Supporting Information

Stereoselective Synthesis of α - and β -Glycosylamide Derivatives from Glycopyranosyl Azides *via* Isoxazoline Intermediates

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Experimental Section.

General Methods. ^1H and ^{13}C NMR spectra were recorded on a Bruker DRX-400 MHz, Bruker DRX-500 MHz, and Bruker DRX-600 MHz spectrometers. Chemical shifts are reported in parts per million (ppm). Coupling constants (J) are given in hertz (Hz). Spin multiplicities are indicated by standard notation.

Infrared spectra were recorded on a Nicolet 5DXC FT-IR spectrophotometer. Band positions are given in reciprocal centimeters (cm^{-1}) and relative intensities are listed as br (broad), s (strong), m (medium) or w (weak).

Melting points were taken in Kimax soft glass capillary tubes using a Thomas-Hoover Uni-Melt capillary melting point apparatus equipped with a calibrated thermometer.

Low resolution (LRMS) and high resolution (HRMS) mass spectra were obtained on a VG-7070E magnetic sector instrument.

Thin-layer chromatography (TLC) was performed on 0.25 mm Merck silica-coated glass plates, with compounds being identified in one or more of the following manners: UV (254 nm) and vanillin/sulfuric acid/ethanol charring.

Tetrahydrofuran (THF) was distilled from sodium/benzophenone ketyl. Methanol (MeOH) was dried and stored over molecular sieves. 1,2-Dichloroethane were distilled from calcium hydride and stored over molecular sieves. Triphenylphosphine (Ph₃P) and benzoic anhydride were recrystallized from hexane. 2,3,4,6-Tetra-*O*-acetyl- α -D-glucopyranosyl azide (**1**) and 2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl azide (**2**) were prepared according to literature procedures.¹ Glassware used in the reactions was dried overnight in an oven at 120 °C. All reactions were performed under an atmosphere of argon unless noted otherwise.

3,4,6-Tri-*O*-acetyl- α -D-glucopyranosyl isoxazoline (**3**).

2,3,4,6-Tetra-*O*-acetyl- α -D-glucopyranosyl azide (**1**) (150 mg, 0.402 mmol) and Ph₃P (116 mg, 0.442 mmol) were dissolved in 1,2-dichloroethane (5 mL) in the presence of 4Å molecular sieves. The resulting solution was heated under reflux for 15h, then was cooled to ambient temperature and concentrated in vacuo. Purification of the residue by flash chromatography (hexanes:EtOAc:Et₃N, 1:3:1%) gave 76 mg (58%) of isoxazoline **3** as a colorless oil. R_f = 0.21 (hexanes:EtOAc, 1:3); IR (CCl₄) 2959 (m), 1751 (s), 1667 (m), 1242 (s), 1214 (s); ¹H NMR (400 MHz, CDCl₃) 2.01 (s, 3H), 2.04 (s, 3H), 2.06 (s, 3H), 2.08 (s, 3H), 3.61 (ddd, J = 8.8, 5.2, 2.4, 1H, H-5), 4.11 (dd, J = 12.4, 2.4, 1H, H-6), 4.23 (dd, J = 12.4, 5.2, 1H, H-6'), 4.37 (dd, J = 7.6, 4.0, 1H, H-2), 4.88 (dd, J = 8.8, 4.0, 1H, H-4), 5.12 (t, J = 4.0, 1H, H-3), 5.80 (d, J = 7.6, 1H, H-1); ¹³C NMR (100 MHz, CDCl₃) 14.1, 20.6, 20.7, 20.7, 63.1, 67.3, 67.7, 70.7, 75.9, 92.8, 168.6, 169.4, 169.5, 170.6; LRMS (FAB) 330 ((M + H)⁺, 100); HRMS (FAB) calcd for C₁₄H₂₀O₈N 330.1189 (M + H)⁺, found 330.1194.

