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Synthesis of Novel 6-Amido-6-deoxy-L-galactose Derivatives as Sialyl Lewis X Mimetics

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Abstract—The synthesis and biological potency of several sialyl Lewis X (SLe^x) mimetics is described. These mimics incorporate all of the critical functional groups present in SLe^x necessary for binding to E-selectin. L-Galactose is used to mimic the naturally occurring L-fucose residue in SLe^x due to the identical arrangement of the 2-, 3-, and 4-hydroxyl groups. Several synthetically and enzymatically prepared amino acids were used to mimic the D-galactose residue. Because of the variability incorporated in the synthesis of these amino acids the spatial requirements necessary for efficient binding were investigated. A carboxylate bearing side chain was introduced as a sialic acid mimic and the chain length was varied to maximize biological activity. By investigating the optimal arrangement of these two factors mimics were produced which were up twofold more active than SLe^x.

Introduction

Carbohydrates are ubiquitous in all biological systems. Recently, tremendous effort has focused on the discovery of new naturally occurring carbohydrates and elucidation of their biological mechanism. Through this research a clearer understanding of the role of carbohydrates is emerging. It is now understood that carbohydrates play a critical role in a host of biological phenomena. For example, it is understood that both embryonic development and cellular differentiation[1] are controlled to a large extent by a series of carbohydrate–protein interactions.[2] Furthermore, a crucial step in the mechanism of cancer metastasis involves the adhesion of cancerous cells with healthy tissues in the body.[3] It is now known that this adhesion process is mediated by the interaction of a glycoprotein found on cancerous cells and carbohydrate binding proteins throughout the body usually reserved for normal cellular trafficking events.

Inflammation is another example of a cellular adhesion process that is mediated by carbohydrates.[4] Inflammation is the result of an accumulation of leukocytes at the sight of tissue injury. Although usually helpful, excess accumulation of leukocytes can result in a retardation of the healing process. Arthritis is an autoimmune disease in which leukocytes are incorrectly directed to attack healthy cells. Recently, it has been discovered that the initial stages of leukocyte adhesion are mediated by interaction of a membrane-bound protein (*E*-selectin) found on the endothelial cells with a glycoprotein on the leukocytes.[5] At the terminus of the leukocyte-bound glycoprotein is a tetrasaccharide, sialyl Lewis X[6] (**1**, SLe^x), (Fig. 1), which is critical to the initial interaction in this adhesion process.

SLe^x (**1**) is a tetrasaccahride consisting of a D-*N*-acetylglucosamine amine, L-fucose, D-galactose, and a sialic acid residue. Although no crystal structure has been determined for the *E*-selectin/SLe^x complex, several groups have helped define the functional groups necessary for efficient binding.[7] As indicated (bold atoms in **1**) the 2-, 3-, and 4-hydroxyl groups of the fucose, the 4- and 6-hydroxyl groups of the galactose, and the carboxylate residue form the sialic acid are necessary for binding. In order to design efficient mimetics of SLe^x, and therefore cell adhesion, the mimics must incorporate all of the functional groups necessary for binding discussed above.

Herein we report the synthesis of a series of SLe^x mimetics **2–14** which incorporate all of the functionality necessary for binding to *E*-selectin.[8] These mimics utilize L-galactose as a mimic of the L-fucose residue because of the identical nature of the spatial arrangement of the 2-, 3-, and 4-hydroxyls. The D-galactose is replaced by a series of unnatural amino acids which were prepared by both enzymatic and synthetic methods. The unnatural amino acids allow us to probe, and therefore maximize, their ability to mimic the D-galactose residue. The sialic acid is replaced by a side chain, of variable length, which bears a carboxylate group. By controlling all of these factors we were able to synthesize mimics with 2-fold greater activity than SLe^x.

Results and Discussion

Synthesis of the galactose amine core 16

We chose to use L-galactose as a mimic of the L-fucose in SLe^x. A recent study indicates that L-galactose can

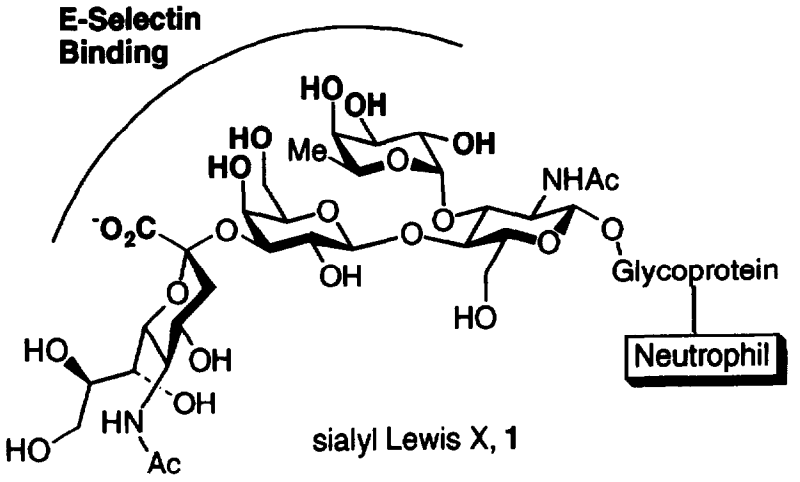


Figure 1. The structure of sialyl Lewis X showing the five functional groups essential for binding to *E*-selectin.

be substituted for L-fucose in a naturally occurring system without incident.[9] We anticipated that this would be an effective method since the spatial arrangement of the 2-, 3-, and 4-hydroxyl groups of the L-galactose would be identical to that of the 2-, 3-, and 4-hydroxyl groups of the L-fucose.

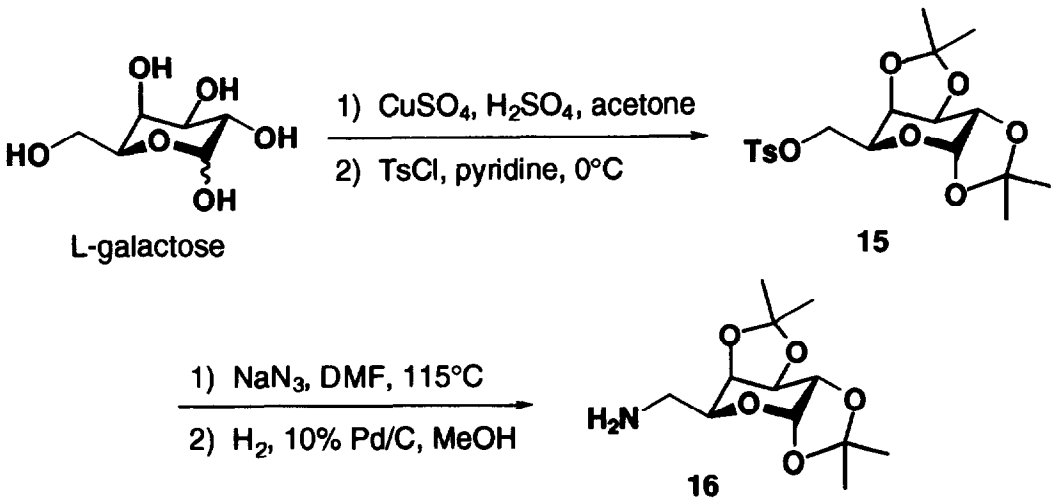
Because the galactose amine core is central to all of the mimics it was important to develop an efficient synthesis which was amenable to large scale process. Furthermore, suitable protecting groups are needed which would allow for deprotection in the late stages of the synthesis without complication.

Our synthesis follows the procedure reported by May[10] and begins with the commercially available L-galactose (Scheme 1). Selective protection of the 1,2- and 3,4-hydroxyl groups as the acetonide was high yielding and allowed for further functionalization of the C6-OH. Conversion of the primary alcohol to the tosylate under standard conditions afforded **15**. Displacement with sodium azide produced the C6-N_3 in 72% yield from L-galactose. Hydrogenation of the azide proceeded without incident affording the primary amine **16** in quantitative yield and set the stage for the subsequent coupling reactions.

Synthesis of unnatural amino acids

Our decision to use dihydroxy amino acids was based on two factors. First, molecular modeling studies suggested that these compounds would be efficient mimics of the 4- and 6-hydroxyl groups of the D-galactose in SLe^x. Secondly, methodology recently developed in this group has resulted in the efficient production of dihydroxy amino acids and would allow for the introduction of significant variability in the side-chain.[10]

Amino acids **17**, **18**, and **19** were synthesized via a threonine aldolase catalysed reaction of glycine with the appropriately protected hydroxyl aldehyde following the published literature procedure (Scheme



Scheme 1. Preparation of the galactose amine core.

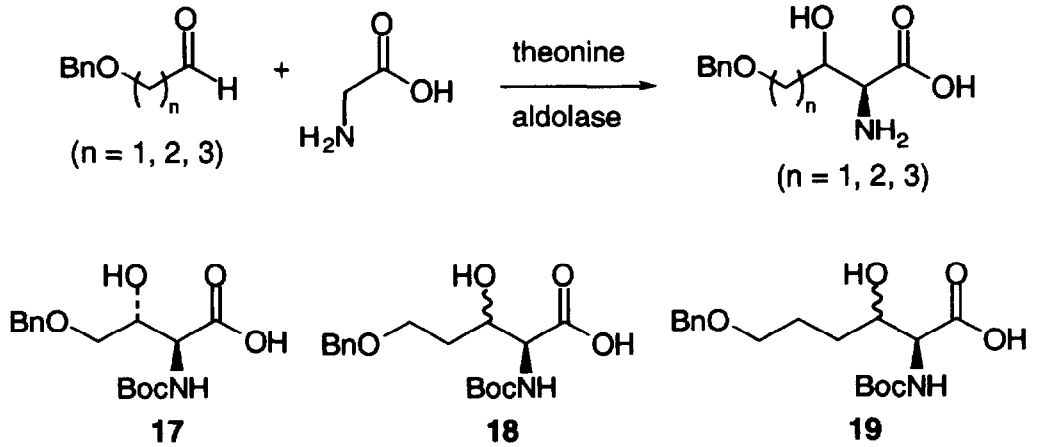
2).[11] The resulting benzyl-protected dihydroxy amino acids were treated with BOC-anhydride affording amino acids **17** (99%), **18** (83%), and **19** (85%) in high yield. Amino acids **18** and **19** were isolated as a 1:1 mixture about the 2° OH center and were carried on without separation.

Amino acid **21** was prepared synthetically as shown in Scheme 3 following the procedure described by Otani.[12] Treatment of serine with Na_2CO_3 and formaldehyde in the presence of $CuSO_4$ afforded the desired diol which was converted to the BOC derivative **20**[13] in 37% yield for this two-step conversion. Perbenzylation with excess BnBr in THF followed by hydrolysis of the ester and acidification afforded the protected amino acid **21** in 37% yield which was used in the subsequent coupling studies.

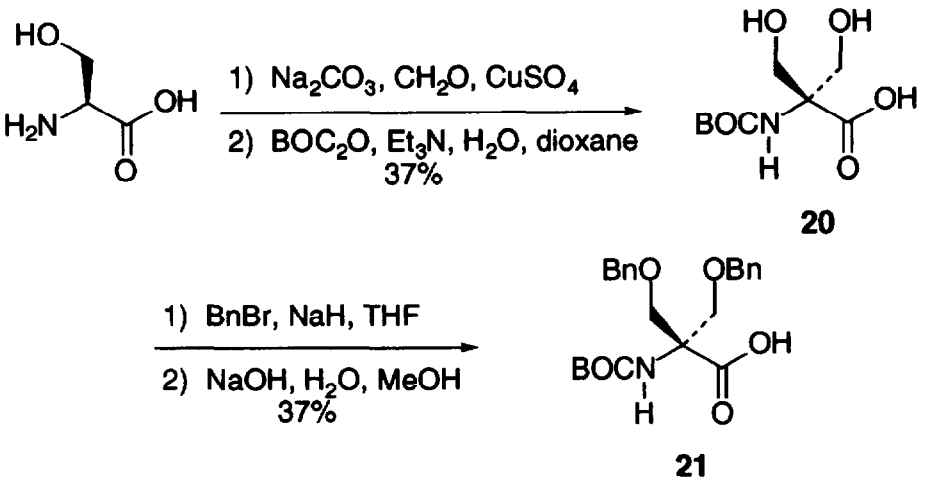
For amino acid **24** we felt that protection of the less hindered hydroxyl was necessary in order to circumvent any problems associated with lactonization in the coupling sequence. To this end 2-butyne-1,4-diol (**22**) was converted to the 4-benzloxy-2-butanone derivative using mercuric oxide and concentrated sulfuric acid (Scheme 4).[14] The resulting ketone was subjected to Bucherer conditions (KCN, $(NH_4)_2CO_3$)[15] which afforded the desired hydantoin **23** in 43% yield from **22**. Barium hydroxide hydrolysis of the hydantoin and ion-exchange chromatography afforded the desired amino acid (93%) which was converted to the N-BOC derivative **24** in a modest 44% yield.

