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Effective synthesis of nucleosides with glycosyl trifluoroacetimidates as donors

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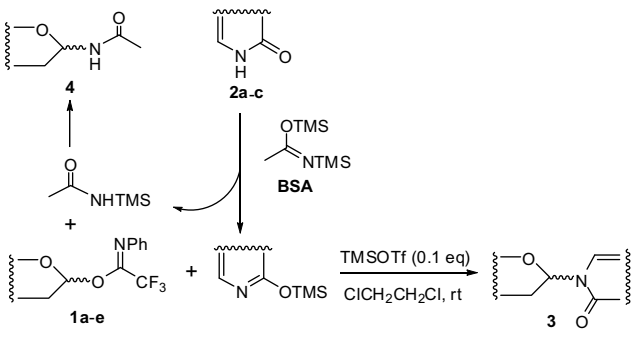
ABSTRACT

Glycosyl trifluoroacetimidates have been disclosed to be effective glycosyl donors for the synthesis of nucleosides; the present N-glycosylation protocol requires only a catalytic amount of TMSOTf as promoter and proceeds smoothly at room temperature.

Since the introduction of the silyl variation of the Hilbert-Johnson reaction[1] by Iwai and Nishimura in 1964,[2] many types of glycosyl donors have been applied in the synthesis of a large variety of the nucleosides. Among them, 1-*O*-acetyl sugars, in the presence of a strong Lewis acid, are the most frequently used glycosyl donors.[3] However, in all these methods, either stoichiometric amount of the promoter or high temperature is required to secure high-yielding of the N-glycosylation. Glycosyl trichloroacetimidates,[4] one of the most favorable types of glycosyl donors for O-glycosylation, which require a catalytic amount of Lewis acid (e.g., TMSOTf and $BF_3{\cdot}OEt_2$) at low temperature for activation, have rarely been employed in the nucleosides synthesis.[5] Recently, glycosyl trifluoroacetimidates have been found to be valuable alternatives to the trichloroacetimidates as glycosylation donors,[6] showing advantages especially in the sialylation,[7] glycosylation of hydroxamic acids,[8] and N-glycosylation of amides.[9] Herein, we report effective glycosylation of nucleobases employing glycosyl trifluoroacetimidates as donors under mild conditions.

The tri-*O*-benzoyl- and -acetyl-D-ribofuranosyl trifluoroacetimidates **1a**[19] and **1b**,[8] tetra-*O*-acetyl-, -benzoyl-, and -benzyl-D-glucopyranosyl trifluoroacetimidates **1c**,[6] **1d**,[6] and **1e**[6] were readily prepared by condensation of the corresponding 1-OH sugars and *N*-phenyl trifluoroacetimidoyl chloride in the presence of K_2CO_3 in acetone.[6,8] Uracil, thymine, and pyridin-2-one (**2a**–**c**) were chosen as the nucleobases. These nucleobases were treated with *N,O*-bis(trimethylsilyl)acetamide (BSA)[10] in dry acetonitrile to provide the corresponding silylated bases, which are sensitive toward moisture, and therefore were used directly after removal of the solvent.[11] As shown in Scheme 1 and Table 1, glycosylation of the silylated uracil and thymine with the ribofuranosyl trifluoroacetimidates **1a** and **1b** proceeded smoothly in the presence of 0.1 equiv of TMSOTf at room temperature, providing the corresponding β-nucleosides (**3aa**,[12] **3ab**,[13] **3ba**,[12] and **3bb**[14]) in 88–98% yields (entries 1, 2, 4, and 5). Glycosylation of the pyridin-2-one (**2c**) with the tri-*O*-benzoyl-ribofuranosyl trifluoroacetimidate **1a** gave the β-nucleoside **3ac**[15] in 98% yield (entry 3), however, with the tri-*O*-acetyl-ribofuranosyl trifluoroacetimidate **1b** led to the desired nucleoside **3bc** in only 64% yield (entry 6). *N*-Trimethylsilylacetamide, resulting from the silylation reagent BSA, competed for the N-glycosylation to afford the 1-*N*-acetyl-β-ribofuranosylamine **4b** in a remarkable 30% yield. Glycosylation of the nucleobases with the tetra-*O*-acetyl- and -benzoyl-D-glucopyranosyl trifluoroacetimidates **1c** and **1d** under similar conditions was found unsuccessful. While coupling of **1c** with uracil gave the



Scheme 1. Nucleoside synthesis employing glycosyl trifluoroacetimidates as donors and BSA as a silylation reagent.