General procedure for the coupling reactions. 2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl azide (**1**) (200 mg, 0.536 mmol) and Ph_3P (155 mg, 0.590 mmol) were dissolved in 1,2-dichloroethane (6 mL) in the presence of 4Å molecular sieves. The resulting solution was heated under reflux for 15h, then was cooled to RT. The acylating reagent and additive, respectively, were added to the reaction mixture and heated at given temperature for given time as shown in the Table. The reaction mixture was diluted with 100 mL Et_2O and washed with 2x100 mL H_2O . The organic layer was dried over Na_2SO_4 and concentrated in vacuo to give crude product, which was purified by flash chromatography (hexanes:EtOAc, 1:1).

2,3,4,6-Tetra-*O*-acetyl-1-*N*-phenyl acetyl- β -D-glucopyranosylamine (β -7) and 2,3,4,6-Tetra-*O*-acetyl-1-*N*-phenyl acetyl- α -D-glucopyranosylamine (α -7).

Compounds **7** (entry 9) were prepared following the general coupling procedure outlined above employing β -azide (**1**), Ph_3P , and 2-thiopyridyl phenylacetate (160 mg, 0.697 mmol) as the acylating reagent. Purification of the residue by flash chromatography (hexanes:EtOAc, 1:1) gave 166 mg (67%) of α/β mixture (5:1) of **7** as a white solid. TLC R_f = 0.33 (hexanes:EtOAc, 1:1). The anomers were separated by HPLC using Hypersilica 5 μm column (hexane: CH_2Cl_2 :MeOH, 90:10:1), and isolated pure anomers were recrystallized from hexanes:EtOAc (1:1) solvent mixture.

(α -7): m.p. 156-158 $^{\circ}\text{C}$; IR (CCl_4) 3258 (w), 3062 (w), 2962 (w), 1754 (s), 1655 (m), 1220 (s); ^1H NMR (400 MHz, CDCl_3) 1.83 (s, 3H), 1.98 (s, 6H), 2.02 (s, 3H), 3.61 (s, 2H), 3.74 (m, 1H), 3.99 (d, J = 12.0, 1H), 4.22 (dd, J = 12.0, 4.0, 1H), 4.95-5.10 (m, 3H), 5.78 (t, J = 5.5, 1H), 6.46 (d, J = 7.0, 1H, NH), 7.25-7.35 (m, 5H); ^{13}C

NMR (100 MHz, CDCl₃) 20.7, 21.0, 21.0, 21.1, 44.2, 62.0, 68.4, 68.6, 68.7, 70.4, 74.7, 128.1, 129.4, 129.6, 134.7, 169.3, 169.7, 170.7, 170.2, 172.1; LRMS (FAB) 466 ((M + H)⁺, 16), 43 (100), 91 (57); HRMS (FAB) calcd for C₂₂H₂₈O₁₀N 466.1713 (M + H)⁺, found 466.1716.

(β-7): m.p. 158-159 °C; IR (KBr) 3457 (w), 3060 (w), 2955 (w), 1750 (s), 1662 (m), 1536 (m) 1229 (s); ¹H NMR (400 MHz, CDCl₃) 1.81 (s, 3H), 1.96 (s, 3H), 1.99 (s, 3H), 2.06

(s, 3H), 3.47 (d, *J* = 15.2, 1H, CH₂), 3.57 (d, *J* = 15.2, 1H, CH₂), 3.78 (ddd, *J* = 9.6, 4.4, 2.0, 1H, H₅), 4.05 (dd, *J* = 12.4, 2.0, 1H, H₆), 4.28 (dd, *J* = 12.4, 4.4, 1H, H_{6'}), 4.80 (t, *J* = 9.6, 1H, H₂), 5.00 (t, *J* = 9.6, 1H, H₄), 5.17 (t, *J* = 9.6, 1H, H₁), 5.23 (t, *J* = 9.6, 1H, H₃), 6.17 (d, *J* = 9.6, 1H, NH), 7.19 (d, *J* = 7.2, 2H), 7.25-7.35 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) 20.3, 20.5, 20.6, 20.7, 43.9, 61.6, 68.1, 70.1, 72.5, 73.6, 78.3, 127.5, 129.1, 129.2, 133.7, 169.5, 169.8, 170.6, 170.6, 171.2; LRMS (FAB) 466 ((M + H)⁺, 100); HRMS (FAB) calcd for C₂₂H₂₈O₁₀N 466.1713 (M + H)⁺, found 466.1725.