Coupling of the amino acids 17–19, 21, and 24 with the galactose amine core 16

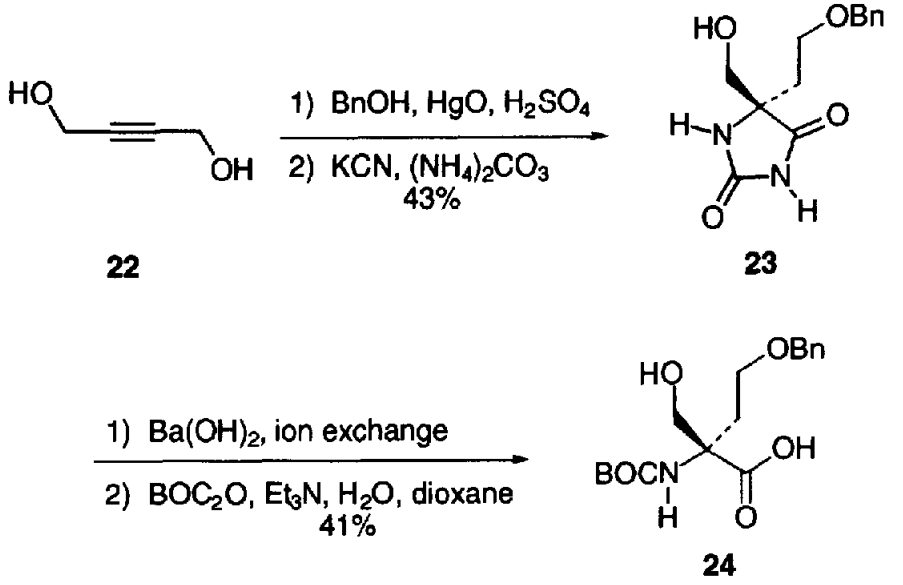
The next stage in the synthesis involved coupling of the galactose amine core **16** with the unnatural amino acids in hopes that they would provide a suitable mimic for the D-galactose in the naturally occurring SLe^x. To this end amino acids **17–19**, **21**, and **24** were coupled to the aminoglycoside core **16** using EDCI and HOBt without incident. Subsequent deprotection of the BOC (10%



Scheme 2. Synthesis of amino acids **17–19**.



Scheme 3. Synthesis of dihydroxy amino acid **21**.

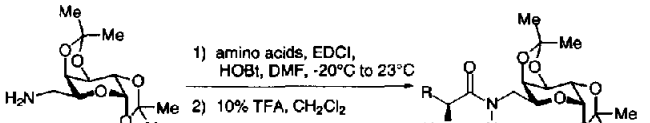


Scheme 4. Synthesis of amino acid **24**.

TFA in CH_2Cl_2) afforded the desired amines **25–29** in excellent yield. Table 1 summarizes our results for the coupling and deprotection sequence.

With coupled aminoglycoside in hand we turned our attention to the sialic acid mimic. We felt that by controlling the length of the carboxylate side chain we could probe the optimum length needed for binding. This idea was reduced to practice by coupling amines **25–29** with a suitably activated carboxylate side chain (methods A–G, Table 2). Initial attempts at hydrogenolysis of the benzyl protecting group using methanol as the solvent resulted in partial transesterification of

Table 1. Coupling of amino acids **17–19**, and **24** with galactose amine core **16**



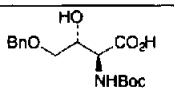
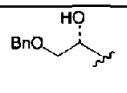
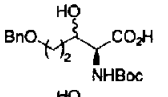
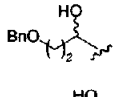
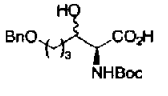
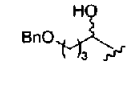
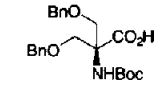
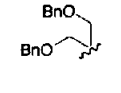
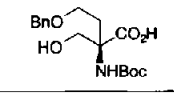
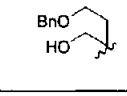
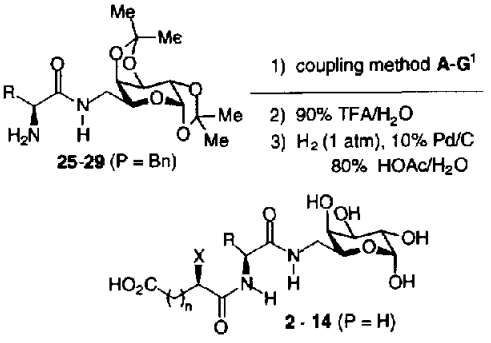
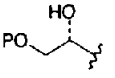
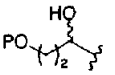
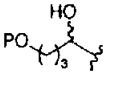
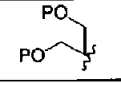
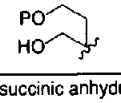
	amino acid	R	yield from 16
17			**25**, 59%
18			**26**, 75%
19			**27**, 74%
21			**28**, 57%
24			**29**, 57%

Table 2. Introduction of the sialic acid mimic and final deprotection



Amine	Coupling Method[1]	R	n	X	Final Compounds	Yield
25	A		1	H	**2**	52%
25	B		2	H	**3**	50%
25	C		1	NH_2	**4**	65%
26	A		1	H	**5**	49%
26	B		2	H	**6**	56%
26	C		1	NH_2	**7**	49%
27	A		1	H	**8**	65%
27	B		2	H	**9**	63%
27	C		1	NH_2	**10**	50%
28	D		1	H	**11**	68%
28	E		2	H	**12**	53%
29	F		1	H	**13**	45%
29	G		2	H	**14**	29%

[1]coupling methods: A) succinic anhydride, MeOH; B) glutaric anhydride, MeOH; C) EDCI, HOBt, DMF, *N*-Cbz-benzyloxyaspartic acid; D) $BnO_2C(CH_2)_2COCl$, CH_2Cl_2, Et_3N; E) $BnO_2C(CH_2)_3COCl$, CH_2Cl_2, Et_3N; F) EDCI, HOBt, DMF, $BnO_2C(CH_2)_2CO_2H$; G) EDCI, HOBt, DMF, $BnO_2C(CH_2)_3CO_2H$.

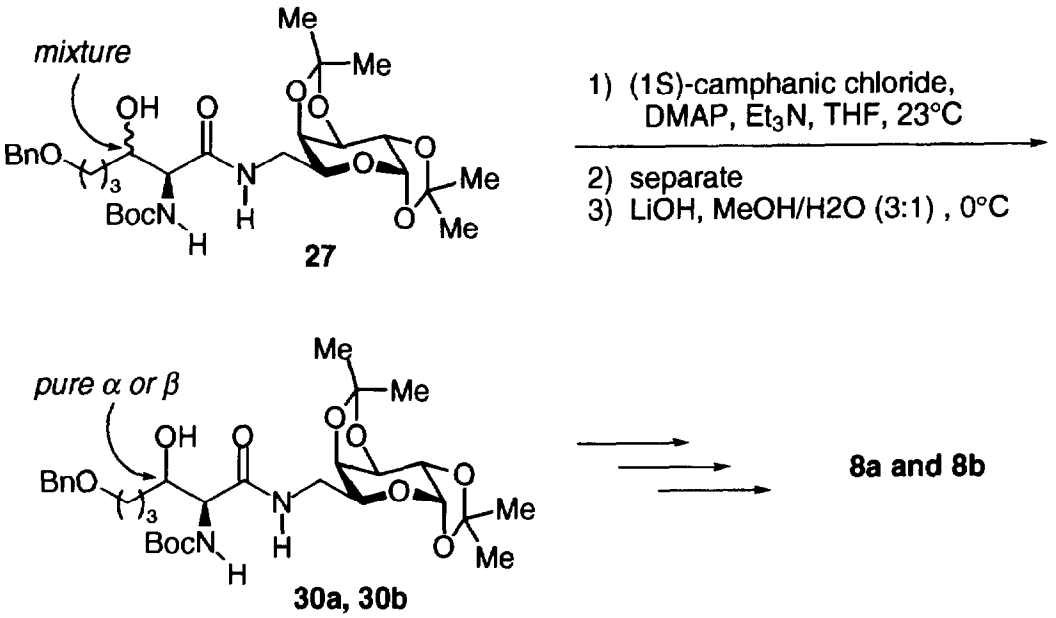
the carboxylate side group. Using 80% HOAc as the solvent resulted in complete removal of all protecting groups affording the fully deprotected mimics in good yield (Table 2).

Production of enantiomerically pure mimics 8a and 8b

The enzymatically prepared amino acid used in the production of mimic **8** was an epimeric mixture at the β-center. In addition to submitting the mixture (e.g. **8**) to biological evaluation, we decided to evaluate each epimer (**8a** and **b**) in order to evaluate the effect that this center may have on the biological activity. Unfortunately, simple chromatographic separation of compounds **8a** and **b** was not possible. However, conversion of the secondary alcohol to the chiral camphanate derivative allowed separation of the diastereomeric mixture (Scheme 5). Hydrolysis of the auxiliary afforded the single diastereomerically pure compounds which were converted to mimics **8a** and **b** following the procedures used for all of the other mimics.

Biological activities

The biological activities were assayed in a system that measured the binding of SLe^a glycoconjugate to immobilized recombinant *E*-selectin.[16] The results of the binding assay are shown in Tables 3 and 4. Table 3 shows the mimics that incorporate the enzymatically



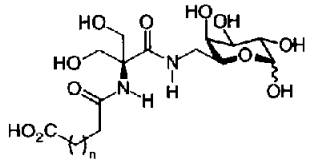
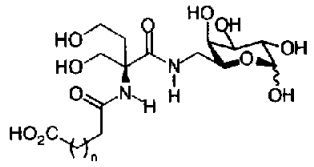
Scheme 5. Resolution of compound **8**.

Table 3. IC_{50} values of mimics derived from the enzymatically synthesized amino acids. SLe^x = 0.5 mM

Structure	*m*	*n*	X	Final compounds	IC_{50}
HO_2C	1	1	H	**2**	10 mM[a]
	1	2	H	**3**	10 mM[a]
	1	1	NH_2	**4**	0.6 mM[a]
	2	1	H	**5**	inactive[b]
	2	2	H	**6**	4.2 mM[b]
	2	1	NH_2	**7**	1 mM[b]
	3	1	H	**8**	1 mM[b]
	3	1	H	**8a**	1 mM[c]
	3	1	H	**8b**	1 mM[c]
	3	2	H	**9**	inactive
	3	1	NH_2	**10**	1.5 mM[c]

[a]The activity shown is derived from a mixture at the anomeric center only, the amino acid stereochemistry (indicated by an asterisk is *R*).
[b]These compounds were submitted as a mixture at the 2°OH on both the amino acid side chain (indicated with an asterisk) and the anomeric center.
[c]**8a** and **8b** are enantiomerically pure at the amino acid center but the absolute stereochemistry is unknown.

Table 4. IC_{50} values of mimics derived from synthetically prepared amino acids. $SLe^x = 0.5$ mM

Structure	*n*	Final compounds	IC_{50}
	1	**11**	inactive
	2	**12**	0.3 mM
	1	**13**	0.3 mM
	2	**14**	0.2 mM

prepared amino acids and Table 4 includes those mimetics which contain the synthetically prepared amino acids. The data in Table 3 indicate that the distance between the hydroxyl groups ($m = 1, 2, 3$) in the amino acid plays a role in the biological activity, when comparing mimics **2–4** to **8–10**. Interestingly the stereochemistry of the amino acid side chain has no effect on the biological activity, compare **8**, **8a**, and **8b**. The length of the carboxylate side chain seems to be critical for efficient binding, and this result is more clearly demonstrated in Table 4 (**11** and **13** compared to **12** and **14**). Overall the α-disubstituted amino acids (Table 4) show better activity than the enzymatically prepared amino acids suggesting that they are better mimics of the D-galactose in the naturally occurring SLe^x. Mimic **14** which incorporates the α-dihydroxy amino acid and a longer carboxylate side chain proved to be the best mimic showing activity twofold better that SLe^x. The design and synthesis of second generation mimetics are currently underway and will be reported in due course.

Experimental

6-Amino-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-L-galactopyranose (16). Aminoglycoide **16** was prepared following May's procedure.[10]

The following procedure is representative for BOC protection of the enzymatically prepared amino acids.

(2*S*,3*R*)-2-Amino-4-benzyloxy-3-hydroxybuteric acid (17). A soln of di-tert butyl dicarbonate (524 mg, 2.4 mmol) in dioxane (10 mL) was added to a stirred soln of (2*S*,3*R*) 2-amino-4-benzyloxy-3-hydroxy butanoic acid (450 mg, 2.0 mmol) in H_2O (10 mL) containing Et_3N (310 μL, 2.2 mmol) at 23 °C. After 10 h, the mixture was poured into Et_2O:H_2O (1:1, 100 mL) and the upper organic layer discarded. The lower aq layer was washed with Et_2O (3 × 50 mL) and then acidified to pH 3 using 1 M HCl soln. The acidic soln was then extracted with EtOAc (5 × 30 mL). The combined organic extracts were washed with satd $NaHCO_3$ (3 × 25 mL), dried ($MgSO_4$) and evapd giving **17** (644 mg, 99%) as a colorless oil: $[\alpha]_D$ +27 (*c*, 1.02 in $CHCl_3$); ^1H NMR (250 MHz; CD_3OD): δ 7.38–7.22 (5H, m, aromatic), 4.54 (2H, s, OCH_2Ph), 4.32 (1H, br d, $J = 4.9$ Hz, H2), 4.07 (1H, q, $J = 5.0$ Hz, H3), 3.62 (1H, dd, $J = 10.1$ and 4.7 Hz, $H4_aH4_b$), 3.56 (1H, dd, $J = 10.1$ and 5.6 Hz, $H4_aH4_b$), 1.32 (9H, s, ^{t}Bu); ^{13}C NMR (63 MHz; CD_3OD): δ 173.86, 157.95, 139.48, 129.34, 128.87, 128.66, 80.73, 74.41, 72.46, 71.70, 57.93, 28.68; HRMS (FAB, doped with CsI): found $M + Cs^+$, 458.0590. $C_{16}H_{23}NO_6$ requires $M + Cs^+$ 458.0580.

