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Facile synthesis of glycosylated Fmoc amino acid building blocks assisted by microwave irradiation

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Abstract

The synthesis of glycosylated Fmoc amino acids by reaction of mono- and disaccharide peracetates with Fmoc amino acids having free carboxyl groups was rapidly promoted by Lewis acids (SnCl₄, BF₃·Et₂O) under microwave irradiation. The products are useful building blocks for the synthesis of glycopeptides.

Keywords

Fmoc amino acids; Glycosylation; Microwave irradiation

Carbohydrates are important components of glycoproteins, playing pivotal roles in many biological processes, such as cell adhesion, inflammation, the immune response, and tumor metastasis.¹ It is therefore of great interest to synthesize glycopeptides. Currently, there are two approaches to synthesize glycopeptides including the convergent approach² and the building block approach.³ The former is based on glycosylation of a peptide in solution or on solid-phase. This direct O-glycosylation of a peptide often results in low yields.⁴ Alternatively, the versatile and general building block approach has a lot of advantages. A glycosylated amino acid building block is easily introduced into a solid phase peptide synthesis using peptide chemistry. This method has been widely applied to prepare a large variety of complex glycopeptides and even larger glycopeptides libraries.⁵

Several methods exist for the preparation of glycosylated Fmoc amino acid building blocks.⁶ However, the previous approaches to glycosylated amino acids require the synthetic glycosyl donors and amino acids to be protected at both the α -carboxyl and α -amino groups. Kihlberg and co-workers reported that Fmoc amino acids with unprotected carboxyl groups could be directly glycosylated with commercial carbohydrate 1, 2-*trans* peracetates.⁷ However, these methods suffered from low yields or long reaction times. Microwave irradiation has been demonstrated to dramatically accelerate the conversion in synthetic chemistry.⁸ Seibel et al. reported on the glycosylation of Fmoc-Ser-OBn in a microwave oven.⁹ These building blocks cannot be directly used for the solid-phase synthesis of glycopeptides. Therefore, the direct synthesis of glycosylated Fmoc amino acids from Fmoc

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amino acids with unprotected carboxyl groups and mono- and disaccharide peracetates should be efficiently carried out under microwave irradiation.

It has been reported that Fmoc amino acids are glycosylated with peracetylated glycosides under the influence of Lewis acids such as FeCl_3 , SnCl_4 or $\text{BF}_3 \cdot \text{Et}_2\text{O}$ as promoters and CH_2Cl_2 , CH_3CN and toluene as solvents.^{7, 9} A microwave reactor (Personal Chemistry, Emrys Optimizer) is compatible with various solvents and reaction temperatures. Initially, glycosylated Fmoc-Ser-OH with β -D-galactose pentaacetate was investigated to determine which Lewis acid and solvent could afford higher yield (Table 1) using microwave reactor. Fmoc-Ser-OH (0.01 mmol) and β -D-galactose pentaacetate (0.01 mmol) were added to a 5-mL microwave vial, followed by addition of 2 mL of solvent and Lewis acid (0.01 mmol). The mixture was irradiated in the microwave oven for 5 min. The product **1** was purified by preparative HPLC and confirmed to be of the β -configuration by ^1H NMR spectroscopy. The reaction conversion was directly determined by HPLC. FeCl_3 provided lower conversion, suggesting heterogeneous system ($\text{FeCl}_3/\text{CH}_2\text{ClCH}_2\text{Cl}$ or C_6H_6) may limit the reaction rates. The use of CH_2Cl_2 as solvent resulted in a higher conversion than that of reactions performed in $\text{CH}_2\text{ClCH}_2\text{Cl}$, C_6H_6 or CH_3CN .