2,3,4,6-Tetra-*O*-acetyl-1-*N*-[1-benzyl-*N*-(benzyloxy)carbonyl-L-aspart-4-oyl]-α-D-glucopyranosylamine (8).

Asparagine derivative **8** was prepared following the general coupling procedure outlined above employing azide (**1**) (100 mg, 0.268 mmol), Ph₃P (77.0 mg, 0.295

mmol), Z-Asp(SPy)-OBn (157 mg, 0.348 mmol) as the acylating reagent, and CuCl₂•2H₂O (60.0 mg, 0.348 mmol) as the additive. Purification of the residue by flash chromatography (hexanes:EtOAc, 1:1) gave 138 mg (75%) of **8** as a white solid: m.p. 159-160 °C; R_f = 0.30 (hexanes:EtOAc, 1:1); IR (CCl₄) 3429 (w), 3345 (w), 3035 (w),

2956 (w), 1754 (s), 1701 (s), 1685 (m), 1220 (s), 1042 (s); ^1H NMR (400 MHz, CDCl_3) 1.96 (s, 3H), 2.00 (s, 3H), 2.02 (s, 3H), 2.04 (s, 3H), 2.87 (dm, $J = 16$, 1H), 2.95 (dm, $J = 16$, 1H), 3.84 (m, 1H), 3.97 (dd, $J = 2, 8$, 1H), 4.24 (dd, $J = 4, 8$, 1H), 4.67 (m, 1H), 5.00-5.20 (m, 6H), 5.25-2.30 (m, 1H), 5.80 (t, $J = 6$, 1H), 5.92 (s, 1H), 6.57 (m, 1H), 7.30-7.35 (m, 10H); LRMS (EI) 686 ($(\text{M}^+, 12)$), 91 (100); HRMS (EI) calcd for $\text{C}_{33}\text{H}_{38}\text{O}_{14}\text{N}_2$ 686.2323, found 687.2305. ^1H NMR and ^{13}C NMR data were consistent with the data reported by Zhang *et al.*²

2,3,4-Tri-*O*-acetyl-6-*O*-[2,3,4,6-tetra-*O*-acetyl- α -D-galactopyranosyl]- β -D-glucopyranosyl acetate.

Melibiose (4.00 g, 11.1 mmol) was added to the refluxing mixture of NaOAc (4.55 g, 55.5 mmol) and Ac_2O (27 mL, 279 mmol). The solution was refluxed until one spot was observed by TLC. The solution was cooled to RT, diluted with 500 mL Et_2O , washed with 3 x 400 mL sat. aq. NaHCO_3 solution and 2 x 400 mL H_2O , dried over Na_2SO_4 , and concentrated in vacuo to give colorless gummy oil. The gummy oil was crystallized from mixture of Et_2O and petroleum ether to afford 7.01 g (93 %) of ~ 90% pure octa-*O*-acetate- -melibioside, which was used in the formation of -azide **9a** without further purification. IR (CCl_4) 2956 (w), 1750 (s), 1218 (s), 1038 (s); ^1H NMR (400 MHz, CDCl_3) 1.92 (s, 3H), 1.95 (s, 3H), 1.96 (s, 3H), 1.98 (s, 3H), 1.99 (s, 3H), 2.04 (s, 3H), 2.06 (s, 3H), 2.07 (s, 3H), 3.56 (dd, $J = 11.6, 2.4$ 1H, H6), 3.66 (dd, $J = 11.6, 4.4$, 1H, H6'), 3.72 (ddd, $J = 9.6, 4.4, 2.4$, 1H, H5), 3.95-4.05 (m, 2H, H6'), 4.10-4.10 (m, 1H, H5'), 4.95-5.10 (m, 4H, H2, H2', H1', H4), 5.18 (t, $J = 9.6$, 1H, H3), 5.28 (dd, $J = 10.0, 3.2$, 1H, H3'), 5.35-5.40 (m, 1H, H4'), 5.60 (d, $J = 8.4$, 1H, H1); ^{13}C

NMR (100 MHz, CDCl₃) 20.8, 20.8, 20.9, 20.9, 20.9, 20.9, 21.0, 21.0, 61.9, 65.8, 66.6, 67.6, 68.2, 68.3, 68.5, 70.4, 73.1, 73.7, 91.8, 96.6, 169.1, 169.5, 169.5, 170.0, 170.3, 170.4, 170.6, 170.8; LRMS (FAB) 685 ((M + Li)⁺, 100); HRMS (FAB) calcd for C₂₈H₃₈O₁₉Li 685.2167, found 685.2164.

