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Stereoselective Synthesis of *N*-Glycosyl Amino Acids by Traceless Staudinger Ligation of Unprotected Glycosyl Azides

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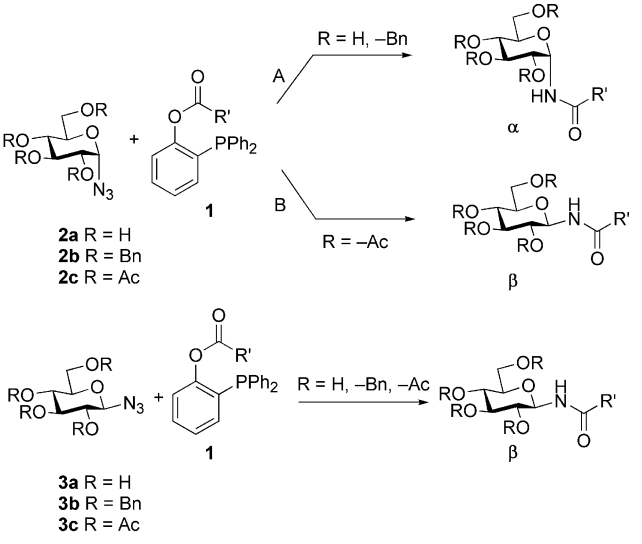
The stereoconservative Staudinger ligation of unprotected α- and β-glycosyl azides with 2-(diphenylphosphanyl)-4-fluorophenyl esters to afford α- and β-*N*-glycosyl amino acids is described. The ligation method works reliably well for unprotected β-azides of the *gluco*, *galacto* and *fuco* series. Lower yields (ca. 50 %) were obtained with a β-glucosyl-*N*-acetyl azide. The reaction of an α-glucosyl azide also led to major improvements compared with the use of non-fluorinated phosphanes. All the *N*-glycosyl amino acid products can be isolated and byproducts removed from the crude reaction mixtures by simple water extraction.

Introduction

The synthesis of neo-glycoconjugates has gained increasing attention in the past 10 years.[1] Our laboratory has recently shown that the traceless Staudinger ligation[2] of glycosyl azides with functionalized phosphanes **1** allows the stereoselective synthesis of both α- and β-glycosyl amides (Scheme 1).[3,4] With α-glycosyl azides, the stereoselectivity of the process depends critically on the sugar protecting groups: the unprotected monosaccharide (**2a**: R = H) or its *O*-benzyl ether (**2b**: R = Bn) can be transformed into the corresponding amides with retention of configuration at the anomeric carbon atom, whereas the *O*-acetyl derivative (**2c**: R = Ac) completely isomerizes to give the epimeric β-amides. In contrast, β-glycosyl azides **3** can be transformed into the corresponding amides with retention of configuration, irrespective of the nature of the R group (R = Bn, Ac, H).



Scheme 1. Traceless Staudinger ligation of glycosyl azides with functionalized phosphane **1**.

Ligation of the unprotected α- and β-glucosyl azides[4] **2a** and **3a** was particularly remarkable because in both cases it occurred stereoconservatively and allowed simple isolation of the resulting glucosyl amides from the phosphane oxide byproduct by water extraction. The anomeric ratios of the products were consistently good and the yields moderate-to-good for most of the alkyl chains R′, particularly under MW irradiation. The only notable exception was presented by the aspartic and glutamic acid derivatives **1a** and **1b** (Scheme 2), which gave poor yields of the corresponding glucosyl amino acids for both the α and β series. This is particularly disappointing because these amides are important glycoconjugates, mimicking the conserved core of natural *N*-asparagine-linked glycopeptides and glycoproteins.[5,6]

Herein we present novel functionalized phosphanes **4** (Scheme 4) that were designed to improve the Staudinger ligation of glycosyl azides with amino acids. We show that indeed monofluorophosphanes **4** improve the yields of amino acid transfer in comparison with the non-fluorinated analogues **1** and afford the corresponding *N*-glycosyl amino acids in a synthetically practical manner.

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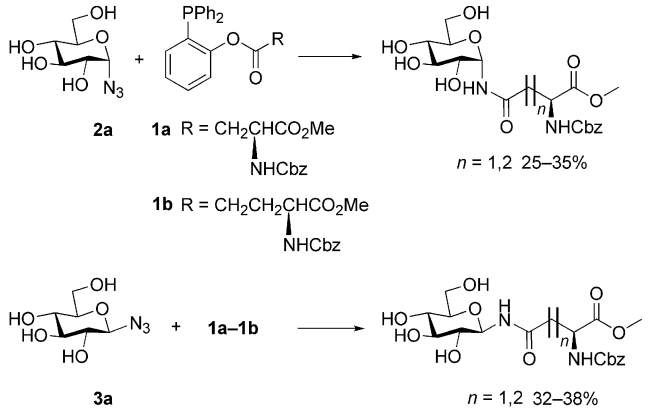


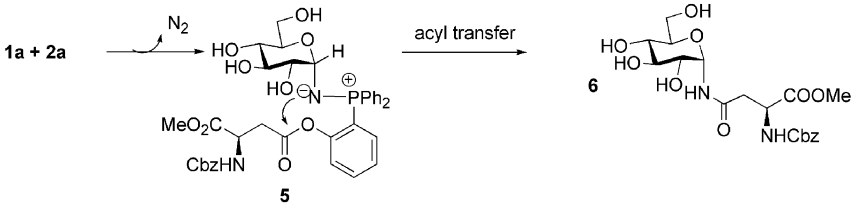
Scheme 2. Phosphanes **1a**,**b** give poor yields of *N*-glycosyl amino acids.

Results and Discussion

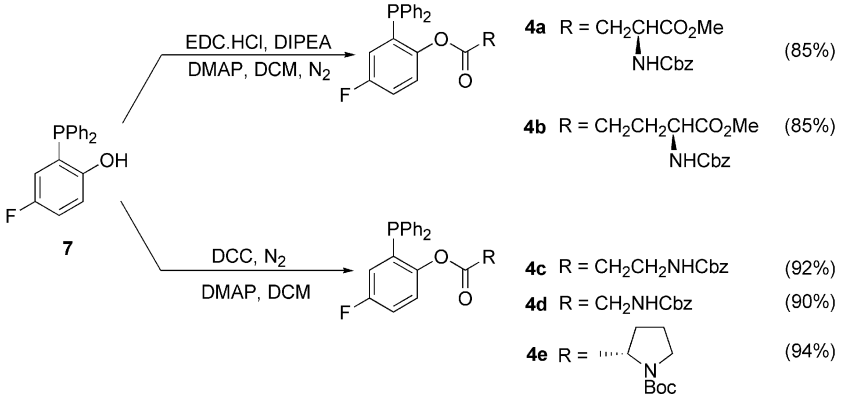
The Staudinger ligation of phosphanes **1** can be envisaged as taking place in two steps, as depicted in Scheme 3 for the reaction of **1a** with α-glucosyl azide **2a**. In the first step, nucleophilic addition of the phosphane to the γ nitrogen of the azide followed by nitrogen extrusion leads to the iminophosphorane **5**. In the second step, **5** undergoes an intramolecular reaction in which the acyl chain is transferred from the phenolic activated ester to the iminophosphorane nitrogen and an amide bond is generated. Our previous observations indicated that the poor amide yields obtained for the reaction of glucosyl azides with phosphanes **1a** and **1b** were caused by inefficient acyl chain transfer in the iminophosphorane **5**.[3,4] Hence, improving the leaving group ability of the activated ester should result in higher yields for this difficult transfer step.

Fluorophenyl esters are well known to act as good activating groups in acyclic nucleophilic substitution reactions. Thus, we replaced phosphanes **1** with the corresponding monofluoro derivatives **4** (Scheme 4), which could be obtained in high yields from the known phosphane **7**[7] by reaction with the appropriate amino acids and condensing agents (Scheme 4). The functionalized phosphanes **4a**–**e** were synthesized to examine the Staudinger ligation of the aspartic and glutamic acid side-chains (**4a** and **4b**, respectively) as well as the reactions of simple α- and β-amino acids such as β-alanine **4c**, glycine **4d** and proline **4e**. Optimal yields were obtained by using either *N*-[3-(dimethylamino)propyl]-*N*′-ethylcarbodiimide (EDC) (**4a** and **4b**) or DCC (**4c**–**e**) as the condensing agent. The ligation reagents could be isolated by simple filtration through a silica gel plug. Analytical samples were purified by flash chromatography. In general, and like the parent non-fluorinated compounds, phosphanes **4a**–**e** were found to be air-stable compounds that could be handled under standard conditions with minimal precautions.