(2*S*,3*R* and 3*S*)-2-Amino-5-benzyloxy-3-hydroxypropionic acid (18). As for **17** above to giving **18** as a colorless oil (83%): ^1H NMR (250 MHz; CD_3OD): δ 7.22–7.11 (5H, m, aromatics), 4.39 (1H, s, CH_2Ph), 4.38 (1H, s, CH_2Ph), 4.22–4.18 (0.5H, m, H2), 4.08–4.05 (1H, m, H2 + H3), 3.96–3.89 (0.5H, m, H3), 3.56–3.44 (2H, m, 2 × C5H_2), 1.78–1.59 (2H, m, 2 × C4H_2), 1.32 (9H, m, 2 × ^{t}Bu); ^{13}C NMR (63 MHz; CD_3OD): δ 174.54, 173.49, 156.35, 156.13, 137.42, 128.48, 127.80, 80.51, 80.25, 73.27, 71.80, 71.27, 68.45, 67.99, 58.10, 57.61, 32.71, 28.25; HRMS (FAB, doped with CsI): found M + Cs, 472.0728. $C_{17}H_{25}NO_6$ requires M − Cs, 472.0736.

(2*R*,3*R* and 3*S*)-2-Amino-6-benzyloxy-3-hydroxyhexanoic acid (19). As for **17** above to give **19** as a colorless oil (85%): ^1H NMR (250 MHz; CD_3OD:) δ 7.23–7.13 (5H, m, aromatics), 4.38 (2H, s, 2 × CH_2Ph), 4.07–3.97 (1.5H, m, 2 × H2 + H3), 3.72–3.68 (0.5H, m, H3), 3.43–3.38 (2H, m, C6H_2), 1.67–1.46 (4H, m, 2 × H4 + 2 × H5), 1.33 (9H, s, 2 × ^{t}Bu); ^{13}C NMR (63 MHz; CD_3OD): δ 174.57, 173.40, 156.38, 156.14, 137.63, 128.40, 127.79, 80.18, 72.89, 71.65, 70.00, 58.12, 57.61, 30.79, 30.46, 28.23, 26.07; HRMS (FAB, doped with CsI): found M + Cs, 486.0914. $C_{18}H_{27}NO_6$ requires M + Cs, 486.0893.

1-Hydroxymethyl-1-benzyloxyethylhydantoin (23). The ketone intermediate was synthesized from 2-butyne-1,4-diol **22** (1.004 g, 11.66 mmol) according to the procedure described by Hennion and Kupiecki.[14] However, instead of EtOH, BnOH (3.33 mL total) was used. When the conversion was complete, the mixture was extracted with CH_2Cl_2 (3 times) and the collected organic layers were washed with 1 M Na_2CO_3, 1 N HCl, brine, dried ($MgSO_4$) and coned under vacuum silica gel CG (EtOAc:hexanes, 3:7) affording the product as a colorless oil in 54% yield (1.217 g): ^1H NMR (250 MHz, $CDCl_3$): δ 2.68 (t, 2H, $J = 6.0$ Hz, $COCH_2CH_2$), 3.17 (br, 1H, OH), 3.76 (t, 2H, $J = 6.0$ Hz, CH_2O), 4.28 (s, 2H, CH_2OH), 4.50 (s, 2H, CH_2Ph), 7.25–7.38 (m, 5H, Ph); ^{13}C NMR (63 MHz, $CDCl_3$): δ 38.83, 64.80, 68.70, 73.12, 127.55, 127.66, 128.32, 137.57, 208.38.

The above ketone (1.00 g, 5.15 mmol) was converted to the hydantoin **23** following the procedure described by Krüger.[15] Recrystallization from EtOH:H_2O afforded **23** (1.092 g, 80% yield): mp 157.5–158.5 °C; ^1H NMR (400 MHz, MeOD:$CDCl_3$): δ 2.12, 2.24 (m 8 lines (H_a),

dt (H_b), 2H, $J_{AX}=5.9$ Hz, $J_{AY}=8.3$ Hz, $J_{BX}=4.6$ Hz, $J_{AB}=14.3$ Hz, CCH_2), 3.59–3.63 (m, 2H, CH_2O), 4.31, 4.55 (two d, 2H, $J=9.1$ Hz, CH_2OH), 4.48, 4.52 (two d, 2H, $J=11.9$ Hz, CH_2Ph), 7.28–7.38 (m, 5H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 36.15, 63.40, 65.72, 72.98, 73.30, 127.36, 127.42, 127.96, 128.03, 137.06, 159.01, 175.28; HRMS calcd for $C_{13}H_{16}N_2O_4$ ($M+H^+$): 265.1188; found 265.1184.

***N*-Butyloxycarbonyl-1-benzyloxyethylserine (24).** The title amino acid was prepared from the hydantoin **23** (0.695 g, 2.63 mmol) by hydrolysis using $Ba(OH)_2$ as described by Krüger.[15] After a reaction time of 48 h, 1 M $NaHCO_3$ was added and the precipitate filtered. The filtrate was evapd to a small vol under red. pres. and acidified with HOAc to pH 3. Ion exchange column chromatography (Dowex 50W H^+, gradient of 0.5 N NH_4OH), followed by lyophilization afforded the product (0.583 g, 93%) as a white solid: ^1H NMR (250 MHz, D_2O, ref. CH_3CN): δ 1.78–2.07 (m, 2H, CCH_2CH_2), 3.55, 3.81 (two d, 2H, $J=11.4$ Hz, CH_2OH), 3.62–3.67 (m, 2H, CH_2O), 4.54 (s, 2H, CH_2Ph), 7.35–7.47 (m, 5H, Ph); ^{13}C NMR (63 MHz, D_2O, Ref. CH_3CN): δ 34.27, 64.00, 67.38, 67.62, 73.62, 1 .02, 129.22, 129.46, 138.05, 179.33; HRMS calcd for $C_{12}H_{17}NO_4$ ($M+Na^+$): 262.1055; found 262.1060.

The above amino acid (92 mg, 0.385 mmol) was dissolved in a mixture of H_2O (1 mL) and dioxane (1 mL). Triethylamine (64 μL, 0.46 mmol) and Boc_2O (101 mg, 0.46 mmol) were added and the mixture was stirred for 2 days at 23 °C, during which time 3 additional portions of Boc_2O (101 mg, 0.46 mmol) and Et_3N (64 mg, 0.46 mmol) were added. The dioxane was evapd under red. pres. and the residue acidified with 1 N HCl to pH 3 and extracted with CH_2Cl_2 (3 × 5 mL). The collected organic layers were washed with brine, dried ($MgSO_4$) and concd under red. pres. Purification by CG (CH_2Cl_2:MeOH, 96:4) afforded **24** as an oil (57 mg, 44%): ^1H NMR (250 MHz, $CDCl_3$): δ 1.42 (s, 9H, $C(CH_3)_3$), 2.15–2.34 (m, 2H, CCH_2), 3.59–3.63 (m, 2H, CH_2CH_2O), 3.83, 4.03 (two d, 2H, $J=11.0$ Hz, CH_2OH), 4.45, 4.51 (two d, 2H, $J=11.7$ Hz, CH_2Ph), 5.50 (br, 1H, COOH), 6.25 (br, 1H, NH), 7.26–7.35 (m, 5H, Ph); ^{13}C NMR (63 MHz, $CDCl_3$): δ 28.25, 32.35, 63.62, 66.25, 73.20, 80.15, 127.73, 128.40, 137.51, 155.93, 175.95; HRMS calcd for $C_{17}H_{25}NO_6$ ($M+Na^+$): 362.1580; found 362.1573.

Coupling of N-protected amino acids 18, 19, 21, and 24 to 6-amino-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-L-galactopyranose (16). The following coupling and deprotection procedure is identical to that which was used in the synthesis of compounds **25–29**.

Glycopeptide 25. 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (124 mg, 0.65 mmol) was added to a stirred soln of 6-amino-6-deoxy-1,2:3,4-diisopropylidene-α-L-galactopyranoside **16** (155 mg, 0.6 mmol), N-Boc amino acid **17** (211 mg, 0.65 mmol), 1-hydroxy benzotriazole (HOBt) (88 mg, 0.65 mmol) and 4-methyl morpholine (143 μL, 1.3 mmol) in dry DMF (2 mL) under argon at −20 °C. The resulting mixture was stirred at −20 °C for 1 h and then allowed to warm slowly to 23 °C. After 14 h, the reaction soln was quenched with a 5% citric acid soln (20 mL) and extracted with EtOAc (6 × 25 mL). The combined organic extracts were washed with satd $NaHCO_3$ soln (50 mL), a satd NaCl soln (50 mL), dried ($MgSO_4$) and evapd down under red. pres. The residual oil was purified by silica gel flash chromatography (40%→50%→66% EtOAc in hexanes) to give the product (287 mg, 84%) as a white amorphous foam: $[\alpha]_D$ +7.4 (*c*. 1.02 in $CHCl_3$); ^1H NMR (400 MHz; $CDCl_3$): δ 7.33–7.25 (5H, m, aromatic), 6.72 (1H, m, C6NH), 5.62 (1H, br d, $J=7.4$ Hz, C2′NH), 5.49 (1H, d, $J=5.0$ Hz, H1), 4.56 (1H, dd, $J=7.9$ and 2.4 Hz, H3), 4.55 (2H, s, OCH_2Ph), 4.28 (1H, dd, $J=5.0$ and 2.4 Hz, H2), 4.23–4.20 (1H, br m, H2′), 4.16 (1H, dd, $J=7.9$ and 1.8 Hz, H4), 3.95–3.91 (2H, m, H5 + H3′), 3.66 (1H, ddd, $J=14.0$, 7.5 and 3.6 Hz, $H6_aH6_b$), 3.65–3.58 (2H, m, $C4'H_2$), 3.46 (1H, br d, $J=7.0$ Hz, C3′OH), 3.17 (1H, ddd, $J=14.0$, 9.1 and 4.5 Hz, $H6_aH6_b$), 1.45 (3H, s, acetonide Me), 1.43 (3H, s, acetonide Me), 1.41 (9H, s, ^{t}Bu), 1.31 (3H, s, acetonide Me), 1.28 (3H, s, acetonide Me); ^{13}C NMR (100 MHz; $CDCl_3$): δ 170.64, 155.60, 137.77, 128.41, 128.22, 127.84, 109.48, 108.79, 96.37, 79.95, 73.45, 71.76, 71.48, 71.45, 70.80, 70.43, 65.63, 55.75, 40.03, 28.26, 25.93, 24.88, 24.32; IR 3349, 2979, 2933, 1712, 1666, 1497, 1454, 1382, 1369, 1253, 1211, 1167, 1110, 1070, 1006, 901, 859, 736, 698 cm^{-1}; HRMS (FAB, doped with CsI): found $M+Cs^+$, 699.1876. $C_{28}H_{42}N_2O_{10}$ requires $M+Cs^+$ 699.1894. Elemental analysis found: C, 59.07; H, 7.39; N, 4.94. $C_{28}H_{42}N_2O_{10}$ requires C, 59.35; H, 7.47; N, 4.94.

A soln of the above glycopeptide (187 mg, 322 μmol) with 10% TFA in dry CH_2Cl_2 (2 mL) was stirred under argon at 23 °C. After 2 h, the soln was evapd down under red. pres. and the residual oil dissolved up in n-BuOH:H_2O:MeOH (5:3:2 10 mL). To the soln was added Dowex (Cl^- form, prewashed with MeOH, 100 mg) and the mixture stirred for 30 min, filtered and the solid washed with MeOH (3 × 5 mL). The combined filtrate and washings were then evapd down under red. pres. The residual oil was purified by silica gel flash chromatography (19:0.9:0.1→14:0.9:0.1 CH_2Cl_2:MeOH:NH_4OH) to give **25** (108 mg, 70%): $[\alpha]_D$ +2.6 (*c*. 2.22 in $CHCl_3$); ^1H NMR (400 MHz; $CDCl_3$): δ 7.51 (1H, br dd, $J=7.3$ and 4.4 Hz, C6NH), 7.31–7.21 (5H, m, aromatic), 5.45 (1H, d, $J=5.0$ Hz, H1), 4.54 (1H, d, $J=11.9$ Hz, OCH_aH_bPh), 4.52 (1H, dd, $J=7.9$ and 2.4 Hz, H3), 4.45 (1H, d, $J=11.9$ Hz, OCH_aH_bPh), 4.24 (1H, dd, $J=5.0$ and 2.4 Hz, H2), 4.13 (1H, dd, $J=7.9$ and 1.7 Hz, H4), 3.88–3.83 (2H, m, H5+H3′), 3.66–3.55 (2H, m, $H6_aH6_b$ + $C4'H_2$), 3.41 (1H, d, $J=11.9$ Hz, H2′), 3.17 (1H, ddd, $J=14.0$, 9.1 and 4.4 Hz, $C6H_aH_b$), 2.80–1.50 (2H, br s, $C2'NH_2$), 1.42 (3H, s, acetonide Me), 1.40 (3H, s, acetonide Me), 1.27 (3H, s, acetonide Me), 1.25 (3H, s, acetonide Me); ^{13}C NMR (100 MHz; $CDCl_3$): δ 174.27, 137.93, 128.39, 127.68, 127.65, 109.38, 108.70, 96.28, 73.41, 72.26, 71.59, 71.42, 70.76, 70.46, 66.16, 56.58, 39.70, 25.95, 25.93, 24.91, 24.29; IR 3367, 2986, 2932, 1654, 1529, 1454, 1382,

1254, 1211, 1166, 1108, 1068, 1005, 900, 738, 698 cm^{-1}; HRMS (FAB, doped with CsI) found: $M+Cs^+$, 599.1353. $C_{23}H_{34}N_2O_8$ requires $M+Cs^+$ 599.1369.