2,3,4-Tri-*O*-acetyl-6-*O*-[2,3,4,6-tetra-*O*-acetyl- α -D-galactopyranosyl]- β -D-glucopyranosyl azide (9a).

The azide was prepared according to the procedure of Peto *et. al.*⁵ 2,3,4-Tri-*O*-acetyl-6-*O*-[2,3,4,6-tetra-*O*-acetyl- α -D-galactopyranosyl]- β -D-glucopyranosyl acetate (200 mg, 0.295 mmol) was dissolved in 10 mL of CH₂Cl₂.

Trimethylsilyl azide (55 μ L, 0.413 mmol) was added via syringe followed by SnCl₄ (35 μ L, 0.295 mmol). The solution was stirred for 20 h at 20 °C. The reaction mixture was diluted with 100 mL CH₂Cl₂, washed with 100 mL sat. aq. NaHCO₃ solution, and with 2x100 mL H₂O. The organic layer was dried over Na₂SO₄ and concentrated in vacuo to give crude product, which was crystallized from absolute ethanol to afford 144 mg (74 %) of azide **9a** as a white solid: m.p. 140-142 °C (lit. m.p. 142-143 °C)⁵; IR (CCl₄) 2964 (w), 2118 (s), 1758 (s), 1225 (s); ¹H NMR (400 MHz, CDCl₃) 1.97 (s, 3H), 2.00 (s, 3H), 2.03 (s, 6H), 2.06 (s, 3H), 2.10 (s, 3H), 2.12 (s, 3H), 3.55-3.60 (m, 1H, H5), 3.70-3.80 (m, 2H, H6), 4.07 (d, *J* = 6.8, 2H, H6'), 4.21 (t, *J* = 6.8, 1H, H5'), 4.60 (d, *J* = 9.0, 1H, H1), 4.90 (t, *J* = 9.0, 1H, H2), 5.08 (t, *J* = 9.0, 1H, H4), 5.10 (dd, *J* = 10.8, 3.8, 1H, H2'), 5.15 (d, *J* = 3.8, 1H, H1'), 5.21 (t, *J* = 9.0, 1H, H3), 5.35 (dd, *J* = 10.8, 3.8, 1H, H3'), 5.44 (d, *J* = 3.8, 1H, H4'); ¹³C NMR (100 MHz, CDCl₃) 20.5, 20.5, 20.6, 20.6, 20.6, 20.7, 20.8, 61.6, 66.0, 66.4, 67.4, 68.0, 68.0, 68.4, 70.6, 72.6, 74.8, 87.6, 96.2,

169.2, 169.2, 169.9, 170.1, 170.2, 170.4, 170.5; LRMS (FAB) 668 ((M + Li)⁺, 53); HRMS (FAB) calcd for C₂₆H₃₅O₁₇N₃Li 668.2127, found 668.2135. Since the coupling constant between H4' and H5' is smaller than 1 Hz, and it is undistinguishable on the spectrum, it was reported as no coupling. The ¹H-NMR and ¹³C-NMR data were consistent with the data reported by Petö *et al.*⁵

2,3,6-Tri-*O*-acetyl-4-*O*-[2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl- α -D-glucopyranosyl)- α -D-glucopyranosyl]- α -D-glucopyranosyl chloride.