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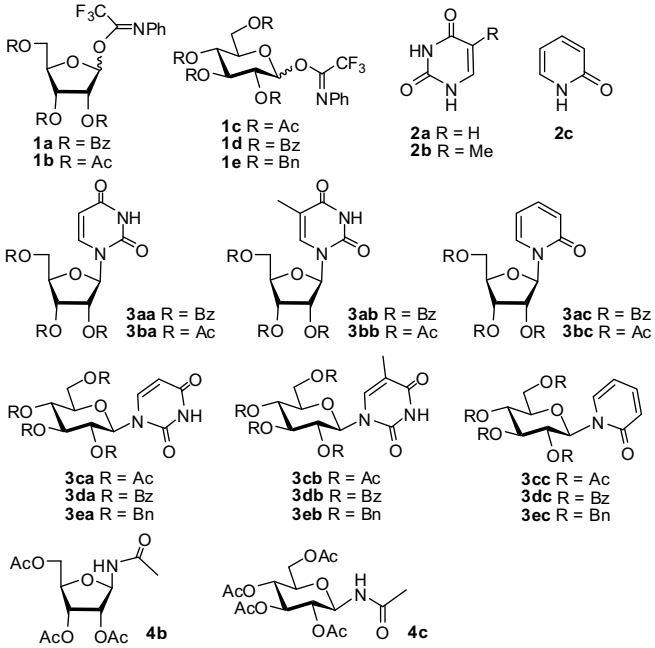
Table 1
Nucleoside synthesis employing glycosyl trifluoroacetimidates as donors and BSA as a silylation reagent[a]

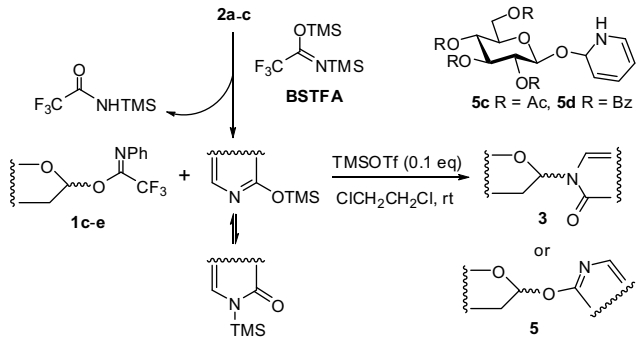


Entry	Donor	Acceptor	Product	Yield[b] (%)	α:β[c]
1	**1a**	**2a**	**3aa**	98	β
2		**2b**	**3ab**	88	β
3		**2c**	**3ac**	98	β
4	**1b**	**2a**	**3ba**	98	β
5		**2b**	**3bb**	88	β
6		**2c**	**3bc** + **4b**	64 + 30	β
7	**1c**	**2a**	**3ca**	45	β
8		**2b**	**4c**	60	β
9		**2c**	**4c**	—	—
10	**1d**	**2a**	NR	—	—
11		**2b**	NR	—	—
12		**2c**	NR	—	—
13	**1e**	**2a**	**3ea**	87	1:2
14		**2b**	**3eb**	84	1:2.5
15		**2c**	Complex	—	—