Glycopeptide 26. Following the coupling procedure described above afforded 88% of a pale yellow amorphous foam: ^1H NMR (400 MHz; $CDCl_3$) 7.33–7.22 (5H, m, aromatic), 6.96 (0.5H, br m, C6NH), 6.89 (0.5H, br m, C6NH), 5.58 (0.5H, br d, C2'NH), 5.55 (0.5H, br d, C2'NH), 5.47 (1H, apparent t, 2×H1), 4.55 (1H, dt, $J=7.9$ and 2.3 Hz, 2×H3), 4.52–4.45 (2H, m, 2×C$\underline{H}_2$Ph), 4.26 (0.5H, dd, $J=5.0$ and 2.3 Hz, H2), 4.25–4.21 (0.5H, m, H2'), 4.24 (0.5H, dd, $J=5.0$ and 2.3 Hz, H2), 4.16 (1H, dt, $J=7.9$ and 1.8 Hz, 2×H4), 4.14–4.10 (0.5H, m, H2'), 4.09–4.06 (0.5H, m, H3'), 3.95–3.90 (1H, m, 2×H5), 3.87–3.80 (0.5H, m, H3'), 3.70–3.58 (4H, m, 2×$\underline{H}6_aH6_b$ + 2×C3'OH + 2×C5'H_2), 3.23 (0.5H, ddd, $J=13.9$, 8.7 and 4.3 Hz, $H6_a\underline{H}6_b$), 3.22 (0.5H, ddd, $J=13.9$, 9.3 and 4.5 Hz, $H6_a\underline{H}6_b$), 2.01–1.66 (2H, m, 2×C4'H_2), 1.42 (6H, s, acetonide Me), 1.41 (4.5H, s, 'Bu), 1.40 (4.5H, s, 'Bu), 1.30 (3H, s, acetonide Me), 1.25 (1.5H, s, acetonide Me), 1.23 (1.5H, s, acetonide Me); ^{13}C NMR (100 MHz; $CDCl_3$): δ 171.00, 170.80, 155.96, 155.63, 137.99, 137.87, 128.48, 128.44, 128.42, 128.38, 128.32, 127.70, 127.65, 109.46, 109.40, 108.78, 108.69, 96.39, 96.28, 79.92, 79.79, 73.24, 73.21, 71.53, 71.44, 70.79, 70.69, 70.46, 70.42, 68.45, 67.49, 65.72, 65.58, 57.66, 57.44, 39.96, 33.51, 31.82, 29.65, 28.29, 25.90, 25.82, 24.93, 24.85, 24.31; IR 3343, 2979, 2933, 1707, 1654, 1497, 1454, 1369, 1254, 1211, 1167, 1110, 1071, 1008, 902, 860, 735, 698 cm^{-1}; HRMS (FAB, doped with CsI) Found M+Cs, 713.2081. $C_{29}H_{44}N_2O_{10}$ requires $M+Cs^+$, 713.2050; elemental analysis found: C, 59.90; H, 7.77; N, 4.74. $C_{29}H_{44}N_2O_{10}$ requires C, 60.00; H, 7.64; N, 4.82.

Deprotection of the BOC group as above gave **26** (85%) as a yellow foam: ^1H NMR (400 MHz; $CDCl_3$): δ 7.63 (0.5H, br m, C6NH), 7.50 (0.5H, br m, C6NH), 7.34–7.24 (5H, m, aromatic), 5.50 (0.5H, d, $J=5.0$ Hz, H1), 5.49 (0.5H, d, $J=5.0$ Hz, H1), 4.57 (1H, dd, $J=7.9$ and 2.3 Hz, 2×H3), 4.49 (2H, s, 2×OC$\underline{H}_2$Ph), 4.28 (0.5H, dd, $J=5.0$ and 2.4 Hz, H2), 4.27 (0.5H, dd, $J=5.0$ and 2.4 Hz, H2), 4.17 (1H, dt, $J=7.9$ and 2.0 Hz, 2×H4), 4.06–4.03 (0.5H, m, H3'), 3.95–3.87 (1.5H, m, 2×H5+H3'), 3.75–3.63 (3H, m, 2×$H6_aH6_b$ + 2×C5'H_2), 3.32 (0.5H, br d, $J=6.3$, H2'), 3.30 (0.5H, br d, $J=4.4$, H2'), 3.24–3.14 (1H, m, 2×$H6_a\underline{H}6_b$), 1.98–1.73 (4H, m, 2×C2'NH_2 + 2×C4'H_2), 1.44 (3H, s, acetonide Me), 1.43 (3H, s, acetonide Me), 1.31 (3H, s, acetonide Me), 1.28 (3H, s, acetonide Me); ^{13}C NMR (63 MHz; $CDCl_3$): δ 173.70,137.81, 128.39, 127.66, 109.35, 108.66, 96.29, 73.31, 72.59, 71.62, 71.29, 70.76, 70.46, 68.12, 66.21, 66.12, 58.45, 39.69, 39.61, 32.24, 25.91, 24.91, 24.27; IR 3362, 2984, 2923, 1654, 1527, 1454, 1382, 1255, 1211, 1167, 1109, 1069, 1006, 901, 859, 739, 698 cm^{-1}; HRMS (FAB, doped with CsI) Found M+H, 481.2573. $C_{21}H_{36}N_2O_8$ requires $M+H$, 481.2550; elemental analysis found: C, 59.76; H, 7.57; N, 5.60. $C_{21}H_{36}N_2O_8$ requires C, 60.00; H, 7.55; N, 5.83.

Glycopeptide 27. Via the procedure described above, the product was obtained (86%) as a pale yellow amorphous foam: ^1H NMR (400 MHz; $CDCl_3$): δ 7.33–7.25 (5H, m, aromatic), 6.82 (0.5H, br m, C6NH), 6.64 (0.5H, br m, C6NH), 5.49–5.45 (1H, br s, 2×C2'NH), 5.48 (0.5H, d, $J=5.0$, H1), 5.47 (0.5H, d, $J=5.0$, H1), 4.58–4.55 (1H, dm, $J=7.9$, 2×H3), 4.49 (1H, s, CH_2Ph), 4.48 (1H, s, C$\underline{H}_2$Ph), 4.27 (0.5H, dd, $J=5.0$ and 2.3, H2), 4.26 (0.5H, dd, $J=5.0$ and 2.3, H2), 4.17 (1H, dd, $J=7.9$ and 1.5, 2×H4), 4.12 (0.5H, br d, H2'), 4.09–4.06 (0.5H, m, H2'), 3.98–3.92 (1.5H, m, 2×H5+H3'), 3.78–3.76 (1H, m, 2×C3'OH), 3.69–3.56 (1.5H, m, 2×$H6_aH6_b$+H3'), 3.51–3.43 (2H, m, 2×C6'H_2), 3.26–3.15 (1H, m, 2×$H6_a\underline{H}6_b$), 1.85–1.49 (4H, m, 2×C4'H_2+2×C5'H_2), 1.44 (3H, s, acetonide Me), 1.42 (9H, s, 2×'Bu), 1.41 (3H, s, acetonide Me), 1.31 (3H, s, acetonide Me), 1.27 (3H, s, acetonide Me); ^{13}C NMR (100 MHz; $CDCl_3$): δ 171.63, 171.43, 156.02, 155.69, 138.36, 138.08, 128.40, 128.34, 127.71, 127.63, 127.53, 109.53, 109.42, 108.73, 96.39, 96.31, 79.91, 72.99, 72.86, 71.52, 71.46, 71.29, 70.79, 70.45, 70.26, 70.11, 65.63, 65.50, 57.77, 57.27, 39.98, 30.49, 29.62, 28.28, 26.40, 26.03, 25.92, 24.95, 24.85, 24.30; IR 3345, 2980, 2933, 1707, 1662, 1497, 1454, 1369, 1254, 1167, 1110, 1070, 1007, 918, 902, 859, 736, 698 cm^{-1}; HRMS (FAB, doped with CsI): found M+Cs, 727.2237. $C_{30}H_{46}N_2O_{10}$ requires M+Cs, 727.2207.

Via the deprotection procedure described, **27** was obtained (86%) as a yellow foam: ^1H NMR (400 MHz; $CDCl_3$): δ 7.59 (0.5H, br m, C6NH), 7.44 (0.5H, br m, C6NH), 7.35–7.26 (5H, m, aromatic), 5.49 (1H, d, $J=5.0$ Hz, 2×H1), 4.57 (1H, dd, $J=7.9$ and 2.3 Hz, 2×H3), 4.50 (2H, s, 2×OC$\underline{H}_2$Ph), 4.30–4.27 (1H, m, 2×H2), 4.19 (1H, d, $J=7.9$ Hz, 2×H4), 4.01–3.98 (0.5H, m, H3'), 3.95–3.89 (1.0H, m, 2×H5), 3.71–3.64 (1.5H, m, 2×$\underline{H}6_aH6_b$ + H3'), 3.56–3.49 (2H, m, 2×C6'H_2), 3.28–3.18 (1H, m, 2×H6a$\underline{H}6_b$), 3.24 (0.5H, br d, $J=3.6$ Hz, H2'), 3.21 (0.5H, br d, $J=4.5$ Hz, H2'), 1.85–1.45 (6H, m, 2×C2'NH_2+2×C4'H_2 + 2×C5'H_2), 1.45 (3H, s, acetonide Me), 1.44 (3H, s, acetonide Me), 1.32 (3H, s, acetonide Me), 1.29 (3H, s, acetonide Me); ^{13}C NMR (63 MHz; $CDCl_3$): δ 174.71, 174.07, 138.22, 138.13, 128.33, 127.64, 109.35, 108.65, 96.27, 73.21, 72.90, 71.89, 71.62, 70.76, 70.46, 70.23, 66.18, 66.00, 58.79, 58.64, 39.66, 30.04, 29.86, 29.62, 26.36, 25.92, 25.71, 24.89, 24.24; IR 3368, 2987, 2932, 2857, 1657, 1526, 1454, 1383, 1255, 1211, 1167, 1109, 1070, 1007, 919, 902, 736, 698 cm^{-1}; HRMS (doped with CsI): found M+H, 495.2727. $C_{25}H_{38}N_2O_8$ requires M+H, 495.2706. Elemental analysis: found; C, 61.01; H, 8.02; N, 5.36. $C_{25}H_{38}N_2O_8$ requires; C, 60.71; H, 7.74; N, 5.66.

Glycopeptide 28. Via the coupling procedure described above affording the product (87%) as a colorless oil: $[\alpha]_D$ +14 (*c*. 2.88 in $CHCl_3$); ^1H NMR (400 MHz; $CDCl_3$): δ 7.33–7.24 (11H, m, 2×aromatics+C6NH), 5.64 (1H, br s, C2'NH), 5.45 (1H, d, $J=5.0$ Hz, H1), 4.55 (1H, dd, $J=8.0$ and 2.4 Hz, H3), 4.53–4.47 (4H, m, 2×OCH_2Ph), 4.27 (1H, dd, $J=5.0$ and 2.4 Hz, H2), 4.17 (1H, dd, $J=7.9$ and 1.7 Hz, H4),

3.98–3.95 (2H, br m, 2 × C$\underline{H}_a H_b$OBn), 3.91 (1H, ddd, J = 8.5, 4.8 and 1.8 Hz, H5), 3.88–3.83 (2H, br m, 2 × $CH_a\underline{H}_b$OBn), 3.60 (1H, ddd, J = 13.7, 7.4 and 4.8 Hz, $\underline{H}6_a H6_b$), 3.32 (1H, ddd, J = 13.7, 8.5 and 4.5, $H6_a\underline{H}6_b$), 1.43 (3H, s, acetonide Me), 1.42 (3H, s, acetonide Me), 1.40 (9H, s, ^{t}Bu), 1.29 (3H, s, acetonide Me), 1.28 (3H, s, acetonide Me); ^{13}C NMR (100 MHz; $CDCl_3$): δ 171.28, 154.74, 137.74, 137.69, 128.48, 128.42, 128.35, 128.26, 127.67, 127.58, 109.34, 108.69, 96.26, 73.55, 73.47, 71.44, 70.79, 70.53, 70.04, 65.94, 62.07, 39.85, 28.29, 26.05, 25.96, 25.03, 24.43; IR 3380, 2979, 2923, 1715, 1678, 1484, 1454, 1367, 1253, 1211, 1167, 1097, 1070, 1006, 901, 739, 698 cm^{-1}; HRMS (FAB, doped with CsI): found M + Cs, 789.2385. $C_{35}H_{48}N_2O_{10}$ requires M + Cs, 789.2363; elemental analysis found: C, 64.04; H, 7.58; N, 4.36. $C_{35}H_{48}N_2O_{10}$ requires C, 64.00; H, 7.36; N, 4.26.