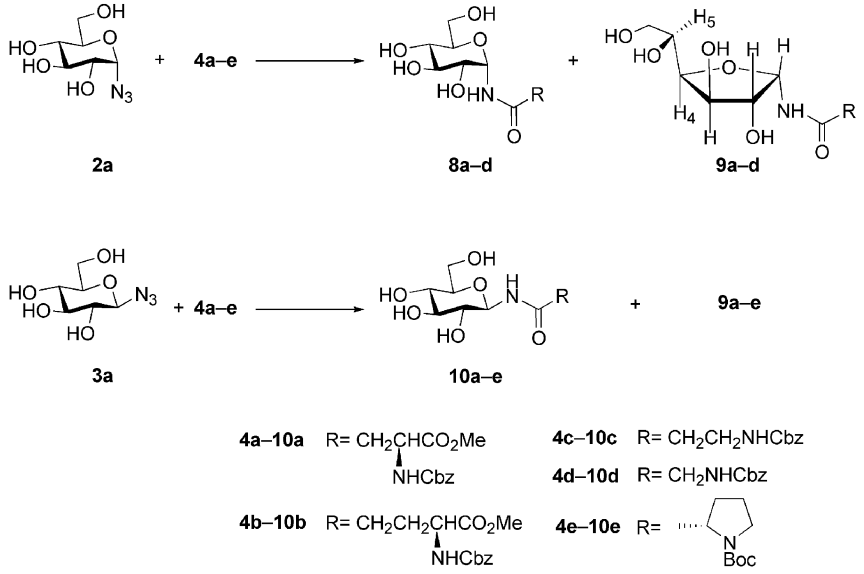
The initial experiments were performed by treating the unprotected α- and β-glucosyl azides **2a** and **3a** with 2 equiv. of phosphane in DMA/DMPU (98:2) at 40 °C for 18 h. After completion of the reaction, the crude mixtures were stirred with water for an additional 2 h, then diluted with water and extracted with CH_2Cl_2 to eliminate the phosphane byproducts. The aqueous layers were analyzed by ^1H NMR (typically in D_2O) and the product ratios established on the basis of the integration of the anomeric protons. Typical reaction crudes contained both the expected α- or β-pyranosyl amides **8** or **10** and variable amounts of the corresponding furanosyl amides **9** (Scheme 5). As we have previously shown,[4] the latter are



Scheme 3. Two-step mechanism for the Staudinger ligation.



Scheme 4. Synthesis of the fluorinated phosphanes **4a**–**e**.



Scheme 5. Synthesis of α- and β-glucosyl amino acids **8a**–**d** and **10a**–**e**.

formed by ring-opening/ring-closure of the intermediate iminophosphoranes.[8] Free glucose (equilibrium anomeric mixtures) is also formed by hydrolysis of the same intermediates. The glucosyl amides were purified by flash chromatography on silica gel (4:1 $CHCl_3$/MeOH) and fully characterized as their acetylated counterparts.

The phosphanes **4** afforded major improvements in the Staudinger ligation of **2a** and **3a** with amino acids. The reactions with β-glucosyl azide **3a** (Table 1, entries 1–5) gave good-to-excellent yields of the corresponding pyranosyl amides **10a**–**e**, which were essentially pure after water extraction. The ^{1}H NMR spectra of the reaction crudes showed no trace of the anomeric α-pyranosyl epimer and very minor quantities (≤3%) of a byproduct to which the furanosyl amide structure **9** was tentatively assigned; α-, β- and γ-amino acids were transferred with equal efficiency. The aspartic acid amide **10a** (Table 1, entry 1) was the most difficult to obtain, but could still be isolated in 77% yield, as opposed to the yield of 32% obtained under the same conditions with phosphane **1a**.[4]

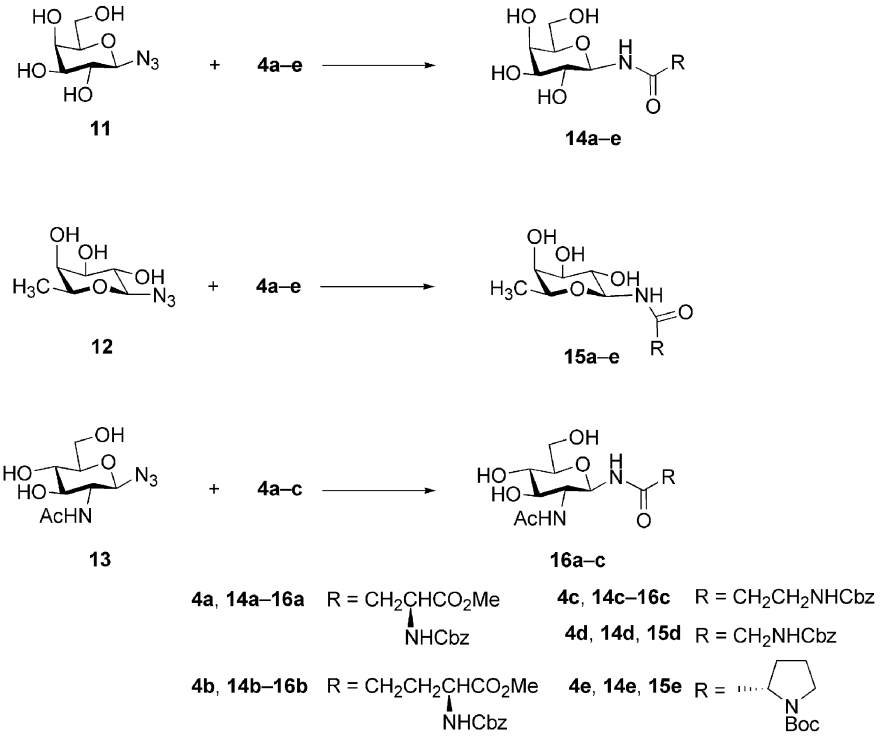
The reactions of α-glucosyl azide **2a** (Table 1, entries 6–9) with **4a**–**d** also led to major improvements compared with the use of non-fluorinated phosphanes, although it afforded the corresponding α-amides **8a**–**d** in modest yields in comparison with the β anomer. As an example, the aspartic acid side-chain was transferred giving a yield of 55% with phosphane **4a** (entry 6) as opposed to the 35% yield obtained with the non-fluorinated phosphane **1a**. Ligation of the α-azide was generally accompanied by ring contraction and sizeable quantities of the glucofuranosyl amides **9** were formed (Table 1, entries 6–9). Strict control of anhydrous conditions was found to minimize the formation of ring-contraction byproducts. In our previous studies with phosphanes **1**, the use of MW irradiation proved beneficial for reducing the amount of furanose formation,[4] but this was not the case with phosphanes **4** as MW irradiation (50 °C, 50 min) gave lower yields of the desired pyranosyl amides and more byproducts.

To probe the scope of the fluorinated phosphanes **4**, other β-unprotected glycosyl azides were tested in the Staudinger ligation (Scheme 6, Table 2). The reactions of phosphanes **4a**–**e** with β-galactosyl azide **11**, β-fucosyl azide **12** and β-glucosyl-*N*-acetyl azide **13** were performed and afforded the corresponding glycosyl amides **14**–**16** in good

Table 1. Synthesis of α- and β-glucosyl amino acids **8** and **10** by ligation of α- and β-glucosyl azides **2a** and **3a** with **4a**–**e**.

