OCH_2CH_2), 64.5 (C-5), 58.8 (OCH_3), 54.8 (C-4), 39.3 (CH_2NH_2), 29.2 to 28.5 (NCH_3 and CH_2 x 6), 17.7 (CCH_3), 16.3 (C-6); ^{13}C NMR (125 MHz, CD_3OD, δ_C) for minor atropisomer 174.2 (CH_3NC=O), 168.6 (HNC=O), 99.0 (C-1), 83.2 (CH_3OCH), 75.7 (CH_3COH), 69.9 (C-3), 69.2 (C-2), 68.1 (CCO_2H), 67.9 (OCH_2CH_2), 64.9 (C-

5), 59.6 (OCH_3), 54.7 (C-4), 39.3 (CH_2NH_2), 29.2 to 28.5 (NCH_3 and CH_2 x 6), 22.0 (CCH_3), 16.1 (C-6); HRMS (ESI) calcd for (M+Na) $C_{23}H_{41}N_3NaO_{10}$: 542.2684. Found: 542.2678.

8-Azidooctyl 4-[(2′*S*,3′*S*,4′*R*)-3′-(hydroxy)-4′-methoxy-2′-carboxyl-1′,3′-dimethyl-5′-oxopyrrolidine-2′-carboxamido]-4,6-dideoxy-α-D-galactopyranoside (**6**) To a solution of **47** (15 mg , 0.018 mmol) in CH_3OH (5 mL), water (0.5 mL) and acetic acid (0.1 mL) was added palladium on charcoal (10%, 7 mg) and subjected to hydrogen atmosphere for 20 h. The mixture was filtered through Celite and the filtrate was concentrated. The residue was subjected to flash chromatography (C18 column, 0→50% CH_3OH–H_2O) to yield **6** (8 mg, 88% yield) as a white soild. $[\alpha]_D$ = +117.8 (*c* 0.3, CH_3OH); The NMR data showed that there were two atropisomers in CD_3OD in a 5:1 ratio.^{1}H NMR for major atropisomer: ^{1}H NMR (500 MHz, CD_3OD, δ_H) 4.77 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1), 4.26 (dd, 1 H, $J_{3,4}$ = 4.5 Hz, $J_{4,5}$ = 1.5 Hz, H-4), 4.15 (qd, 1 H, $J_{5,6}$ = 6.5 Hz, $J_{4,5}$ = 1.5 Hz, H-5), 3.96 (s, 1 H, CH_3OCH), 3.84 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 4.5 Hz, H-3), 3.67–3.62 (m, 2 H, octyl OCH_2 and H-2), 3.56 (s, 3 H, OCH_3), 3.46 (dt, 1 H, *J* = 10.0, 6.5 Hz, octyl OCH_2), 2.91 (t, *J* = 8.0 Hz, 2 H, CH_2NH_2), 2.85 (s, 3 H, NCH_3), 1.67–1.60 (m, 4 H, CH_2 x 2), 1.42–1.36 (m, 8 H, CH_2 x 4), 1.31 (s, 3 H, CCH_3), 1.07 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR for major atropisomer: ^{13}C NMR (125 MHz, CD_3OD, δ_C) 173.7 (CH_3NC=O), 169.1 (HNC=O), 99.0 (C-1), 84.3 (CH_3OCH), 79.1 (CH_3COH), 70.3 (C-2), 69.8 (C-3), 67.9 (octyl OCH_2), 64.3 (C-5), 58.9 (OCH_3), 55.0 (C-4), 39.3 (CH_2NH_2), 29.0 (CH_2), 28.8 (CH_2), 28.7 (CH_2), 28.6 (NCH_3), 27.2 (CH_2), 25.9 (CH_2), 25.7 (CH_2), 17.8 (CCH_3), 15.7 (C-6); HRMS (ESI) calcd for (M+Na) $C_{23}H_{41}N_3NaO_{10}$: 542.2684. Found: 542.2677.

8-Azidooctyl 4-[(2′*S*,3′*S*,4′*R*)-3′-(hydroxy)-4′-methoxy-1′,3′-dimethyl-5′-oxopyrrolidine-2′-carboxamido]-4,6-dideoxy-α-D-galactopyranoside (**7**) A solution of **50** (15.0 mg , 0.019 mmol) in CH_3OH (5 mL), water (0.5 mL) and acetic acid (0.1 mL) was treated with palladium on charcoal (10%, 8 mg) and subjected to hydrogen atmosphere for 20 h. The mixture was filtered through Celite and the filtrate was concentrated. The residue was triturated with CH_2Cl_2 to yield **7** (8.1 mg, 0.016 mmol, 87% yield) as a white amorphous solid. $[\alpha]_D$ = +118.3 (*c* 0.3, CH_3OH); ^{1}H NMR (600 MHz, CD_3OD, , δ_H) 4.78 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1), 4.34 (dd, 1 H, $J_{3,4}$ = 4.5 Hz, $J_{4,5}$ = 1.5 Hz, H-4), 4.15 (qd, 1 H, $J_{5,6}$ = 6.5 Hz, $J_{4,5}$ = 1.5 Hz, H-5), 4.06 (s, 1 H, CH_3OCH), 4.01 (s, 1 H, C*H*C=ONH), 3.87 (dd, 1 H, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 4.5 Hz, H-3), 3.67 (dt, 1 H, *J* = 9.5, 7.0 Hz, octyl OCH_2), 3.62 (dd, 1 H, $J_{2,3}$ = 10.5 Hz, $J_{1,2}$ = 4.0 Hz, H-2), 3.59 (s, 3 H, OCH_3), 3.45 (dt, 1 H, *J* = 9.5, 6.5 Hz, octyl OCH_2), 2.90 (t, 2 H, *J* = 7.5 Hz, CH_2NH_2), 2.75 (s, 3 H, NCH_3), 1.68−1.62 (m, 4 H, CH_2 x 2), 1.43−1.38 (m, 8 H, CH_2 x 4), 1.37 (s, 3 H, CCH_3), 1.11 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR (125 MHz, CD_3OD, δ_C) 172.8 (CH_3NC=O), 170.0 (HNC=O), 98.9 (C-1), 84.1 (CH_3OCH), 76.1 (CH_3COH), 70.1 (*C*HC=ONH), 69.4 (C-3), 69.2 (C-2), 67.9 (octyl OCH_2), 64.1 (C-5), 58.9 (OCH_3), 54.7 (C-4), 39.2 (CH_2NH_2), 29.0 (CH_2), 28.8 (CH_2), 28.7 (CH_2), 27.8 (NCH_3), 27.2 (CH_2), 25.9 (CH_2), 25.7 (CH_2), 20.5 (CCH_3), 15.6 (C-6); HRMS (ESI) calcd for (M+H) $C_{22}H_{42}N_3O_8$: 476.2966. Found: 476.2961.

8-Azidooctyl 4-[(2′*S*,3′*R*)-3′-(hydroxy)-1′,3′-dimethyl-5′-oxopyrrolidine-2′- carboxamido]-4,6-dideoxy-α-D-galactopyranoside (**8**) A solution of **58** (5.1 mg , 0.0077 mmol) in CH_3OH (5 mL), water (0.5 mL) and acetic acid (0.1 mL) was treated with palladium on charcoal (10%, 5 mg) and subjected to a hydrogen atmosphere for 8 h. The mixture was filtered through Celite and the filtrate was concentrated. The residue was triturated with CH_2Cl_2 to afford **8** (2.8 mg, 81%

yield) as a white amorphous solid. $[\alpha]_D$ = +89.0 (*c* 0.1, CH_3OH); ^1H NMR (700 MHz, CD_3OD, δ_H) 8.02 (d, 1 H, *J* = 10.5 Hz, NH), 4.77 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1), 4.33–4.35 (m, 1 H, H-4), 4.14 (q, 1 H, $J_{5,6}$ = 6.5 Hz, H-5), 4.09 (s, 1 H, C*H*C=ONH), 3.85 (dd, 1 H, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 4.5 Hz, H-3), 3.66 (dt, 1 H, *J* = 10.0, 7.0 Hz, octyl OCH_2), 3.59 (dd, 1 H, $J_{2,3}$ = 10.5 Hz, $J_{1,2}$ = 4.0 Hz, H-2), 3.44 (dt, 1 H, *J* = 10.0, 6.5 Hz, octyl OCH_2), 2.90 (t, 2 H, *J* = 7.5 Hz, CH_2NH_2), 2.76 (s, 3 H, NCH_3), 2.61 (d, 1 H, *J* = 16.5 Hz, CH_2C=O), 1.31 (d, 1 H, *J* = 16.5 Hz, CH_2C=O), 1.68−1.60 (m, 4 H, CH_2 x 2), 1.49 (s, 3 H, CCH_3), 1.44−1.36 (m, 8 H, CH_2 x 4), 1.12 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR (125 MHz, CD_3OD, δ_C) 176.4 (CH_3NC=O), 171.5 (HNC=O), 100.5 (C-1), 74.3 (*C*HC=ONH), 73.2 (CH_3*C*OH), 70.9 (C-3 or C-2), 70.8 (C-3 or C-2), 69.4 (octyl O*C*H_2), 65.2 (C-5), 56.0 (C-4), 46.2 (*C*H_2C=O), 40.8 (*C*H_2NH_2), 30.5 (*C*H_2), 30.3 (*C*H_2), 30.2 (*C*H_2), 29.1 (NCH_3), 28.9 (C*C*H_3), 28.6 (*C*H_2), 27.4 (*C*H_2), 27.2 (*C*H_2), 17.1 (C-6); HRMS (ESI) calcd for (M+H) $C_{21}H_{40}N_3O_7$: 446.2861. Found: 446.2860.

8-Azidooctyl 4-amino-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galacatopyranoside (9) To a solution of **24** (350 mg, 0.59 mmol) in CH_3OH (16 mL) at room temperature was added NaOH (aq.) (4 mL, 1 N, 4 mmol). The mixture was heated at reflux for 4 days, before being cooled, diluted with water and extracted with CH_2Cl_2. The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated to afford **9** (281 mg, 96% yield) as a colorless oil. R_f 0.17 (2:3 hexane–EtOAc); $[\alpha]_D$ = +42.3 (*c* 0.4, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$, δ_H) δ 7.42–7.30 (m, 10 H, ArH), 4.83 (d, 1 H, *J* = 12.0 Hz, PhCH_2, C-2), 4.79 (d, 1 H, *J* = 11.5 Hz, PhCH_2, C-3), 4.77 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1), 4.72 (d, 1 H, *J* = 11.5 Hz, PhCH_2, C-3), 4.69 (d, 1 H, *J* = 12.0 Hz, PhCH_2, C-2), 4.05 (qd, 1 H, $J_{5,6}$ = 6.5 Hz, $J_{4,5}$ = 1.5 Hz, H-5), 3.89 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 4.0 Hz, H-3), 3.78 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{1,2}$ = 4.0 Hz, H-2), 3.65 (dt, 1 H, *J* = 10.0, 7.0

Hz, octyl OCH_2), 3.47 (dt, 1 H, J = 10.0, 7.0 Hz, octyl OCH_2), 3.29 (t, 2 H, J = 7.0 Hz, CH_2N_3), 3.20 (dd, 1 H, $J_{3,4}$ = 4.0 Hz, $J_{4,5}$ = 1.5 Hz, H-4), 1.68–1.60 (m, 4H, CH_2 x 2), 1.48 (br, 2H, NH_2), 1.42–1.37 (m, 8H, CH_2 x 4), 1.26 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) δ 138.8 (Ar), 128.4 (Ar), 128.3 (Ar), 127.8 (Ar), 127.6 (Ar), 127.63 (Ar), 127.61 (Ar), 97.4 (C-1), 78.6 (C-3), 75.5 (C-2), 73.1 (PhCH$_2$, C-2), 72.3 (PhCH$_2$, C-3), 68.1 (OCH$_2$CH$_2$), 65.1 (C-5), 53.4 (C-4), 51.5 (CH$_2$N$_3$), 29.4 (CH$_2$), 29.3 (CH$_2$), 29.1 (CH$_2$), 28.8 (CH$_2$), 26.7 (CH$_2$), 26.1 (CH$_2$), 16.8 (C-6); HRMS (ESI) calcd for (M+H) $C_{28}H_{41}N_4O_4$: 497.3122. Found: 497.3113.