Via the deprotection procedure described above, **28** was obtained (66%) as a colorless oil: $[\alpha]_D$ +9.7 (*c* 5.7 in $CHCl_3$); ^{1}H NMR (400 MHz; $CDCl_3$): δ 8.05–8.01 (1H, m, C6NH), 7.34–7.24 (10H, m, 2 × aromatics), 5.47 (1H, d, J = 5.0 Hz, H1), 4.53 (1H, dd, J = 7.9 and 2.4 Hz, H3), 4.54–4.44 (4H, m, 2 × OC$\underline{H}_2$Bn), 4.27 (1H, dd, J = 5.0 and 2.4 Hz, H2), 4.15 (1H, dd, J = 7.9 and 1.7 Hz, H4), 3.87 (1H, ddd, J = 8.6, 4.2 and 1.6 Hz, H5), 3.77 (1H, d, J = 8.9 Hz, C$\underline{H}_a$H$_b$OBn) 3.64 (1H, d, J = 9.0, C$\underline{H}_a$H$_b$OBn), 3.64–3.58 (1H, m, $\underline{H}6_a H6_b$), 3.53 (1H, d, J = 8.8 Hz, $CH_a\underline{H}_b$OBn) 3.52 (1H, d, J = 9.0 Hz, $CH_a\underline{H}_b$OBn) 3.25 (1H, ddd, J = 13.8, 8.6 and 4.4 Hz, $H6_a\underline{H}6_b$), 1.97 (2H, br s, C2′NH_2), 1.43 (3H, s, acetonide Me), 1.38 (3H, s, acetonide Me), 1.30 (3H, s, acetonide Me), 1.28 (3H, s, acetonide Me); ^{13}C NMR (100 MHz; $CDCl_3$): δ 175.84, 109.50, 108.76, 96.40, 71.50, 70.81, 70.46, 65.65, 65.43, 61.96, 39.79, 25.89, 25.80, 24.83, 24.24; IR 3378, 2985, 2917, 2861, 1670, 1517, 1453, 1382, 1254, 1211, 1169, 1097, 1070, 1006, 902, 738, 698 cm^{-1}; HRMS (FAB, doped with CsI): found M + Cs, 689.1818. $C_{30}H_{40}N_2O_8$ requires M + Cs, 689.1839. Elemental analysis found: C, 64.57; H, 6.97; N, 4.96. $C_{30}H_{40}N_2O_8$ requires C, 64.73; H, 7.24; N, 5.03.

Glycopeptide 29. Via the coupling procedure described above, the product was obtained (78%) as a pale yellow amorphous foam: ^{1}H NMR (400 MHz; $CDCl_3$): δ 7.35–7.25 (5H, m, aromatic), 6.96 (0.5H, br s, C6NH), 6.83 (0.5H, br s, C6NH), 6.41 (0.5H, br s, C2′NH), 5.93 (0.5H, br s, C2′NH), 5.48 (1H, t, J = 5.2 Hz, 2 × H1), 4.57 (0.5H, dd, J = 7.9 and 2.4 Hz, H3), 4.56 (0.5H, dd, J = 7.9 and 2.4 Hz, H3), 4.51–4.45 (2H, m, 2 × OCH_2Ph), 4.28 (0.5H, dd, J = 5.0 and 2.4 Hz, H2), 4.27 (0.5H, dd, J = 5.0 and 2.4 Hz, H2), 4.19 (0.5H, dd, J = 7.9 and 1.8 Hz, H4), 4.16 (0.5H, dd, J = 7.9 and 1.7 Hz, H4), 4.15–4.10 (1H, m, 2 × C$\underline{H}_a$H$_b$OH), 4.00–3.90 (2.0H, m, 2 × H5 + 2 × $CH_a\underline{H}_b$OH), 3.70–3.51 (4H, m, 2 × $\underline{H}6_a H6_b$ + 2 × C4′H_2 + 2 × CH_2OH), 3.25–3.18 (1H, m, 2 × $H6_a\underline{H}6_b$), 2.31–2.09 (2H, m, 2 × C3′H_2), 1.45 (1.5H, s, acetonide Me), 1.44 (1.5H, s, acetonide Me), 1.43 (3H, s, acetonide Me), 1.39 (9H, s, 2 × ^{t}Bu), 1.30 (3H, s, acetonide Me), 1.29 (1.5H, s, acetonide Me), 1.28 (1.5H, s, acetonide Me); ^{13}C NMR (100 MHz; $CDCl_3$): δ 173.99, 173.09, 155.08, 137.53, 137.48, 128.45, 127.84, 127.73, 109.38, 108.75, 96.35, 80.08, 73.31, 73.27, 71.53, 70.79, 70.48, 66.74, 66.58, 66.48, 65.61, 65.40, 63.26, 62.70, 39.99, 33.55, 32.79, 29.67, 28.40, 28.31, 28.25, 25.97, 24.96, 24.91, 24.31, 24.27; IR 3374, 2979, 2935, 1717, 1667, 1486, 1455, 1369, 1254, 1212, 1167, 1070, 1005, 902, 734, 698 cm^{-1}; HRMS (FAB, doped with CsI): found M + Cs, 713.2074. $C_{29}H_{44}N_2O_{10}$ requires M + Cs, 713.2050. Elemental analysis found: C, 60.26; H, 7.78; N, 4.92. $C_{29}H_{44}N_2O_{10}$ requires C, 60.00; H, 7.64; N, 4.82.

Via the deprotection procedure described above affording **29** (73%) as a yellow foam: ^{1}H NMR (400 MHz; $CDCl_3$): δ 8.13 (0.5H, br m, NH), 8.04 (0.5H, br m, NH), 7.34–7.24 (5H, m, aromatic), 5.50 (1H, d, J = 5.0, 2 × H1), 4.58–4.55 (1H, dm, J = 7.9 Hz, 2 × H3), 4.50 (0.5H, d, J = 11.7 Hz, OC$\underline{H}_a$H$_b$Ph), 4.45 (1H, s, OCH_2Ph), 4.44 (0.5H, d, J = 11.7 Hz, $OCH_a\underline{H}_b$Ph), 4.28 (1H, dd, J = 5.0 and 2.4 Hz, 2 × H2), 4.17 (1H, dm, J = 7.9, 2 × H4), 4.05–4.02 (0.5H, m, H5), 3.91–3.88 (0.5H, m, H5), 3.79 (0.5H, d, J = 11.0 Hz, C$\underline{H}_a$H$_b$OH), 3.72 (0.5H, d, J = 10.9, C$\underline{H}_a$H$_b$OH), 3.69–3.55 (3H, m, 2 × $\underline{H}_{6a}H6_b$ + 2 × C4′H_2), 3.46 (0.5H, d, J = 10.9, $CH_a\underline{H}_b$OH), 3.34 (0.5H, d, J = 11.0 Hz, $CH_a\underline{H}_b$OH), 3.21 (0.5H, ddd, J = 14.1, 9.1 and 4.6 Hz, $H6_a\underline{H}6_b$), 3.15 (0.5H, ddd, J = 14.0, 9.7 and 4.9, $H6_a\underline{H}6_b$), 2.20–1.60 (2H, br s, C2′NH_2), 2.09–2.00 (1H, m, C3′H_2), 1.87 (0.5H, ddd, J = 14.7, 7.0 and 4.6 Hz, $H3'_a$H3′$_b$), 1.79 (0.5H, ddd, J = 14.6, 7.4 and 4.5 Hz, H3′$_a\underline{H}3'_b$), 1.47 (1.5H, s, acetonide Me), 1.43 (4.5H, s, acetonide Me), 1.31 (3H, s, acetonide Me), 1.28 (3H, s, acetonide Me); ^{13}C NMR (100 MHz; $CDCl_3$): δ 176.89, 176.71, 138.00, 137.92, 128.40, 128.36, 128.33, 128.30, 127.69, 127.66, 109.46, 109.40, 108.75, 108.63, 96.53, 96.35, 73.21, 73.15, 71.70, 71.54, 70.91, 70.82, 70.47, 69.28, 68.83, 66.90, 66.83, 66.03, 65.10, 60.86, 60.43, 39.79, 39.72, 35.53, 35.37, 25.98, 25.96, 25.93, 25.76, 24.96, 24.87, 24.31; IR 3372, 2973, 2933 , 1650, 1522, 1382, 1254, 1211, 1166, 1103, 1069, 1005, 902 cm^{-1}; HRMS (FAB, doped with CsI): found M + Cs, 613.1550. $C_{24}H_{36}N_2O_8$ requires M + Cs, 613.1526.

The coupling reaction of amine **25** with succinic anhydride is shown below and is representative of the procedure used for the synthesis of all mimics. This procedure was also used for the glutaric derivatives:

Coupling procedure of amine 25 with succinic anhydride. Succinic anhydride (6.6 mg, 66 μmol) was added to a stirred solution of amino glycopeptide **25** (28.8 mg, 56 μmol) in MeOH (2 mL) at 23 °C. After 30 min, the solution was evaporated down under reduced pressure. The residual solid was purified by silica gel flash chromatography (2→5% acetic acid in EtOAc) to give the product (24.6 mg, 71%) as a white amorphous foam: $[\alpha]_D$ +1.8 (*c* 2.52 in $CHCl_3$); ^{1}H NMR (400 MHz; CD_3OD): δ 7.90 (1H, br t, J = 5.6 Hz, C6NH), 7.38–7.24 (5H, m, aromatic), 5.46 (1H, d, J = 5.0 Hz, H1), 4.60 (1H, dd, J = 7.9 and 2.4 Hz, H3), 4.56–4.51 (3H, m, H2′ + $OC\underline{H}_2$Ph), 4.33 (1H, dd, J = 5.0 and 2.4 Hz, H2), 4.20 (1H, dd, J = 7.9 and 1.8 Hz, H4), 4.03 (1H, br dd, J = 10.2 and 5.2 Hz, H3′), 3.94 (1H, ddd,

J=8.4, 4.4 and 1.7 Hz, H5), 3.62 (1H, dd, J=10.2 and 4.1 Hz, H4′$_a$H4′$_b$), 3.58 (1H, dd, J=10.2 and 5.2 Hz, H4′$_a$H4′$_b$), 3.47–3.41 (1H, m, H6$_a$H6$_b$), 3.28–3.24 (1H, m, H6$_a$H6$_b$), 2.60–2.46 (4H, m, C2″H$_2$+C3″H$_2$), 1.46 (3H, s, acetonide Me), 1.40 (3H, s, acetonide Me), 1.32 (3H, s, acetonide Me), 1.30 (3H, s, acetonide Me); ^{13}C NMR (100 MHz; CD_3OD): δ 174.54, 172.38, 139.55, 129.39 129.04, 129.00, 128.73, 110.48, 109.99, 97.81, 74.43, 72.65, 72.15, 71.87, 71.33, 67.51, 57.10, 41.06, 40.94, 31.62, 26.41, 26.33, 25.19, 24.57; IR 3304, 2986, 2933, 1721, 1643, 1536, 1453, 1382, 1254, 1211, 1166, 1109, 1069, 1004, 900, 752, 698 cm^{-1}; HRMS (FAB, doped with CsI): found M+Cs$^+$, 699.1510. $C_{27}H_{38}N_2O_{11}$ requires M+Cs$^+$ 699.1530.

The coupling reaction of amine **25** with the *N*-Cbz-γ-benzyl ester of aspartic acid is shown below and is representative of the procedure used for the synthesis of all mimics:

Coupling of amine 25 with the *N*-Cbz-γ-benzyl ester of aspartic acid. EDCI (14.3 mg, 75 μmol) was added to a stirred soln of **25** (33.4 mg, 71.5 μmol), *N*-Cbz-γ-benzyl ester of aspartic acid (26.8 mg, 75 μmol), HOBt (10.1 mg, 75 μmol) and 4-methyl morpholine (17 μL, 150 μmol) in dry DMF (2 mL) under argon at −20 °C. The resulting mixture was stirred at −20 °C for 1 h and then allowed to warm slowly to 23 °C. After 12 h, the reaction soln was quenched 5% w/v citric acid solution (20 mL) and extracted with EtOAc (6×25 mL). The combined organic extracts were washed with satd $NaHCO_3$ soln (50 mL) and satd NaCl soln (50 mL), dried ($MgSO_4$) and evapd down under red. pres. The residual oil was then purified by silica gel flash chromatography (40%→50%→66% EtOAc in hexanes) to give the product (43.2 mg, 75%) as a pale yellow oil: $[\alpha]_D$ +2.4 (*c* 1.57 in $CHCl_3$); ^{1}H NMR (400 MHz; $CDCl_3$): δ 7.56 (1H, br d, J=7.9 Hz, C2′NH), 7.35–7.24 (15H, m, aromatic), 6.92–6.90 (1H, br m, C6NH), 5.88 (1H, br d, J=8.7 Hz, C2″NH), 5.48 (1H, d, J=5.0 Hz, H1), 5.12–5.03 (4H, m, OCH$_2$Ph [ester & Cbz]), 4.60–4.47 (4H, m, H2′+H2″+OCH$_2$Ph [Et2O]), 4.56 (1H, dd, J=7.9 and 2.3 Hz, H3), 4.27 (1H, dd, J=5.0 and 2.4 Hz, H2), 4.15 (1H, dd, J=7.9 and 1.7 Hz, H4), 4.04–4.00 (1H, br m, H3′), 3.90–3.87 (1H, m, H5), 3.70–3.54 (4H, m, H6$_a$H6$_b$+C3′OH+C4′H2), 3.15 (1H, ddd, J=14.0, 9.4 and 4.2 Hz, H6$_a$H6$_b$), 3.07 (1H, dd, J=17.2 and 4.5 Hz, H3′$_a$H3′$_b$), 2.78 (1H, dd, J=17.2 and 4.5 Hz, H3′$_a$H3′$_b$), 1.44 (3H, s, acetonide Me), 1.43 (3H, s, acetonide Me), 1.31 (3H, s, acetonide Me), 1.27 (3H, s, acetonide Me); ^{13}C NMR (100 MHz; $CDCl_3$): δ 171.68, 170.39, 169.47, 155.99, 137.69, 135.85, 135.22, 138.59, 128.56, 128.43, 128.41, 128.29, 128.25, 127.89, 127.81, 109.47, 108.85, 96.30, 73.42, 71.45, 71.24, 70.76, 70.66, 70.41, 67.39, 66.96, 66.12, 55.45, 51.30, 39.96, 36.26, 25.94, 24.90, 24.31; IR 3304, 2986, 2934, 1729, 1647, 1533, 1498, 1454, 1328, 1255, 1212, 1167, 1109, 1068, 1003, 901, 739, 697 cm^{-1}; HRMS (FAB, doped with CsI): found M+Cs$^+$, 938.2453. $C_{42}H_{51}N_2O_{13}$ requires M+Cs$^+$ 938.2476. Elemental analysis found: C, 62.35; H, 6.15; N, 4.99. $C_{42}H_{51}N_2O_{13}$ requires C, 62.60; H, 6.38; N, 5.21.

