Supporting Information

Site-Selective Photobromination of O-Acetylated Carbohydrates in Benzotrifluoride

Guoqing Zhang,¹ Nicholas W. See,¹,² Norbert Wimmer,¹ Michael J. Godinez,² Scott A. Cameron,²
Richard H. Furneaux² and Vito Ferro¹,*

¹School of Chemistry and Molecular Biosciences, The University of Queensland, Brisbane QLD
4072, Australia
²Ferrier Research Institute, Victoria University of Wellington, 69 Gracefield Road, Lower Hutt 5040,
New Zealand
**Contents**

**Supporting Information**

- Experimental .................................................................................................................. 1
- General procedure for photobromination ......................................................................... 3
- Synthesis and Characterization of Products ...................................................................... 3

<table>
<thead>
<tr>
<th>Compound Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,2,3,4,6-Penta-O-acetyl-5-C-bromo-β-D-glucopyranose (2a)</td>
<td>5</td>
</tr>
<tr>
<td>1,2,3,4,6-Penta-O-acetyl-5-C-bromo-β-D-galactopyranose (2b)</td>
<td>5</td>
</tr>
<tr>
<td>Methyl 1,2,3,4-tetra-O-acetyl-5-C-bromo-β-D-glucopyranuronate (2c)</td>
<td>6</td>
</tr>
<tr>
<td>Methyl 1,2,3,4-tetra-O-acetyl-5-C-bromo-α-D-glucopyranuronate (2d)</td>
<td>6</td>
</tr>
<tr>
<td>1,2,3,4-Tetra-O-acetyl-α-L-rhamnopyranose (1e)</td>
<td>7</td>
</tr>
<tr>
<td>Tetra-O-acetyl-β-D-xylopyranose (1f)</td>
<td>7</td>
</tr>
<tr>
<td>(5S)-Tetra-O-acetyl-5-C-bromo-β-D-xylopyranose (2f)</td>
<td>8</td>
</tr>
<tr>
<td>Methyl (2,3,4-tri-O-acetyl-5-C-bromo-β-D-glucopyranosyl fluoride)uronate (2g)</td>
<td>8</td>
</tr>
<tr>
<td>Methyl (2,3,4-tri-O-acetyl-5-C-bromo-β-D-mannopyranosyl fluoride)uronate (2h)</td>
<td>9</td>
</tr>
<tr>
<td>Methyl (2,3,4-tri-O-acetyl-β-D-galactopyranosyl fluoride)uronate (1i)</td>
<td>9</td>
</tr>
<tr>
<td>2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl fluoride (1j)</td>
<td>12</td>
</tr>
<tr>
<td>2,3,4,6-Tetra-O-acetyl-5-C-bromo-β-D-glucopyranosyl fluoride (2j)</td>
<td>12</td>
</tr>
<tr>
<td>2-Acetamido-1,3,4,6-tetra-O-acetyl-2-deoxy-β-D-glucopyranose (1k)</td>
<td>13</td>
</tr>
<tr>
<td>Tetra-O-acetyl-2-phthalamido-2-deoxy-β-D-glucopyranose (1l)</td>
<td>14</td>
</tr>
<tr>
<td>1,3,4,6-Tetra-O-acetyl-5-C-bromo-2-deoxy-2-phthalamido-β-D-glucopyranose (2l)</td>
<td>14</td>
</tr>
<tr>
<td>1,2,2',3,3',4',6,6'-Octa-O-acetyl-β-maltose (1m)</td>
<td>15</td>
</tr>
<tr>
<td>1,2,2',3,3',4',6,6'-Octa-O-acetyl-5-C-bromo-β-maltose (2m)</td>
<td>15</td>
</tr>
</tbody>
</table>

**NMR Spectra** .............................................................................................................. 17

**References** ................................................................................................................... 48
Experimental