In order to further improve yields, a number of conditions including reaction time and promoter (Table 2) were conducted in CH_2Cl_2 . An increase in the amount of SnCl_4 from 1 equivalent to 2 equivalents resulted in higher glycosylation. A further increase in the amount of SnCl_4 , however, did not increase the yield of glycosylated Fmoc amino acid. Interestingly, variations in the amount of $\text{BF}_3 \cdot \text{Et}_2\text{O}$ did not lead to any change in yield, and prolonged microwave irradiation was discovered to give side products. Furthermore, a wider range of amino acids and mono- and oligosaccharides were explored to synthesize various glycosylated Fmoc amino acid building blocks under microwave irradiation for 5 min using SnCl_4 or $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (2 equiv) as promoters and CH_2Cl_2 as solvent. Their conversions are presented in Table 3. Glycosylation of Fmoc-Ser-OH with different peracetylated glycosylation donors such as galactose, glucose, xylose, lactose and maltose gave higher yields (52 – 72%). In comparison, lower yields (31 – 47%) were obtained in the glycosylation of Fmoc-Tyr-OH under identical conditions. It was noteworthy that disaccharide peracetates of lactose and maltose as glycosyl donors were found to give lower yields than monosaccharide peracetates of galactose, glucose, and xylose.

In conclusion, we have developed a microwave-assisted glycosylation of Fmoc amino acids with unprotected carboxyl groups, which can be used to efficiently synthesize glycosylated Fmoc amino acid building blocks. To our knowledge, this is the first report of glycosylation of Fmoc amino acids without prior protection of the amino acid carboxyl groups under microwave conditions. The reactions were readily carried out under microwave irradiation for only 5 min, resulting in β -glycosides in moderate yields. The products could be easily purified via flash chromatography. Furthermore Fmoc amino acids and carbohydrate peracetates are commercially available. This method provides easy access to numerous valuable building blocks, which can be directly used for constructing parallel and combinatorial glycopeptide libraries as well as the synthesis of various glycopeptides.

1. Experimental

1.1. General Methods

All solvents and chemical reagents were purchased from Sigma – Aldrich Chemical Co. (Milwaukee, WI) and were of analytical grade. NMR spectra were recorded on a Bruker DRX spectrometer in $\text{DMSO}-d_6$ at 25 °C (500 M Hz for ^1H NMR). HRMS was performed with a Finnigan LTQ FT™ instrument. Analytical HPLC was performed on a Waters 2996 HPLC system equipped with a 4.6×150 mm Waters Xterra® MS C18 5.0- μm column, and

employed a 20-min gradient from 100% aqueous H₂O (0.1% TFA) to 100% CH₃CN (0.1% TFA) at a flow rate of 1.0 mL/min. Preparative HPLC was performed on a System Gold 126NMP Solvent Module (Beckman) with a C18 column (Vydac, 5μM, 2.5 cm i.d. × 25 cm). A gradient elution of 0 – 60% B over 25 min, followed by 60 – 100% B over 25 min, followed by 100% B for 5 min, was used at a flow rate of 7 mL/min (solvent A: H₂O – 0.1% TFA; B: Acetonitrile – 0.1% TFA).

1.2. General procedure for glycosylation of Fmoc amino acids

Fmoc amino acids (0.2 mmol) and mono- and disaccharide peracetates (0.26 mmol) were added to a 5-mL round-bottom microwave vial, followed by addition of 3 mL of CH₂Cl₂ and SnCl₄, or BF₃·Et₂O (0.4 mmol). The vessel was sealed and heated to 100 °C for 5 min in a microwave reactor (Personal Chemistry, Emrys Optimizer). The reaction temperature increased from 25 to 100 °C in 90 s and was maintained at 100 °C for the duration of the reaction. The reaction conversion was determined by analytical HPLC. The mixture was concentrated and purified by preparative HPLC. All of the products were characterized by ESIMS and ¹H NMR spectroscopy.