[a] A typical procedure: To a stirred suspension of the nucleobase (1.5 equiv) in dry acetonitrile was added BSA (2 equiv for **2a** and **2b**, 1 equiv for **2c**). The mixture was stirred at rt for 30 min, leading to a clear solution. The solvent was removed under reduced pressure to provide a clear oil. Under argon atmosphere, the resulting oil was dissolved in dry 1,2-dichloroethane, followed by addition of the activated 4 Å MS and the glycosyl trifluoroacetimidate (1.0 equiv). After subsequent addition of TMSOTf (0.1 equiv), the mixture was stirred at rt until the imidate was consumed completely (12–48 h), as monitored by TLC.
[b] Isolated yield.
[c] Determined by ^{1}H NMR.

nucleoside **3ca**[16] in a moderate 45% yield, coupling of **1c** with thymine and pyridin-2-one led to the 1-*N*-acetyl-β-glucosylamine **4c** as the major product (entries 7–9). The tetra-*O*-benzoyl-D-glucopyranosyl trifluoroacetimidate **1d** remained intact under these conditions (entries 10–12). The glycosylation of uracil and thymine with the 'armed' tetra-benzyl-glucopyranosyl trifluoroacetimidate **1e** afforded the desired nucleosides **3ea**[19] and **3eb**[19] in 87% and 84% yields, respectively; albeit each in a pair of the anomers, in the absence of a neighboring participating group in the donors (entries 13 and 14). The reaction of **1e** with pyridin-2-one failed, leading to a complex mixture (entry 15).

The unsuccessful glycosylation encountered above are partially due to the competing glycosylation of the *N*-trimethylsilylacetamide resulting from the silylation reagent BSA. Thus, *N,O*-bis(trimethylsilyl)trifluoroacetamide (BSTFA)[17] was used instead. The resultant *N*-trimethylsilyltrifluoroacetamide, a much weaker nucleophile, could hardly compete with the nucleobases for glycosylation. Thus, the previously unsuccessful coupling reactions with BSA were examined with BSTFA as the silylation reagent. The results are listed in Scheme 2 and Table 2.



Scheme 2. Nucleoside synthesis employing glucopyranosyl trifluoroacetimidates as donors and BSTFA as a silylation reagent.

Expectedly, glycosylation of uracil and thymine with the tetra-acetyl-glucopyranosyl trifluoroacetimidate **1c** provided the corresponding β-nucleosides **3ca**[16] and **3cb**[18] in excellent 87% and 91% yields, respectively (entries 1 and 2). However, under similar conditions, coupling of **1c** with pyridin-2-one provided the O-glycosylation product **5c**[19] (C1 at 93.2 ppm) dominantly (80%, entry 4). When the silylation time was prolonged (from the original 0.5 h to 12 h), the otherwise similar coupling procedure afforded the N-glycosylation product **3cc**[19] (C1 at 79.0 ppm) as the major product (86%, entry 3). The glycosylation of uracil with the tetra-benzoyl-glucopyranosyl trifluoroacetimidate **1d** again led to a complex mixture (entry 5). Nevertheless, glycosylation of thymine with **1d** proceeded smoothly, providing the nucleoside **3db**[19] in an excellent 91% yield (entry 6). Glycosylation of pyridin-2-one with **1d** led to the O-glycosylation product **5d**[19] in good yield, regardless of the variation of the silylation time (entry 7). Finally, glycosylation of pyridin-2-one with **1e** took place under the present conditions, furnishing the nucleoside **3ec**[19] as a pair of the anomers in 63% yield (entry 8).

In summary, glycosyl trifluoroacetimidates have been disclosed to be effective glycosyl donors for the synthesis of nucleosides. The present N-glycosylation protocol requires only a catalytic amount of TMSOTf as promoter and proceeds smoothly at room temperature. The procedure for the silylation of the bases also affects the subsequent glycosylation reaction. BSTFA has been shown to be superior to BSA for the subsequent glycosylation with pyranosyl donors.