Entry	Phosphane	Azide	Product	Isolated yield[a] [%]	α/β Ratio[b]	Pyr/fur[c]
1	**4a**	**3a**	**10a**	77	≤1:99	98:2[d]
2	**4b**	**3a**	**10b**	87	≤1:99	98:2[d]
3	**4c**	**3a**	**10c**	85	≤1:99	98:2[d]
4	**4d**	**3a**	**10d**	75	≤1:99	97:3[d]
5	**4e**	**3a**	**10e**	70	≤1:99	98:2[d]
6	**4a**	**2a**	**8a**	56	98:2	85:15[e]
7	**4b**	**2a**	**8b**	59	98:2	87:13[e]
8	**4c**	**2a**	**8c**	60	98:2	90:10[e]
9	**4d**	**2a**	**8d**	36 (12)[f]	98:2	67:33[e]

[a] Yields based on glucopyranosyl amide. [b] Ratio of the anomeric proton signals of the α- and β-pyranosyl amides **8** and **10** in the crude ^{1}H NMR spectrum. [c] Ratio of the anomeric proton signals in the crude ^{1}H NMR spectrum. [d] Ratio of **10/9**. [e] Ratio of **8/9** ratio. [f] Isolated yield of furanosyl amide **9d**.



Scheme 6. Synthesis of amides **14**–**16** with **4a**–**e**.

Table 2. Synthesis of amides **14**–**16** with **4a**–**e**.

Entry	Phosphane	Azide	Product	Isolated yield[a] [%]	Furanose[b] [%]
1	**4a**	**11**	**14a**	74	–
2	**4b**	**11**	**14b**	70	5
3	**4c**	**11**	**14c**	71	10
4	**4d**	**11**	**14d**	73	5
5	**4a**	**12**	**15a**	60[c]	9
6	**4b**	**12**	**15b**	68[c]	9
7	**4c**	**12**	**15c**	70[c]	13
8	**4d**	**12**	**15d**	75[c]	6
9	**4e**	**12**	**15e**	87[c]	–
10	**4a**	**13**	**16a**	56	–
11	**4b**	**13**	**16b**	54	–
12	**4c**	**13**	**16c**	60	–

[a] Yields based on β-pyranosyl amide. [b] Estimated by integration of the anomeric proton signals in the ^{1}H NMR spectra of the crude reaction mixtures. [c] Around 10% of hydrolysis product (fucose) was also observed.

yields. ^{1}H NMR analysis of the crude reaction mixtures showed no trace of the anomeric α-pyranosyl epimer. Variable quantities (5–13%) of the isomeric furanosyl amides were formed, depending both on the nature of the azide and the amino acid transferred (see Table 2). In all cases, this byproduct could be separated from the pyranose isomer by flash chromatography. With the β-galactosyl azide **11**, β- and γ-amino acids were transferred with an average yield of 70% (Table 2, entries 1–4). Similar results were obtained with β-fucosyl azide **12** (Table 2, entries 5–9). β-Glucosyl-*N*-acetyl azide **13** was found to be less reactive and the corresponding amides were formed in an average yield of 55% (Table 2, entries 10–12).[9] Comparison with the yields obtained with the corresponding β-glucosyl azide **3a** (Table 1), which on average are higher by 30%, suggests a deactivating role of the acetamido group in **13**.

Conclusions

The results reported herein show that unprotected α- and β-glycosyl azides can be stereoselectively ligated to α-, β- and γ-amino acids by traceless Staudinger ligation using phosphanes **4**. All the *N*-glycosyl amino acid products could be isolated from the crude reaction mixtures by simple water extraction and were further purified by flash chromatography on silica gel.

The starting phosphane **7** is not commercially available, but it can be easily prepared on the gram scale by following the reported procedure.[7] It is stable to air at room temperature for weeks and can be handled with no special precautions. Acylation followed by silica gel filtration affords the ligation agents **4**, which can be used without further purification. The stereoselective synthesis of the required

azide precursors has been reviewed.[3] A recently developed methodology also allows the direct conversion of unprotected sugars to glycosyl azides,[12–14] often stereoselectively.

The ligation method described herein works reliably well for unprotected β-azides of the *gluco*, *galacto* and *fuco* series. Lower yields (ca. 50%) were obtained with β-glucosyl-*N*-acetyl and α-glycosyl azides. Only one method for the synthesis of β-D-2-deoxy-2-*N*-acetylglucopyranosyl-asparagine from unprotected *N*-acetylglucosamine has been described.[15]

There are only a handful of methods that can be used to synthesize α-*N*-glycosyl amides,[3,4,10,11] among them, the traceless Staudinger ligation of α-glycosyl azides with functionalized phosphanes was found to perform poorly with amino acids. The fluorophenylphosphanes **4** described herein overcome most of the limitations previously described and allow the synthesis of α-*N*-glucosyl amino acids in reasonable yields and in a synthetically practical manner.

The elaboration of unprotected carbohydrates has received considerable attention in recent years.[16–18] Unprotected glycosyl amino acid can be used directly for the linear synthesis of glycopeptides (direct insertion of the glycosyl amino acid into a growing peptide chain).[15,19] Methods of glycopeptide synthesis that do not involve protected sugars do not require further manipulation of the sugar, which can lead to racemization of the amino acid.[20]

Beyond affording *N*-glycosylated Asn and Gln building blocks, the functionalized phosphanes described herein could also be used to achieve traceless ligation of glycosyl azides to glycine, proline and the non-proteinogenic amino acid β-Ala. The resulting compounds are not meant to be incorporated into *N*-glycopeptide sequences, but can be used for the bioconjugation of carbohydrates to aglycons using chemically stable bonds and for the design of carbohydrate mimics which may resist in vivo to hydrolytic enzymes.[21,22]

Experimental Section

General: Solvents were dried by standard procedures: dichloromethane, methanol, *N*,*N*-diisopropylethylamine and triethylamine were dried with calcium hydride; *N*,*N*-dimethylacetamide (DMA), 1,3-dimethyltetrahydro-2(1*H*)-pyrimidinone (DMPU), chloroform and pyridine were dried with activated molecular sieves. Reactions requiring anhydrous conditions were performed under nitrogen. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded at 400 MHz with a Bruker AVANCE-400 instrument. Chemical shifts (δ) for the ^{1}H and ^{13}C NMR spectra are expressed in ppm relative to internal Me_4Si as standard. Signal multiplicities are abbreviated as follows: s, singlet; br. s, broad singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Mass spectra were obtained with a Bruker ion-trap Esquire 3000 (ESI ionization) or Autospec Fission spectrometer (FAB ionization) and FT-ICR Mass Spectrometer APEX II & Xmass 4.7 Magnet software (Bruker Daltonics). Thin-layer chromatography (TLC) was carried out on precoated Merck F_{254} silica gel plates. Flash chromatography (FC) was carried out on Macherey–Nagel silica gel 60 (230–400 mesh). Compounds **8a**,**b**,[4] **10a**,**b**,[4] **10d**[23] and **16a**[24] have been previously described.

1-Methyl 5-[2-(Diphenylphosphanyl)-4-fluorophenyl] *N*-(Benzyloxycarbonyl)-L-aspartate (4a): A solution of *o*-(diphenylphosphanyl)-*p*-fluorophenol (**7**; 253 mg, 0.85 mmol, 1 equiv.), the commercially available 1-methyl *N*-(benzyloxycarbonyl)-L-aspartate (380 mg, 1.02 mmol, 1.2 equiv.) and 4-(dimethylamino)pyridine (10.4 mg, 0.085 mmol, 0.1 equiv.) in dry CH_2Cl_2 (8.5 mL, 0.1 M) were added, at room temperature and under nitrogen, to a suspension of *N*-[3-(dimethylamino)propyl]-*N*′-ethylcarbodiimide hydrochloride (EDC) (228 mg, 1.19 mmol, 1.4 equiv.) and dry *N*,*N*-diisopropylethylamine (203.7 μL, 1.19 mmol, 1.4 equiv.) in dry CH_2Cl_2. The mixture was stirred at room temp. for 2 h, monitoring by TLC (7:3 hexane/AcOEt). The reaction mixture was diluted with CH_2Cl_2 and extracted with 5% aqueous HCl and water. The organic layer was dried with Na_2SO_4 and concentrated. The crude product was purified by flash chromatography using 6:4 hexane/AcOEt as the eluent to afford **4a** (404 mg, 0.72 mmol) in 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.48–7.27 (m, 15 H, Ar-H), 7.12–7.02 (m, 2 H, 2-H, 3-H), 6.55 (m, 1 H, 1-H), 5.70 (d, J_{NH-CH} = 8.6 Hz, 1 H, NH), 5.18 (d, J = 6 Hz, 2 H, CH_2-O), 4.61 (q, J_{CH-CH2} = 4.4 Hz, 1 H, CH), 3.72 (s, 3 H, O-CH_3), 3.01 (dd, J = 4.6, J = 17.2 Hz, 1 H, H_a, CH_2), 2.75 (dd, J = 4.2, 17.2 Hz, 1 H, H_b, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 170.9, 169.2, 161.8, 159.4 (CO_{Cbz}), 134.2, 134.1, 133.9, 133.8, 129.7, 129.6, 129.0, 128.9, 128.7, 128.6, 128.4, 128.3, 128.1 (5 C_{Ar}), 123.9, 123.8, 120.2, 120, 116.9, 116.6, 67.2 (CH_2-O), 52.9 (O-CH_3), 50.3 (CH), 36.5 (CH_2) ppm. ^{31}P NMR: δ = –15.3 ppm [oxide ^{31}P = +26.7 ppm]. MS (ESI): m/z = 582.2 [M + Na]$^+$. R_f = 0.61 (6:4 hexane/AcOEt).