(2*S*,3*S*,4*R*)-methyl 3-(benzyloxy)-2-(hydroxymethyl)-4-methoxy-1,3-dimethyl-5-oxopyrrolidine-2-carboxylate (10) To a solution of **38** (46 mg, 0.10 mmol) in THF (5 mL) was added *n*-Bu_4NF solution (0.5 mL, 1.0 M, 0.50 mmol) dropwise at room temperature. The mixture was stirred for 3 h. Then water was added and the mixture was extracted with EtOAc. The organic phases were washed with brine, dried over Na_2SO_4 and concentrated. The crude residue was purified by flash column chromatography (silica gel, gradient 30→50% EtOAc–hexane) to afford **10** (30 mg, 89% yield) as a white amorphous solid. R_f 0.32 (2:3 hexane–EtOAc); $[\alpha]_D$ = +82.1 (*c* 0.1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) δ 7.36–7.26 (m, 5 H, ArH), 4.67 (d, 1 H, J = 11.5 Hz, PhCH_2), 4.53 (d, 1 H, J = 11.5 Hz, PhCH_2), 4.13 (d, 1 H, J = 12.5 Hz, CH_2OH), 4.10 (s, 1 H, CH_3OCH), 4.02 (d, 1 H, J = 12.5 Hz, CH_2OH), 3.75 (s, 3 H, CO_2CH_3), 3.73 (s, 3 H, OCH_3), 2.92 (s, 3 H, NCH_3), 1.48 (s, 3 H, CCH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 172.3 (NC=O), 170.9 (CO$_2$CH$_3$), 138.1 (Ar), 128.3 (Ar), 127.5 (Ar), 126.8 (Ar), 83.4 (PhCH$_2$OC), 82.2 (CH_3OCH), 74.5 (CCO$_2$CH$_3$), 66.0 (PhCH$_2$), 62.5 (CH$_2$OH), 59.3 (OCH_3), 52.7 (CO_2CH_3), 27.7 (NCH_3), 12.8 (CCH_3); HRMS (ESI) calcd for (M+Na) $C_{17}H_{23}NNaO_6$: 360.1418. Found: 360.1420.

(3*S*,6*R*,7*S*,7a*S*)-methyl 3-(*tert*-butyl)-7-hydroxy-6-methoxy-7-methyl-5-oxohexahydropyrrolo[1,2-c]oxazole-7a-carboxylate (11) To a solution of **12**（1.50 g, 5.0 mmol）in dry toluene (100 mL) was added 1,8 diazabicyclo[5.4.0]undec-7-ene (DBU, 0.38 g, 2.5 mmol) and the mixture was heated at 60 °C for 12 h and then cooled to room temperature. The mixture was concentrated and the crude product was purified by flash column chromatography (silica gel, gradient 9→13% EtOAc–hexane) to afford **11** (1.12 g, 70% yield) as a white amorphous solid. R_f 0.52 (2:3 hexane–EtOAc); $[\alpha]_D$ = +35.8 (*c* 0.2, CH_2Cl_2); a sample was recrystallized from hexane and EtOAc, m.p. 136–137 °C; ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 4.95 (s, 1 H, C*H*$(CH_3)_3$), 4.69 (d, 1 H, *J* = 9.5 Hz, OCH_RH$_S$C), 4.61 (s, 1 H, CH_3OC*H*), 3.95 (d, 1 H, *J* = 9.5 Hz, OCH$_R$$H_S$C), 3.85 (s, 3 H, CO_2CH_3), 3.70 (s, 3 H, OCH_3), 2.12 (s, 1 H, OH), 1.33 (s, 3 H, CCH_3), 0.91 (s, 9 H, C$(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 173.0 (NC=O), 171.2 (*C*O_2CH_3), 96.1 (*C*H$(CH_3)_3$), 85.6 (CH_3O*C*H), 81.2 (HO*C*CH_3), 75.8 (*C*CO_2CH_3), 69.0 (O*C*H$_R$H$_S$C), 59.8 (OCH_3), 52.8 (CO_2*C*H_3), 36.4 (*C*$(CH_3)_3$), 24.9 (C$(CH_3)_3$), 18.6 (C*C*H_3); HRMS (ESI) calcd for (M+Na) $C_{14}H_{23}NNaO_6$: 324.1418. Found: 324.1419.

(2*S*,4*R*)-methyl 2-(*tert*-butyl)-3-(2-methoxy-3-oxobutanoyl)oxazolidine-4-carboxylate (12) To a stirred suspension of $PhI(OAc)_2$ (1.3 g, 7.2 mmol) in anhydrous CH_3OH (25 mL) at room temperature was added BF_3•OEt_2 (0.9 mL, 7.2 mmol). After the solution became clear, compound **28** (1.5 g, 5.5 mmol) in CH_3OH (3 mL) was added dropwise and the mixture was stirred at room temperature for 16 h. At that point, half of the solvent was removed and the BF_3•OEt_2 was quenched by the addition of a satd aq solution of $NaHCO_3$. The mixture was then extracted with EtOAc. The organic phases were washed with brine, dried over Na_2SO_4, concentrated, and the residue was purified by flash column chromatography (silica gel, gradient

0→25% EtOAc–hexane) to yield **12** (1.5 g, 90% yield, 96:4 = keto–enol tautomers, 3:1 for two inseparable diastereoisomeric α-methoxy-β-keto amides) as a colorless oil; R_f 0.20 (3:1 hexane–EtOAc); NMR data for major isomer: ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 5.31 (s, 1 H, C*H*$(CH_3)_3$), 5.30 (dd, 1 H, *J* = 7.0, 1.5 Hz, C*H*CO_2CH_3), 4.73 (s, 1 H, C*H*OCH_3), 4.60 (dd, 1 H, *J* = 8.5, 1.5 Hz, OC*H*$_2$), 3.98 (dd, 1 H, *J* = 8.5, 7.0 Hz, OC*H*$_2$), 3.82 (s, 3 H, CO_2CH_3), 3.51 (s, 3 H, CHOC*H*$_3$), 2.34 (s, 3 H, CH_3C=O), 0.94 (s, 9 H, C$(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 207.0 (CH_3C=O), 170.1 (CO_2CH_3), 167.9 (NC=O), 97.1 (*C*H$(CH_3)_3$), 86.8 (*C*HOCH_3), 67.7 (OCH_2), 58.2 (*C*HCO_2CH_3), 57.5 (OCH_3), 52.7 (CO_2CH_3), 37.2 (*C*$(CH_3)_3$), 26.8 (*C*H_3C=O), 25.7 (C(*C*$H_3)_3$); NMR data for minor isomer: ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 5.34 (s, 1 H, C*H*$(CH_3)_3$), 4.79 (dd, 1 H, *J* = 7.0, 2.0 Hz, C*H*CO_2CH_3), 4.63 (s, 1 H, C*H*OCH_3), 4.46 (dd, 1 H, *J* = 8.5, 2.0 Hz, OC*H*$_2$), 3.94 (dd, 1 H, *J* = 8.5, 7.0 Hz, OC*H*$_2$), 3.81 (s, 3 H, CO_2CH_3), 3.49 (s, 3 H, CHOC*H*$_3$), 2.31 (s, 3 H, CH_3C=O), 0.99 (s, 9 H, C$(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 202.5.0 (CH_3C=O), 170.0 (CO_2CH_3), 168.6 (NC=O), 97.6 (*C*H$(CH_3)_3$), 88.8 (*C*HOCH_3), 68.8 (OCH_2), 59.3 (*C*HCO_2CH_3), 58.6 (OCH_3), 52.5 (CO_2CH_3), 37.1 (*C*$(CH_3)_3$), 27.0 (*C*H_3C=O), 26.0 (C(*C*$H_3)_3$); HRMS (ESI) calcd for (M+H) $C_{14}H_{24}NO_6$: 302.1598. Found: 302.1597.

(2*S*,3*R*)-3-hydroxy-1,3-dimethyl-5-oxopyrrolidine-2-carboxylic acid (14) Compound **57** (80 mg, 0.35 mmol) was dissolved in TEA (5 mL), CH_3OH (10 mL) and water (10 mL) and the mixture was stirred at room temperature over night. Then the solution was concentrated, and the resulting residue was subjected to flash column chromatography (latrobeads 6RS-8060, gradient 10%→50% CH_3OH–CH_2Cl_2) to yield **14** (49 mg, 82% yield) as a white amorphous solid; R_f 0.2 (2:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ = +11.6 (*c* 0.3, CH_2Cl_2); ^{1}H NMR (500 MHz, CD_3OD, δ_H) 3.98 (s, 1 H, NC*H*), 2.83 (s, 3 H, NCH_3), 2.56 (d, 1 H, *J* = 17.0 Hz, C*H*$_2$C=O), 2.41 (d, 1 H, *J* = 17.0 Hz,

C*H*$_2$C=O), 1.50 (s, 3 H, CCH$_3$); ^{13}C NMR (125 MHz, CDCl$_3$, δ_C) 176.1 (NC=O), 170.0 (*C*O$_2$H), 75.0 (N*C*H), 73.0 (CH$_3$*C*OH), 46.6 (*C*H$_2$C=O), 29.4 (NCH$_3$), 28.1 (C*C*H$_3$); HRMS (ESI) (M-H) calcd for $C_7H_{10}NO_4$: 172.0615. Found: 172.0618.

(2*S*,3*R*)-1-*tert*-butyl 2-methyl 3-hydroxy-3-methyl-5-oxopyrrolidine-1,2-dicarboxylate (15) Compound **16**[14] (0.91g, 3.31 mmol) was dissolved in CCl_4 (15 mL), CH_3CN (15 mL), and water (18 mL). With vigorous stirring, $NaIO_4$ (2.12 g, 9.9 mmol) and $RuCl_3 \cdot H_2O$ (30 mg) were added at 0 °C. The mixture was stirred at room temperature for 1 h, and then EtOAc (30 mL) was added. The mixture was washed with a satd aq solution of $NaHCO_3$, brine, dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (silica gel, gradient 50→150% EtOAc–hexane) to give **15** as a colorless liquid (0.61 g, 69% yield). R_f 0.3 (4:3 EtOAc–Hexane); $[\alpha]_D$ = +0.19 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 4.34 (s, 1 H, NC*H*), 3.84 (s, 3 H, OCH_3), 2.90 (d, 1 H, *J* = 17.0 Hz, COC*H*$_2$), 2.60 (d, 1 H, *J* = 17.0 Hz, COC*H*$_2$), 2.26 (br, 1 H, OH), 1.52 (s, 9 H, C(CH$_3$)$_3$), 1.45 (s, 3 H, CCH$_3$); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.6 (NC=O), 169.1 (*C*O$_2$CH$_3$), 149.0 (*C*O$_2$C(CH$_3$)$_3$), 84.1 (O*C*(CH$_3$)$_3$), 70.8 (CH$_3$*C*OH), 69.6 (N*C*H), 52.5 (OCH_3), 46.4 (CH_2), 28.2 (C*C*H$_3$), 27.9 (C(*C*H$_3$)$_3$); HRMS (ESI) calcd for (M+Na) $C_{12}H_{19}NNaO_6$: 296.1105. Found: 296.1105.

Allyl 2,3-di-*O*-benzyl-6-*O*-tosyl-α-D-glucopyranoside (19) To a solution of allyl 2,3-di-*O*-benzyl-α-D-glucopyranoside (**18**,[15] 1.60 g, 4.07 mmol) in anhydrous pyridine (10 mL) was added TsCl (1.16 g, 6.10 mmol) at 0 °C. After being stirred for 12 h at room temperature, the mixture was diluted with EtOAc (30 mL), washed with 1 N HCl, a satd aq solution of $NaHCO_3$, brine, dried over Na_2SO_4 and concentrated. The crude residue was purified by flash column

chromatography (silica gel, gradient 20→25% EtOAc–hexane) to afford **19** (2.14 g, 95% yield) as a colorless oil. R_f 0.45 (2:1 hexane–EtOAc); $[\alpha]_D$ = +38.1 (*c* 0.7, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.80 (d, 2 H, *J* = 8.5 Hz, ArH), 7.39–7.22 (m, 12 H, ArH), 5.92 (dddd, 1 H, *J* = 17.0, 10.0, 6.5, 5.0 Hz, CH_2=C*H*), 5.32 (app dq, 1 H, *J* = 17.0, 1.5 Hz, CH_2=CH), 5.24 (app dq, 1 H, *J* = 10.0, 1.0 Hz, CH_2=CH), 5.02 (d, 1 H, *J* = 12.0 Hz, PhCH_2, C-3), 4.79 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.74 (d, 1 H, *J* = 12.0 Hz, PhCH_2, C-2), 4.71 (d, 1 H, *J* = 12.0 Hz, PhCH_2, C-3), 4.65 (d, 1 H, *J* = 12.0 Hz, PhCH_2, C-2), 4.28–4.22 (m, 2 H, H-4 and H-5), 4.13 (app ddt, 1 H, *J* = 13.0, 5.0, 1.5 Hz, CH_2=CHCH_2), 3.97 (app ddt, 1 H, *J* = 13.0, 6.5, 1.0 Hz, CH_2=CHCH_2), 3.79 (app t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz, H-3), 3.79 (dd, 1 H, $J_{6R,6S}$ = 10.0 Hz, $J_{5,6}$ = 2.5 Hz, H-6), 3.49 (dd, 1 H, $J_{2,3}$ = 9.5 Hz, $J_{1,2}$ = 3.5 Hz, H-2), 3.45 (dd, 1 H, $J_{6R,6S}$ = 10.0 Hz, $J_{5,6}$ = 3.0 Hz, H-6), 2.45 (s, 3 H, $PhCH_3$), 2.23 (d, 1 H, *J* = 3.0 Hz, OH); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 144.8 (Ar), 138.7 (Ar), 137.9 (Ar), 133.5 (*C*H=CH_2), 133.0 (Ar), 129.8 (Ar), 128.6 (Ar), 128.5 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 118.5 (CH=*C*H_2), 95.6 (C-1), 81.1 (C-3), 79.5 (C-2), 75.4 (Ph*C*H_2, C-3), 73.0 (Ph*C*H_2, C-2), 69.5 (C-6), 69.2 and 68.9 (C-4 and C-5), 68.4 (*C*H_2CH=CH_2), 21.7 (*C*H_3PhSO_2); HRMS (ESI) calcd for (M+Na) $C_{30}H_{34}NaO_8S$: 577.1867. Found: 577.1864.