1.3. N^α-(9-Fluorenylmethoxycarbonyl)-3-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-L-serine (1)

White powder, Purity, 97%; ¹H NMR (500 M Hz, DMSO-*d*₆): δ 7.90(d, *J* 5 Hz, 2H), 7.72(d, *J* 10 Hz, 2H), 7.43 (m, 2H), 7.33 (m, 2H), 5.25 (d, *J* 2.5 Hz, 1H), 5.15 (dd, *J* 9 Hz, 3.0 Hz, 1H), 4.91 (dd, *J* 9 Hz, 6.5 Hz, 1H), 4.76 (d, *J* 6.5 Hz, 1H), 4.28–4.34 (m, 2H), 4.19–4.24 (m, 3H), 4.04 (m, 1H), 3.90 (m, 1H), 3.79 (m, 1H), 2.11 (s, 3H), 2.00 (s, 3H), 1.93 (s, 3H), 1.91 (s, 3H). HRESIFTMS [M+K]⁺: calcd for C₃₂H₃₅KNO₁₄ 696.1695; found: 696.1697

1.4. N^α-(9-Fluorenylmethoxycarbonyl)-3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-L-serine (2)

White powder, purity, 99%; ¹H NMR (500 M Hz, DMSO-*d*₆): δ 7.90(d, *J* 5 Hz, 2H), 7.72 (d, *J* 5 Hz, 2H), 7.43 (m, 2H), 7.33 (m, 2H), 5.25 (t, *J* 10 Hz, 1H), 4.90 (dd, 1H), 4.87 (d, *J* 10 Hz, 1H), 4.73 (t, *J* 5 Hz, 1H), 4.16–4.33 (overlap, 5H), 3.99 (m, 1H), 3.90 (m, 1H), 3.77 (dd, 1H), 2.01 (s, 3H), 1.98(s, 3H), 1.93(s, 3H), 1.90(s, 3H). HRESIFTMS [M+K]⁺: calcd for C₃₂H₃₅KNO₁₄ 696.1695; found: 696.1696.

1.5. N^α-(9-Fluorenylmethoxycarbonyl)-3-O-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-L-serine (3)

White powder, purity, 96%; ¹H NMR (500 M Hz, DMSO-*d*₆): δ 7.90(d, *J* 10 Hz, 2H), 7.73(d, *J* 10 Hz, 2H), 7.43(m, 2H), 7.33(m, 2H), 5.12(t, *J* 5 Hz, 1H), 4.80(d, *J* 5 Hz, 1H), 4.73(m, 2H), 4.25–4.33(m, 2H), 4.20–4.23(m, 2H), 3.88(m, 1H), 3.74(m, 1H), 2.00(s, 3H), 1.96(s, 3H), 1.93(s, 3H). HRESIFTMS [M+K]⁺: calcd for C₂₉H₃₁KNO₁₂, 624.1483, found: 624.1486

1.6. N^α-(9-Fluorenylmethoxycarbonyl)-3-O-[(2,3,6-tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-β-D-glucopyranosyl]-L-serine (4)

White powder, purity, 98%; ¹H NMR (500 M Hz, DMSO-*d*₆): δ 7.90(d, *J* 10 Hz, 2H), 7.71(d, *J* 10 Hz, 2H), 7.43(m, 2H), 7.33(m, 2H), 5.22(brs, 1H), 5.15(m, 2H), 4.84(dd, 1H), 4.80(d, *J* 5.0 Hz, 1H), 4.73(d, *J* 10 Hz, 1H), 4.65(dd, 1H), 4.29(m, 3H), 4.21(m, 3H), 4.05(m, 1H), 4.00(m, 2H), 3.81–3.88(m, 2H), 3.75–3.79(m, 2H), 2.11(s, 3H), 2.07(s, 3H), 2.00(s, 6H), 1.93(s, 3H), 1.89(s, 6H). HRESIFTMS [M+K]⁺: calcd for C₄₄H₅₁KNO₂₂, 984.2540, found: 984.2542.