1-Methyl 5-[2-(Diphenylphosphanyl)-4-fluorophenyl] *N*-(Benzyloxycarbonyl)-L-glutamate (4b): A solution of *o*-(diphenylphosphanyl)-*p*-fluorophenol (**7**; 324 mg, 1.09 mmol, 1 equiv.), the commercially available 1-methyl *N*-(benzyloxycarbonyl)-L-glutamate (386 mg, 1.31 mmol, 1.2 equiv.) and 4-(dimethylamino)pyridine (13.5 mg, 0.11 mmol, 0.1 equiv.) in dry CH_2Cl_2 (0.1 M) were added, at room temperature and under nitrogen, to a suspension of *N*-[3-(dimethylamino)propyl]-*N*′-ethylcarbodiimide hydrochloride (293.3 mg, 1.53 mmol, 1.4 equiv.) and dry *N*,*N*-diisopropylethylamine (262 μL, 1.53 mmol, 1.4 equiv.) in dry CH_2Cl_2. The mixture was stirred at room temp. for 2 h, monitoring by TLC (8:2 hexane/AcOEt). The reaction mixture was diluted with CH_2Cl_2 and extracted with 5% aqueous HCl and water. The organic layer was dried with Na_2SO_4 and concentrated. The crude product was purified by flash chromatography using 6:4 hexane/AcOEt as the eluent to afford **4b** (531 mg, 0.93 mmol) in 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.40–7.27 (m, 15 H, Ph), 7.09 (m, 1 H, 2-H), 7.00 (m, 1 H, 3-H), 6.47 (m, 1 H, 1-H), 5.34 (d, J_{NH-CH} = 7.9 Hz, 1 H, NH), 5.11 (d, J = 3.8 Hz, 2 H, CH_2-O), 4.35 (m, 1 H, CH), 3.74 (s, 3 H, O-CH_3), 2.28 (m, 2 H, CH_2-CO), 2.01 (m, 1 H, H_a, CH_2-CH), 1.80 (m, 1 H, H_b, CH_2-CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 170.8, 161.9, 159.4 (CO_{Cbz}), 134.4, 134.4, 134.2, 134.2, 129.8, 129.2, 129.1, 128.9, 128.6, 128.5 (5 C_{Ar}), 124.3, 124.2, 120.2, 119.9, 116.9, 116.7, 67.5 (CH_2-O), 53.5 (CH), 52.8 (O-CH_3), 30.3 (CH_2-CO), 27.6 (CH_2) ppm. ^{31}P NMR: δ = –14.2 ppm [oxide ^{31}P = +26.8 ppm]. MS (ESI): m/z = 596.3 [M + Na]$^+$. R_f = 0.56 (6:4 hexane/AcOEt).

***N*-(Benzyloxycarbonyl)-β-alanine 2-(Diphenylphosphanyl)-4-fluorophenyl Ester (4c):** A solution of *o*-(diphenylphosphanyl)-*p*-fluorophenol (**7**; 283.3 mg, 0.96 mmol, 1 equiv.), the protected amino acid *N*-(benzyloxycarbonyl)-L-β-alanine (257.1 mg, 1.15 mmol, 1.2 equiv.) and 4-(dimethylamino)pyridine (11.7 mg, 0.096 mmol, 0.1 equiv.) in dry CH_2Cl_2 (9.6 mL, 0.1 M) was added, at room temperature and under argon, to a solution of *N*,*N*′-dicyclohexylcarbodiimide (277.3 mg, 1.34 mmol, 1.4 equiv.) in dry CH_2Cl_2. The

mixture was stirred at room temperature for 2 h, monitoring by TLC (7:3 hexane/AcOEt). The reaction mixture was filtered and washed with CH_2Cl_2. The crude product was purified by flash chromatography using 7:3 hexane/AcOEt as the eluent to afford **4c** (460 mg, 0.88 mmol) in 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.42–7.27 (m, 15 H, Ph), 7.15–7.05 (m, 2 H, 2-H, 3-H), 6.52 (m, 1 H, 1-H), 5.27 (m, 1 H, NH), 5.12 (s, 2 H, CH_2-O), 3.48 (q, J_{CH2-NH} = 12 Hz, 2 H, CH_2-NH), 2.50 (t, $J_{CH2-CH2}$ = 6 Hz, 2 H, CH_2-CO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 170.8, 161.9, 159.5 (CO_{Cbz}), 156.5, 134.8, 134.7, 134.4, 134.2, 132.1, 132, 129.8, 129.3, 129.2, 128.8, 128.5, 128.4 (5 C_{Ar}), 124.3, 124.2, 120.4, 120.2, 117.1, 116.8, 67 (CH_2-O), 36.6 (CH_2), 34.8 (CH_2CO) ppm. ^{31}P NMR: δ = –15.2 ppm [oxide ^{31}P NMR: δ = +27.9 ppm]. MS (ESI): *m*/*z* = 524.2 [M + Na]$^+$. R_f = 0.42 (7:3 hexane/AcOEt).

***N*-(Benzyloxycarbonyl)glycine 2-(Diphenylphosphanyl)-4-fluorophenyl Ester (4d):** A solution of *o*-(diphenylphosphanyl)-*p*-fluorophenol (**7**; 158.3 mg, 0.53 mmol, 1 equiv.), the protected amino acid *N*-(benzyloxycarbonyl)-L-glycine (134 mg, 0.64 mmol, 1.2 equiv.) and 4-(dimethylamino)pyridine (6.5 mg, 0.053 mmol, 0.1 equiv.) in dry CH_2Cl_2 (5.3 mL, 0.1 M) was added, at room temperature and under argon, to a solution of *N*,*N*′-dicyclohexylcarbodiimide (152.7 mg, 0.74 mmol, 1.4 equiv.) in dry CH_2Cl_2. The mixture was stirred at room temperature for 2 h, monitoring by TLC (7:3 hexane/AcOEt). The reaction mixture was filtered and washed with CH_2Cl_2. The crude product was purified by flash chromatography using 7:3 hexane/AcOEt as the eluent to afford **4d** (232.5 mg, 0.48 mmol) in 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.48–7.30 (m, 15 H, Ph), 7.15 (m, 1 H, 2-H), 7.11 (m, 1 H, 3-H), 6.53 (m, 1 H, 1-H), 5.12 (s, 2 H, CH_2-O), 4.99 (m, 1 H, NH), 3.85 (d, J_{NH-CH2} = 5.2 Hz, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 168.4, 159.6 (CO_{Cbz}), 156.4, 162.1, 136.4 (C_{ipso}), 134.8, 134.7, 134.4, 134.2, 129.9, 129.2, 129.1, 128.9, 128.6, 128.4 (5 C_{Ar}), 124.2, 124.1, 120.4, 120.3, 120.1, 120.1, 117, 116.8, 67.5 (CH_2-O), 42.8 (CH_2) ppm. ^{31}P NMR: δ = –14.0 ppm. [oxide ^{31}P NMR: δ = +27.5 ppm]. MS (ESI): *m*/*z* = 510.4 [M + Na]$^+$. R_f = 0.51 (7:3 hexane/AcOEt).