Table 2
Nucleoside synthesis employing glucopyranosyl trifluoroacetimidates as donors and BSTFA as a silylation reagent[a]

Entry	Donor	Acceptor	Product	Yield[b] (%)	α:β[c]
1	**1c**	**2a**	**3ca**	87	β
2		**2b**	**3cb**	91	β
3[d]		**2c**	**3cc**	86	β
4		**2c**	**5c**	80	β
5	**1d**	**2a**	NR	—	—
6		**2b**	**3db**	91	β
7		**2c**	**5d**	86	β
8	**1e**	**2c**	**3ec**	63	1:3

[a] A similar procedure as that described in Table 1 was used.
[b] Isolated yield.
[c] Determined by ^{1}H NMR.
[d] The silylation time was prolonged from the standard 0.5–12 h.

Acknowledgments

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References and notes

1. Nishimura, T.; Iwai, I. *Chem. Pharm. Bull. (Tokyo)* **1964**, *12*, 352.
2. Hilbert, G. E.; Johnson, T. B. *J. Am. Chem. Soc.* **1930**, *52*, 4489.
3. (a) Vorbrüggen, H.; Ruh-Pohlenz, C. *Org. React.* **2000**, *55*, 1; (b) Vorbrüggen, H. *Acc. Chem. Res.* **1995**, *28*, 509.
4. Schmidt, R. R.; Michel, J. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 731.
5. (a) Chanteloup, L.; Thuong, N. T. *Tetrahedron Lett.* **1994**, *35*, 877; (b) Shohda, K.; Wada, T.; Sekine, M. *Nucleosides Nucleotides* **1998**, *17*, 2199.
6. (a) Yu, B.; Tao, H. *Tetrahedron Lett.* **2001**, *42*, 2405; (b) Yu, B.; Tao, H. *J. Org. Chem.* **2002**, *67*, 9099; (c) Adinolfi, M.; Barone, G.; Iadonisi, A.; Schiattarella, M. *Synlett* **2002**, 269.
7. Cai, S.; Yu, B. *Org. Lett.* **2003**, *21*, 3827.
8. Thomas, M.; Gesson, J. P.; Papot, S. *J. Org. Chem.* **2007**, *72*, 4262.
9. Tanaka, H.; Iwata, Y.; Takahashi, D.; Adachi, M.; Takahashi, T. *J. Am. Chem. Soc.* **2005**, *127*, 1630.
10. (a) Klebe, J. F. *Acc. Chem. Res.* **1970**, *3*, 299; (b) Sell, T. B.; Nair, V. *Tetrahedron* **1994**, *50*, 117; (c) Caplar, V.; Zinic, M. *Tetrahedron Lett.* **1995**, *36*, 4455.
11. (a) Dudycz, L. W.; Wright, G. E. *Nucleosides Nucleotides* **1984**, *3*, 34; (b) Matulic-Adamic, J.; Gonzalez, C.; Usman, N.; Beigelman, L. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 373.
12. Nowal, I.; Robins, M. J. *Org. Lett.* **2005**, *7*, 4903.
13. Sheng, J.; Jiang, J.-S.; Salon, J.; Huang, Z. *Org. Lett.* **2007**, *9*, 749.
14. Chow, K.; Danishefsky, S. *J. Org. Chem.* **1990**, *55*, 4211.
15. Matulic-Adamic, J.; Gonale, C.; Usman, N.; Beigelman, L. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 373.
16. Haeckel, R.; Weber, K.; Germann, C.; Haberkorn, V.; Zeisler, S.; Eisenbarth, J.; Wiessler, M.; Oberdor, F. *J. Labbel. Compds. Radiopharm.* **1996**, *38*, 1061.