1.7. N^α-(9-Fluorenylmethoxycarbonyl)-3-O-[(2,3,6-tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-β-D-glucopyranosyl]-L-serine (5)

White powder, purity, 97%; ¹H NMR (500 M Hz, DMSO-*d*₆): δ 7.90(d, *J* 10 Hz, 2H), 7.71(d, *J* 10 Hz, 2H), 7.43(m, 2H), 7.33(m, 2H), 5.29(m, 1H), 5.27(bris, 1H), 5.22(t, *J* 10 Hz, 1H), 4.98(dd, 1H), 4.87(dd, 1H), 4.84(d, *J* 10 Hz, 1H), 4.63(t, *J* 5 Hz, 1H), 4.14–4.36(m, 4H), 3.86–4.01(m, 4H), 3.76(dd, 1H), 3.40–3.70(overlap), 2.06(s, 3H), 2.01(s, 3H), 1.98(s, 6H), 1.95(s, 3H), 1.91(s, 3H), 1.88(s, 3H). HRESIFTMS [M+K]⁺: calcd for C₄₄H₅₁KNO₂₂, 984.2540, found: 984.2542.

1.8. N^α-(9-Fluorenylmethoxycarbonyl)-3-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-L-threonine (6)

White powder, purity, 99%; ¹H NMR(500 M Hz, DMSO-*d*₆): δ 7.90(d, *J* 10 Hz, 2H), 7.73(d, *J* 10 Hz, 2H), 7.42(t, *J* 10 Hz, 2H), 7.33(t, *J* 10 Hz, 2H), 6.60(d, *J* 5 Hz, 1H), 5.25(d, *J* 5.0 Hz, 1H), 5.17(dd, *J* 10 Hz, 5.0 Hz, 1H), 4.87(dd, 1H), 4.79(d, *J* 10 Hz, 1H), 4.30(m, 1H), 4.29(m, 1H), 4.22(m, 2H), 4.17(t, *J* 10 Hz, 1H), 4.10(dd, *J* 10 Hz, 5.0 Hz, 1H), 4.02(t, *J* 5 Hz, 2H), 2.09(s, 3H), 1.99(s, 3H), 1.92(s, 3H), 1.13(d, *J* 5 Hz, 3H). HRESIFTMS [M+K]⁺: calcd for C₃₃H₃₇KNO₁₄, 710.1851, found: 710.1854.

1.9. N^α-(9-Fluorenylmethoxycarbonyl)-3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-L-threonine (7)

White powder, purity, 97%; ¹H NMR(500 M Hz, DMSO-*d*₆): δ 7.90(d, *J* 10 Hz, 2H), 7.74(d, *J* 5 Hz, 2H), 7.42(t, *J* 5 Hz, 2H), 7.32(t, *J* 5 Hz, 2H), 6.75(d, *J* 5 Hz, 1H), 5.26(t, *J* 10 Hz, 1H), 4.90(dd, 1H), 4.88(d, *J* 10 Hz, 1H), 4.70(t, *J* 5 Hz, 1H), 4.27–4.31(m, 2H), 4.17–4.24(m, 3H), 4.11(dd, 1H), 3.97(m, 1H), 1.98(s, 6H), 1.97(s, 3H), 1.94(s, 3H), 1.13(d, *J* 5 Hz, 3H). HRESIFTMS [M+K]⁺: calcd for C₃₃H₃₇KNO₁₄, 710.1851, found: 710.1854.

1.10. N^α-(9-Fluorenylmethoxycarbonyl)-3-O-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-L-threonine (8)

White powder, purity, 98%; ¹H NMR (500 M Hz, DMSO-*d*₆): δ 7.90(d, *J* 10 Hz, 2H), 7.73(d, *J* 5 Hz, 2H), 7.42(t, *J* 5 Hz, 2H), 7.32(t, *J* 5 Hz, 2H), 6.75(d, *J* 5 Hz, 1H), 5.10(t, *J* 5 Hz, 1H), 4.76(d, *J* 5 Hz, 1H) 4.75(m, 1H), 4.69(t, *J* 5 Hz, 1H), 4.23–4.31(m, 4H), 4.12(dd, *J* 5 Hz, 5 Hz, 1H), 4.93(dd, *J* 5 Hz, 5 Hz, 1H), 2.01(s, 3H), 2.00(s, 6H), 1.12(d, *J* 5 Hz, 3H). HRESIFTMS [M + K]⁺:calcd for C₃₀H₃₃KNO₁₂, 638.1640, found: 638.1642.