Allyl 2,3-di-*O*-benzyl-6-deoxy-α-D-glucopyranoside (20) Tosylate **19** (2.10 g, 3.79 mmol) was dissolved in THF (30 mL) and $LiAlH_4$ (288 mg, 7.58 mmol) was added. The reaction mixture was heated at reflux for 3 h. After completion of the reaction, the $LiAlH_4$ was quenched by slowly adding the mixture to ice, then the mixture was filtered through Celite. The filter cake was washed with EtOAc, and the resulting cloudy solution was filtered again through Celite. The combined organic layers were washed with 1 N HCl, a satd aq solution of $NaHCO_3$, brine, dried over Na_2SO_4 and concentrated. The crude residue was purified by flash column chromatography

(silica gel, gradient 10→15% EtOAc–hexane) to afford **20** (1.25 g, 85% yield) as a colorless oil. R_f 0.39 (4:1 hexane–EtOAc); $[\alpha]_D$ = +70.4 (*c* 0.2, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.41–7.29 (m, 10 H, ArH), 5.98 (dddd, 1 H, *J* = 17.0, 10.0, 6.5, 5.0 Hz, CH_2=C*H*), 5.37 (app dq, 1 H, *J* = 17.0, 1.0 Hz, CH_2=CH), 5.27 (app dq, 1 H, *J* = 10.0, 1.0 Hz, CH_2=CH), 5.08 (d, 1 H, *J* = 11.5 Hz, PhCH_2, C-3), 4.81 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.76 (d, 1 H, *J* = 12.0 Hz, PhCH_2, C-2), 4.73 (d, 1 H, *J* = 11.5 Hz, PhCH_2, C-3), 4.70 (d, 1 H, *J* = 12.0 Hz, PhCH_2, C-2), 4.20 (app ddt, 1 H, *J* = 13.0, 5.0, 1.0 Hz, CH_2=CHCH_2), 4.05 (app ddt, 1 H, *J* = 13.0, 6.5, 1.0 Hz, CH_2=CHCH_2), 3.81 (app t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz, H-3), 3.75 (dq, 1 H, $J_{4,5}$ = 9.5 Hz, $J_{5,6}$ = 6.0 Hz, H-5), 3.57 (dd, 1 H, $J_{2,3}$ = 9.5 Hz, $J_{1,2}$ = 3.5 Hz, H-2), 3.21 (app td, 1 H, $J_{4,5}$ = $J_{3,4}$ = 9.5 Hz, $J_{4,OH}$ = 2.0 Hz, H-4), 2.19 (d, 1 H, *J* = 2.0 Hz, OH), 1.27 (d, 3 H, $J_{5,6}$ = 6.0 Hz, H-6); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 138.8 (Ar), 138.1 (Ar), 133.9 (*C*H=CH_2), 128.7 (Ar), 128.5 (Ar), 128.1 (Ar), 128.0 (Ar), 127.92 (Ar), 127.91 (Ar), 118.1 (CH=*C*H_2), 95.5 (C-1), 81.3 (C-3), 80.1 (C-2), 75.4 (C-4), 75.3 (Ph*C*H_2, C-3), 72.8 (Ph*C*H_2, C-2), 68.2 (*C*H_2CH=CH_2), 67.1 (C-5), 17.7 (C-6); HRMS (ESI) calcd for (M+Na) $C_{23}H_{28}NaO_5$: 407.1829. Found: 407.1825.

Allyl 4-azido-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (21) To a solution of **20** (1.25 g, 3.25 mmol) and pyridine (3 mL) in anhydrous CH_2Cl_2 at 0 °C was added Tf_2O (1.37 g, 4.88 mmol) slowly. After being stirred for 1 h, the mixture was diluted with CH_2Cl_2, washed with water, a satd aq solution of $NaHCO_3$, brine, dried over Na_2SO_4 and concentrated to obtain the crude triflate, which was dissolved into DMF (15 mL). Excess NaN_3 (845 mg, 13 mmol) was added and the mixture was stirred overnight at room temperature. After completion of the reaction, the mixture was filtered through Celite and the residue was washed with EtOAc. The combined solutions were concentrated and the resulting residue was purified by flash column

chromatography (silica gel, gradient 4→6% EtOAc–hexane) to afford **21** (1.13 g, 85% yield) as a colorless oil. R_f 0.61 (4:1 hexane–EtOAc); $[\alpha]_D$ = +85.1 (*c* 0.4, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.44–7.29 (m, 10 H, ArH), 5.95 (dddd, 1 H, *J* = 17.0, 10.0, 6.0, 5.0 Hz, CH_2=C*H*), 5.34 (d, 1 H, *J* = 17.0 Hz, CH_2=CH), 5.25 (d, 1 H, *J* = 10.0 Hz, CH_2=CH), 4.89 (d, 1 H, *J* = 12.0 Hz, PhCH_2, C-3), 4.84 (d, 1 H, *J* = 12.0 Hz, PhCH_2, C-2), 4.80 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.79 (d, 1 H, *J* = 12.0 Hz, PhCH_2, C-3), 4.68 (d, 1 H, *J* = 12.0 Hz, PhCH_2, C-2), 4.12 (dd, 1 H, *J* = 12.5, 5.0 Hz, CH_2=CHCH_2), 4.10 (dd, 1 H, $J_{2,3}$ = 9.5 Hz, $J_{3,4}$ = 3.5 Hz, H-3), 4.03 (dd, 1 H, *J* = 12.5, 6.0 Hz, CH_2=CHCH_2), 4.01 (q, 1 H, $J_{5,6}$ = 6.5 Hz, H-5), 3.89 (dd, 1 H, $J_{2,3}$ = 9.5 Hz, $J_{1,2}$ = 3.5 Hz, H-2), 3.75 (d, 1 H, $J_{3,4}$ = 3.5 Hz, H-4), 1.26 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 138.4 (Ar), 138.3 (Ar), 133.9 (*C*H=CH_2), 128.5 (Ar), 128.4 (Ar), 128.0 (Ar), 127.8 (Ar), 127.7 (Ar), 127.6 (Ar), 118.1 (CH=*C*H_2), 96.3 (C-1), 78.1 (C-3), 76.0 (C-2), 73.6 (Ph*C*H_2, C-2), 73.2 (Ph*C*H_2, C-3), 68.5 (*C*H_2CH=CH_2), 65.2 (C-4), 64.5 (C-5), 17.3 (C-6); HRMS (ESI) calcd for (M+Na) $C_{23}H_{27}N_3NaO_4$: 432.1894. Found: 432.1893.

Allyl 4-amino-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (22) To a solution of **21** (1.05 g, 2.56 mmol) in THF (40 mL) at room temperature was added NaOH (1 M, 10 mL). Then a solution of PMe_3 (10.0 mL, 1M in THF, 10.0 mmol) was added dropwise. The mixture was stirred at room temperature for 10 h. After completion of the reaction, the mixture was diluted with water, extracted with CH_2Cl_2. The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated. The crude residue was purified by flash column chromatography (silica gel, gradient 0→2% CH_3OH–EtOAc) to afford **22** (0.91 g, 92% yield) as a colorless oil. R_f 0.17 (2:3 hexane–EtOAc); $[\alpha]_D$ = +98.3 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.42–7.29 (m, 10 H, ArH), 5.97 (dddd, 1 H, *J* = 17.0, 10.0, 6.5, 5.0 Hz, CH_2=C*H*), 5.36 (apt dq,

1 H, J = 17.0, 1.5 Hz, CH_2=CH), 5.25 (apt dq, 1 H, J = 10.0, 1.0 Hz, CH_2=CH), 4.83 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1), 4.81 (d, 1 H, J = 12.0 Hz, PhCH_2, C-2), 4.79 (d, 1 H, J = 11.5 Hz, PhCH_2, C-3), 4.72 (d, 1 H, J = 11.5 Hz, PhCH_2, C-2), 4.68 (d, 1 H, J = 12.0 Hz, PhCH_2, C-3), 4.17 (apt ddt, 1 H, J = 13.0, 5.0, 1.0 Hz, CH_2=CHCH_2), 4.06 (q, 1 H, $J_{5,6}$ = 6.5 Hz, H-5), 4.05 (apt ddt, J = 13.0, 6.5, 1.5 Hz, 1H, CH_2=CHCH_2), 3.92 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 4.0 Hz, H-3), 3.78 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{1,2}$ = 4.0 Hz, H-2), 3.22 (d, 1 H, $J_{3,4}$ = 4.0 Hz, H-4), 2.06 (br, 2 H, NH_2), 1.26 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 138.7 (Ar), 138.6 (Ar), 134.1 (*C*H=CH_2), 128.4 (Ar), 128.3 (Ar), 127.9 (Ar), 127.7 (Ar), 127.6 (Ar), 117.9 (CH=*C*H_2), 96.2 (C-1), 78.3 (C-3), 75.3 (C-2), 73.2 (Ph*C*H_2, C-2), 72.4 (Ph*C*H_2, C-3), 68.3 (*C*H_2CH=CH_2), 65.2 (C-5), 53.5 (C-4), 16.7 (C-6); HRMS (ESI) calcd for (M+H) $C_{23}H_{30}NO_4$: 384.2169. Found: 384.2165.

Allyl 4-trifluoroacetamido-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (23) To a solution of **22** (590 mg, 1.5 mmol) in anhydrous pyridine (15 mL) at 0 °C was added trifluoroacetic anhydride (594 mg, 3.0 mol) dropwise. The mixture was slowly warmed to room temperature and stirred for 6 h. After completion of the reaction, the mixture was concentrated under vacuum and diluted with CH_2Cl_2. The organic solution was washed with 1 N HCl, brine, dried over Na_2SO_4 and concentrated. The crude residue was purified by flash column chromatography (silica gel, gradient 10→15% EtOAc–hexane) to afford **23** (634 mg, 86% yield) as a colorless oil. R_f 0.48 (4:1 hexane–EtOAc); $[\alpha]_D$ = +71.1 (*c* 0.3, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.40–7.30 (m, 10 H, ArH), 6.32 (d, 1 H, J = 10.0 Hz, NH), 5.96 (dddd, 1 H, J = 17.0, 10.0, 6.5, 5.0 Hz, CH_2=C*H*), 5.37 (apt dq, 1 H, J = 17.0, 1.5 Hz, CH_2=CH), 5.28 (apt dq, 1 H, J = 10.0, 1.0 Hz, CH_2=CH), 4.84 (d, 1 H, J = 12.0 Hz, PhCH_2, C-2), 4.83 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1),

4.83 (d, 1 H, J = 11.0 Hz, PhCH_2, C-3), 4.68 (d, 1 H, J = 12.0 Hz, PhCH_2, C-2), 4.60 (d, 1 H, J = 11.0 Hz, PhCH_2, C-3), 4.57 (dd, 1 H, $J_{4,NH}$ = 10.0 Hz, $J_{3,4}$ = 4.0 Hz, H-4), 4.23 (qd, 1 H, $J_{5,6}$ = 6.5 Hz, $J_{4,5}$ = 1.5 Hz, H-5), 4.19 (apt ddt, 1 H, J = 13.0, 5.0, 1.5 Hz, CH_2=CHCH_2), 4.07 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 4.0 Hz, H-3), 4.06 (apt ddt, 1 H, J = 13.0, 6.5, 1.0 Hz, CH_2=CHCH_2), 3.47 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{1,2}$ = 4.0 Hz, H-2), 1.18 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 158.0 (q, $^2J_{C,F}$ = 37.5 Hz, C=O), 138.1 (Ar), 137.9 (Ar), 133.5 (CH=CH_2), 128.4 (Ar), 128.3 (Ar), 128.0 (Ar), 127.9 (Ar), 127.7 (Ar), 118.4 (CH=CH_2), 115.9 (q, $^1J_{C,F}$ = 287.5 Hz, CF_3), 96.3 (C-1), 76.2 (C-3), 75.1 (C-2), 73.4 (PhCH$_2$, C-2), 72.1 (PhCH$_2$, C-3), 68.8 (CH$_2$CH=CH_2), 63.8 (C-5), 52.1 (C-4), 16.4 (C-6); HRMS (ESI) calcd for (M+Na) $C_{25}H_{28}F_3NNaO_5$: 502.1812. Found: 502.1808.