Resolution of enantiomerically pure alcohol 30a and b

Compound **27** was resolved by conversion of the secondary alcohol to the chiral camphanate derivative, separation using HPLC, and hydrolysis of the chiral auxiliary using conditions reported in the literature.[17] Experimental data for selected intermediates is shown below. After resolution the coupling and deprotection sequence is identical to those used for all of the mimics.

Conversion of 27 to 30a. Data for the camphanate derivative. ^{1}H NMR (400 MHz; $CDCl_3$): δ 7.34–7.23 (5H, m, aromatic), 6.56–6.54 (1H, br m, C6NH), 5.46 (1H, d, J=5.0 Hz, H1), 5.38 (1H, br d, J=8.4 Hz, C2′NH), 5.07–5.04 (1H, br m, H3′), 4.64–4.61 (1H, br m, H2′), 4.57 (1H, dd, J=7.9 and 2.4 Hz, H3), 4.46 (2H, s, OCH$_2$Ph), 4.27 (1H, dd, J=5.0 and 2.4 Hz, H2), 4.17 (1H, dd, J=7.9 and 1.8 Hz, H4), 3.91 (1H, ddd, J=8.1, 4.3 and 1.7 Hz, H5), 3.62 (1H, ddd, J=14.0, 7.0 and 4.4 Hz, H6$_a$H6$_b$), 3.49–3.40 (2H, m, C6′H$_2$), 3.27 (1H, ddd, J=14.0, 8.2 and 4.4, H6$_a$H6$_b$), 2.39 (1H, ddd, J=13.6, 10.8 and 4.2, camphanate), 2.05 (1H, ddd, J=13.6, 9.3 and 4.3 Hz, camphanate), 1.88 (1H, ddd, J=13.1, 10.8 and 4.6 Hz, camphanate), 1.80–1.56 (5H, m, C4′H$_2$+C5′H$_2$+camphanate), 1.44 (3H, s, acetonide Me), 1.43 (3H, s, acetonide Me), 1.41 (9H, s, ^{t}Bu), 1.31 (3H, s, acetonide Me), 1.26 (3H, s, acetonide Me), 1.08 (3H, s, camphanate Me), 1.04 (3H, s, camphanate Me), 0.96 (3H, s, camphanate Me); ^{13}C NMR (100 MHz; $CDCl_3$): δ 178.23, 168.35, 167.66, 155.35, 138.26, 128.36, 127.73, 127.58, 109.49, 108.68, 96.27, 91.13, 80.07, 76.48, 72.97, 71.61, 70.77, 70.49, 69.59, 65.23, 55.65, 54.86, 54.19, 40.20, 30.72, 28.95, 28.28, 25.96, 25.76, 25.69, 24.93, 24.28, 16.55, 16.51, 9.69; IR 3350, 2977, 2934, 1789, 1716, 1673, 1494, 1454, 1369, 1312, 1258, 1211, 1167, 1104, 1069, 1006, 754, 698 cm^{-1}; MS (FAB, doped with CsI): found M+Cs$^+$, 907.3033. $C_{40}H_{58}N_2O_{13}$ requires M+Cs$^+$ 907.2993; found: C, 61.74; H, 7.33; N, 3.48. $C_{40}H_{58}N_2O_{13}$ requires C, 61.99; H, 7.54; N, 3.61.

Data for 30a. ^{1}H NMR (400 MHz; $CDCl_3$): δ 7.34–7.23 (5H, m, aromatic), 6.63 (1H, br s, C6NH), 5.49–5.47 (1H, br m, C2′NH), 5.48 (1H, d, J=5.0 Hz, H1), 4.56 (1H, dd, J=7.9 and 2.4 Hz, H3), 4.47 (2H, s, OCH$_2$Ph), 4.27 (1H, dd, J=5.0 and 2.4 Hz, H2), 4.17 (1H, dd, J=7.9 and 1.7 Hz, H4), 3.98–3.92 (2H, m, H5+H2′), 3.77 (1H, br d, J=5.0 Hz, C3′-OH; disappears when shaken with D_2O), 3.67 (1H, ddd, J=14.0, 7.5 and 3.7 Hz, H6$_a$H6$_b$), 3.60–3.55 (1H, m, H3′; when shaken with D_2O gives a ddd, J=8.9, 6.2 and 2.9 Hz), 3.52–3.43 (2H, m, C6′H$_2$), 3.17 (1H, ddd, J=14.0, 9.0 and 4.4, H6$_a$H6$_b$), 1.86–1.52 (4H, m, C4′H$_2$+C5′H$_2$), 1.43 (3H, s, acetonide Me), 1.42 (3H, s, acetonide Me), 1.41 (9H, s, 'Bu), 1.31 (3H, s, acetonide Me), 1.27 (3H, s, acetonide Me); ^{13}C NMR (100 MHz; $CDCl_3$): δ 171.62, 155.68, 138.34, 128.35, 127.64, 127.53, 109.52, 108.73, 96.38, 79.95, 77.23, 72.93, 72.86, 71.44, 70.78, 70.41, 70.10, 65.47, 57.78, 39.98, 30.46, 28.28, 26.04, 25.90, 24.85, 24.30; IR 3337, 2979, 2934, 1703, 1657, 1497, 1454, 1368, 1254, 1211, 1167, 1110,

1070, 1006, 902, 737, 698 cm $^{-1}$; MS (FAB, doped with CsI): found M+Cs$^+$, 727.2229. $C_{30}H_{46}N_2O_{10}$ requires M+Cs$^+$ 727.2209; found: C, 60.24; H, 7.57; N, 4.59. $C_{30}H_{46}N_2O_{10}$ requires C, 60.59; H, 7.80; N, 4.71.

Conversion of 27 to 30b. Data for the camphanate derivative. ^{1}H NMR (400 MHz; $CDCl_3$): δ 7.32–7.22 (5H, m, aromatic), 6.69 (1H, br s, C6NH), 5.58–5.54 (1H, br m, H3′), 5.44 (1H, d, J=5.0, H1), 5.29 (1H, br d, J=9.3, C2′NH), 4.55 (1H, dd, J=7.9 and 2.3 Hz, H3), 4.44 (2H, s, OCH_2Ph), 4.38 (1H, br dd, J=9.1 and 3.0 Hz, H2′), 4.25 (1H, dd, J=5.0 and 2.3 Hz, H2), 4.12 (1H, dd, J=7.9 and 1.5, H4), 3.85–3.80 (1H, m, H5), 3.61–3.55 (1H, br m, H6$_a$H6$_b$), 3.45–3.42 (2H, m, C6′H$_2$), 3.15 (1H, ddd, J=13.9, 8.4 and 3.7, H6$_a$H6$_b$), 2.41–2.34 (1H, br m, camphanate), 1.98–1.84 (2H, m, 2×camphanate), 1.78–1.57 (5H, m, C4′H$_2$+C5′H$_2$+camphanate), 1.41 (15H, s, ^{t}Bu+2×acetonide Me), 1.30 (3H, s, acetonide Me), 1.25 (3H, s, acetonide Me), 1.06 (3H, s, camphanate Me), 1.00 (3H, s, camphanate Me), 0.87 (3H, s, camphanate Me); ^{13}C NMR (100 MHz; $CDCl_3$): δ 178.34, 169.16, 166.58, 155.57, 138.33, 128.32, 127.61, 127.50, 109.44, 108.70, 96.14, 91.09, 80.55, 74.82, 72.77, 71.64, 70.74, 70.42, 69.42, 65.79, 56.49, 54.86, 54.35, 40.14, 30.88, 28.86, 28.22, 27.66, 25.98, 25.46, 24.95, 24.29, 16.58, 16.36, 9.65; IR 3328, 2977, 2934, 1790, 1753, 1712, 1675, 1516, 1454, 1368, 1309, 1258, 1211, 1167, 1106, 1088, 1006, 753, 698 cm^{-1}; MS (FAB, doped with CsI): found M+Cs$^+$, 907.3031. $C_{40}H_{58}N_2O_{13}$ requires M+Cs$^+$ 907.2993; found: C, 61.83; H, 7.34; N, 3.47. $C_{40}H_{58}N_2O_{13}$ requires C, 61.99; H, 7.54; N, 3.61.

Data for 30b. ^{1}H NMR (400 MHz; $CDCl_3$): δ 7.35–7.25 (5H, m, aromatic), 6.83–6.80 (1H, br m, C6NH), 5.47 (2H, br d, J=5.0 Hz, H1+C2′NH), 4.57 (1H, dd, J=7.9 and 2.4 Hz, H3), 4.49 (2H, s, OCH_2Ph), 4.27 (1H, dd, J=5.0 and 2.4 Hz, H2), 4.17 (1H, dd, J=7.9 and 1.7 Hz, H4), 4.12 (1H, br d m, J=7.7 Hz, H2′), 4.09–4.03 (1H, br m, H3′; when shaken with D_2O gives a ddd, J=8.9, 6.2 and 2.9 Hz), 3.93 (1H, ddd, J=8.7, 3.8 and 1.6 Hz, H5), 3.79 (1H, br s, C3′-OH; disappears when shaken with D_2O), 3.62 (1H, ddd, J=14.0, 7.2 and 4.0 Hz, H6$_a$H6$_b$), 3.52–3.49 (2H, m, C6′H$_2$), 3.22 (1H, ddd, J=14.0, 8.7 and 4.6 Hz, H6$_a$H6$_b$), 1.81–1.51 (4H, m, C4′H$_2$+C5′H$_2$), 1.44 (6H, s, 2×acetonide Me), 1.42 (9H, s, ^{t}Bu), 1.31 (3H, s, acetonide Me), 1.27 (3H, s, acetonide Me); ^{13}C NMR (100 MHz; $CDCl_3$): δ 171.42, 155.02, 138.05, 128.42, 127.72, 127.65, 109.42, 108.73, 96.38, 79.92, 73.00, 71.51, 71.31, 70.79, 70.45, 70.28, 65.60, 57.25, 39.96, 29.63, 28.28, 26.42, 25.94, 24.96, 24.30; IR 3350, 2979, 2934, 1702, 1661, 1495, 1454, 1368, 1253, 1211, 1167, 1109, 1070, 1007, 901, 735, 697 cm^{-1}; MS (FAB, doped with CsI): found M+Cs$^+$, 727.2227. $C_{30}H_{46}N_2O_{10}$ requires M+Cs$^+$ 727.2209; found C, 60.24; H, 7.72; N, 4.57. $C_{30}H_{46}N_2O_{10}$ requires C, 60.59; H, 7.80; N, 4.71.

Deprotection to give the final mimics

The following procedure is representative of the deprotection sequence used for all of the mimics. A solution of glycopeptide (0.01 M solution in 90% TFA in H_2O) was stirred at 23 °C. After 3 h, the reaction soln was evapd down under red. pres. and azeotroped twice with toluene (2×5 mL). An ^{1}H NMR and accurate mass were performed on the crude product to ensure that the isopropylidene moieties were removed and then the crude reaction mixture was taken on to the next step without purification.

10% Palladium on carbon (50 mg) was added carefully to a stirred solution of crude glycopeptide in 80% acetic acid in H_2O (5 mL) and hydrogenated (1 atm) at 23 °C. After 14 h, the 10% palladium on carbon was filtered through Celite® and the solid washed twice with 80% acetic acid in H_2O (2×5 mL). The combined filtrate and washings were evapd down under red. pres. The crude product was purified by Biogel P2 column, and lyophilization of the fractions containing the compound gave the required compound.