Hendeca-*O*-acetyl- -maltotriose (1.80 g, 1.86 mmol) was dissolved in 20 mL of dry chloroform, followed by addition of 1M titanium tetrachloride solution (2.05 mL, 2.05 mmol) via syringe. The

solution was refluxed for 3 h, and cooled to RT. The reaction mixture was diluted with 100 mL CH₂Cl₂, washed twice with 100 mL water, filtered through a plug of silica gel, dried over Na₂SO₄, and concentrated in vacuo to give yellow oil. The oil was crystallized from mixture of Et₂O and petroleum ether to afford 1.53 g (87 %) of ~ 90% pure deca-*O*-acetyl- -maltotriosyl chloride as a white solid, and was used in the formation of azide **9b** without further purification. ¹H NMR (400 MHz, CDCl₃) 2.01 (s, 3H), 2.02 (s, 3H), 2.03 (s, 3H), 2.04 (s, 3H), 2.06 (s, 3H), 2.08 (s, 6H), 2.11 (s, 3H), 2.16 (s, 3H), 2.19 (s, 3H), 3.90-4.10 (m, 5H), 4.15-4.20 (m, 1H), 4.25-4.35 (m, 3H), 4.50-4.55 (m, 2H), 4.75 (dd, *J* = 10.4, 4.0, 1H, H2'), 4.86 (dd, *J* = 10.4, 4.0, 1H, H2''), 4.89 (dd, *J* = 10.4, 4.0, 1H, H2), 5.08 (t, *J* = 10.4, 1H, H4''), 5.30 (d, *J* = 4.0, 1H, H1'), 5.37 (t, *J* = 10.4, 1H, H3''), 5.40-5.45 (m, 1H, H3'), 5.43 (d, *J* = 4.0, 1H, H1''), 5.62 (t, *J* = 10.4, 1H, H3), 6.18 (d, *J* = 4.0, 1H, H1); ¹³C NMR (100 MHz, CDCl₃) 20.5, 20.6, 20.8, 20.9,

20.9, 21.0, 61.3, 62.1, 62.1, 67.9, 68.4, 69.2, 69.3, 70.1, 70.4, 70.9, 71.2, 71.6, 71.8, 72.2, 72.8, 89.7, 95.6, 95.9, 169.4, 169.5, 169.7, 169.8, 170.0, 170.3, 170.4, 170.5, 170.7, 170.8; LRMS (FAB) 1075 ((M + Cs)⁺, 45); HRMS (FAB) calcd for C₃₈H₅₁O₂₅ClCs 1075.1462, found 1075.1483.

2,3,6-Tri-*O*-acetyl-4-*O*-[2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl- α -D-glucopyranosyl)- α -D-glucopyranosyl]- β -D-glucopyranosyl azide (9b**).**

The deca-*O*-acetyl- β -maltotriosyl azide was prepared according to the procedure of Soli *et al.*¹ The deca-*O*-acetyl- β -maltotriosyl chloride (1.52 g, 1.61 mmol) was dissolved in 15 mL of THF. Trimethylsilyl azide (278 μ L, 2.10 mmol)

was added via syringe followed by TBAF (2.10 mL, 2.10 mmol). The solution was stirred for 29 h at 65 °C. The reaction was cooled to ambient temperature, filtered through a plug of silica gel, dried over Na₂SO₄, and concentrated in vacuo to give yellow oil. The oil was crystallized from absolute ethanol to afford 1.22 mg (80 %) of β -azide **9b** as a white solid: IR (CCl₄) 2956 (w), 2117 (m), 1759 (s), 1368 (s), 1227 (s), 1053 (s); ¹H NMR (600 MHz, CDCl₃) 1.97 (s, 3H), 1.98 (s, 3H), 1.98 (s, 3H), 1.99 (s, 3H), 2.01 (s, 3H), 2.03 (s, 3H), 2.03 (s, 3H), 2.08 (s, 3H), 2.14 (s, 3H), 2.17 (s, 3H), 3.80 (ddd, *J* = 2.7, 4.5, 12.4, 1H, H5), 3.85-4.00 (m, 4H, H5'', H5', H4, H4'), 4.03 (dd, *J* = 2.3, 12.4, 1H, H6''), 4.16 (dd, *J* = 3.6, 12.4, 1H, H6'), 4.23 (dd, *J* = 3.6, 12.4, 1H, H6''), 4.30 (dd, *J* = 4.5, 12.4, 1H, H6), 4.44 (dd, *J* = 2.3, 12.4, 1H, H6'), 4.48 (dd, *J* = 2.7, 12.4, 1H, H6), 4.69 (d, *J* = 8.9, 1H, H1), 4.72 (dd, *J* = 4.1, 10.2, 1H, H2'), 4.76 (t, *J* = 8.9, 1H, H2), 4.83 (dd, *J* = 4.1, 10.2, 1H, H2''), 5.05 (t, *J* = 10.2, 1H, H4''), 5.20-5.25 (m, 2H, H3, H1'),