17. (a) Johnson, F.; Pillai, K. M. R.; Grollman, A-P.; Tseng, L.; Takeshita, M. *J. Med. Chem.* **1984**, *27*, 954; (b) Siddiqui, A. P.; Driscoll, J. S.; Marquez, V. E.; Roth, J. S.; Shirasaka, T.; Mitsuya, H.; Barchi, J. J.; Kelley, J. A. *J. Med. Chem.* **1992**, *35*, 2195.
18. Ermolinsky, B-S.; Fomitcheva, M-V.; Efimtseva, E-V.; Meshkov, S-V.; Mikhailov, S-N. *Nucleosides Nucleotides* **1996**, *15*, 1619.
19. Selected data for new compounds: *2,3,5-Tri-O-benzoyl-D-ribofuranosyl(N-phenyl)trifluoroacetimidate* (**1a**): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12–7.82 (m, 6H), 7.62–7.23 (m, 11H), 7.12 (t, J = 7.5 Hz, 1H), 6.86 (d, J = 8.1 Hz, 2H), 6.60 (s, 1H), 6.01–5.92 (m, 2H), 4.90–4.85 (m, 1H), 4.78 (dd, J = 3.9, 12.0 Hz, 1H), 4.65 (dd, J = 5.4, 12.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 165.2, 164.9, 143.2, 133.7, 133.5, 133.2, 129.8, 129.7, 129.6, 129.3, 128.6, 128.5 (2C), 128.4 (2C), 128.3 (2C), 124.3, 119.3, 101.4, 80.5, 74.8, 71.4, 63.8. HRMS (ESI) calcd for $C_{38}H_{38}N_2O_7Na$ $[M+Na]^+$: 656.1503. Found: 656.1506.
1-(2,3,5-Tri-O-acetyl-β-D-ribofuranosyl)-1,2-dihydropyridin-2-one (**3bc**): $[\alpha]_D^{25}$ 110.1 (c 0.45, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (dd, J = 1.2, 7.2 Hz, 1H), 7.36 (dt, J = 1.8, 9.0 Hz, 1H), 6.53 (d, J = 9.0 Hz, 1H), 6.30 (d, J = 4.2 Hz, 1H), 6.24 (dt, J = 6.0, 1.2 Hz, 1H), 5.41–5.29 (m, 2H), 4.35–4.33 (m, 3H), 2.14, 2.11, 2.08 (s each, 3H each); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 169.5, 169.3, 162.0, 139.8, 132.0, 121.0, 106.2, 88.0, 79.2, 73.8, 69.5, 62.6, 20.6, 20.4. HRMS (ESI) calcd for $C_{16}H_{19}NO_8Na$ $[M+Na]^+$: 376.1003. Found: 376.1005.
1-(2,3,4,6-Tetra-O-benzyl-D-glucopyranosyl)uracil (**3ea**): For the α isomer: $[\alpha]_D^{25}$ −30.4 (c 0.45, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.53 (d, J = 8.1 Hz, 1H), 7.27–7.07 (m, 20H), 5.96 (s, 1H), 5.54 (d, J = 7.5 Hz, 1H), 4.52–4.21 (m, 9H), 3.98 (s, 1H), 3.76 (s, 1H), 3.67–3.60 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.0, 149.8, 142.1, 137.8, 137.5, 137.1, 136.4, 128.6, 128.5, 128.40, 128.36, 128.3, 128.1, 128.1, 127.8, 127.7, 127.6, 100.8, 79.3, 76.6, 76.2, 74.9, 73.7, 73.4, 73.0, 72.2, 71.9, 69.3. For the β isomer: $[\alpha]_D^{25}$ −22.7 (c 0.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28–7.11 (m, 20H), 6.81 (dd, J = 3.6, 8.4 Hz, 1H), 5.52 (d, J = 8.7 Hz, 1H), 5.28 (d, J = 8.4 Hz, 1H), 4.87–4.42 (m, 8H), 3.80–3.40 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.8, 150.3, 137.9, 137.6, 136.8, 128.7, 128.5, 128.4, 128.4, 128.3, 127.83, 127.82,127.7, 127.7, 102.8, 85.7, 78.3, 77.4, 77.3, 75.8, 75.0, 74.5, 73.3, 68.1. HRMS (ESI) calcd for $C_{38}H_{38}N_2O_7Na$ $[M+Na]^+$: 657.2571. Found: 657.2556.