8-Azidooctyl 4-trifluoroacetamido-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (24)

To a solution of **23** (500 mg, 1.04 mmol) in CH_3OH (10 mL) and CH_2Cl_2 (10 mL) at room temperature was added $PdCl_2$ (18 mg, 0.10 mol, 0.1 equiv). The mixture was stirred at room temperature for 16 h. After completion of the reaction, the mixture was filtered through a plug of Celite and the filtrate was concentrated to obtain crude 4-trifluoroacetamido-2,3-di-*O*-benzyl-4,6-dideoxy-D-galactopyranoside, which was carried forward without further purification. This crude product was dissolved in anhydrous CH_2Cl_2 (20 mL) with 4 Å molecular sieves and this mixture was treated with trichloroacetonitrile (1.5 g, 10.4 mmol) and Cs_2CO_3 (676 mg, 2.08 mmol). The mixture was stirred at room temperature for 6 h and then filtered through Celite. The filtrate was concentrated to obtain the corresponding glycosyl trichloroacetimidate, which was dissolved in Et_2O (5 mL) and added to a mixture of 8-azidooctanol (355 mg, 2.08 mmol) and 4 Å molecular sieves in Et_2O (5 mL). The mixture was cooled to 0 °C and TMSOTf (15 μL) was

added and the solution was stirred at 0 °C for 1 h. The TMSOTf was quenched by the addition of Et_3N (1 mL) and the solution was concentrated. The residue was purified by flash column chromatography (silica gel, gradient 10→15% EtOAc–hexane) to afford **24** (415 mg, 68% yield) as a colorless oil. R_f 0.58 (4:1 hexane–EtOAc); $[\alpha]_D$ = +66.3 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.39–7.30 (m, 10 H, ArH), 6.33 (d, 1 H, *J* = 10.0 Hz, NH), 4.84 (d, 1 H, *J* = 12.0 Hz, PhC*H*$_2$, C-2), 4.83 (d, 1 H, *J* = 11.0 Hz, PhC*H*$_2$, C-3), 4.76 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1), 4.67 (d, 1 H, *J* = 12.0 Hz, PhC*H*$_2$, C-2), 4.60 (d, 1 H, *J* = 11.0 Hz, PhC*H*$_2$, C-3), 4.57 (ddd, 1 H, $J_{4,NH}$ = 10.0 Hz, $J_{3,4}$ = 4.5 Hz, $J_{4,5}$ = 1.5 Hz, H-4), 4.21 (qd, 1 H, $J_{5,6}$ = 6.5 Hz, $J_{4,5}$ = 1.5 Hz, H-5), 4.05 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 4.5 Hz, H-3), 3.65 (dt, 1 H, *J* = 10.0, 7.0 Hz, octyl OC*H*$_2$), 3.47 (dt, 1 H, *J* = 10.0, 7.0 Hz, octyl OC*H*$_2$), 3.46 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{1,2}$ = 4.0 Hz, H-2), 3.29 (t, 2 H, *J* = 7.0 Hz, CH_2N_3), 1.70–1.60 (m, 4H, CH_2 x 2), 1.43–1.34 (m, 8H, CH_2 x 4), 1.18 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 158.0 (q, $^2J_{C,F}$ = 37.5 Hz, C=O), 138.3 (Ar), 137.9 (Ar), 128.4 (Ar), 128.3 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 115.9 (q, $^1J_{C,F}$ = 287.5 Hz, CF_3), 97.5 (C-1), 76.2 (C-3), 75.3 (C-2), 73.3 (Ph*C*H$_2$, C-2), 72.1 (Ph*C*H$_2$, C-3), 68.7 (O*C*H$_2$CH$_2$), 63.6 (C-5), 52.1 (C-4), 51.5 (*C*H$_2$N$_3$), 29.4 (*C*H$_2$), 29.3 (*C*H$_2$), 29.1 (*C*H$_2$), 28.8 (*C*H$_2$), 26.7 (*C*H$_2$), 26.1 (*C*H$_2$), 16.5 (C-6); HRMS (ESI) calcd for (M+Na) $C_{30}H_{39}F_3N_4NaO_5$: 615.2765. Found: 615.2754.

(2*S*,4*R*)-methyl 2-(*tert*-butyl)-3-(3-oxobutanoyl)oxazolidine-4-carboxylate (**28**) To a stirred suspension of D-serine methyl ester hydrochloride (3.23 g, 20.8 mmol) in pentane (100 mL) were added *t*-butyl aldehyde (2.32 g, 27.0 mmol) and Et_3N (2.73 g, 27.0 mmol) at room temperature. The mixture was heated at reflux for 15 h using a Dean-Stark apparatus. The resulting mixture was cooled to room temperature, filtered, and the cake was washed with pentane (2 x 50 mL).

The combined filtrate was concentrated to afford crude product as clear oil, which was used in the next step without further purification. To a solution of the crude product in dry CH_2Cl_2 (100 mL) at 0 °C were added acetoacetic acid (2.55 g, 25.0 mmol), EDC hydrochloride (4.8 g, 25.0 mmol) and DMAP (0.25 g, 2.1 mmol). The mixture was warmed to room temperature and stirred for 16 h, before being diluted with water and extracted with CH_2Cl_2. The organic phases were washed with brine, dried over Na_2SO_4 and concentrated. The crude residue was purified by flash column chromatography (silica gel, gradient 20→50% EtOAc–hexane) to afford **25** (4.3 g, 77% yield) as a mixture of keto–enol tautomers (1.7: 1 ratio). R_f 0.16 (3:1 hexane–EtOAc); $[\alpha]_D$ = +46.3 (*c* 0.4, CH_2Cl_2); NMR data for keto form: ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 5.35 (s, 1 H, C*H*$(CH_3)_3$), 4.66 (d, 1 H, *J* = 6.0 Hz, C*H*CO_2CH_3), 4.56 (d, 1 H, *J* = 8.0 Hz, OC*H*$_2$), 4.08–4.03 (m, 1H, OC*H*$_2$), 3.82 (s, 3 H, CO_2CH_3), 3.73 (s, 2 H, CH_2C=ON), 2.34 (s, 3 H, CH_3C=O), 0.93 (s, 9 H, C$(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 202.6 (CH_3C=O), 170.0 (CO_2CH_3), 168.0 (NC=O), 96.7 (*C*H$(CH_3)_3$), 67.8 (OCH_2), 59.4 (*C*HCO_2CH_3), 52.7 (CO_2CH_3), 51.9 (CH_2C=ON), 37.4 (*C*$(CH_3)_3$), 30.7 (*C*H_3C=O), 25.8 (C(*C*$H_3)_3$); NMR data for enol form: ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 5.13 (s, 1 H, C*H*$(CH_3)_3$), 4.50 (d, 1 H, *J* = 8.5 Hz, OC*H*$_2$), 4.08–4.03 (m, 1 H, OC*H*$_2$), 3.83 (s, 3 H, CO_2CH_3), 2.01 (s, 3 H, CH_3C=O), 0.97 (s, 9 H, C$(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 176.5 (NC=O), 170.4 (CO_2CH_3), 89.6 (*C*H$(CH_3)_3$), 67.9 (OCH_2), 52.8 (CO_2CH_3), 37.7 (*C*$(CH_3)_3$), 25.9 (C(*C*$H_3)_3$), 22.0 (*C*H_3C=O); HRMS (ESI) calcd for (M+H) $C_{13}H_{22}NO_5$: 272.1492. Found: 272.1487.

(3*S*,6*R*,7*S*,7a*S*)-methyl 7-(benzyloxy)-3-(*tert*-butyl)-6-methoxy-7-methyl-5-oxohexahydropyrrolo[1,2-c]oxazole-7a-carboxylate (33) To a solution of **11** (222 mg, 0.73 mmol) in DMF (1 mL) and benzyl bromide (3 mL) was added *n*-Bu_4NI (323 mg, 0.87 mmol).

The mixture was cooled to −15 °C and NaH (44 mg, 60% in mineral oil, 1.09 mmol) was added in two portions. After 1 h, the mixture was slowly warmed to 0 °C and a satd aq solution of NH_4Cl (5 mL) was added dropwise. Thereafter, the mixture was extracted with EtOAc. The organic phases were washed with brine, dried over Na_2SO_4 and concentrated. The crude residue was purified by flash column chromatography (silica gel, gradient 9→14% EtOAc–hexane) to afford **33** (245 mg, 85% yield) as a white amorphous solid and the by-product **34** (25 mg, 9% yield) as a white amorphous solid. Data for **33**: R_f 0.50 (3:1 hexane–EtOAc); $[\alpha]_D$ = + 36.6 (*c* 0.3, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) δ 7.37–7.29 (m, 5 H, ArH), 4.96 (s, 1 H, C*H*$(CH_3)_3$), 4.78 (d, 1 H, *J* = 9.5 Hz, OCH_RH$_S$C), 4.77 (s, 1 H, CH_3OC*H*), 4.59 (d, 1 H, *J* = 11.0 Hz, PhCH_2), 4.52 (d, 1 H, *J* = 11.0 Hz, PhCH_2), 4.05 (d, 1 H, *J* = 9.5 Hz, OCH$_R$$H_S$C), 3.71 (s, 3 H, CO_2CH_3), 3.70 (s, 3 H, OCH_3), 1.59 (s, 3 H, CCH_3), 0.91 (s, 9 H, C$(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 173.3 (NC=O), 171.0 (*C*O_2CH_3), 137.8 (Ar), 128.3 (Ar), 127.6 (Ar), 127.1 (Ar), 95.9 (*C*H$(CH_3)_3$), 85.9 (PhCH_2O*C*), 85.5 (CH_3O*C*H), 75.7 (*C*CO_2CH_3), 69.1 (O*C*H$_R$H$_S$C), 67.0 (Ph*C*H_2), 59.2 (OCH_3), 52.7 (CO_2*C*H_3), 36.5 (*C*$(CH_3)_3$), 24.9 (C(*C*$H_3)_3$), 13.9 (C*C*H_3); HRMS (ESI) calcd for (M+Na) $C_{21}H_{29}NNaO_6$: 414.1887. Found: 414.1885. Data for **34**: R_f 0.47 (3:1 hexane–EtOAc); $[\alpha]_D$ = + 40.3 (*c* 0.6, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) δ 7.33–7.26 (m, 5 H, ArH), 4.96 (s, 1 H, C*H*$(CH_3)_3$), 4.92 (d, 1 H, *J* = 11.5 Hz, PhCH_2), 4.62 (d, 1 H, *J* = 11.5 Hz, PhCH_2), 4.59 (d, 1 H, *J* = 8.5 Hz, OCH_RH$_S$C), 4.42 (s, 1 H, CH_3OC*H*), 4.31 (d, 1 H, *J* = 8.5 Hz, OCH$_R$$H_S$C), 3.83 (s, 3 H, CO_2CH_3), 3.75 (s, 3 H, OCH_3), 1.48 (s, 3 H, CCH_3), 0.91 (s, 9 H, C$(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 175.0 (NC=O), 171.5 (*C*O_2CH_3), 138.6 (Ar), 128.3 (Ar), 127.3 (Ar), 127.1 (Ar), 96.4 (*C*H$(CH_3)_3$), 86.6 (CH_3O*C*H), 82.5 (PhCH_2O*C*), 77.5 (*C*CO_2CH_3), 68.4 (O*C*H$_R$H$_S$C), 67.8 (Ph*C*H_2), 60.3 (OCH_3), 52.8 (CO_2*C*H_3), 36.3 (*C*$(CH_3)_3$),

24.9 (C(CH_3)$_3$), 17.6 (CCH_3); HRMS (ESI) calcd for (M+Na) $C_{21}H_{29}NNaO_6$: 414.1887. Found: 414.1883.