Mimic 2. 73% as an amorphous brown foam: ^{1}H NMR (400 MHz; D_2O): δ 5.18 (d, J=3.4, H1$_\gamma$), 4.50 (d, J=7.8, H1$_\beta$), 4.38–4.35 (m, H2′$_{(\gamma+\beta)}$), 4.05–4.02 (m, H5$_\gamma$+H3′$_\gamma$), 3.96–3.93 (m, H3′$_\beta$), 3.88 (br d, J=3.4 Hz, H4$_\gamma$), 3.81 (d, J=3.1 Hz, H4$_\beta$), 3.80–3.77 (m, H3$_\gamma$), 3.75 (dd, J=11.5 and 3.6 Hz, H2$_\gamma$), 3.68–3.54 (m, H3$_\beta$+H5$_\beta$+C4′H$_{2(\gamma+\beta)}$), 3.57–3.49 (m, H2$_\beta$+H6$_a$H6$_{b(\gamma+\beta)}$), 3.40–3.30 (m, H6$_a$H6$_{b(\gamma+\beta)}$), 2.53 (m, C2″H$_{2(\gamma+\beta)}$+C3″H$_{2(\gamma+\beta)}$); ^{13}C NMR (100 MHz; D_2O): δ 184.12, 179.39, 178.95, 174.93, 174.44, 98.87, 94.78, 75.22, 75.09, 74.20, 71.95, 71.50, 71.37, 70.73, 70.66, 70.60, 70.33, 70.16, 61.03, 60.95, 60.81, 60.75, 60.55, 42.25, 42.17, 38.40, 37.69, 37.34, 24.31; HRMS (FAB, doped with NaI): found M+H, 397.1446. $C_{14}H_{24}N_2O_{11}$ requires M+H, 397.1458.

Mimic 3. 81% as a white foam: ^{1}H NMR (400 MHz; D_2O): δ 5.20 (d, J=3.6 Hz, H1$_\gamma$), 4.52 (d, J=7.8 Hz, H1$_\beta$), 4.41–4.36 (m, H2′$_{(\gamma+\beta)}$), 4.08–4.05 (m, H3′$_\beta$), 4.01–3.93 (m, H5$_\gamma$+H3′$_\gamma$), 3.91 (br d, J=3.4 Hz, H4$_\gamma$), 3.86 (d, J=3.3 Hz, H4$_\beta$), 3.82 (dd, J=10.4 and 3.1 H3$_\gamma$), 3.75 (dd, J=10.4 and 3.6 Hz, H2$_\gamma$), 3.71–3.53 (m, H3$_\beta$+C4′H$_{2(\gamma+\beta)}$), 3.51–3.42 (m, H2$_\beta$+H6$_a$H6$_{b(\gamma+\beta)}$), 3.37–3.31 (m, H6$_a$H6$_{b(\gamma+\beta)}$), 2.35–2.27 (m, C2″H$_{2(\gamma+\beta)}$+C4″H$_{2(\gamma+\beta)}$), 1.88–1.82 (m, C3″H$_{2(\gamma+\beta)}$); ^{13}C NMR (100 MHz; D_2O, using CH_3CN as reference with the CH_3 signal set at 1.3 ppm): δ 176.61, 172.32, 96.85, 92.75, 73.08, 72.16, 71.23, 71.19, 70.57, 70.13, 69.87, 69.75, 69.47, 69.31, 68.63, 68.41, 63.64, 62.80, 55.92, 42.81, 40.25, 40.16, 35.08, 21.67, 21.64; MS (electrospray$^+$, doped with NaI): found M+Na, 433. (electrospray$^-$): found M−H, 409.

Mimic 4. 87% as a fluffy white foam: ^{1}H NMR (400 MHz; D_2O): δ 5.22 (d, J=3.5 Hz, H1$_\gamma$), 4.53 (d, J=7.8 Hz, H1$_\beta$), 4.49–4.45 (m, H2′$_{(\gamma+\beta)}$), 4.20 (br s, H2″$_{(\gamma+\beta)}$), 4.08–4.05 (m, H3′$_\beta$), 3.99 (br s, H5$_\gamma$+H3′$_\gamma$), 3.90 (br d, J=2.3, H4$_\gamma$), 3.86 (d, J=2.8, H4$_\beta$), 3.85–3.80 (m, H3$_\gamma$), 3.75 (dd, J=10.3 and 3.5 Hz, H2$_\gamma$), 3.71–3.57 (m, H3$_\beta$+H5$_\beta$+C5′H$_{2(\gamma+\beta)}$), 3.54–3.42 (m, H2$_\beta$+H6$_a$H6$_{b(\gamma+\beta)}$), 3.38–3.33 (m, H6$_a$H6$_{b(\gamma+\beta)}$), 2.84–2.69 (m, C3″H$_{2(\gamma+\beta)}$), 1.90 (s, C2″NH$_{2(\gamma+\beta)}$); ^{13}C NMR (100 MHz; D_2O, using CH_3CN as reference with the CH_3 signal

set at 1.3 ppm): δ 171.63, 96.83, 92.77, 73.09, 72.16, 71.07, 69.91, 69.48, 69.34, 68.66, 62.71, 56.20, 51.01, 40.35, 40.21, 37.89; MS (electrospray$^+$, doped with NaI): found M+Na, 434. (electrospray$^-$): found M−H, 410.

Mimic 5. 75% as a white foam: ^{1}H NMR (400 MHz; D_2O): δ 5.23 (d, J=3.5, $H1_\alpha$), 4.55 (dd, J=7.9 and 4.6, $H1_\beta$), 4.40–4.35 (m, $H2'_{(\alpha+\beta)}$), 4.30–4.27 (m, $H3'_\beta$), 4.11–4.05 (m, $H5_\gamma+H3'_\gamma$), 3.92 (br d, J = 2.8 Hz, $H4_\gamma$), 3.86 (d, J = 3.4 Hz, $H4_\beta$), 3.83 (dd, J=10.4 and 3.2 Hz, $H3_\gamma$), 3.77 (dd, J=10.4 and 3.7, $H2_\gamma$), 3.76–3.68 (m, $H5_\beta+C4'H_{2(\alpha+\beta)}$), 3.62 (dd, J = 10.0 and 3.4 Hz, $H3_\beta$), 3.56–3.34 (m, $H2_{\beta+}C6H_{2(\alpha+\beta)}$), 2.61–2.40 (m, $C2''H_{2(\alpha+\beta)}+C3''H_{2(\alpha+\beta)}$) 1.82–1.69 (m, $C4'H_{2(\alpha-\beta)}$); ^{13}C NMR (100 MHz; D_2O, using CH_3CN as reference with the CH_3 signal set at 1.3 ppm): δ 176.81, 176.23, 172.96, 172.87, 172.40, 172.28, 96.83, 92.77, 73.15, 73.07, 72.96, 72.16, 69.83, 69.78, 69.47, 69.27, 69.18, 68.66, 68.50, 68.20, 68.14, 59.00, 58.57, 58.53, 40.25, 40.16, 40.00, 35.62, 35.22, 35.10, 31.77, 31.70; HRMS (FAB, doped with NaI): found M+Na, 433.1447. $C_{15}H_{26}N_2O_{11}$ requires M+Na, 433.1434.

Mimic 6. 76% as a white foam: ^{1}H NMR (400 MHz; D_2O): δ 5.22 (d, J=3.6 Hz, $H1_\alpha$), 4.54 (dd, J=7.9 and 3.3 Hz, $H1_\beta$), 4.39–4.33 (m, $H2'_{(\alpha-\beta)}$), 4.23–4.18 (m, $H3'_\beta$), 4.11–4.08 (m, $H5_\gamma+H3'_\gamma$), 3.92 (br d, J=2.4 Hz, $H4_\gamma$), 3.87 (d, J=3.4, $H4_\beta$), 3.82 (dd, J=10.4 and 3.1 Hz, $H3_\gamma$), 3.77 (dd, J=10.4 and 3.6 Hz, $H2_\gamma$), 3.75–3.65 (m, $H5_\beta+C5'H2_{(\alpha+\beta)}$), 3.62 3.54 (dd, J=9.9 and 3.4 Hz, $H3_\beta$), 3.57–3.49 (m, $\underline{H6_a}H6_{b(\alpha+\beta)}$), 3.46 (dd, J=10.4 and 3.6 Hz, $H2_\beta$), 3.39–3.30 (m, $H6_a\underline{H6_b}_{(\alpha+\beta)}$), 2.44–2.22 (m, $C2''H_{2(\alpha+\beta)}+C4''H_{2(\alpha+\beta)}$), 1.90–1.63 (m, $C4'H_{2(\alpha+\beta)}+C3''H_{2(\alpha+\beta)}$); ^{13}C NMR (100 MHz; D_2O): δ 184.12, 179.39, 178.95, 174.93, 174.44, 98.87, 94.78, 75.22, 75.09, 74.20, 71.95, 71.50, 71.37, 70.73, 70.66, 70.60, 70.33, 70.16, 61.03, 60.95, 60.81, 60.75, 60.55, 42.25, 42.17, 38.40, 37.69, 37.34, 24.31; HRMS (FAB, doped with NaI): found M+Na, 447.1579. $C_{16}H_{28}N_2O_{11}$ requires M+Na, 447.1591.

Mimic 7. 75% as a white foam: ^{1}H NMR (400 MHz; D_2O): δ 5.23 (d, J=3.5 Hz, $H1_\alpha$), 4.54 (dd, J=7.8 and 5.3 Hz, $H1_\beta$), 4.45–4.41 (m, $H2'_{(\alpha-\beta)}$), 4.31–4.22 (m, $H3'_{\beta+}H2''_{(\alpha+\beta)}$), 4.09–4.07 (m, $H5_\gamma+H3'_\gamma$), 3.92 (br d, J=2.5 Hz, $H4_\gamma$), 3.86 (d, J=3.1, $H4_\beta$), 3.85–3.82 (m, $H3_\gamma$), 3.79–3.76 (m, $H2_\gamma$), 3.75–3.71 (m, $H5_\beta+C5'H2_{(\alpha+\beta)}$), 3.62 (dd, J=9.9 and 3.2 Hz, $H3_\beta$), 3.58–3.44 (m, $H2_{\beta+}H6_aH6_{b(\alpha-\beta)}$), 3.42–3.33 (m, $H6_aH6_{b(\alpha+\beta)}$), 2.86–2.72 (m, $C3''H_{2(\alpha+\beta)}$), 1.91 (s, $C2''NH_{2(\alpha+\beta)}$), 1.82–1.68 (m, $C4'H_{2(\alpha-\beta)}$); ^{13}C NMR (100 MHz; D_2O, using CH_3CN as reference with the CH_3 signal set at 1.3 ppm): δ 176.45, 172.19, 172.12, 171.63, 171.51, 96.83, 92.78, 73.19, 73.09, 72.98, 72.18, 69.97, 69.91, 69.49, 69.41, 69.33, 68.71, 68.67, 68.53, 68.21, 68.17, 68.13, 68.07, 59.15, 59.12, 59.03, 58.52, 58.42, 40.46, 40.36, 40.23, 37.79, 37.63, 35.60, 35.16, 34.99; MS (electrospray$^+$, doped with NaI): found M+H, 426 and M+Na, 448. (electrospray$^-$): found M−H, 424.

Mimic 8. 76% as a white foam: ^{1}H NMR (400 MHz; D_2O): δ 5.23 (d, J=3.6 Hz, $H1_\gamma$), 4.55 (dd, J=7.9 and 4.7 Hz, $H1_\beta$), 4.36–4.32 (m, $H2'_{(\alpha+\beta)}$), 4.15–4.06 (m, $H5_\gamma+H3'_\beta$), 3.96–3.92 (m, $H3'_\gamma$), 3.91 (br d, J=3.0, $H4_\gamma$), 3.86 (d, J=3.4 Hz, $H4_\beta$), 3.84 (dd, J=10.3 and 3.2 Hz, $H3_\gamma$), 3.77 (dd, J=10.3 and 3.7 Hz, $H2_\gamma$), 3.74–3.68 (m, $H5_\beta$), 3.64–3.61 (m, $H3_\beta+C6'H_{2(\alpha+\beta)}$), 3.56–3.31 (m, $H2_{\beta+}C6H_{2(\alpha-\beta)}$), 2.66–2.48 (m, $C2''H_{2(\alpha+\beta)}+C3''H_{2(\alpha-\beta)}$), 1.75–1.47 (m, $C4'H_{2(\alpha+\beta)}+C5'H_{2(\alpha+\beta)}$). ^{13}C NMR (100 MHz; D_2O): δ 182.93, 179.11, 175.20, 174.66, 98.86, 94.80, 75.19, 75.08, 75.02, 74.21, 72.91, 71.78, 71.48, 71.28, 71.18, 70.71, 70.52, 63.84, 63.80, 61.00, 60.90, 60.48, 42.15, 42.03, 34.71, 34.19, 34.12, 31.84, 31.44, 30.14. HRMS (FAB, doped with NaI): found M+Na, 447.1570. $C_{16}H_{28}N_2O_{11}$ requires M+Na, 447.1591.

Mimica 8a. 78% as a white foam: ^{1}H NMR (400 MHz; D_2O): δ 5.21 (d, J = 3.6 Hz, $H1_\gamma$), 4.53–4.51 (m, $H1_\beta$), 4.33–4.30 (m, $H2'_{(\alpha+\beta)}$), 4.07–4.04 (m, $H3'_\beta$), 3.99–3.92 (m, $H5_\gamma+H4_\alpha+H3'_a$), 3.84 (br s, $H4_b$), 3.82–3.80 (m, $H3_\alpha$), 3.78–3.59 (m, $H2_\alpha+H3_\beta+H5_\beta+C6'H_{2(\alpha+\beta)}$), 3.55–3.42 (m, $H2_{\beta+}H6_aH6_{b(\alpha+\beta)}$), 3.36–3.30 (m, $H6_a\underline{H6_b}_{(\alpha+\beta)}$) 2.65–2.49 (m, $C2''H_{2(\alpha+\beta)}+C3''H_{2(\alpha-\beta)}$), 1.71–1.46 (m, $C4'H_{2(\alpha+\beta)}+C5'H_{2(\alpha+\beta)}$); ^{13}C NMR (100 MHz; D_2O, using CH_3CN as reference with the CH_3 signal set at 1.3 ppm): δ 180.96, 176.42, 176.09, 175.28, 172.64, 172.54, 96.86, 92.78, 73.17, 73.07, 72.19, 70.89, 69.84, 69.48, 69.34, 69.26, 68.68, 61.83, 58.99, 58.88, 52.78, 52.62, 40.18, 40.13, 40.01, 32.65, 32.10, 30.61, 30.32, 29.54, 29.42, 29.33, 28.16, 28.06; HRMS (FAB, doped with NaI): found M+Na, 447.1607. $C_{16}H_{28}N_2O_{11}$ requires M+Na, 447.1591.