1-(2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosyl)thymine (**3eb**): For the α isomer: $[\alpha]_D^{25}$ −21.4 (c 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.38–7.06 (m, 21H), 5.98 (s, 1H), 4.53–4.22 (m, 9H), 3.98 (s, 1H), 3.77 (s, 1H), 3.69–3.60 (m, 3H), 1.74 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.1, 149.8, 138.0, 137.8, 137.5, 137.2, 136.6, 128.5, 128.43, 128.39, 128.3, 128.2, 128.1, 128.0, 127.7, 109.0, 78.8, 76.6, 76.0, 75.0, 74.1, 73.5, 73.1, 72.3, 71.9, 69.4, 12.3. For the β isomer: $[\alpha]_D^{25}$ −42.9 (c 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.37–7.16 (m, 20H), 6.65 (s, 1H), 5.59 (d, J = 9.0 Hz, 1H), 4.86 (s, 2H), 4.95–4.45 (m, 6H), 3.87 (t, J = 8.7 Hz, 1H), 3.74–3.58 (m, 4H), 3.46 (t, J = 8.7 Hz, 1H), 1.67 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.4, 150.5, 138.0, 137.61, 137.56, 136.9, 128.6, 128.43, 128.40, 128.36, 128.3, 128.1, 127.8, 127.7, 110.9, 85.9, 77.8, 77.4, 75.7, 75.0, 74.2, 73.2, 68.0. HRMS (ESI) calcd for $C_{39}H_{40}N_2O_7Na$ $[M+Na]^+$: 671.2728. Found: 671.2709.
1-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-1,4-dihydropyridin-2-one (**3cc**): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (d, J = 6.6 Hz, 1H), 7.34 (dd, J = 8.7, 6.9 Hz, 1H), 6.53 (d, J = 9.0 Hz, 1H), 6.34 (d, J = 9.3 Hz, 1H), 6.28 (t, J = 6.9 Hz, 1H), 5.46 (t, J = 9.3 Hz, 1H), 5.24 (m, 2H), 4.30 (dd, J = 4.8, 12.6 Hz, 1H), 4.13 (d, J = 11.1 Hz, 1H), 3.96 (dd, J = 3.3, 9.9 Hz, 1H), 2.05, 2.03, 2.00, 1.91 (s each, 3H each); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 169.4, 169.3, 169.1, 161.5, 139.9, 132.5, 120.1, 106.4, 79.0, 74.6, 72.5, 70.3, 67.7, 61.5, 20.4, 20.3, 20.2, 19.9. HRMS (ESI) calcd for $C_{19}H_{23}NO_{10}Na$ $[M+Na]^+$: 448.1214. Found: 448.1214.
2-[(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-oxy]pyridine (**5c**): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (d, J = 4.2 Hz, 1H), 7.65 (t, J = 7.8 Hz, 1H), 7.00 (t, J = 6 Hz, 1H), 6.81 (d, J = 8.4 Hz, 1H), 6.21 (d,J = 7.2 Hz, 1H), 5.34–5.30 (m, 2H), 5.23 (t, J = 8.7 Hz, 1H), 4.34 (dd, J = 3.9, 12.3 Hz, 1H), 4.13 (d, J = 12.3 Hz, 1H), 3.96 (d, J = 9.3, 1H), 2.04, 2.02, 1.98 (s each, 3H each); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 170.1, 169.32, 169.28, 161.1, 146.6, 139.2, 118.7, 111.6, 93.2, 72.9, 71.9, 70.6, 67.9, 61.5, 20.5, 20.44, 20.39. HRMS (ESI) calcd for $C_{19}H_{23}NO_{10}Na$ $[M+Na]^+$: 448.1214. Found: 448.1214.