(2*S*,3*S*,4R)-methyl 3-(benzyloxy)-2-(hydroxymethyl)-4-methoxy-3-methyl-5-oxopyrrolidine -2-carboxylate (36) To a solution of **33** (620 mg, 1.58 mmol) in CF_3CH_2OH (4.0 mL) were added 1,3-propanedithiol (4.0 mL) and HCl (12 N, 60 μL). The mixture was stirred at 60 °C for 2 h, cooled, concentrated and the resulting crude product was purified by flash chromatography (silica gel, gradient 75→100% EtOAc–hexane) to afford **36** (414 mg, 81% yield) as a white amorphous solid; R_f 0.18 (2:3 hexane–EtOAc); $[\alpha]_D$ = +61.7 (*c* 0.1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) δ 7.36–7.23 (m, 5 H, ArH), 6.27 (br, 1 H, NH), 4.60 (d, 1 H, *J* = 11.5 Hz, PhCH_2), 4.50 (d, 1 H, *J* = 11.5 Hz, PhCH_2), 4.25 (dd, 1 H, *J* = 11.0, 5.5 Hz, CCH_2OH), 4.04 (s, 1 H, CH_3OC*H*), 3.78 (dd, 1 H, *J* = 11.0, 5.5 Hz, CCH_2OH), 3.75 (s, 3 H, CO_2CH_3), 3.67 (s, 3 H, OCH_3), 2.25 (t, 1 H, *J* = 5.5 Hz, OH), 1.45 (s, 3 H, CCH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 172.9 (NC=O), 171.0 (CO_2CH_3), 137.9 (Ar), 128.3 (Ar), 127.6 (Ar), 126.8 (Ar), 84.4 ($PhCH_2OC$), 82.3 (CH_3OCH), 72.1 (CCO_2CH_3), 65.8 (PhCH_2), 64.6 (CCH_2OH), 59.3 (OCH_3), 52.8 (CO_2CH_3), 12.7 (CCH_3); HRMS (ESI) calcd for (M+Na) $C_{16}H_{21}NNaO_6$: 346.1261. Found: 346.1259.

(2*S*,3*S*,4*R*)-methyl 3-(benzyloxy)-2-(((*tert*-butyldimethylsilyl)oxy)methyl)-4-methoxy-3-methyl-5-oxopyrrolidine-2-carboxylate (37) To a solution of **36** (60.0 mg, 0.19 mmol) in CH_2Cl_2 (5.0 mL) were added imidazole (19.4 mg, 0.28 mmol) and TBSCl (42 mg, 0.28 mmol). The mixture was stirred at room temperature for 12 h. Thereafter, the organic phase was washed with brine, dried over Na_2SO_4, concentrated, and subjected to flash column chromatography (silica gel, gradient 20→25% EtOAc–hexane) to yield **37** (73.6 mg, 92% yield) as a colorless oil;

R_f 0.26 (3:1 hexane–EtOAc); $[\alpha]_D$ = +26.9 (*c* 0.6, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) δ 7.31–7.21 (m, 5 H, ArH), 6.20 (br, 1 H, NH), 4.57 (d, 1 H, *J* = 11.4 Hz, PhCH_2), 4.47 (d, 1 H, *J* = 11.4 Hz, PhCH_2), 4.23 (d, 1 H, *J* = 8.8 Hz, CCH_2OTBS), 3.87 (s, 1 H, CH_3OC*H*), 3.69 (d, 1 H, *J* = 8.8 Hz, CCH_2OTBS), 3.76 (s, 3 H, CO_2CH_3), 3.63 (s, 3 H, OCH_3), 1.41 (s, 3 H, CCH_3), 0.85 (s, 9 H, $SiC(CH_3)_3$), 0.05 (s, 3 H, $SiCH_3$), 0.04(s, 3 H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 172.5 (NC=O), 170.5 (CO_2CH_3), 138.0 (Ar), 128.3 (Ar), 127.5 (Ar), 126.8 (Ar), 83.8 ($PhCH_2OC$), 82.2 (CH_3OCH), 73.0 (CCO_2CH_3), 65.49 (PhCH_2), 65.48 (CCH_2OTBS), 59.2 (OCH_3), 52.4 (CO_2CH_3), 25.6 ($SiC(CH_3)_3$), 18.1 ($SiC(CH_3)_3$), 12.7 (CCH_3), −5.5 ($SiCH_3$) , −5.7($SiCH_3$); HRMS (ESI) calcd for (M+Na) $C_{22}H_{35}NNaO_6Si$: 460.2126. Found: 460.2125.

(2*S*,3*S*,4*R*)-methyl 3-(benzyloxy)-2-(((*tert*-butyldimethylsilyl)oxy)methyl)-4-methoxy-1,3-dimethyl-5-oxopyrrolidine-2-carboxylate (38) To a solution of **37** (50 mg, 0.11 mmol) in DMF (3 mL) was added CH_3I (162 mg, 1.14 mmol). Then the mixture was cooled to 0 °C and NaH (11 mg, 60% in mineral oil, 0.28 mmol) was added. After 1 h, a satd aq solution of NH_4Cl (5 mL) was added dropwise and the mixture was extracted with EtOAc. The organic phases were washed with brine, dried over Na_2SO_4 and concentrated. The crude residue was purified by flash column chromatography (silica gel, gradient 20→25% EtOAc–hexane) to afford **38** (46 mg, 90% yield) as a colorless oil. R_f 0.33 (3:1 hexane–EtOAc); $[\alpha]_D$ = +31.3 (*c* 0.3, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.35–7.25 (m, 5 H, ArH), 4.64 (d, 1 H, *J* = 11.5 Hz, PhCH_2), 4.52 (d, 1 H, *J* = 11.5 Hz, PhCH_2), 4.23 (d, 1 H, *J* = 11.0 Hz, CCH_2OTBS), 4.01 (s, 1 H, CH_3OC*H*), 3.98 (d, 1 H, *J* = 11.0 Hz, CCH_2OTBS), 3.69 (s, 3 H, OCH_3), 3.68 (s, 3 H, CO_2CH_3), 2.94 (s, 3 H, NCH_3), 1.41 (s, 3 H, CCH_3), 0.89 (s, 9 H, $SiC(CH_3)_3$), 0.105 (s, 3 H, $SiCH_3$), 0.098(s, 3 H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 172.5 (NC=O), 170.1 (CO_2CH_3), 138.3 (Ar), 128.3 (Ar), 127.4 (Ar),

126.8 (Ar), 83.2 ($PhCH_2OC$), 82.4 (CH_3OCH), 75.2 (CCO_2CH_3), 65.8 ($PhCH_2$), 63.1 (CCH_2OTBS), 59.3 (OCH_3), 52.2 (CO_2CH_3), 28.4 (NCH_3), 25.6 ($SiC(CH_3)_3$), 18.0 ($SiC(CH_3)_3$), 13.3 (CCH_3), −5.7 ($SiCH_3$) , −5.9($SiCH_3$); HRMS (ESI) calcd for (M+Na) $C_{23}H_{37}NNaO_6Si$: 474.2282. Found: 474.2283.

(2*R*,3*S*,4*R*)-methyl 3-(benzyloxy)-2-formyl-4-methoxy-1,3-dimethyl-5-oxopyrrolidine-2-carboxylate (39) To a mixture of **10** (90 mg, 0.27 mmol) and 4 Å molecular sieves in dry CH_2Cl_2 (8 mL) were added NMO (47 mg, 0.40 mmol) and TPAP (4.9 mg, 0.014 mmol) at room temperature. The mixture was stirred for 6 h and then concentrated. The crude product was purified by flash column chromatography (silica gel, gradient 20→25% EtOAc–hexane) to afford **39** (76 mg, 84% yield) as a colorless oil. R_f 0.65 (3:1 hexane–EtOAc); $[\alpha]_D$ = +89.2 (*c* 0.4, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 10.08 (s, 1 H, CHO), 7.38–7.27 (m, 5 H, ArH), 4.64 (d, 1 H, *J* = 14.5 Hz, $PhCH_2$), 4.56 (d, 1 H, *J* = 14.5 Hz, $PhCH_2$), 4.18 (s, 1 H, CH_3OCH), 3.79 (s, 3 H, CO_2CH_3), 3.68 (s, 3 H, OCH_3), 2.84 (s, 3 H, NCH_3), 1.34 (s, 3 H, CCH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 194.3 (CHO), 172.5 (NC=O), 167.8 (CO_2CH_3), 137.5 (Ar), 128.5 (Ar), 127.8 (Ar), 127.0 (Ar), 84.4 ($PhCH_2OC$), 82.3 (CH_3OCH), 80.2 (CCO_2CH_3), 66.9 ($PhCH_2$), 59.4 (OCH_3), 53.2 (CO_2CH_3), 28.9 (NCH_3), 14.3 (CCH_3); HRMS (ESI) calcd for (M+Na) $C_{17}H_{21}NNaO_6$: 358.1261. Found: 358.1260.

(2*R*,3*S*,4*R*)-3-(benzyloxy)-4-methoxy-2-(methoxycarbonyl)-1,3-dimethyl-5-oxopyrrolidine-2-carboxylic acid (40) A solution of **39** (155 mg, 0.44 mmol) in *t*-BuOH (5 mL) and 2-methyl-2-butene (3 mL) was treated with a freshly prepared solution of $NaClO_2$ (396 mg, 4.4 mmol, 10 equiv) in 20% aqueous NaH_2PO_4 (3 mL) at room temperature. The mixture was stirred for 2 h

and then water was added and the aqueous phase was extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated to afford **40** (149 mg, 92% yield) as a white amorphous solid. R_f 0.55 (3:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ = +46.6 (*c* 0.1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) δ 7.41–7.27 (m, 5 H, ArH), 4.74 (d, 1 H, *J* = 11.5 Hz, PhC*H*$_2$), 4.58 (d, 1 H, *J* = 11.5 Hz, PhC*H*$_2$), 4.11 (s, 1 H, CH_3OCH), 3.88 (s, 3 H, CO_2CH_3), 3.74 (s, 3 H, OCH_3), 2.90 (s, 3 H, NCH_3), 1.52 (s, 3 H, CCH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 172.1 (NC=O), 171.2 (CO_2CH_3), 164.6 (CO_2H), 137.3 (Ar), 128.5 (Ar), 127.9 (Ar), 127.0 (Ar), 84.3 ($PhCH_2OC$), 82.5 (CH_3OCH), 78.0 (CCO_2CH_3), 66.8 ($PhCH_2$), 59.5 (OCH_3), 54.5 (CO_2CH_3), 28.8 (NCH_3), 15.2 (CCH_3); HRMS (ESI) calcd for (M+Na) $C_{17}H_{21}NNaO_7$: 374.1210. Found: 374.1212.

8-Azidooctyl 4-[(2′*R*,3′*S*,4′*R*)-3′-(benzyloxy)-4′-methoxy-2′-(methoxycarbonyl)-1′,3′-dimethyl-5′-oxopyrrolidine-2′-carboxamido]-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (**41**) To a solution of **9** (40 mg, 0.08 mmol) in DMF (5 mL) was added **40** (35 mg, 0.10 mmol), TBTU (35 mg, 0.11 mmol) and DIEA (16 mg, 0.12 mmol). The mixture was stirred at room temperature over night and then water was added and the mixture was extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4, and concentrated. The resulting residue was purified by flash column chromatography (silica gel, gradient 30→50% EtOAc–hexane) to afford **41** (50 mg, 76% yield) as a colorless oil. R_f 0.52 (1:1 hexane–EtOAc); $[\alpha]_D$ = +128.3 (*c* 0.2, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.20 (d, 1 H, *J* = 10.0 Hz, NH), 7.41–7.25 (m, 15 H, ArH), 4.88 (d, 1 H, *J* = 11.0 Hz, PhC*H*$_2$, C-3), 4.85 (d, 1 H, *J* = 12.0 Hz, PhC*H*$_2$, C-2), 4.83 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1), 4.69 (d, 1 H, *J* = 12.0 Hz, PhC*H*$_2$, C-2), 4.69 (d, 1 H, *J* = 11.5 Hz, PhC*H*$_2$O lactam), 4.61 (dd, 1 H, $J_{NH,4}$ = 10.0 Hz, $J_{3,4}$ =

4.0 Hz, H-4), 4.59 (d, 1 H, J = 11.0 Hz, PhCH_2, C-3), 4.53 (d, 1 H, J = 11.5 Hz, PhCH_2O lactam), 4.21 (qd, 1 H, $J_{5,6}$ = 6.5 Hz, $J_{4,5}$ = 1.5 Hz, H-5), 4.03 (dd, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 4.0 Hz, 1H, H-3), 3.95 (s, 1 H, CH_3OCH), 3.72 (s, 3 H, CO_2CH_3), 3.67 (dt, 1 H, J = 10.0, 6.5 Hz, octyl OCH_2), 3.65 (s, 3 H, OCH_3), 3.61 (dd, 1 H, $J_{2,3}$ =10.0 Hz, $J_{1,2}$ = 4.0 Hz, H-2), 3.50 (dt, 1 H, J = 10.0, 6.5 Hz, octyl OCH_2), 3.29 (t, 2 H, J = 7.0 Hz, CH_2N_3), 2.69 (s, 3 H, NCH_3), 1.69–1.62 (m, 4 H, CH_2 x 2), 1.51 (s, 3 H, CCH_3), 1.43–1.34 (m, 8 H, CH_2 x 4), 1.20 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 172.3 (CH_3NC=O), 169.5 (CO_2CH_3), 164.7 (HNC=O), 138.7 (Ar), 138.6 (Ar), 137.8 (Ar), 128.4 (Ar), 128.2 (Ar), 128.1 (Ar), 127.8 (Ar), 127.6 (Ar), 127.4 (Ar), 126.9 (Ar), 97.5 (C-1), 83.7 ($PhCH_2OCCH_3$), 82.3 (CH_3OCH), 79.3 (CCO_2CH_3), 77.5 (C-3), 75.5 (C-2), 73.1 (PhCH_2, C-2), 71.8 (PhCH_2, C-3), 68.4 (octyl OCH_2), 66.2 (PhCH_2O lactam), 64.0 (C-5), 59.3 (OCH_3), 53.1 (CO_2CH_3), 51.9 (C-4), 51.5 (CH_2N_3), 29.4 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 29.0 (NCH_3), 28.8 (CH_2), 26.7 (CH_2), 26.1 (CH_2), 17.3 (C-6), 14.8 (CCH_3); HRMS (ESI) calcd for (M+Na) $C_{45}H_{59}N_5NaO_{10}$: 852.4154. Found: 852.4138.