***N*-(*tert*-Butoxycarbonyl)-L-proline 2-(Diphenylphosphanyl)-4-fluorophenyl Ester (4e):** A solution of *o*-(diphenylphosphanyl)-*p*-fluorophenol (**7**; 119.6 mg, 0.40 mmol, 1 equiv.), the protected amino acid *N*-Boc-L-proline (103.3 mg, 0.48 mmol, 1.2 equiv.) and 4-(dimethylamino)pyridine (4.9 mg, 0.04 mmol, 0.1 equiv.) in dry CH_2Cl_2 (4 mL, 0.1 M) was added, at room temperature and under argon, to a solution of *N*,*N*′-dicyclohexylcarbodiimide (115.5 mg, 0.56 mmol, 1.4 equiv.) in dry CH_2Cl_2. The mixture was stirred at room temperature for 2 h, monitoring by TLC (8:2 hexane/AcOEt). The reaction mixture was filtered and washed with CH_2Cl_2. The crude product was purified by flash chromatography using 8:2 hexane/AcOEt as the eluent to afford **4e** (185.3 mg, 0.37 mmol) in 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.30–7.25 (m, 5 H, Ar), 7.24–7.09 (m, 5 H, Ar), 7.06–6.92 (m, 2 H, 2-H, 3-H), 6.36 (m, 1 H, 1-H), 4.24 (m, 1 H, CH), 3.26 (t, $J_{Hc,Hd}$ = 6.8 Hz, 1 H, H_c, CH_2), 3.18 (t, $J_{Hc,Hd}$ = 6.8 Hz, 1 H, H_d, CH_2), 2.03–1.95 (m, 1 H, H_a), 1.78–1.62 (m, 3 H, H_b, CH_2), 1.39–1.36 (2 s, 9 H, Boc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 171.2, 161.9, 159.4, 154.8, 153.9, 148.9, 135.1, 134.4, 134.2, 133.9, 132.1, 129.7, 129, 124.3, 123.5, 119.9, 117.2, 116.9, 80.4, 80.1, 59.4, 46.8, 30.6, 29.6, 28.8 (Boc), 24.9, 23.8 ppm. ^{31}P NMR: δ = –15.5, –15.8 ppm. [oxide ^{31}P NMR: δ = +27.7, 28.0 ppm]. MS (ESI): *m*/*z* = 516.2 [M + Na]$^+$. R_f = 0.43 (8:2 hexane/AcOEt).

General Procedure for the Stereoselective Ligation of Glycosyl Azides in DMA/DMPU Mixtures: The phosphane (2 equiv.) was added, at room temperature, to a 0.1 M solution of the azide (1 equiv.) in 98:2 *N*,*N*-dimethylacetamide/DMPU. The solution was stirred for 16 h at 40 °C, then water was added and the mixture was stirred for an additional 2 h at the same temperature. The solvent was evaporated under reduced pressure and the residue was diluted with water and extracted with CH_2Cl_2. The water layer was evaporated under reduced pressure and the crude was purified as indicated below for each compound. The reactions were performed on the 0.1–1 mmol scale. Yields are reported in Tables 1 and 2.

***N*-(*N*-Benzyloxycarbonyl-β-alanyl)-α-D-glucopyranosylamine (8c):** The compound was purified by flash chromatography (80:20:2 $CHCl_3$/MeOH/H_2O, R_f = 0.38). $[\alpha]_D^{25}$ = +46.4 (*c* = 1, MeOH). ^{1}H NMR (400 MHz, D_2O, 25 °C): δ = 7.41–7.33 (m, 5 H, Ph), 5.52 (d, $J_{1,2}$ = 5.4 Hz, 1 H, 1-H) 5.05 (s, 2 H, CH_2-O), 3.78–3.58 (m, 4 H, 2-H, 6-H, 6′-H), 3.50–3.27 (m, 4 H, CH_2), 2.53–2.48 (m, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, D_2O, 25 °C): δ = 175.9, 158.2 (CO_{Cbz}), 136.4 (C_{ipso}), 128.8, 128.5, 127.7 (5 Ar), 76.6 (C-1), 73.0, 72.6, 69.3, 69.2, 66.9 (CH_2-O), 60.4 (C-6), 38.1 (CH_2), 36.1 (CH_2) ppm.

***N*-(*N*-Benzyloxycarbonylglycyl)-α-D-glucopyranosylamine (8d):** The compound was purified by flash chromatography (80:20:2$CHCl_3$/MeOH/H_2O, R_f = 0.23). $[\alpha]_D^{25}$ = +16.3 (*c* = 0.5, MeOH). ^{1}H NMR (400 MHz, D_2O, 25 °C): δ = 7.43–7.29 (m, 5 H, Ph), 5.53 (d, $J_{1,2}$ = 5.6 Hz, 1 H, 1-H), 5.09 (s, 2 H, CH_2-O), 3.89 (br. s, 2 H, CH_2), 3.87–3.34 (m, 6 H, 2-H, 3-H, 4-H, 5-H, 6-H, 6′-H) ppm. ^{13}C NMR (100 MHz, D_2O, 25 °C): δ = 170.3, 128.8, 128.4, 127.8 (5 C_{Ar}), 79.4 (C-1), 76.7, 72.7, 72.4, 69.4, 67.3 (CH_2-O), 60.6 (C-6), 43.4 (CH_2) ppm.

***N*$^{\alpha}$-(Benzyloxycarbonyl)-*N*$^{\gamma}$-(β-D-glucopyranosyl)-L-asparagine *O*-Methyl Ester (10a):** The compound was purified by flash chromatography (80:20:2 $CHCl_3$/MeOH/H_2O, R_f = 0.43). $[\alpha]_D^{25}$ = –0.6 (*c* = 1, MeOH). ^{1}H NMR (400 MHz, D_2O, 25 °C): δ = 7.45–7.35 (m, 5 H, Ph), 5.10 (s, 2 H, CH_2-O), 4.96 (d, $J_{1,2}$ = 9.2 Hz, 1 H, 1-H), 4.65 (t, *J* = 6.4 Hz, 1 H, CH-N), 3.88 (dd, $J_{6,6'}$ = 12.4, $J_{5,6}$ = 2.4 Hz, 1 H, 6-H), 3.80–3.69 (m, 4 H, 6′-H, O-CH_3), 3.60–3.51 (m, 2 H, 4-H, 5-H), 3.46–3.37 (m, 2 H, 3-H, 2-H), 2.95–2.89 (m, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, D_2O, 25 °C): δ = 173.4, 173.1, 157.7 (CO_{Cbz}), 136.2 (C_{ipso}), 128.8, 128.4, 127.6 (5 C_{Ar}), 79.2 (C-1), 77.5 (C-5), 76.4 (C-4), 71.7 (C-2), 69.2 (C-3), 67.2 (CH_2-O), 53.1 (O-CH_3), 50.6 (CH), 37.1 (CH_2) ppm. MS (FAB): *m*/*z* = 465 [M + Na]$^+$.

***N*$^{\alpha}$-(Benzyloxycarbonyl)-*N*$^{\delta}$-(β-D-glucopyranosyl)-L-glutamine *O*-Methyl Ester (10b):** The compound was purified by flash chromatography (80:20:2 $CHCl_3$/MeOH/H_2O, R_f = 0.47). $[\alpha]_D^{25}$ = –10 (*c* = 1, MeOH). ^{1}H NMR (400 MHz, D_2O, 25 °C): δ = 7.49–7.38 (m, 5 H, Ph), 5.14 (s, 2 H, CH_2-O), 4.95 (d, $J_{1,2}$ = 9.2 Hz, 1 H, 1-H), 4.25 (m, 1 H, CH-N), 3.86 (dd, $J_{5,6}$ = 2, $J_{6,6'}$ = 12.4 Hz, 1 H, 6-H), 3.72 (s, 3 H, O-CH_3), 3.67 (dd, $J_{5,6'}$ = 5.2, $J_{6,6'}$ = 12.4 Hz, 1 H, 6′-H), 3.54–3.47 (m, 2 H, 4-H, 5-H), 3.44–3.35 (m, 2 H, 3-H, 2-H), 2.44 (t, *J* = 7.6 Hz, 2 H, CH_2-CO), 2.27–2.18 (m, 1 H, H_a, CH_2-CH), 2.04–1.95 (m, 1 H, H_b, CH_2-CH) ppm. ^{13}C NMR (100 MHz, D_2O, 25 °C): δ = 176.2, 174.2, 158 (CO_{Cbz}), 136.3 (C_{ipso}), 128.8, 128.4, 127.6 (5 C_{Ar}), 79.2 (C-1), 77.5 (C-5), 76.4 (C-4), 71.8 (C-2), 69.2 (C-3), 67.2 (CH_2-O), 60.5 (C-6), 53.5 (CH), 52.9 (O-CH_3), 31.7 (CH_2-CO), 26.2 (CH_2) ppm. MS (FAB): *m*/*z* = 479 [M + Na]$^+$.