Mimic 8b. 83% as a white foam: ^{1}H NMR (400 MHz; D_2O): δ 5.20 (d, J = 3.6 Hz, $H1_\gamma$), 4.53–4.51 (m, $H1_\beta$), 4.35–4.33 (m, $H2'_{(\alpha+\beta)}$), 4.12–4.04 (m, $H5_\alpha+H3'(_{\gamma+\beta})$), 3.89 (br s, $H4_\gamma$), 3.85–3.78 (br s, $H3_\gamma+H4_b$), 3.77–3.57 (m, $H2_\alpha+H3_\beta+H5_\beta+C6'H_{2(\alpha+\beta)}$), 3.51–3.33 (m, $H2_{\beta+}C6H_{2(\alpha+\beta)}$), 2.59–2.52 (m, $C2''H_{2(\alpha+\beta)}+C3''H_{2(\alpha+\beta)}$), 1.65–1.52 (m, $C4'H_{2(\alpha+\beta)}+C5'H_{2(\alpha-\beta)}$); ^{13}C NMR (100 MHz; D_2O, using CH_3CN as reference with the CH_3 signal set at 1.3 ppm) 176.83, 176.13, 175.88, 173.16, 173.09, 173.06, 96.86, 92.79, 73.11, 73.07, 72.99, 72.18, 70.92, 69.87, 69.78, 69.46, 69.34, 69.19, 68.69, 68.65, 68.50, 61.78, 58.44, 58.37, 52.80, 40.25, 40.06, 31.96, 31.75, 30.36, 30.29, 29.82, 29.44, 28.12, 27.70, 27.52; HRMS (FAB, doped with NaI): found M+Na, 447.1609. $C_{16}H_{28}N_2O_{11}$ requires M+Na, 447.1591.

Mimic 9. 84% as a white foam: ^{1}H NMR (400 MHz; D_2O): δ 5.23 (d, J=3.6, $H1_\gamma$), 4.55 (dd, J=7.9 and 2.8 Hz, $H1_\beta$), 4.37 (apparent t, $H2'_\beta$), 4.32 (t, J=6.5 Hz, $H2'_a$), 4.12–4.09 (m, $H5_\gamma+H3'_\beta$), 4.02–3.90 (m, $H4_\gamma+H3'_\gamma$), 3.88 (d, J = 3.4 Hz, $H4_\beta$), 3.83 (dd, J=10.3 and 3.1 Hz, $H3_\gamma$), 3.78 (dd, J=10.3 and 3.6 Hz, $H2_\gamma$), 3.75–3.68 (m, $H5_\beta$), 3.64–3.60 (m, $H3_\beta+C6'H_{2(\alpha+\beta)}$), 3.58–3.50 (m, $\underline{H6_a}H6_{b(\alpha+\beta)}$), 3.47 (dd, J=9.9 and 7.9 Hz, $H2_\beta$), 3.40–3.31 (m, $H6_a\underline{H6_b}_{(\alpha-\beta)}$), 2.41–2.18 (m, $C2''H_{2(\alpha+\beta)}+C4''H_{2(\alpha-b)}$), 1.92–1.54 (m, $C4'H_{2(a+b)}+C5'H_{2(\alpha-b)}+C3''H_{2(\alpha-b)}$); ^{13}C NMR (100 MHz; D_2O): δ 184.96, 179.51, 178.99, 175.17, 175.09, 174.70, 98.89,

94.79, 75.24, 75.09, 74.21, 73.05, 72.85, 71.95, 71.50, 71.37, 70.67, 70.60, 63.84, 63.79, 61.00, 60.93, 60.58, 60.51, 42.39, 42.24, 42.15, 39.11, 37.48, 31.88, 31.59, 31.51, 30.13, 30.10, 24.66; HRMS (FAB, doped with NaI): found M+Na, 461.1735. $C_{17}H_{30}N_2O_{11}$ requires M+Na, 461.1747.

Mimic 10. 72% as a white foam: ^{1}H NMR (400 MHz; D_2O) 5.22 (d, J=3.6 Hz, $H1_\gamma$), 4.54 (dd, J=7.9 and 5.1 Hz, $H1_\beta$), 4.40–4.26 (m, $H2'_{(\gamma+\beta)}+H2''_{(\gamma+\beta)}$), 4.11–4.07 (m, $H5_\gamma+H3'_\beta$), 3.96–3.92 (m, $H3'_\gamma$), 3.91 (br d, J = 2.9 Hz, $H4_\gamma$), 3.85 (d, J = 3.0 Hz, $H4_\beta$), 3.83 (dd, J=10.6 and 3.0 Hz, $H3_\gamma$), 3.74 (dd, J=10.6 and 3.6 Hz, $H2_\gamma$), 3.72–3.68 (m, $H5_\beta$), 3.63–3.53 (m, $H3_\beta+C6'H_{2(\gamma+\beta)}$), 3.51–3.33 (m, $H2_\beta+C6H_{2(\gamma+\beta)}$), 2.86–2.75 (m, $C3''H_{2(\gamma+\beta)}$), 1.70–1.52 (m, $C4'H_{2(\gamma+\beta)}+C5'H_{2(\gamma+\beta)}$); ^{13}C NMR (100 MHz; D_2O, using CH_3CN as reference with the CH_3 signal set at 1.3 ppm): δ 176.39, 172.39, 172.33, 171.87, 171.76, 170.64, 170.15, 96.85, 92.79, 73.22, 73.09, 73.01, 72.19, 70.83, 69.96, 69.91, 69.48, 69.42, 69.33, 68.75, 68.68, 68.52, 59.13, 58.94, 58.82, 61.77, 59.13, 58.94, 58.82, 51.07, 40.45, 40.265, 37.73, 37.57, 29.88, 29.44, 29.33, 28.11, 28.05; MS (electrospray$^+$, doped with NaI): found M+H, 440 and M+Na, 462. (electrospray$^-$): found M−H, 438.

Mimic 11. 81% as a white foam: ^{1}H NMR (400 MHz; D_2O) 5.20 (d, J=3.5 Hz, $H1_\gamma$), 4.52 (d, J=7.8 Hz, $H1_\beta$), 4.06–4.03 (m, $H5_\gamma$), 3.96–3.88 (m, $H4_\gamma+2\times C\underline{H}_aH_bOH_{(\gamma+\beta)}$), 3.82–3.79 (m, $H3_\gamma+H4_\beta+2\times C\underline{H}_aH_bOH_{(\gamma+\beta)}$), 3.77 (dd, J=10.2 and 3.6 Hz, $H2_\gamma$), 3.66–3.63 (m, $H5_\beta$), 3.59 (dd, J = 9.9 and 3.2 Hz, $H3_\beta$), 3.48–3.39 (m, $H2_\beta+\underline{H}6_aH6_{b(\gamma+\beta)}$), 3.36–3.29 (m, $H6_a\underline{H}6_{b(\gamma+\beta)}$), 2.52 (br s, $C2''H_{2(\gamma+\beta)}+C3''H_{2(\gamma+\beta)}$); ^{13}C NMR (100 MHz; D_2O, using CH_3CN as reference with the CH_3 signal set at 1.3 ppm): δ 176.18, 176.09, 173.68, 96.83, 92.81, 86.17, 73.05, 72.98, 72.19, 69.54, 69.43, 69.02, 68.70, 68.40, 64.93, 64.82, 61.36, 61.19, 39.87, 39.72, 32.08; MS (electrospray$^+$, doped with NaI): found M+H, 397 and M+Na, 419. (electrospray$^-$): found M−H, 395.

Mimic 12. 68% as a white foam: ^{1}H NMR (400 MHz; D_2O): δ 5.20 (d, J=3.7 Hz, $H1_\gamma$), 4.55 (d, J=7.8 Hz, $H1_\beta$), 4.07–4.04 (m, $H5_\gamma$), 3.95–3.90 (m, $H4\alpha+2\times C\underline{H}_aH_bOH_{(\gamma+\beta)}$), 3.85–3.80 (m, $H3_\gamma+H4_\beta+2\times C\underline{H}_aH_bOH_{(\gamma+\beta)}$), 3.75 (dd, J=10.3 and 3.7 Hz, $H2_\gamma$), 3.68–3.64 (m, $H5_\beta$), 3.60 (dd, J=9.9 and 3.4 Hz, $H3_\beta$), 3.54–3.46 (m, $\underline{H}6_aH6_{b(\gamma+\beta)}$), 3.44 (dd, J=9.9 and 7.8 Hz, $H2_\beta$), 3.34–3.26 (m, $H6_aH6_{b(\gamma+\beta)}$), 2.35–2.28 (m, $C2''H_{2(\gamma+\beta)}+C4''H_{2(\gamma+\beta)}$), 1.87–1.82 (m, $C3''H_{2(\gamma+\beta)}$). ^{13}C NMR (100 MHz; D_2O, using CH_3CN as reference with the CH_3 signal set at 1.3 ppm): δ 180.95, 176.38, 176.31, 173.77, 173.72, 96.87, 92.80, 73.14, 73.14, 73.05, 72.19, 69.77, 69.46, 69.27, 68.67, 68.53, 64.45, 64.39, 61.30, 61.04, 60.91, 60.84, 55.75, 43.08, 39.90, 36.81, 35.41, 35.24, 33.16, 25.45, 21.56, 21.62; HRMS (FAB, doped with NaI): found M+Na, 433.1446. $C_{15}H_{26}N_2O_{11}$ requires M+Na, 433.1434.

Mimic 13. 82% as a white foam: ^{1}H NMR (400 MHz; D_2O): δ 5.20 (d, J=3.3 Hz, $H1_\gamma$), 4.60–4.46 (m, $H1_\beta+C4'H_{2(\gamma+\beta)}$), 4.10–3.30 (m, $H2_{(\gamma+\beta)}+H3_{(\gamma+\beta)}+H4_{(\gamma+\beta)}+H5_{(\gamma+\beta)}+C6\underline{H}_{2(\gamma+\beta)}+CH_2OH_{(\gamma+\beta)}$), 2.69–2.50 (m, $C2''H_{2(\gamma+\beta)}+C3''H_{2(\gamma+\beta)}$), 2.19–1.98 (m, $C3'H_{2(\gamma+\beta)}$). ^{13}C NMR (100 MHz; D_2O, using CH_3CN as reference with the CH_3 signal set at 1.3 ppm): δ 180.87, 175.81, 174.74, 174.58, 169.46, 96.88, 96.82, 92.79, 73.23, 73.06, 72.88, 72.75, 72.20, 70.51, 70.37, 70.01, 69.63, 69.49, 69.44, 69.13, 69.06, 68.92, 68.70, 68.65, 68.53, 68.40, 63.64, 63.12, 63.03, 62.94, 62.78, 62.70, 57.40, 57.12, 43.53, 40.92, 40.93, 40.01, 39.90, 34.80, 34.75, 34.12, 32.25, 31.9, 30.43. HRMS (FAB, doped with NaI): found M+Na, 433.1448. $C_{15}H_{26}N_2O_{11}$ requires M+Na, 425.1771.

Mimic 14. 90% yield as a white foam: ^{1}H NMR (400 MHz; D_2O): δ 5.19 (d, J=3.3 Hz, $H1_\gamma$), 4.64–4.41 (m, $H1_\beta+C4'H_{2(\gamma+\beta)}$), 4.11–3.38 (m, $H2_{(\gamma+\beta)}+H3_{(\gamma+\beta)}+H4_{(\gamma+\beta)}+H5_{(\gamma+\beta)}+C6H_{2(\gamma+\beta)}+CH_2OH_{(\gamma+\beta)}$), 2.47–2.16 (m, $C3'H_{2(\gamma+\beta)}+C2''H_{2(\gamma+\beta)}+C4''H_{2(a+b)}$), 1.87–1.81 (m, $C3'H_{2(\gamma+\beta)}$); ^{13}C NMR (100 MHz; D_2O, using CH_3CN as reference with the CH_3 signal set at 1.3 ppm): δ 181.47, 176.05, 174.91, 174.86, 169.19, 96.93, 96.90, 92.75, 73.30, 73.23, 73.12, 73.09, 72.79, 72.23, 70.06, 70.01, 69.52, 68.98, 68.66, 68.55, 65.87, 63.02, 62.93, 62.68, 62.44, 62.35, 57.35, 57.10, 57.05, 52.73, 43.74, 43.37, 41.04, 40.95, 40.91, 40.12, 35.72, 35.39, 34.52, 34.06, 33.98, 33.55, 33.21, 21.68, 20.94; HRMS (FAB, doped with NaI): found M+Na, 425.1784. $C_{16}H_{28}N_2O_{11}$ requires M+H, 425.1771.

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