8-Azidooctyl 4-[(2′*R*,3′*S*,4′*R*)-3′-(benzyloxy)-4′-methoxy-2′-carboxyl-1′,3′-dimethyl-5′-oxopyrrolidine-2′-carboxamido]-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (**42**)

To a solution of **41** (45 mg, 0.054 mmol) in THF (5 mL) and water (5 mL) was added LiOH monohydrate (34 mg, 0.81 mmol) at room temperature. The mixture was stirred at room temperature for 16 h. Then 1 M HCl was added to adjust the pH to 1. The mixture was diluted with water (5 mL) and extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated to afford **42** (42 mg, 96% yield) as a colorless oil. R_f 0.65 (10:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ = +106.7 (*c* 0.2, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.38–7.20 (m, 15 H, ArH), 6.61 (d, 1 H, J = 10.0 Hz, NH), 4.87 (d, 1 H, J = 10.5 Hz, PhCH_2, C-

3), 4.84 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1), 4.79 (d, 1 H, J = 12.0 Hz, PhCH_2, C-2), 4.66 (d, 1 H, J = 12.0 Hz, PhCH_2, C-2), 4.65 (d, 1 H, J = 10.5 Hz, PhCH_2, C-3), 4.64 (dd, 1 H, $J_{NH,4}$ = 10.0 Hz, $J_{3,4}$ = 4.0 Hz, H-4), 4.48 (d, 1 H, J = 11.5 Hz, PhCH_2O lactam), 4.29 (d, 1 H, J = 11.5 Hz, PhCH_2O lactam), 4.26 (qd, 1 H, $J_{5,6}$ = 6.5 Hz, $J_{4,5}$ = 1.0 Hz, H-5), 4.21 (s, 1 H, CH_3OCH), 4.05 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 4.0 Hz, H-3), 3.67 (dt, 1 H, J = 10.0, 6.5 Hz, octyl OCH_2), 3.61 (s, 3 H, OCH_3), 3.50 (dt, 1 H, J = 10.0, 6.5 Hz, octyl OCH_2), 3.43 (dd, 1 H, $J_{2,3}$ =10.0 Hz, $J_{1,2}$ = 4.0 Hz, H-2), 3.29 (t, 2 H, J = 7.0 Hz, CH_2N_3), 2.91 (s, 3 H, NCH_3), 1.70–1.61 (m, 4 H, CH_2 x 2), 1.45–1.34 (m, 8 H, CH_2 x 4), 1.32 (s, 3 H, CCH_3), 1.19 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 172.3 (CH_3NC=O), 170.9 (HNC=O), 167.0 (CO_2H), 138.0 (Ar), 137.7 (Ar), 137.6 (Ar), 128.4 (Ar), 128.32 (Ar), 128.31 (Ar), 128.2 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 127.5 (Ar), 126.9 (Ar), 97.2 (C-1), 84.5 (CH_3OCH), 82.6 ($PhCH_2OCCH_3$), 77.4 (C-3), 77.2 (CCO_2CH_3), 75.8 (C-2), 73.3 (PhCH_2, C-2), 72.9 (PhCH_2, C-3), 68.8 (octyl OCH_2), 66.4 (PhCH_2O lactam), 63.6 (C-5), 59.6 (OCH_3), 53.3 (C-4), 51.5 (CH_2N_3), 31.0 (NCH_3), 29.4 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 28.8 (CH_2), 26.7 (CH_2), 26.1 (CH_2), 17.2 (C-6), 15.7 (CCH_3); HRMS (ESI) calcd for (M-H) $C_{44}H_{56}N_5O_{10}$: 814.4033. Found: 814.4029.

(2*S*,3*S*,4*R*)-3-(benzyloxy)-2-(hydroxymethyl)-4-methoxy-1,3-dimethyl-5-oxopyrrolidine-2-carboxylic acid (44) To a solution of **10** (200 mg, 0.59 mmol) in THF (8 mL) and water (8 mL) was added LiOH monohydrate (124 mg, 2.95 mmol) at room temperature. The mixture was stirred at room temperature for 16 h. Then 1 M HCl was added to adjust the pH to 1. The mixture was diluted by water and extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated to afford **44** (175 mg, 0.54 mmol, 92% yield) as a white amorphous solid. R_f 0.63 (3:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ = +58.2 (*c* 0.2, CH_2Cl_2); ^{1}H NMR

(500 MHz, $CDCl_3$, δ_H) δ 7.27–7.21 (m, 5 H, ArH), 4.63 (d, 1 H, *J* = 11.5 Hz, PhC*H*$_2$), 4.49 (d, 1 H, *J* = 11.5 Hz, PhC*H*$_2$), 4.10 (s, 1 H, CH_3OCH), 4.09 (d, 1 H, *J* = 12.5 Hz, C*H*$_2$OH), 3.99 (d, 1 H, *J* = 12.5 Hz, C*H*$_2$OH), 3.65 (s, 3 H, OCH_3), 2.89 (s, 3 H, NCH_3), 1.44 (s, 3 H, CCH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 173.4 (*C*O_2H), 172.6 (NC=O), 138.0 (Ar), 128.3 (Ar), 127.5 (Ar), 126.7 (Ar), 83.4 ($PhCH_2OC$), 81.9 (CH_3OCH), 74.6 (CCO_2CH_3), 66.0 (Ph*C*H$_2$), 62.2 (*C*H$_2$OH), 59.4 (OCH_3), 27.8 (NCH_3), 12.8 (CCH_3); HRMS (ESI) (M+Na) calcd for $C_{16}H_{21}NNaO_6$: 346.1261. Found: 346.1256.

8-Azidooctyl 4-[(2′*S*,3′*S*,4′*R*)-3′-(benzyloxy)-4′-methoxy-2′-hydroxymethyl-1′,3′-dimethyl-5′-oxopyrrolidine-2′-carboxamido]-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (**45**)

To a solution of **44** (60 mg, 0.12 mmol) in DMF (5 mL) was added compound **9** (39 mg, 0.12 mmol), TBTU (51 mg, 0.16 mmol) and DIEA (23 mg, 0.18 mmol). The mixture was stirred at room temperature over night. Then water was added and the mixture was extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (silica gel, gradient 30→70% EtOAc–hexane) to afford **45** (64 mg, 67% yield) as a colorless oil. R_f 0.39 (2:3 hexane–EtOAc); $[\alpha]_D$ = +121.1 (*c* 0.5, CH_2Cl_2,); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) δ 7.40–7.23 (m, 15 H, ArH), 6.01 (d, 1 H, *J* = 10.0 Hz, NH), 4.78 (d, 1 H, *J* = 10.5 Hz, PhC*H*$_2$, C-3), 4.72 (d, 1 H, *J* = 12.5 Hz, PhC*H*$_2$, C-2), 4.69 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1), 4.66 (d, 1 H, *J* = 12.5 Hz, PhC*H*$_2$, C-2), 4.62 (d, 1 H, *J* = 12.0 Hz, PhC*H*$_2$O lactam), 4.59 (d, 1 H, *J* = 10.5 Hz, PhC*H*$_2$, C-3), 4.57 (ddd, 1 H, $J_{NH,4}$ = 10.0 Hz, $J_{3,4}$ = 4.5 Hz, $J_{4,5}$ = 1.5 Hz, H-4), 4.50 (d, 1 H, *J* = 12.0 Hz, PhC*H*$_2$O lactam), 4.02 (qd, 1 H, $J_{5,6}$ = 6.5 Hz, $J_{4,5}$ = 1.5 Hz, H-5), 4.01 (dd, 1 H, *J* = 12.5, 3.0 Hz, C*H*$_2$OH), 3.94 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 4.5 Hz, H-3), 3.85 (s, 1 H, CH_3OCH), 3.82 (dd, 1 H, *J* = 12.5, 8.0 Hz, C*H*$_2$OH),

3.66 (s, 3 H, OCH_3), 3.58 (dt, 1 H, J = 13.5, 6.5 Hz, octyl OCH_2), 3.44 (dt, 1 H, J = 13.5, 6.5 Hz, octyl OCH_2), 3.29 (t, 2 H, J = 7.0 Hz, CH_2N_3), 3.28 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{1,2}$ = 4.0 Hz, H-2), 2.71 (s, 3 H, NCH_3), 1.64–1.60 (m, 4 H, CH_2 x 2), 1.52 (s, 3 H, CCH_3), 1.42–1.32 (m, 8 H, CH_2 x 4), 0.73 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 172.5 (CH_3NC=O), 169.7 (HNC=O), 138.3 (Ar), 138.1 (Ar), 137.9 (Ar), 128.4 (Ar), 128.327 (Ar), 128.321 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 127.6 (Ar), 127.5 (Ar), 127.4 (Ar), 97.0 (C-1), 82.9 (CH_3OCH), 81.3 ($PhCH_2OCCH_3$), 77.2 (C-3), 75.7 (CCH_2OH), 74.9 (C-2), 72.6 (PhCH_2, C-2), 71.9 (PhCH_2, C-3), 68.4 (octyl OCH_2), 66.2 (PhCH_2O lactam), 63.9 (C-5), 62.9 (CH_2OH), 59.4 (OCH_3), 51.5 (CH_2N_3), 51.0 (C-4), 29.4 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 28.8 (CH_2), 28.3 (NCH_3), 26.7 (CH_2), 26.1 (CH_2), 16.4 (C-6), 13.2 (CCH_3); HRMS (ESI) calcd for (M+H) $C_{44}H_{60}N_5O_9$: 802.4386. Found: 802.4376.

8-Azidooctyl 4-[(2′*R*,3′*S*,4′*R*)-3′-(benzyloxy)-4′-methoxy-2′-formyl-1′,3′-dimethyl-5′-oxopyrrolidine-2′-carboxamido]-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (46)

To a mixture of **45** (60 mg, 0.075 mmol) and 4 Å molecular sieves in dry CH_2Cl_2 (8 mL) were added NMO (18 mg, 0.15 mmol) and TPAP (2.6 mg, 0.0075 mmol) at room temperature. The mixture was stirred for 6 h and then the mixture was concentrated and the crude product was purified by flash column chromatography (silica gel, gradient 30→50% EtOAc–hexane) to afford **46** (51 mg, 0.064 mmol, 85% yield) as a colorless oil. R_f 0.76 (1:1 hexane–EtOAc); $[\alpha]_D$ = +124.3 (*c* 0.2, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 10.09 (s, 1 H, CHO), 7.32–7.22 (m, 15 H, ArH), 6.43 (d, 1 H, J = 10.0 Hz, NH), 4.75 (d, 1 H, J = 10.5 Hz, PhCH_2, C-3), 4.67 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1), 4.65 (d, 1 H, J = 11.5 Hz, PhCH_2O lactam), 4.62 (d, 1 H, J = 12.0 Hz, PhCH_2, C-2), 4.60 (ddd, 1 H, $J_{NH,4}$ = 10.0 Hz, $J_{3,4}$ = 4.5 Hz, $J_{4,5}$ = 1.5 Hz, H-4), 4.54 (d, 1 H, J = 10.5 Hz,

PhCH_2, C-3), 4.53 (d, 1 H, J = 12.0 Hz, PhCH_2, C-2), 4.47 (d, 1 H, J = 11.5 Hz, PhCH_2O lactam), 4.06 (qd, 1 H, $J_{5,6}$ = 6.5 Hz, $J_{4,5}$ = 1.5 Hz, H-5), 3.94 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 4.5 Hz, H-3), 3.91 (s, 1 H, CH_3OCH), 3.60 (dt, 1 H, J = 10.7, 7.0 Hz, octyl OCH_2), 3.56 (s, 3 H, OCH_3), 3.44 (dt, 1 H, J = 10.0, 6.5 Hz, octyl OCH_2), 3.29 (t, 2 H, J = 7.0 Hz, CH_2N_3), 3.25 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{1,2}$ = 4.0 Hz, H-2), 2.75 (s, 3 H, NCH_3), 1.66–1.60 (m, 4 H, CH_2 x 2), 1.46 (s, 3 H, CCH_3), 1.42–1.32 (m, 8 H, CH_2 x 4), 0.87 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 197.8 (CHO), 172.5 (CH_3NC=O), 165.7 (HNC=O), 138.3 (Ar), 138.2 (Ar), 137.6 (Ar), 128.4 (Ar), 128.3 (Ar), 128.2 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 127.6 (Ar), 127.5 (Ar), 127.4 (Ar), 97.0 (C-1), 84.2 (PhCH_2O*C*CH_3), 81.5 (CH_3O*C*H), 80.6 (*C*CHO), 76.5 (C-3), 75.2 (C-2), 72.7 (Ph*C*H_2, C-2), 71.8 (Ph*C*H_2, C-3), 68.5 (octyl O*C*H_2), 66.3 (Ph*C*H_2O lactam), 63.8 (C-5), 59.1 (OCH_3), 51.5 (*C*H_2N_3), 51.4 (C-4), 29.4 (NCH_3), 29.3 (*C*H_2), 29.2 (*C*H_2), 29.1 (*C*H_2), 28.8 (*C*H_2), 26.7 (*C*H_2), 26.1 (*C*H_2), 16.5 (C-6), 14.4 (C*C*H_3); HRMS (ESI) calcd for (M+H) $C_{44}H_{58}N_5O_9$: 800.4229. Found: 800.4214.