5.30-5.37 (m, 2H, H3'', H3'), 5.38 (d, $J = 4.1$, 1H, H1'); ^{13}C NMR (100 MHz, CDCl_3) 20.6, 20.6, 20.7, 20.8, 20.8, 61.3, 62.2, 62.7, 67.8, 68.5, 69.0, 69.3, 70.0, 70.4, 71.5, 71.6, 72.4, 73.4, 74.1, 74.9, 87.4, 95.6, 95.9, 169.4, 169.5, 169.7, 169.8, 170.0, 170.3, 170.4, 170.5, 170.6, 170.6; LRMS (FAB) 956 (($\text{M} + \text{Li}$) $^+$, 100); HRMS (FAB) calcd for $\text{C}_{38}\text{H}_{51}\text{N}_3\text{O}_{25}\text{Li}$ 956.2972, found 956.2997.

2,3,4-Tri-*O*-acetyl-6-*O*-[2,3,4,6-tetra-*O*-acetyl- α -D-galactopyranosyl]-1-*N*-phenyl acetyl- α -D-glucopyranosylamine (10a).

Hepta-*O*-acetyl-1-*N*-phenyl acetyl melibiosyl amine

(**10a**) was prepared following the general coupling procedure outlined above employing α -azide (**9a**) (125 mg, 0.189 mmol), Ph_3P (55.0 mg, 0.208 mmol), 2-thiopyridyl phenylacetate (57.0 mg, 0.246 mmol) as the

acylating reagent, and $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (42.1 mg, 0.246 mmol) as the additive. Purification of the residue by flash chromatography (hexanes:EtOAc, 1:1) gave 110 mg (77%) of **10a** as a white foam: $R_f = 0.19$ (hexanes:EtOAc, 1:1); IR (CCl_4) 3398 (w), 3030 (w), 2926 (m), 1754 (s), 1706 (m), 1370 (s), 1227 (s); ^1H NMR (400 MHz, CDCl_3) 1.96 (s, 3H), 1.99 (s, 3H), 2.01 (s, 3H), 2.02 (s, 3H), 2.04 (s, 3H), 2.09 (s, 3H), 2.12 (s, 3H), 3.60-3.75 (m, 5H, H5, H6, H6, CH₂), 4.00 (dd, $J = 11.2, 6.4$, 1H, H6'), 4.11 (dd, $J = 11.2, 6.4$, 1H, H6'), 4.22 (t, $J = 6.4$, 1H, H5'), 4.98 (t, $J = 9.0$, 1H, H4), 4.99 (dd, $J = 9.0, 5.0$, 1H, H2), 5.00-5.10 (m, 3H, H3, H1', H2'), 5.29 (dd, $J = 8.8, 3.0$, 1H, H3'), 5.44 (d, $J = 3.0$, 1H, H4'), 5.72 (dd, $J = 7.6, 5.0$, 1H, H1), 6.28 (d, $J = 7.6$, 1H, NH), 7.25-7.30 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3) 20.3, 20.6, 20.7, 20.7, 20.8, 43.8, 61.5, 66.3, 66.6, 67.4, 68.0, 68.1, 68.4, 69.0, 69.0, 69.9, 73.9, 96.4, 127.6, 129.1, 129.1, 134.3, 168.9, 169.3, 169.9,

170.1, 170.2, 170.5, 170.7, 171.4; LRMS (FAB) 760 ((M + Li)⁺, 100); HRMS (FAB) calcd for C₃₄H₄₃NO₁₈Li 760.2640, found 760.2639.

2,3,6-Tri-*O*-acetyl-4-*O*-[2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl- α -D-glucopyranosyl)- α -D-glucopyranosyl]-1-*N*-phenyl acetyl- α -D-glucopyranosylamine (10b).