1.11. N^α-(9-Fluorenylmethoxycarbonyl)-3-O-[(2,3,6-tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)- β-D-glucopyranosyl]-L-threonine (9)

White powder, purity, 96%; ¹H NMR(500 M Hz, DMSO-*d*₆): δ 7.90(d, *J* 10 Hz, 2H), 7.72(d, *J* 10 Hz, 2H), 7.42(t, *J* 10 Hz, 5 Hz, 2H), 7.33(t, *J* 5 Hz, 2H), 6.69(d, *J* 10 Hz, 1H), 5.22(bris, 1H), 5.12–5.17(m, 2H), 4.82–4.85(m, 2H), 4.73(d, *J* 5 Hz, 1H), 4.63(t, *J* 10 Hz, 1H), 4.22–4.29(m, 6H), 4.11(dd, 1H), 4.00–4.05(m, 3H), 3.75–3.79(m, 2H), 2.10(s, 3H), 2.05(s, 3H), 2.00(s, 6H), 1.97(s, 3H), 1.95(s, 3H), 1.89(s, 3H), 1.12(d, *J* 5 Hz, 3H). HRESIFTMS [M+H]⁺: calcd for C₄₅H₅₄NO₂₂, 960.3137, found: 960.3140.

1.12. N^α-(9-Fluorenylmethoxycarbonyl)-3-O-[(2,3,6-tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)- β-D-glucopyranosyl]-L-threonine (10)

White powder, purity, 98%; ¹H NMR(500 M Hz, DMSO-*d*₆): δ 7.89(d, *J* 10 Hz, 2H), 7.73(d, *J* 10 Hz, 5 Hz, 2H), 7.42(t, *J* 10 Hz, 2H), 7.32(t, *J* 5 Hz, 2H), 6.78(d, *J* 5 Hz, 1H), 5.29(dd, 1H), 5.27(bris, 1H), 4.98(t, *J* 10 Hz, 1H), 4.88(dd, 1H), 4.87(d, *J* 10 Hz, 1H), 4.61(t, *J* 10 Hz, 1H), 4.10–4.31(m, 7H), 3.98–4.09(m, 5H), 2.05(s, 3H), 2.00(s, 3H), 1.99(s, 3H), 1.98(s, 3H), 1.95(s, 3H), 1.94(s, 6H), 1.13(d, *J* 10 Hz, 3H). HRESIFTMS [M+H]⁺: calcd for C₄₅H₅₄NO₂₂, 960.3137, found: 960.3140.

1.13. N^α-(9-Fluorenylmethoxycarbonyl)-O-(2, 3, 4, 6-tetra-O-acetyl-β-D-galactopyranosyl)-L-tyrosine (11)

White powder, purity, 99%; ¹H NMR(500 M Hz, DMSO-*d*₆): δ 7.88(d, *J* 10 Hz, 2H), 7.63(dd, *J* 10 Hz, 5 Hz, 2H), 7.41(m, 2H), 7.31(m, 2H), 7.23(d, *J* 10 Hz, 2H), 7.00(d, *J* 10 Hz, 2H), 5.73(d, *J* 5 Hz, 1H), 5.40(dd, 1H), 5.39(brs, 1H), 5.32(dd, 1H), 5.15(d, *J* 5 Hz, 1H), 5.13(t, *J* 5 Hz, 1H), 4.28(dd, 1H), 4.12–4.20(m, 3H), 4.01(dd, *J* 5 Hz, 5 Hz, 1H), 3.90(dd, *J* 5 Hz, 5 Hz, 1H), 3.05(dd, *J* 10 Hz, 5 Hz, 1H), 3.81(dd, *J* 10 Hz, 5 Hz, 1H), 2.14(s, 3H), 2.04(s, 3H), 1.97(s, 3H), 1.83(s, 3H). HRESIFTMS [M + H]⁺: calcd for C₃₈H₄₀NO₁₄, 734.2449, found: 734.2451.