8-Azidooctyl 4-[(2′*S*,3′*S*,4′*R*)-3′-(benzyloxy)-4′-methoxy-2′-carboxyl-1′,3′-dimethyl-5′-oxopyrrolidine-2′-carboxamido]-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (47)

To a solution of **46** (45 mg, 0.056 mmol) in *t*-BuOH (5 mL) and 2-methyl-2-butene (3 mL) was treated with a freshly prepared solution of $NaClO_2$ (99 mg, 1.1 mmol, 20 equiv) in 20% aqueous NaH_2PO_4 (3 mL) at room temperature. The mixture was stirred for 2 h and then water was added and the aqueous phase was extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated to afford **47** (43 mg, 95% yield) as a colourless oil. R_f 0.38 (10:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ = +80.8 (*c* 0.4, CH_2Cl_2); ^{1}H NMR (500 MHz, CD_3OD, δ_H) δ 7.36–7.21 (m, 15 H, ArH), 4.78 (d, 1 H, J = 10.5 Hz, PhCH_2, C-3), 4.72 (d, 1 H, J = 13.0

Hz, PhCH_2O lactam), 4.68 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.54 (d, 1 H, $J_{3,4}$ = 4.0 Hz, H-4), 4.49 (d, 1 H, J = 11.5 Hz, PhCH_2O lactam), 4.42 (d, 1 H, J = 10.5 Hz, PhCH_2, C-3), 4.29 (d, 1 H, J = 11.5 Hz, PhCH_2, C-2), 4.21 (d, 1 H, J = 11.5 Hz, PhCH_2, C-2), 4.13 (q, 1 H, $J_{5,6}$ = 6.5 Hz, H-5), 4.11 (s, 1 H, CH_3OCH), 3.91 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 4.5 Hz, H-3), 3.63 (dt, 1 H, J = 13.0, 6.5 Hz, octyl OCH_2), 3.44 (s, 3 H, OCH_3), 3.40–3.36 (m, 2 H, octyl OCH_2 and H-2), 3.24 (t, 2 H, J = 7.0 Hz, CH_2N_3), 2.89 (s, 3 H, NCH_3), 1.63–1.52 (m, 4 H, CH_2 x 2), 1.41–1.28 (m, 8 H, CH_2 x 4), 1.30 (s, 3 H, CCH_3), 1.08 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR (125 MHz, CD_3OD, δ_C) 172.6 (CH_3NC=O), 168.1 (HNC=O), 141.6 (Ar), 141.0 (Ar), 140.8 (Ar), 130.4 (Ar), 130.2 (Ar), 130.1 (Ar), 130.0 (Ar), 129.5 (Ar), 129.4 (Ar), 129.0 (Ar), 128.6 (Ar), 99.4 (C-1), 86.1 ($PhCH_2OCCH_3$), 85.5 (CH_3OCH), 79.0 (C-3), 78.7 (C-2), 74.8 (PhCH_2, C-2), 73.6 (PhCH_2, C-3), 70.2 (octyl OCH_2), 68.0 (PhCH_2O lactam), 66.5 (C-5), 61.0 (OCH_3), 54.8 (C-4), 53.3 (CH_2N_3), 31.3 (CH_2), 31.2 (NCH_3), 31.1 (CH_2), 30.8 (CH_2), 28.6 (CH_2), 28.1 (CH_2), 18.0 (CCH_3), 16.6 (C-6); HRMS (ESI) calcd for (M-H) $C_{44}H_{56}N_5O_{10}$: 814.4033. Found: 814.4027.

(3*S*,4*R*)-methyl 3-(benzyloxy)-4-methoxy-1,3-dimethyl-5-oxopyrrolidine-2-carboxylate (**48**) A solution of **40** (250 mg , 0.71 mmol) in toluene (25 mL) was heated at reflux for 24 h. Then the mixture was concentrated and the crude product was purified by flash column chromatography (silica gel, gradient 10→25% EtOAc–hexane) to afford **48** (170 mg, 0.55 mmol, 78% yield) as a 1:1 mixture of inseparable diastereomers. These are defined below as *cis* and *trans*, to describe the relationship between the carboxymethyl and benzyloxy groups. R_f 0.35 (2:3 hexane–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.38–7.29 (m, 10 H, ArH (*cis* and *trans*)), 4.69–4.60 (m, 4 H, $PhCH_2O$(*cis* and *trans*)), 4.25 (s, 1 H, CH_3OCH(*cis*)), 4.22 (s, 1 H, $CHCO_2CH_3$(*trans*)), 3.99 (s, 1 H, $CHCO_2CH_3$(*cis*)), 3.86 (s, 1 H, CH_3OCH(*trans*)), 3.85 (s, 3 H,

CO_2CH_3(*trans*)), 3.72 (s, 3 H, OCH_3(*cis*)), 3.71 (s, 3 H, CO_2CH_3(*cis*)), 3.68 (s, 3 H, OCH_3(*trans*)), 2.88 (s, 3 H, NCH_3(*trans*)), 2.85 (s, 3 H, NCH_3(*cis*)), 1.55 (s, 3 H, CCH_3(*cis*)), 1.38 (s, 3 H, CCH_3(*trans*)); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 171.8 (NC=O(*cis*)), 171.4 (NC=O(*trans*)), 169.6 (CO_2CH_3(*cis*)), 168.9 (CO_2CH_3(*trans*)), 138.1 (Ar), 138.0 (Ar), 128.5 (Ar), 128.3 (Ar), 127.7 (Ar), 127.5 (Ar), 127.1 (Ar), 126.8(Ar), 83.5 (CH_3OCH(*trans*)), 82.5 (CH_3OCH(*cis*)), 81.6 ($PhCH_2OC$), 81.4 ($PhCH_2OC$), 70.1 ($CHCO_2CH_3$(*trans*)), 68.8 ($CHCO_2CH_3$(*cis*)), 66.3 ($PhCH_2$), 65.7 ($PhCH_2$), 59.4 (OCH_3), 59.3 (OCH_3), 52.5 (CO_2CH_3), 52.4 (CO_2CH_3), 29.2 (NCH_3(*cis*)), 28.9 (NCH_3(*trans*)), 18.0 (CCH_3(*cis*)), 14.8 (CCH_3(*trans*)); HRMS (ESI) calcd for (M+Na) $C_{16}H_{21}NNaO_5$: 330.1312. Found: 330.1307.

8-Azidooctyl 4-[(2′*S*,3′*S*,4′*R*)-3′-(benzyloxy)-4′-methoxy-1′,3′-dimethyl-5′-oxopyrrolidine-2′-carboxamido]-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (**50**) To a solution of **48** (47 mg, 0.16 mmol) in THF (10 mL) and water (10 mL) was added LiOH monohydrate (67 mg, 1.6 mmol) at room temperature. The mixture was stirred at room temperature for 16 h. Then 1 M HCl was added to adjust the pH to 1. The mixture was diluted with water and extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated to afford crude acid **49**. Then, to a solution of **9** (40 mg, 0.080 mmol) in DMF (5 mL) was added the above crude acid, TBTU (38 mg, 0.12 mmol) and DIEA (16 mg, 0.12 mmol). The mixture was stirred at room temperature over night. Water was then added and the mixture was extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (silica gel, gradient 30→70% EtOAc–hexane) to afford **50** (39.8 mg, 64% yield) and **51** (9.8 mg, 16% yield). Data for **50**: R_f 0.45 (2:3 hexane–EtOAc); $[\alpha]_D$ = +124.2 (*c* 0.4, CH_2Cl_2,); ^{1}H NMR (600

MHz, $CDCl_3$, δ_H) 7.36–7.21 (m, 15 H, ArH), 5.85 (d, 1 H, *J* = 10.5 Hz, NH), 4.75 (d, 1 H, *J* = 11.0 Hz, PhC*H*$_2$, C-3), 4.69 (d, 1 H, *J* = 11.5 Hz, PhC*H*$_2$O lactam), 4.68 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.67 (d, 1 H, *J* = 12.0 Hz, PhC*H*$_2$, C-2), 4.60 (ddd, 1 H, $J_{4,NH}$ = 10.5 Hz, $J_{3,4}$ = 4.5 Hz, $J_{4,5}$ = 1.5 Hz, H-4), 4.56 (d, 1 H, *J* = 12.0 Hz, PhC*H*$_2$, C-2), 4.52 (d, 1 H, *J* = 11.0 Hz, PhC*H*$_2$, C-3), 4.50 (d, 1 H, *J* = 11.5 Hz, PhC*H*$_2$O lactam), 4.05 (s, 1 H, CH_3OCH), 4.04 (qd, 1 H, $J_{5,6}$ = 6.5 Hz, $J_{4,5}$ = 1.5 Hz, H-5), 3.94 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 4.5 Hz, H-3), 3.90 (s, 1 H, C*H*C=ONH), 3.63 (s, 3 H, OCH_3), 3.58 (dt, 1 H, *J* = 10.0, 7.0 Hz, octyl OC*H*$_2$), 3.42 (dt, 1 H, *J* = 10.0, 6.5 Hz, octyl OC*H*$_2$), 3.27 (t, 2 H, *J* = 7.0 Hz, CH_2N_3), 3.26 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{1,2}$ = 3.5 Hz, H-2), 2.70 (s, 3 H, NCH_3), 1.63–1.58 (m, 4 H, CH_2 x 2), 1.52 (s, 3 H, CCH_3), 1.39–1.28 (m, 8 H, CH_2 x 4), 0.90 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR (150 MHz, $CDCl_3$, δ_C) 171.8 (CH_3NC=O), 167.9 (HNC=O), 138.4 (Ar), 138.3 (Ar), 138.2 (Ar), 128.3 (Ar), 128.2 (Ar), 128.18 (Ar), 128.0 (Ar), 127.7 (Ar), 127.6 (Ar), 127.5 (Ar), 127.4 (Ar), 97.1 (C-1), 82.7 (CH_3OCH), 80.9 ($PhCH_2OCCH_3$), 76.2 (C-3), 75.5 (C-2), 72.8 (Ph*C*H$_2$, C-2), 72.4 (*C*HC=ONH), 71.5 (Ph*C*H$_2$, C-3), 68.4 (octyl O*C*H$_2$), 66.5 (Ph*C*H$_2$O lactam), 64.0 (C-5), 59.3 (OCH_3), 51.5 (*C*H$_2$N$_3$), 51.0 (C-4), 29.4 (NCH_3), 29.3 (*C*H$_2$), 29.2 (*C*H$_2$), 29.1 (*C*H$_2$), 28.8 (*C*H$_2$), 26.7 (*C*H$_2$), 26.1 (*C*H$_2$), 18.3 (C*C*H$_3$), 16.6 (C-6); HRMS (ESI) calcd for (M+H) $C_{43}H_{58}N_5O_8$: 772.4280. Found: 772.4279. Data for **51**: R_f 0.49 (1:1 hexane–EtOAc); $[\alpha]_D$ = +118.3 (*c* 0.1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) δ 7.44–7.26 (m, 15 H, ArH), 6.62 (d, 1 H, *J* = 10.0 Hz, NH), 4.92 (d, 1 H, *J* = 11.0 Hz, PhC*H*$_2$, C-3), 4.85 (d, 1 H, *J* = 12.5 Hz, PhC*H*$_2$, C-2), 4.79 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1), 4.70 (d, 1 H, *J* = 12.5 Hz, PhC*H*$_2$, C-2), 4.67 (d, 1 H, *J* = 11.0 Hz, PhC*H*$_2$, C-3), 4.57 (d, 1 H, *J* = 11.5 Hz, PhC*H*$_2$O lactam), 4.54 (ddd, 1 H, $J_{4,NH}$ = 10.5 Hz, $J_{3,4}$ = 4.0 Hz, $J_{4,5}$ = 1.5 Hz, H-4), 4.53 (d, 1 H, *J* = 11.5 Hz, PhC*H*$_2$O lactam), 4.15 (qd, 1 H, $J_{5,6}$ = 6.5 Hz, $J_{4,5}$ = 1.5 Hz, H-5), 4.03 (s, 1 H, C*H*C=ONH), 4.01 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 4.0 Hz, H-3), 3.66 (dt, 1 H, *J* = 10.0, 7.0 Hz,