1-(2,3,4,6-Tetra-O-benzoyl-β-D-glucopyranosyl)thymine (**3db**): $[\alpha]_D^{25}$ 5.0 (c 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.05–7.74 (m, 8H), 7.62–7.22 (m, 13H), 6.27 (d, J = 9.3 Hz, 1H), 6.11 (dd, J = 9.6, 9.9 Hz, 1H), 5.81 (dd, J = 9.6, 10.2 Hz, 1H), 5.71 (dd, J = 9.9, 9.3 Hz, 1H), 4.69 (dd, J = 2.4, 12.6 Hz, 1H), 4.51–4.39 (m, 2H), 1.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 165.3, 165.09, 165.07, 163.4, 150.5, 134.4, 133.6, 133.5, 133.2, 133.1, 129.8, 129.7, 129.6, 129.5, 129.1, 128.33, 128.26, 128.21, 128.17, 127.7, 112.1, 80.2, 74.9, 72.8, 69.9, 68.7, 62.6, 12.4; HRMS (ESI) calcd for $C_{39}H_{32}N_2O_{11}Na$ $[M+Na]^+$: 727.1898. Found: 727.1907.
2-[(2,3,4,6-Tetra-O-benzoyl-β-D-glucopyranosyl)-oxy]pyridine (**5d**): $[\alpha]_D^{25}$ 56.2 (c 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (d, J = 4.2 Hz, 1H), 8.00–7.85 (m, 8H), 7.60–7.23 (m, 13H), 6.96 (dd, J = 6.3, 5.7 Hz, 1H), 6.82 (d, J = 8.4 Hz, 1H), 6.57 (d, J = 8.1 Hz, 1H), 6.08 (t, J = 9.6 Hz, 1H), 5.88–5.75 (m, 2H), 4.68–4.36 (m, J = 8.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 165.7, 165.12, 165.08, 161.1, 146.5, 139.2, 133.4, 133.2, 132.9, 129.64, 129.60, 129.58, 129.57, 129.4, 128.8, 128.53, 128.51, 128.33, 128.26, 128.1, 118.7, 111.6, 93.8, 73.1, 72.4, 71.3, 69.4, 62.8; HRMS (ESI) calcd for $C_{39}H_{31}NO_{10}Na$ $[M+Na]^+$: 696.1840. Found: 696.1843.
1-(2,3,4,6-Tetra-O-benzyl-D-glucopyranosyl)-1,4-dihydropyridin-2-one (**3ec**): For the α isomer: $[\alpha]_D^{25}$ −89.0 (c 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.42–7.13 (m, 19H), 7.09–7.06 (m, 2H), 6.53 (d, J = 9.3 Hz, 1H), 6.41 (d, J = 2.7 Hz, 1H), 6.21 (dd,J = 6.9, 6.3 Hz, 1H), 4.63–4.29 (m, 10H), 3.83–3.63 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.0, 139.6, 138.0, 137.7, 137.3, 137.2, 134.9, 128.44, 128.38, 128.30, 128.27, 128.1, 128.0, 127.9, 127.82, 127.81, 127.7, 127.6, 127.5, 119.6, 105.1, 79.8, 76.6, 74.8, 73.4, 73.3, 72.9, 71.9, 71.7, 69.8. For the β isomer: $[\alpha]_D^{25}$ 69.9 (c 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38–7.12 (m, 20H), 7.09–7.06 (m, 1H), 6.60 (d, J = 10.2 Hz, 1H), 6.21 (d, J = 9.3 Hz, 1H), 6.09 (dd, J = 6.6, 6.9 Hz, 1H), 4.90–4.84 (m, 3H), 4.62–4.31 (m, 5H), 3.95–3.59 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9, 139.2, 138.0, 137.68, 137.66, 137.0, 132.5, 128.2, 128.1, 127.9, 127.7, 127.6, 127.53, 127.49, 127.47, 120.7, 106.1, 85.3, 80.6, 77.4, 75.4, 74.8, 74.2, 73.1, 68.1. HRMS (ESI) calcd for $C_{39}H_{39}NO_6Na$ $[M+Na]^+$: 640.2670. Found: 640.2661.