***N*-(*N*-Benzyloxycarbonyl-β-alanyl)-β-D-glucopyranosylamine (10c):** The compound was purified by flash chromatography (80:20:2 $CHCl_3$/MeOH/H_2O, R_f = 0.34). $[\alpha]_D^{25}$ = +3.5 (*c* = 0.7, MeOH). ^{1}H NMR (400 MHz, D_2O, 25 °C): δ = 7.50–7.38 (m, 5 H, Ph), 5.11 (s, 2 H, CH_2-O), 4.97 (d, $J_{1,2}$ = 8.8 Hz, 1 H, 1-H), 3.88 (d, $J_{6,6'}$ = 12.4 Hz, 1 H, 6-H), 3.72 (dd, $J_{6,6'}$ = 12.4, $J_{5,6'}$ = 5.2 Hz, 1 H, 6′-H), 3.60–3.30 (m, 6 H, 5-H, 4-H, 2-H, 3-H, CH_2-NHCbz), 2.54 (t,

J = 6.4 Hz, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, D_2O, 25 °C): δ = 175.3, 158.2 (CO_{Cbz}), 136.4 (C_{ipso}), 128.8, 128.3, 127.6 (5 C_{Ar}), 79.2 (C-1), 77.5 (C-5), 76.4 (C-4), 71.7 (C-2), 69.2 (C-3), 66.9 (CH_2-O), 60.5 (C-6), 36.7 (CH_2), 35.8 (CH_2) ppm. MS (FAB): m/z = 407 $[M + Na]^+$.

N-(N-Benzyloxycarbonylglycyl)-β-D-glucopyranosylamine (10d): The compound was purified by flash chromatography (80:20:2 $CHCl_3$/MeOH/H_2O, R_f = 0.32). $[\alpha]_D^{25}$ = +4.1 (c = 1, MeOH). ^1H NMR (400 MHz, D_2O, 25 °C): δ = 7.45–7.30 (m, 5 H, Ph), 5.09 (s, 2 H, CH_2O), 4.94 (d, $J_{1,2}$ = 9.2 Hz, 1 H, 1-H), 3.88–3.77 (m, 3 H, CH_2, 6-H), 3.64 (dd, $J_{5,6'}$ = 5.2, $J_{6,6'}$ = 12.4 Hz, 1 H, 6′-H), 3.53–3.44 (m, 2 H, 5-H, 3-H), 3.39–3.28 (m, 2 H, 2-H, 4-H) ppm. ^{13}C NMR (100 MHz, D_2O, 25 °C): δ = 173.4, 158.6 (CO_{Cbz}), 136.2 (C_{ipso}), 128.8, 128.2, 127.7 (5 C_{Ar}), 79.3 (C-1), 77.6, 76.4, 71.7, 68.9, 66.4 (CH_2-O), 60.5 (C-6), 43.7 (CH_2) ppm.

N-(N-*tert*-Butoxycarbonyl-L-prolyl)-β-D-glucopyranosylamine (10e): The compound was purified by flash chromatography (80:20:2 $CHCl_3$/MeOH/H_2O, R_f = 0.36). $[\alpha]_D^{25}$ = –39.2 (c = 0.6, MeOH). ^1H NMR (400 MHz, MeOD, 25 °C): δ = 4.95 (d, $J_{1,2}$ = 8.8 Hz, 1 H, 1-H), 4.26 (dd, J = 3.6, J = 8.4 Hz, 1 H, CH), 3.87 (br. dd, $J_{6,6'}$ = 11.6 Hz, 1 H, 6-H), 3.75–3.68 (m, 1 H, 6′-H), 3.63–3.52 (m, 1 H, H_a, CH_2-CH), 3.51–3.42 (m, 2 H, 3-H, H_b, CH_2-CH), 3.41–3.30 (m, 3 H, 2-H, 4-H, 5-H), 2.37–2.18 (m,1 H, H_c), 2.08–1.88 (m, 3 H, H_d, CH_2), 1.50 (m, 9 H, Boc) ppm. ^{13}C NMR (100 MHz, MeOD, 25 °C): δ = 81.4 (C-1), 79.8, 79.1, 74.2, 71.6, 62.8 (C-6), 61.8 (CH), 48 (CH_2), 32 (CH_2), 28.8 (Boc), 25.1 (CH_2) ppm. FT-ICR MS (ESI): calcd. for $C_{16}H_{28}N_2O_8Na$ $[M + Na]^+$ 399.17379; found 399.17314.

N^{α}-(Benzyloxycarbonyl)-N^{γ}-(β-D-galactopyranosyl)-L-asparagine O-Methyl Ester (14a): The compound was purified by flash chromatography (80:20:2 $CHCl_3$/MeOH/H_2O, R_f = 0.18). ^1H NMR (400 MHz, MeOD, 25 °C): δ = 7.42–7.28 (m, 5 H, Ph), 5.11 (s, 2 H, CH_2-O), 4.58 (m, 1 H, CH), 3.89 (d, J = 2.4 Hz, 1 H, 4-H), 3.77–3.64 (m, 5 H, 6-H, 6′-H, O-CH_3), 3.63–3.47 (m, 3 H, 2-H, 3-H, 5-H), 2.89–2.78 (m, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, MeOD, 25 °C): δ = 129.6, 129.1, 129 (5 C_{Ar}), 81.6 (C-1), 78.4, 75.9, 71.4, 70.6 (C-4), 67.9 (C-6), 62.7 (CH_2-O), 53.1 (O-CH_3), 52.1 (CH), 38.2 (CH_2) ppm.

N^{α}-(Benzyloxycarbonyl)-N^{δ}-(β-D-galactopyranosyl)-L-glutamine O-Methyl Ester (14b): The crude compound was crystallized from MeOH, filtered and washed with diethyl ether.^1H NMR (400 MHz, DMSO, 25 °C): δ = 7.47–7.26 (m, 5 H, Ph), 5.04 (s, 2 H, CH_2-O), 4.63 (d, $J_{1,2}$ = 5.2 Hz, 1 H, 1-H), 4.10–4.01 (m, 1 H, CH), 3.70–3.67 (m, 1 H, 5-H), 3.64 (s, 3 H, O-CH_3), 3.52–3.31 (m, 5 H, 2-H, 3-H, 4-H, 6-H, 6′-H), 2.25–2.20 (t, J = 7.6 Hz, 2 H, CH_2), 2.03–1.95 (m, 1 H, H_a, CH_2-CH), 1.78–1.73 (m, 1 H, H_b, CH_2-CH) ppm. ^{13}C NMR (100 MHz, DMSO, 25 °C): δ = 172.6, 171.6, 156.1 (CO_{Cbz}), 136.8 (C_{ipso}), 128.3, 127.7, 127.1 (5 C_{Ar}), 79.9 (C-1), 76.7, 74.1, 69.7, 68.2, 65.5 (CH_2-O), 60.4 (C-6), 53.5 (CH), 51.8 (O-CH_3), 31.6 (CH_2-CO), 26.3 (CH_2) ppm.