Deca-*O*-acetyl-1-*N*-phenyl acetyl maltotriosyl amine (**10b**) was prepared following the general coupling procedure outlined above employing -azide **9b** (200 mg, 0.211 mmol), Ph₃P (61.0 mg, 0.232

mmol), 2-thiopyridyl phenylacetate (63.0 mg, 0.275 mmol) as the acylating reagent, and CuCl₂•2H₂O (47.0 mg, 0.275 mmol) as the additive. Purification of the residue by flash chromatography (hexanes:EtOAc, 2:3) gave 138 mg (63%) of **10b** as a white foam: R_f = 0.22 (hexanes:EtOAc, 2:3); IR (CCl₄) 3429 (w), 3030 (w), 2958 (w), 1758 (s), 1699 (m), 1368 (s), 1233 (s), 1040 (s); ¹H NMR (400 MHz, CDCl₃) 1.90 (s, 3H), 1.97 (s, 3H), 1.99 (s, 3H), 2.00 (s, 3H), 2.02 (s, 3H), 2.02 (s, 3H), 2.03 (s, 3H), 2.08 (s, 3H), 2.11 (s, 3H), 2.11 (s, 3H), 3.65-3.70 (m, 3H, CH₂, H₄), 3.85-4.00 (m, 4H, H₄', H₅, H₅', H₅''), 4.03 (dd, *J* = 2.0, 12.4, 1H, H₆''), 4.11 (dd, *J* = 4.0, 12.4, 1H, H₆'), 4.18 (dd, *J* = 5.6, 12.4, 1H, H₆), 4.23 (dd, *J* = 3.6, 12.4, 1H, H₆''), 4.29 (dd, *J* = 3.2, 12.4, 1H, H₆), 4.43 (dd, *J* = 2.0, 12.4, 1H, H₆'), 4.73 (dd, *J* = 4.0, 10.0, 1H, H₂'), 4.85 (dd, *J* = 4.0, 10.0, 1H, H₂''), 4.90 (dd, *J* = 4.4, 7.0, 1H, H₂), 4.96 (m, 1H, H₃), 5.06 (t, *J* = 10.0, 1H, H₄''), 5.15 (d, *J* = 4.0, 1H, H₁'), 5.33 (t, *J* = 10.0, 1H, H₃''), 5.34 (t, *J* = 10.0, 1H, H₃'), 5.38 (d, *J* = 4.0, 1H, H₁''), 5.76 (dd, *J* = 4.4, 8.4, 1H, H₁), 6.25 (d, *J* = 8.4, 1H, NH), 7.29-7.43 (m,

5H, Ph); ^{13}C NMR (100 MHz, CDCl_3) 20.3, 20.4, 20.6, 20.6, 20.6, 20.7, 20.8, 20.8, 20.8, 20.9, 43.9, 61.3, 62.4, 63.0, 67.8, 68.0, 68.5, 68.8, 69.4, 69.8, 70.1, 70.3, 70.5, 71.9, 72.4, 72.8, 74.3, 95.9, 96.4, 127.7, 129.3, 129.4, 134.2, 169.2, 169.4, 169.7, 169.8, 169.9, 170.3, 170.4, 170.4, 170.5, 170.6, 171.1; LRMS (FAB) 1174 ($(\text{M} + \text{Cs})^+$, 12); HRMS (FAB) calcd for $\text{C}_{46}\text{H}_{59}\text{NO}_{26}\text{Cs}$ 1174.2380, found 1174.2327.

1-Succinimidyl phenylacetate.

The ester was prepared according to the procedure of Stefanowicz *et. al.*³ and the recrystallization (hexanes:benzene) gave the ester as white solid: m.p. 114-116 °C (lit.³ 118-119 °C); R_f = 0.30

(hexanes:EtOAc, 2:1); IR (CCl_4) 3034 (w), 2936 (m), 2858 (w), 1747 (s), 1704 (m), 1069 (m); ^1H NMR (400 MHz, CDCl_3) 2.80 (s, 4H), 3.92 (s, 2H), 7.20-7.35 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3) 25.5, 37.6, 127.8, 128.8, 129.2, 131.4, 166.7, 169.0; LRMS (EI) 233 ($(\text{M}^+$, 63), 91 (100); HRMS (EI) calcd for $\text{C}_{12}\text{H}_{11}\text{O}_4\text{N}$ 233.0688, found 233.0699.