1.14. N^α-(9-Fluorenylmethoxycarbonyl)-O-(2,3,4,6-tetra-O-acetyl-β-D-gulcopyranosyl)-L-tyrosine (12)

White powder, purity, 97%; ¹H NMR(500 M Hz, DMSO-*d*₆): δ 7.88(d, *J* 5 Hz, 2H), 7.64(d, *J* 5 Hz, 2H), 7.40(m, 2H), 7.30(m, 2H), 7.22(d, *J* 5 Hz, 2H), 6.90(d, *J* 5 Hz, 2H), 5.73(d, *J* 5 Hz, 1H), 5.45(dd, 1H), 5.37(t, *J* 5 Hz, 1H), 5.05(dd, 1H), 5.03(d, *J* 10 Hz, 1H), 4.97(t, *J* 5 Hz, 1H), 4.10–4.19(m, 5H), 4.01(dd, 1H), 3.03(dd, 1H), 2.83(dd, 1H), 2.00(s, 3H), 1.99(s, 3H), 1.97(s, 3H), 1.96(s, 3H). HRESIFTMS [M + H]⁺: calcd for C₃₈H₄₀NO₁₄, 734.2449, found: 734.2451.

1.15. N^α-(9-Fluorenylmethoxycarbonyl)-O-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-L-tyrosine (13)

White powder, purity, 98%; ¹H NMR(500 M Hz, DMSO-*d*₆): δ 7.88(d, *J* 5 Hz, 2H), 7.64(d, *J* 5 Hz, 2H), 7.40(m, 2H), 7.30(m, 2H), 7.22(d, *J* 10 Hz, 2H), 7.01(d, *J* 10 Hz, 2H), 5.74(brs, 1H), 5.46(t, *J* 10 Hz, 1H), 5.03(d, *J* 10 Hz, 1H), 5.02(m, 1H), 5.01(m, 1H), 4.92(m, 1H), 4.11–4.21(m, 5H), 3.02(dd, 1H), 2.81(dd, 1H), 2.02(s, 3H), 2.00(s, 6H). HRESIFTMS [M + K]⁺: calcd for C₃₅H₃₅KNO₁₂, 700.1796, found: 700.1798.

1.16. N^α-(9-Fluorenylmethoxycarbonyl)-O-[(2,3,6-tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-β-D-glucopyranosyl]-L-tyrosine (14)

White powder, purity, 99%; ¹H NMR(500 M Hz, DMSO-*d*₆): δ 7.88(d, *J* 5 Hz, 2H), 7.64(d, *J* 5 Hz, 2H), 7.40(m, 2H), 7.29(m, 2H), 7.20(d, *J* 10 Hz, 2H), 7.02(d, *J* 5 Hz, 1H), 6.87(d, *J* 10 Hz, 1H), 5.26(dd, 1H), 5.23(brs, 1H), 5.15–5.19(m, 2H), 4.92–4.96(m, 2H), 4.84–4.87(m, 2H), 4.76(d, *J* 10 Hz, 1H), 3.87–4.26(m, 9H), 3.03(dd, 1H), 2.82(dd, 1H), 2.10(s, 3H), 2.03(s, 3H), 2.02(s, 6H), 1.99(s, 3H), 1.96(s, 3H), 1.89(s, 3H). HRESIFTMS [M+K]⁺: calcd for C₅₀H₅₅KNO₂₂, 1060.2853, found: 1060.2855.