General

Reagents were purchased from Merck and co. and were used without further purification. Photobrominations were performed with the CPR-405 Compact PhotoReactor (equipped with 5 purple LEDs, $\lambda=405\text{nm}$, 8.7 W), Fig. S1. The CPR-405 was custom made at the Ferrier Research Institute, Lower Hutt, New Zealand. Reaction solvents were acquired in anhydrous form where possible and stored over 3Å molecular sieves. All acetylated carbohydrate substrates and solid reagents used in this study were dried under vacuum over P$_2$O$_5$ for at least 24 hours prior to use. All experiments were performed in oven-dried glassware under an inter atmosphere (N$_2$ or Ar) and monitored by thin layer chromatography (TLC) and/or NMR spectroscopy. TLC samples were developed on Merck silica gel F$_{254}$ aluminum-backed sheets and visualized under ultraviolet light and/or with anisaldehyde/H$_2$SO$_4$ dip. NMR spectra were measured on Bruker Avance 500 MHz spectrometer and are referenced to the residual solvent peaks ($\delta$H =7.26 ppm; $\delta$C = 77.0 ppm), using CDCl$_3$ as solvent (99.8 atom% D). $^{19}$F NMR spectra were referenced externally to monofluorobenzene (CDCl$_3$; $\delta_F$ = -113.5 ppm). Coupling constants are reported in Hertz (Hz) and chemical shifts are reported in parts per million (ppm). Structure elucidations were made with additional 2D NMR experiments, including gCOSY and gHSQC. The conversions for the reactions were measured by $^1$H NMR analysis of the post-workup product mixture, prior to purification by flash chromatography. Flash chromatography was performed on silica gel (230–400 mesh, Grace) under pressure with specified eluants.

General procedure for photobromination

The substrate (1.0 eq.) and NBS (3.0 eq.) were dissolved in anhydrous PhCF$_3$ to a final substrate concentration of 0.16 M. Br$_2$ (2.5 mol%) was then added dropwise into the reaction mixture with a microliter syringe (5 $\mu$L). The reaction vessel was placed into the compact photoreactor (8.7 W, $\lambda$ = 405 nm) and irradiated under Ar(g). The reactor was cooled by air flow such that the temperature was $\sim$40 °C. The reaction was stopped when the starting material was completely consumed or was no longer being converted into the product as indicated by TLC and NMR spectroscopy. The reaction mixture generally turned from amber to a light yellow color. The reaction mixture was diluted with EtOAc and washed with 50% Na$_2$S$_2$O$_3$ ($\times$1), sat. NaHCO$_3$ ($\times$1) and brine ($\times$3) before it was dried (MgSO$_4$), filtered, and concentrated to dryness. The residue was analysed by $^1$H NMR spectroscopy.
to determine the extent of conversion and was then purified by flash chromatography to give the pure product.

**Figure S1.** The compact photoreactor including specifications.

Specifications:
- LEDs max power output (radiometric flux): **8.7W** (all 5 LEDs, at 1 Amp)
- LEDs: Luminus SST-10-UV-A130-F405-00
- LEDs with boards: New Energy LST1-01G01-UV04-00
- Lenses: Gaggione LLC05N7
- Led Driver: BuckPuck 3023-D-E-1000
Synthesis and Characterization of Products

1,2,3,4,6-Penta-O-acetyl-5-C-bromo-β-D-glucopyranose (2a)

Small scale: 1,2,3,4,6-Penta-O-acetyl-β-D-glucopyranose (1a) (150 mg, 0.38 mmol) was photobrominated according to the general procedure (1.5 h) to afford 150 mg (84%) of the 5-C-bromide 2a as a white foam after purification by flash chromatography, \([\alpha]_D -98.5 \, (c. 1.0, \text{CHCl}_3; \text{lit.} 1^\text{–}91), R_f = 0.6 \, (5:1 \text{PhMe/EtOAc}). 1^H \, \text{and } 13^C \, \text{NMR spectra were consistent with literature values.}^2, ^3 \)

Gram scale: 1,2,3,4,6-Penta-O-acetyl-β-D-glucopyranose (1a) (1.3 g, 3.3 mmol) was photobrominated according to the general procedure (7 h) to afford 1.2 g (78%) of the 5-C-bromide 2a as a white foam.