N-(N-Benzyloxycarbonyl-β-alanyl)-β-D-galactopyranosylamine (14c): The crude compound was crystallized from MeOH, filtered and washed with diethyl ether. ^1H NMR (400 MHz, DMSO, 25 °C): δ = 7.46–7.29 (m, 5 H, Ph), 5.04 (s, 2 H, CH_2-O), 4.70 (d, $J_{1,2}$ = 8.8 Hz, 1 H, 1-H), 3.71 (d, J = 2.4 Hz, 1 H, 4-H), 3.54–3.29 (m, 5 H, 2-H, 3-H, 5-H, 6-H, 6′-H), 3.27–3.23 (m, 2 H, CH_2), 2.41–2.28 (m, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, DMSO, 25 °C): δ = 170.6, 155.9 (CO_{Cbz}), 137.2 (C_{ipso}), 128.4, 127.8, 127.7 (5 C_{Ar}), 79.8 (C-1), 76.6, 73.9, 69.5, 68.1 (C-4), 62.2 (CH_2-O), 60.4 (C-6), 36.6 (CH_2), 35.5 (CH_2) ppm.

N-(N-Benzyloxycarbonylglycyl)-β-D-galactopyranosylamine (14d): The compound was purified by flash chromatography (80:20:2 $CHCl_3$/MeOH/H_2O, R_f = 0.35). ^1H NMR (400 MHz, MeOD, 25 °C): δ = 7.42–7.28 (m, 5 H, Ph), 5.14 (s, 2 H, CH_2-O), 4.92 (d, $J_{1,2}$ = 8.8 Hz, 1 H, 1-H), 3.95–3.83 (m, 3 H, 5-H, CH_2), 3.78–3.70 (m, 2 H), 3.60–3.58 (m, 2 H, 2-H, 6-H), 3.55–3.52 (dd, $J_{5,6'}$ = 3.2, $J_{6,6'}$ = 9.6 Hz, 1 H, 6′-H) ppm. ^{13}C NMR (100 MHz, MeOD, 25 °C): δ = 172.9, 159.1 (CO_{Cbz}), 138.1 (C_{ipso}), 129.5, 129.0, 128.9 (5 C_{Ar}), 81.6 (C-1), 78.3, 75.7, 71.4, 70.4, 67.9 (CH_2-O), 62.6 (C-6), 46.1 (CH_2) ppm.

N^{α}-(Benzyloxycarbonyl)-N^{γ}-β-D-fucopyranosyl-L-asparagine O-Methyl Ester (15a): The compound was purified by flash chromatography (80:20 $CHCl_3$/MeOH, R_f = 0.45). $[\alpha]_D^{25}$ = –0.04 (c = 0.6, MeOH). ^1H NMR (400 MHz, MeOD, 25 °C): δ = 7.41–7.31 (m, 5 H, Ph), 5.12 (s, 2 H, CH_2-O), 4.60 (m, 1 H, H_a, CH-N), 3.68 (s, 3 H, O-CH_3), 3.67–3.56 (m, 3 H, 2-H, 3-H, 5-H), 3.52 (d, J = 6.4 Hz, 1 H, 4-H), 2.84 (m, 2 H, CH_2-CH), 1.25 (d, $J_{5,6}$ = 8 Hz, 3 H, 6-H) ppm. ^{13}C NMR (100 MHz, MeOD, 25 °C): δ = 173.5, 172.8, 158.4 (CO_{Cbz}), 138.1 (C_{ipso}), 129.5, 128.8 (5 C_{Ar}), 81.3 (C-1), 75.9, 73.7, 73.1, 71.1, 67.1 (CH_2-O), 53.0 (O-CH_3), 52.0 (CH), 38.5 (CH_2), 16.9 (C-6) ppm. FT-ICR MS (ESI): calcd. for $C_{19}H_{26}N_2O_9Na$ $[M + Na]^+$ 449.15305; found 449.15235.

N^{α}-(Benzyloxycarbonyl)-N^{δ}-(β-D-fucopyranosyl)-L-glutamine O-Methyl Ester (15b): The compound was purified by flash chromatography (80:20 $CHCl_3$/MeOH, R_f = 0.68). $[\alpha]_D^{25}$ = –23.4 (c = 0.2, MeOH). ^1H NMR (400 MHz, D_2O, 25 °C): δ = 7.52–7.43 (m, 5 H, Ph), 5.18 (s, 2 H, CH_2-O), 4.92 (d, $J_{1,2}$ = 9.2 Hz, 1 H, 1-H), 4.30 (m, 1 H, CH-N), 3.89–3.67 (m, 6 H, 3-H, 4-H, 5-H, O-CH_3), 3.59 (t, $J_{2,3}$ = 9.2 Hz, 1 H, 2-H), 2.47 (m, 2 H, CH_2-CO), 2.24 (m, 1 H, H_a, CH_2-CH), 2.06 (m, 1 H, H_b, CH_2-CH), 1.25 (d, $J_{5,6}$ = 6.4 Hz, 3 H, 6-H) ppm. ^{13}C NMR (100 MHz, D_2O, 25 °C): δ = 175.8, 174.0, 157.8 (CO_{Cbz}), 136.0 (C_{ipso}), 128.6, 128.2, 127.4 (5 C_{Ar}), 79.3 (C-1), 73.3 (C-2), 72.4, 71.2, 68.9, 67.0 (CH_2-O), 53.4 (CH), 52.7 (O-CH_3), 31.5 (CH_2-CO), 26.0 (CH_2-CH), 15.3 (C-6) ppm. MS (FAB): m/z (%) = 441 (56) $[M + 1]^+$, 463 (33) $[M + Na]^+$. FT-ICR MS (ESI): calcd. for $C_{20}H_{28}N_2O_9Na$ $[M + Na]^+$ 463.16870; found 463.16891.

N-(N-Benzyloxycarbonyl-β-alanyl)-β-L-fucopyranosyl amine (15c): The compound was purified by flash chromatography (80:20:2 $CHCl_3$/MeOH/H_2O, R_f = 0.35). $[\alpha]_D^{25}$ = –14.1 (c = 1, MeOH). ^1H NMR (400 MHz, D_2O, 25 °C): δ = 7.49–7.39 (m, 5 H, Ph), 5.11 (s, 2 H, CH_2-O), 4.91 (d, $J_{1,2}$ = 9.2 Hz, 1 H, 1-H), 3.85 (q, $J_{5,6}$ = 6.4 Hz, 1 H, 5-H), 3.79 (d, $J_{3,4}$ = 3.2 Hz, 1 H, 4-H), 3.71 (dd, $J_{2,3}$ = 9.4, $J_{3,4}$ = 3.2 Hz, 1 H, 3-H), 3.59 ("t", $J_{1,2}$ = 9.2, $J_{2,3}$ = 9.4 Hz, 1 H, 2-H), 3.43 (t, J = 6.4 Hz, 2 H, CH_2) 2.53 (m, 2 H, CH_2CO), 1.24 (d, $J_{5,6}$ = 6.4 Hz, 3 H, 6-H) ppm. ^{13}C NMR (100 MHz, D_2O, 25 °C): δ = 175.1, 158.2 (CO_{Cbz}), 136.4 (C_{ipso}), 128.7, 128.3, 127.7 (5 C_{Ar}), 79.4 (C-1), 73.5 (C-3), 72.5 (C-5), 71.4 (C-4), 69.1 (C-2), 66.9 (CH_2-O), 36.7 (CH_2), 35.7 (CH_2CO), 15.6 (C-6) ppm. FT-ICR MS (ESI): calcd. for $C_{17}H_{24}N_2O_7Na$ $[M + Na]^+$ 391.14757; found 391.14714.