1.17. N^α-(9-Fluorenylmethoxycarbonyl)-O-[(2,3,6-tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-gulcopyranosyl)-β-D-gulcopyranosyl]-L-tyrosine (15)

White powder, purity, 98%; ¹H NMR(500 M Hz, DMSO-*d*₆): δ 7.88(d, *J* 5 Hz, 2H), 7.63(d, *J* 5 Hz, 2H), 7.41(m, 2H), 7.31(m, 2H), 7.23(d, *J* 10 Hz, 2H), 7.04(d, *J* 5 Hz, 1H), 6.87(d, *J* 10 Hz, 1H), 5.40(dd, 1H), 5.39(brs, 1H), 5.30(d, *J* 5 Hz, 1H), 5.22–5.26(m, 2H), 4.97(t, *J* 10 Hz, 2H), 4.88–4.93(m, 2H), 4.12–4.22(m, 6H), 3.98–4.03(m, 3H), 3.03(m, 1H), 2.82(m, 1H), 2.02(s, 3H), 2.00(s, 3H), 1.99(s, 6H), 1.96(s, 6H), 1.94(s, 3H). HRESIFTMS [M+K]⁺: calcd for C₅₀H₅₅KNO₂₂, 1060.2853, found: 1060.2855.

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Table 1

Microwave-assisted glycosylation of Fmoc-Ser-OH under different reaction conditions.

Entry	Promoter (1 equiv)	Solvent (2 mL)	Temperature (°C)	Conversion (%)
1	FeCl ₃	CH ₂ ClCH ₂ Cl	150	19
2	SnCl ₄	CH ₂ ClCH ₂ Cl	150	41
3	FeCl ₃	CH ₃ CN	150	7
4	SnCl ₄	CH ₃ CN	150	24
5	FeCl ₃	C ₆ H ₆	150	0
6	SnCl ₄	C ₆ H ₆	150	40
7	FeCl ₃	CH ₂ Cl ₂	100	35
8	SnCl ₄	CH ₂ Cl ₂	100	44

Table 2

Microwave-assisted glycosylation of Fmoc-Ser-OH under different reaction conditions.

Entry	Promoter	Time (min)	Conversion (%)
1	SnCl ₄ (2 equiv)	5 min	73
2	SnCl ₄ (3 equiv)	5 min	68
3	SnCl ₄ (4 equiv)	5 min	64
4	SnCl ₄ (5 equiv)	5 min	63
5	BF ₃ ·Et ₂ O (1 equiv)	5 min	72
6	BF ₃ ·Et ₂ O (2 equiv)	5 min	72
7	BF ₃ ·Et ₂ O (4 equiv)	5 min	73
8	BF ₃ ·Et ₂ O (6 equiv)	5 min	71
9	SnCl ₄ (2 equiv)	15 min	64
10	SnCl ₄ (2 equiv)	30 min	60
11	BF ₃ ·Et ₂ O (6 equiv)	15 min	55
12	BF ₃ ·Et ₂ O (6 equiv)	30 min	36

Table 3

Glycosylation of Fmoc amino acids

Entry	Fmoc amino acid	Donor	Product	Conversion (%)	
				SnCl ₄	BF ₃ ·Et ₂ O
1		β-D-Galactose pentaacetate		73	72
2		β-D-Glucose-pentaacetate		64	61
3		D-Xylose tetraacetate		62	64
4		β-D-Lactose octaacetate		49	57

Entry	Fmoc amino acid	Donor	Product	Conversion (%)	
				SnCl ₄	BF ₃ ·Et ₂ O
5		β-D-Maltose octaacetate		52	52
6		β-D-Galactose pentaacetate		54	58
7		β-D-Glucose- pentaacetate		54	49
8		D-Xylose tetraacetate		45	62
9		β-D-Lactose octaacetate		45	43
10		β-D-Maltose octaacetate		45	43
11		β-D-Galactose pentaacetate		34	38

Entry	Fmoc amino acid	Donor	Product	Conversion (%)	
				SnCl ₄	BF ₃ ·Et ₂ O
12		β-D-Glucose- pentaacetate		33	47
13		D-Xylose tetraacetate		35	40
14		β-D-Lactose octaacetate		24	35
15		β-D-Maltose octaacetate		28	31