\(^1^H \, \text{NMR} \, (500 \, \text{MHz, CDCl}_3): \delta 6.22 \, (d, \, J_{1,2} = 8.6 \, \text{Hz}, \, 1\text{H, H-1}), \, 5.56 \, (dd, \, J_{2,3} = J_{3,4} = 9.7 \, \text{Hz}, \, 1\text{H, H-3}), \, 5.26 \, (dd, \, 1\text{H, H-2}), \, 5.22 \, (d, \, 1\text{H, H-4}), \, 4.57, \, 4.31 \, (\text{ABq, } J_{6a,6b} = 12.3 \, \text{Hz}, \, 2\text{H, H-6a, 6b}), \, 2.12 \, (s, \, 3\text{H, –OAc}), \, 2.10 \, (s, \, 3\text{H, –OAc}), \, 2.06 \, (s, \, 3\text{H, –OAc}), \, 2.04 \, (s, \, 3\text{H, –OAc}), \, 2.00 \, (s, \, 3\text{H, –OAc}). 13^C \, \text{NMR} \, (126 \, \text{MHz, CDCl}_3): \delta 169.8 \, (\text{C=O}), \, 169.7 \, (\text{C=O}), \, 169.4 \, (\text{C=O}), \, 169.2 \, (\text{C=O}), \, 168.4 \, (\text{C=O}), \, 96.0 \, (\text{C-1}), \, 91.5 \, (\text{C-5}), \, 71.2 \, (\text{C-3}), \, 69.6 \, (\text{C-2}), \, 68.4 \, (\text{C-4}), \, 65.8 \, (\text{C-6}), \, 20.8 \, (\text{CH}_3), \, 20.7 \, (\text{CH}_3), \, 20.6 \, (2 \times \text{CH}_3), \, 20.5 \, (\text{CH}_3).

1,2,3,4,6-Penta-O-acetyl-5-C-bromo-β-D-galactopyranose (2b)

β-D-Galactose peracetate (1b) (150 mg, 0.38 mmol) was photobrominated according to the general procedure (2 h) to afford 146 mg (82%) of the 5-C-bromide 2b, as a colourless syrup after purification by flash chromatography, \([\alpha]_D -45.2 \, (c. \, 2.7, \, \text{CHCl}_3), \, R_f = 0.5 \, (5:1 \text{PhMe/EtOAc}). 1^H \, \text{and } 13^C \, \text{NMR spectra were consistent with literature values.}^4, ^5 \)

\(^1^H \, \text{NMR} \, (500 \, \text{MHz, CDCl}_3): \delta 6.32 \, (d, \, J_{1,2} = 8.6 \, \text{Hz}, \, 1\text{H, H-1}), \, 5.56 \, (dd, \, J_{2,3} = J_{3,4} = 9.7 \, \text{Hz}, \, 1\text{H, H-3}), \, 5.26 \, (dd, \, 1\text{H, H-2}), \, 5.22 \, (d, \, 1\text{H, H-4}), \, 4.57, \, 4.31 \, (\text{ABq, } J_{6a,6b} = 12.3 \, \text{Hz}, \, 2\text{H, H-6a, 6b}), \, 2.12 \, (s, \, 3\text{H, –OAc}), \, 2.10 \, (s, \, 3\text{H, –OAc}), \, 2.06 \, (s, \, 3\text{H, –OAc}), \, 2.04 \, (s, \, 3\text{H, –OAc}), \, 2.00 \, (s, \, 3\text{H, –OAc}). 13^C \, \text{NMR} \, (126 \, \text{MHz, CDCl}_3): \delta 169.8 \, (\text{C=O}), \, 169.7 \, (\text{C=O}), \, 169.4 \, (\text{C=O}), \, 169.2 \, (\text{C=O}), \, 168.4 \, (\text{C=O}), \, 96.0 \, (\text{C-1}), \, 91.5 \, (\text{C-5}), \, 71.2 \, (\text{C-3}), \, 69.6 \, (\text{C-2}), \, 68.4 \, (\text{C-4}), \, 65.8 \, (\text{C-6}), \, 20.8 \, (\text{CH}_3), \, 20.7 \, (\text{CH}_3), \, 20.6 \, (2 \times \text{CH}_3), \, 20.5 \, (\text{CH}_3). \)