Pentafluorophenyl phenylacetate.

The ester was prepared according to the procedure used for 1-succinimidyl phenylacetate and the purification by flash chromatography (hexanes:EtOAc, 4:1) gave the ester as

colorless oil: R_f = 0.62 (hexanes:EtOAc, 4:1); IR (CCl_4) 3068 (w), 3034 (m), 2936 (w), 1790 (s), 1704 (m), 1054 (m); ^1H NMR (400 MHz, CDCl_3) 3.98 (s, 2H), 7.30-7.45 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3) 40.0, 125.1(t, J = 13.8), 127.7, 128.8, 129.2, 132.0, 137.8 (dm, J = 250), 139.5 (dm, J = 250), 141.1 (dm, J = 250), 167.5; LRMS (EI) 302

((M⁺, 8), 91 (100); HRMS (FAB) calcd for C₁₄H₈O₂F₅ 303.0444 (M + H)⁺, found 303.0455.

2-Thiopyridyl phenylacetate.

The ester was prepared according to the procedure of Watanabe *et. al.*⁴

and the purification by flash chromatography (hexanes:EtOAc, 4:1) gave the ester as dark orange liquid: R_f = 0.35

(hexanes:EtOAc, 4:1); IR (CCl₄) 3070 (w), 3033 (m), 2912 (w), 1708 (s), 1420 (s); ¹H NMR (400 MHz, CDCl₃) 3.93 (s, 2H), 7.20-7.25 (m, 1H), 7.25-7.35 (m, 5H), 7.54 (d, *J* = 8, 1H), 7.66 (td, *J* = 8, *J* = 1, 1H), 8.58 (dd, *J* = 5, *J* = 1, 1H); ¹³C NMR (100 MHz, CDCl₃) 51.0, 124.1, 128.1, 129.2, 130.2, 130.6, 133.2, 137.7, 150.8, 151.8, 194.9; LRMS (EI) 229 ((M⁺, 21), 118 (100), 91 (80); HRMS (EI) calcd for C₁₄H₈O₂F₅ 229.0561, found 229.0553.

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Table. Acylations of Isoxazoline **3**^a

entry	reagent ^b	equiv	additive ^b	temp (°C)	yield (%) ^c	/ ^d
1		4	-	83	6 (60)	1/3
2	"	2	DIEA ^e	83	6 (25)	6/1
3		1.3	-	83	6 (65)	17/1
4		4	-	83	7 (51)	>19/1
5	"	1.3	-	83	7 (47)	11/1
6		4	-	83	7 (25)	1/4
7		4	-	83	7 (25)	1/3
8		1.3	-	83	7 (67)	5/1
9	"	1.3	-	30	7 (50)	5/1
10	"	1.3	ZnCl ₂	30	7 (60)	1/3
11	"	1.3	NiCl ₂	30	7 (30)	1/1
12	"	1.3	FeCl ₃	30	7 (66)	9/1
13	"	1.3	CuCl ₂ ·2H ₂ O	30	7 (80)	98/2

^a All reactions were performed in 1,2-dichloroethane in the presence of 4Å molecular sieves. All reactions run for 24h,

except entries 1 and 2 (48h). ^b Reagents and additives were added into *in situ* formed isoxazoline **3**. Additives were

added after reagents. ^c Isolated yield (>95%). ^d Determined by ¹H NMR spectroscopy or HPLC analysis. ^e

Diisopropylethyl amine.

S14

14.1
20.6
20.7
20.7

63.1
67.3
67.7
70.7
75.9
76.7
77.0
77.3

92.8

168.6
169.4
169.5
170.6
ppm

S15

S18

S20

8

S26

9b

ppm

S29

S30

S31

6.002
3.231
9.223
6.231
2.994
2.985

3.120
1.008
1.023
1.031
1.096
1.091
1.070
1.084
1.078
2.072
1.050
0.993
3.976
2.950

5.089

Integral

ppm

1-succinimidyl phenylacetate

S33

1-succinimidyl phenylacetate

pentafluorophenyl phenylacetate

S35

pentafluorophenyl phenylacetate

pentafluorophenyl phenylacetate

2-thiopyridyl phenylacetate

S38

2-thiopyridyl phenylacetate