N-(N-Benzyloxycarbonylglycyl)-β-L-fucopyranosylamine (15d): The compound was purified by flash chromatography (80:20:2 $CHCl_3$/MeOH/H_2O, R_f = 0.34). $[\alpha]_D^{25}$ = –12.1 (c = 1, MeOH). ^1H NMR (400 MHz, D_2O, 25 °C): δ = 7.52–7.37 (m, 5 H, Ph), 5.19 (s, 2 H, CH_2-O), 4.96 (d, $J_{1,2}$ = 9 Hz, 1 H, 1-H), 3.95 (d, J = 3.4 Hz, 2 H, CH_2), 3.89 (q, $J_{5,6}$ = 6.4 Hz, 1 H, 5-H), 3.82 (br. d, $J_{3,4}$ = 3.4 Hz, 1 H, 4-H), 3.74 (dd, $J_{2,3}$ = 9.4, $J_{3,4}$ = 3.4 Hz, 1 H, 3-H), 3.64 ("t", $J_{1,2}$ = 9.2, $J_{2,3}$ = 9.4 Hz, 1 H, 2-H), 1.26 (d, $J_{5,6}$ = 6.4 Hz, 3 H, 6-H) ppm. ^{13}C NMR (100 MHz, D_2O, 25 °C): δ = 173.2, 158.6 (CO_{Cbz}), 136.2 (C_{ipso}), 128.8, 128.5, 127.8 (5 C_{Ar}), 79.6 (C-1), 73.5 (C-3), 72.7 (C-5), 71.4 (C-4), 69.1 (C-2), 67.4 (CH_2-O), 43.5 (CH_2), 15.5 (C-6) ppm. FT-ICR MS (ESI): calcd. for $C_{16}H_{22}N_2O_7Na$ $[M + Na]^+$ 377.13192; found 377.13165.

***N*-(*N*-*tert*-Butoxycarbonyl-L-prolyl)-β-L-fucopyranosylamine (15e):** The compound was purified by flash chromatography (80:20:2 $CHCl_3$/MeOH/H_2O, R_f = 0.48). $[\alpha]_D^{25}$ = –49.7 (*c* = 1, MeOH). ^{1}H NMR (400 MHz, MeOD, 25 °C): δ = 4.21–4.13 (m, 1 H, CH), 3.70 (q, $J_{5,6}$ = 6.4 Hz, 1 H, 5-H), 3.64 (s, 1 H, 4-H), 3.56–3.47 (m, 3 H, 2-H, 3-H, H_a), 3.43–3.37 (m, 1 H, H_b), 2.31–2.17 (m, 1 H, H_c, CH_2), 2.15–1.78 (m, 3 H, CH_2, H_d), 1.52–1.39 (br. s, 9 H, Boc), 1.21 (d, $J_{5,6}$ = 6.4 Hz, 3 H, 6-H) ppm. ^{13}C NMR (100 MHz, MeOD, 25 °C): δ = 176.8, 156.3 (CO_{Boc}), 81.5 (C-1), 76.3, 73.7 (C-5), 73.4 (C-4), 71.3, 61.9 (CH), 48.0 (CH_2), 32.6 (CH_2), 28.8 (Boc), 24.8 (CH_2), 17.1 (H-6) ppm. FT-ICR MS (ESI): calcd. for $C_{16}H_{28}N_2O_7Na$ $[M + Na]^+$ 383.17887; found 383.17848.

***N*$^{\alpha}$-(Benzyloxycarbonyl)-*N*$^{\gamma}$-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-L-asparagine *O*-Methyl Ester (16a):** The compound was purified by flash chromatography (80:20 $CHCl_3$/MeOH, R_f = 0.20). $[\alpha]_D^{25}$ = +19.2 (*c* = 1, MeOH). ^{1}H NMR (400 MHz, MeOD, 25 °C): δ = 7.39–7.31 (m, 5 H, Ph), 5.11 (s, 2 H, CH_2-O), 4.96 (d, $J_{1,2}$ = 9.7 Hz, 1 H, 1-H), 4.60 (t, $J_{CH\text{-}CH2}$ = 6.8 Hz, 1 H, CH-N), 3.85 (br. d, $J_{6,6'}$ = 11.8 Hz, 1 H, 6-H), 3.77–3.70 (m, 4 H, 2-H, O-CH_3), 3.66 (dd, $J_{5,6'}$ = 3.8, $J_{6,6'}$ = 11.8 Hz, 1 H, 6′-H) 3.47 (m, 1 H, 3-H), 3.40–3.32 (m, 2 H, 4-H, 5-H), 2.73 (t, *J* = 7.2 Hz, 2 H, CH_2), 1.94 (s, 3 H, NHAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 174.6, 173.5 172.6, 129.6, 129.2, 129.0 (5 C_{Ar}), 80.4 (C-1), 79.9, 76.5 (C-3), 72.0, 67.9 (CH_2-O), 62.8 (C-6), 56.2 (C-2), 53.1 (O-CH_3), 52.2 (CH), 38.7 (CH_2), 23.0 (CO-CH_3) ppm. MS (FAB): *m*/*z* (%) = 484 (17) $[M + 1]^+$, 506 (12) $[M + Na]^+$.

***N*$^{\alpha}$-(Benzyloxycarbonyl)-*N*$^{\delta}$-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-L-glutamine *O*-Methyl Ester (16b):** The compound was purified by flash chromatography (80:20 $CHCl_3$/MeOH, R_f = 0.42). $[\alpha]_D^{25}$ = +3.5 (*c* = 0.6, MeOH). ^{1}H NMR (400 MHz, MeOD, 25 °C): δ = 7.45 (m, 5 H, Ph), 5.15 (s, 2 H, CH_2-O), 5.05 (d, $J_{1,2}$ = 9.7 Hz, 1 H, 1-H), 4.20 (m, 1 H, CH-NH), 3.47–3.81 (m, 6 H, 2-H, 3-H, 4-H, 5-H, 6-H, 6′-H), 3.75 (s, 3 H, O-CH_3), 2.38 (t, *J* = 7.4 Hz, 2 H, CH_2-CO), 2.15–2.05 (m, 1 H, H_a, CH_2-CH), 2.03–1.92 (m, 4 H, H_b, NHAc) ppm. ^{13}C NMR (100 MHz, MeOD, 25 °C): δ = 175.7, 174.8, 152.6 (CO_{Cbz}), 136.4 (C_{ipso}), 128.9, 128.5, 127.7 (5 C_{Ar}), 78.4 (C-1), 77.6, 74.2, 69.6, 67.3 (CH_2-O), 60.6 (C-6), 54.4 (CH-NH), 53.6 (C-2), 53.0 (O-CH_3), 31.8 (CH_2-CO), 26.3 (CH_2-CH), 22.0 (CO-CH_3) ppm. MS (FAB): *m*/*z* (%) = 498 (73) $[M + 1]^+$, 520 (77) $[M + Na]^+$. FT-ICR MS (ESI): calcd. for $C_{22}H_{31}N_3O_{10}Na$ $[M + Na]^+$ 520.19017; found 520.19006.

***N*-(*N*-Benzyloxycarbonyl-β-alanyl)-2-acetamido-2-deoxy-β-D-glucopyranosylamine (16c):** The compound was purified by flash chromatography (80:20:2 $CHCl_3$/MeOH/H_2O, R_f = 0.24). $[\alpha]_D^{25}$ = +18.6 (*c* = 1, MeOH). ^{1}H NMR (400 MHz, MeOD, 25 °C): δ = 7.31–7.24 (m, 5 H, Ph), 5.01 (s, 2 H, CH_2-O), 4.91 (d, $J_{1,2}$ = 9.6 Hz, 1 H, 1-H), 3.78 (d, $J_{6,6'}$ = 11.6 Hz, 1 H, 6-H), 3.69 (t, $J_{3,4}$ = 10 Hz, 1 H), 3.60 (dd, $J_{5,6'}$ = 2.4, $J_{6,6'}$ = 11.6 Hz, 1 H, 6′-H), 3.39 (m, 1 H, 3-H), 3.31–3.24 (m, 4 H, 4-H, 5-H, CH_2), 2.34 (t, *J* = 6.7 Hz, 2 H, CH_2), 1.88 (s, 3 H, NHAc) ppm. ^{13}C NMR (100 MHz, D_2O, 25 °C): δ = 173.0, 172.8, 157.2 (CO_{Cbz}), 136.9 (C_{ipso}), 128.1, 127.6, 127.4 (5 C_{Ar}), 78.9 (C-1), 78.1, 74.9 (C-3), 71.1, 66.1 (CH_2-O), 61.3 (C-6), 54.8 (C-2), 37.9 (CH_2), 35.8 (CH_2), 21.4 (CO-CH_3) ppm. MS (FAB): *m*/*z* = 448 $[M + Na]^+$.

Supporting Information (see also the footnote on the first page of this article): General procedure for the acetylation of glycosyl amino acids, characterization of the *O*-acetylglycosyl amino acids and ^{13}C NMR spectra of all new compounds.

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