octyl OC*H*$_2$), 3.57 (s, 1 H, CH$_3$OC*H*), 3.50 (dt, 1 H, *J* = 10.0, 6.5 Hz, octyl OC*H*$_2$), 3.47 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{1,2}$ = 4.0 Hz, H-2), 3.42 (s, 3 H, OCH$_3$), 3.29 (t, 2 H, *J* = 7.0 Hz, CH$_2$N$_3$), 2.87 (s, 3 H, NCH$_3$), 1.69–1.61 (m, 4H, CH$_2$ x 2), 1.38 (s, 3 H, CCH$_3$), 1.42–1.33 (m, 8 H, CH$_2$ x 4), 1.12 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR (125 MHz, CDCl$_3$, δ_C) 172.1 (CH$_3$NC=O), 168.8 (HNC=O), 138.7 (Ar), 138.5 (Ar), 137.9 (Ar), 128.5 (Ar), 128.4 (Ar), 128.1 (Ar), 128.0 (Ar), 127.8 (Ar), 127.7 (Ar), 127.5 (Ar), 127.4 (Ar), 127.1 (Ar), 97.5 (C-1), 83.7 (CH$_3$O*C*H), 80.4 (PhCH$_2$O*C*CH$_3$), 77.6 (C-3), 75.4 (C-2), 73.0 (Ph*C*H$_2$, C-2), 72.8 (*C*HC=ONH), 71.9 (Ph*C*H$_2$, C-3), 68.5 (octyl O*C*H$_2$), 65.4 (Ph*C*H$_2$O lactam), 64.0 (C-5), 59.3 (OCH$_3$), 51.5 (*C*H$_2$N$_3$), 51.2 (C-4), 29.4 (*C*H$_2$), 29.3 (*C*H$_2$), 29.1 (NCH$_3$), 29.1 (*C*H$_2$), 28.8 (*C*H$_2$), 26.7 (*C*H$_2$), 26.1 (*C*H$_2$), 16.9 (C-6), 14.1 (C*C*H$_3$),; HRMS (ESI) calcd for (M+H) C$_{43}$H$_{58}$N$_5$O$_8$: 772.4280. Found: 772.4270.

(2*S*,3*R*)-1-*tert*-butyl 2-methyl 3-acetoxy-3-methyl-5-oxopyrrolidine-1,2-dicarboxylate (54) To a solution of **15** (0.46 g, 1.7 mmol) in pyridine (15.0 mL) and Ac$_2$O (15.0 mL) were added DMAP (21 mg, 0.17 mmol). The mixture was stirred at room temperature for 12 h. After completion of the reaction, the mixture was concentrated and diluted with CH$_2$Cl$_2$ (30 mL). The organic phase was washed with 1N HCl, brine, dried over Na$_2$SO$_4$ and concentrated. The crude residue was purified by flash column chromatography (silica gel, gradient 20→40% EtOAc–hexane) to yield **54** (472 mg, 89% yield) as a white amorphous solid; R_f 0.65 (4:3 EtOAc–hexane); $[\alpha]_D$ = –18.9 (*c* 0.5, CH$_2$Cl$_2$); ^{1}H NMR (500 MHz, CDCl$_3$, δ_H) 4.56 (s, 1 H, NC*H*), 3.83 (s, 3 H, OCH$_3$), 3.11 (d, 1 H, *J* = 17.5 Hz, COC*H*$_2$), 2.98 (d, 1 H, *J* = 17.5 Hz, COC*H*$_2$), 2.02 (s, 3 H, CH$_3$C=O), 1.78 (s, 3 H, CCH$_3$), 1.52 (s, 9 H, C(CH$_3$)$_3$); ^{13}C NMR (125 MHz, CDCl$_3$, δ_C) 169.8 (NC=O), 169.0 (CH$_3$*C*=O), 168.8 (*C*O$_2$CH$_3$), 148.9 (*C*O$_2$C(CH$_3$)$_3$), 84.4 (O*C*(CH$_3$)$_3$), 77.1 (CH$_3$*C*OAc), 68.6 (N*C*H), 52.5 (OCH$_3$), 44.3 (CH$_2$), 27.9 (C(*C*H$_3$)$_3$), 24.8

(C*C*H$_3$), 21.4 (*C*H$_3$C=O); HRMS (ESI) calcd for (M+Na) $C_{14}H_{21}NNaO_7$: 338.1210. Found: 338.1208.

(2*S*,3*R*)-methyl 3-acetoxy-3-methyl-5-oxopyrrolidine-2-carboxylate (55) To a solution of **54** (0.36 g, 1.7 mmol) in CH_2Cl_2 (30.0 mL) was added TFA (5.0 mL) at 0 °C. The mixture was stirred at room temperature for 2 h. Then, the mixture was concentrated, diluted with CH_2Cl_2 (40 mL), washed with a satd aq solution of $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated. The crude residue was purified by flash column chromatography (silica gel, gradient 100→300% EtOAc–hexane) to yield **55** (227 mg, 93% yield) as a white amorphous solid; R_f 0.15 (4:3 EtOAc–Hexane); $[\alpha]_D$ = +5.7 (*c* 0.7, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 6.52 (br s, 1 H, NH), 4.21 (s, 1 H, NC*H*), 3.82 (s, 3 H, OCH_3), 3.09 (d, 1 H, *J* = 18.0 Hz, COCH_2), 2.65 (d, 1 H, *J* = 18.0 Hz, COCH_2), 2.00 (s, 3 H, CH_3C=O), 1.85 (s, 3 H, CCH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 174.7 (NC=O), 169.5 (CH_3C=O), 169.0 (CO_2CH_3), 82.9 (CH_3COAc), 66.1 (N*C*H), 52.5 (OCH_3), 42.2 (CH_2), 23.6 (C*C*H$_3$), 21.7 (*C*H$_3$C=O); HRMS (ESI) calcd for (M+Na) $C_9H_{13}NNaO_5$: 238.0686. Found: 238.0686.

(2*S*,3*R*)-methyl 3-acetoxy-1,3-dimethyl-5-oxopyrrolidine-2-carboxylate (57) To a solution of **55** (0.2 g, 0.93 mmol) in acetone (25 mL) was added paraformaldehyde (0.1 g, 4.4 mmol), potassium carbonate (20 mg) and water (0.2 mL) at room temperature. The mixture was placed in a sonication bath. After 3 h, the solution was filtered, concentrated and the residue was purified by flash chromatography on silica gel (gradient 50→25% hexane–EtOAc) to afford hemiaminal **56** (190 mg). To this hemiaminal in $CHCl_3$ (25 mL) was added TFA (2.0 mL) and Et_3SiH (2.0 mL). This mixture was stirred at room temperature over night. Thereafter, the

organic phase was washed with a satd aq solution of $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated. The crude residue was purified by flash column chromatography (silica gel, gradient 50→25% hexane–EtOAc) to yield **57** (172 mg, 81% yield over two steps) as a white amorphous solid; R_f 0.25 (4:3 EtOAc–hexane); $[\alpha]_D = -5.1$ (*c* 0.5, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 4.09 (s, 1 H, NC*H*), 3.82 (s, 3 H, OCH_3), 2.97 (d, 1 H, *J* = 17.0 Hz, COCH_2), 2.85 (s, 3 H, NCH_3), 2.79 (d, 1 H, *J* = 17.0 Hz, COCH_2), 2.00 (s, 3 H, CH_3C=O), 1.76 (s, 3 H, CCH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 172.2 (NC=O), 169.2 (CH_3C=O), 168.8 (CO_2CH_3), 79.1 (CH_3COAc), 72.3 (N*C*H), 52.5 (OCH_3), 42.8 (CH_2), 28.8 (NCH_3), 25.1 (C*C*H_3), 21.5 (*C*H_3C=O); HRMS (ESI) calcd for (M+Na) $C_{10}H_{15}NNaO_5$: 252.0842. Found: 252.0840.

8-Azidooctyl 4-[(2′*S*,3′*R*)-3′-(hydroxy)-1′,3′-dimethyl-5′-oxopyrrolidine-2′-carboxamido]-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (**58**) To a solution of **9** (6.0 mg, 0.012 mmol) in DMF (2 mL) was added the **14** (4.1 mg, 0.024 mmol), TBTU (9.6 mg, 0.030 mmol) and DIEA (3.9 mg, 0.030 mmol). The mixture was stirred at room temperature over night. Then water was added and the mixture was extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (silica gel saturated with TEA, gradient 50–16% hexane/EtOAc) to afford **58** (4.0 mg, 52% yield) as a colorless oil. R_f 0.21 (2:3 hexane–EtOAc); $[\alpha]_D = +129.3$ (*c* 0.1, CH_2Cl_2); ^{1}H NMR (700 MHz, $CDCl_3$, δ_H) 7.39–7.27 (m, 10 H, ArH), 5.75 (d, 1 H, *J* = 10.5 Hz, NH), 4.84 (d, 1 H, *J* = 12.0 Hz, PhCH_2, C-2), 4.79 (d, 1 H, *J* = 10.0 Hz, PhCH_2, C-3), 4.65 (dd, 1 H, $J_{NH,4}$ = 10.5 Hz, $J_{3,4}$ = 4.5 Hz, H-4), 4.64 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1), 4.62 (d, 1 H, *J* = 10.0 Hz, PhCH_2, C-3), 4.62 (d, 1 H, *J* = 12.0 Hz, PhCH_2, C-2), 4.19 (q, 1 H, $J_{5,6}$ = 6.5, Hz, H-5), 4.00 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 4.5 Hz, H-3), 3.65 (s, 1 H, C*H*C=ONH), 3.62 (dt, 1 H, *J* =

10.0, 7.0 Hz, octyl OCH_2), 3.50 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{1,2}$ = 4.0 Hz, H-2), 3.45 (dt, 1 H, J = 10.0, 6.5 Hz, octyl OCH_2), 3.27 (t, 2 H, J = 7.0 Hz, CH_2N_3), 3.07 (br s, 1 H, OH), 2.78 (s, 3 H, NCH_3), 2.11 (d, 1 H, J = 16.5 Hz, CH_2C=O), 1.95 (d, 1 H, J = 16.5 Hz, CH_2C=O), 1.66–1.55 (m, 4 H, CH_2 x 2), 1.42 (s, 3 H, CCH_3), 1.39–1.24 (m, 8 H, CH_2 x 4), 1.18 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 173.4 (CH_3NC=O), 168.8 (HNC=O), 138.2 (Ar), 137.2 (Ar), 128.5 (Ar), 128.4 (Ar), 128.2 (Ar), 128.1 (Ar), 127.9 (Ar), 97.6 (C-1), 77.7 (C-3), 74.8 (C-2), 73.7 (*C*HC=ONH), 73.5 (Ph*C*H_2, C-2), 72.8 (Ph*C*H_2, C-3), 68.6 (octyl O*C*H_2), 63.7 (C-5), 51.7 (C-4), 51.5 (*C*H_2N_3), 44.5 (*C*H_2C=O), 29.7 (*C*H_2), 29.4 (*C*H_2), 29.3 (*C*H_2), 29.1 (NCH_3), 28.9 (C*C*H_3), 28.7 (*C*H_2), 26.7 (*C*H_2), 26.0 (*C*H_2), 16.8 (C-6); HRMS (ESI) calcd for (M+H) $C_{35}H_{50}N_5O_7$: 652.3705. Found: 652.3695.

Supporting Information

NMR spectra for compounds **5–58** and X-ray crystallographic data for **11**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(17) A reviewer suggested another possible mechanism: attack of benzylate anion, generated by elimination of **33**, onto alkene **35**. We view this unlikely, however, as such a

mechanism would be expected to generate products with scrambling of the sterochemistry α to the lactam carbonyl group. Such products were not isolated.