S5
spectra were consistent with literature values.\(^3\) \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta \) 6.22 (d, \(J_{1,2} = 8.6\) Hz, 1H, H-1), 5.79 (dd, \(J_{3,4} = 10.5, J_{2,3} = 3.4\) Hz, 1H, H-3), 5.63 (d, 1H, H-2), 5.40 (dd, 1H, H-4), 4.64, 4.36 (ABq, \(J_{6a,6b} = 12.1\) Hz, 2H, H-6a, 6b), 2.13 (s, 6H, 2 × −OAc), 2.07 (s, 3H, −OAc), 2.06 (s, 3H, −OAc), 1.98 (s, 3H, −OAc).\(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \(\delta \) 169.8 (C=O), 169.6 (C=O), 169.5 (C=O), 169.2 (2 × C=O), 93.8 (C-1), 91.5 (C-5), 70.3 (C-3), 68.5 (C-2), 67.3 (C-4), 66.3 (C-6), 20.8 (CH\(_3\)), 20.7 (CH\(_3\)), 20.6 (2 × CH\(_3\)), 20.5 (CH\(_3\)).

**Methyl 1,2,3,4-tetra-\(O\)-acetyl-5-C-bromo-β-D-glucopyranuronate (2c)**

Methyl 1,2,3,4-tetra-\(O\)-acetyl-β-D-glucopyranuronate\(^4\) 1c (165 mg, 0.44 mmol) was photobrominated according to the general procedure (2 h) to afford 186 mg (93%) of the 5-C-bromide 2c as white solid after purification by flash chromatography, m.p. 161–162 °C (lit.\(^5\) 159–161 °C), [\(\alpha\)]\(_D\) −100.8 (c. 2.0, CHCl\(_3\); lit.\(^5\) −107), \(R_f\) = 0.4 (5:1 PhMe/EtOAc). \(^1\)H and \(^{13}\)C NMR spectra were consistent with literature values.\(^4\) \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta \) 6.28 (d, \(J_{1,2} = 8.6\) Hz, 1H, H-1), 5.53 (dd, \(J_{2,3} = J_{3,4} = 9.5\) Hz, 1H, H-3), 5.31 (d, 1H, H-4), 5.24 (dd, 1H, H-2), 3.82 (s, 3H, −CO\(_2\)CH\(_3\)), 2.13 (s, 3H, −OAc), 2.09 (s, 3H, −OAc), 2.04 (s, 3H, −OAc), 2.01 (s, 3H, −OAc).\(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \(\delta \) 169.7 (C=O), 169.2 (C=O), 169.1 (C=O), 168.3 (C=O), 164.3 (C=O), 90.9 (C-1), 89.1 (C-5), 70.8 (C-4), 69.9 (C-2), 69.3 (C-3), 54.2 (OCH\(_3\)), 20.7 (CH\(_3\)), 20.7 (CH\(_3\)), 20.6 (CH\(_3\)), 20.6 (CH\(_3\)).

**Methyl 1,2,3,4-tetra-\(O\)-acetyl-5-C-bromo-α-D-glucopyranuronate (2d)**

Methyl 1,2,3,4-tetra-\(O\)-acetyl-α-D-glucopyranuronate\(^4\) 1d (185 mg, 0.49 mmol) was photobrominated according to the general procedure (2.5 h) to afford 150 mg (67%) of the 5-C-bromide 2d as a colorless syrup after purification by flash chromatography, [\(\alpha\)]\(_D\) = +0.8 (c. 1.6, CHCl\(_3\); lit.\(^6\) +4.7, lit.\(^1\) −6), \(R_f\) =
0.5 (5:1 PhMe/EtOAc). "H and "C NMR spectra were consistent with literature values. "H NMR (500 MHz, CDCl3): δ 6.54 (d, J1,2 = 4.1 Hz, 1H, H-1), 5.81 (dd, 1H, J2,3 = 10.1 Hz, J3,4 = 9.8 Hz, H-3), 5.31 (d, 1H, H-4), 5.19 (dd, H-2), 3.83 (s, 3H, -CO2CH3), 2.21 (s, 3H, -OAc), 2.11 (s, 3H, -OAc), 2.05 (s, 3H, -OAc), 2.05 (s, 3H, -OAc). "C NMR (126 MHz, CDCl3): δ 169.7 (C=O), 169.5 (C=O), 169.1 (C=O), 168.7 (C=O), 164.9 (C=O), 89.6 (C-1), 87.3 (C-5), 69.9 (C-3), 68.1 (C-4), 67.1 (C-2), 54.2 (OCH3), 21.3 (CH3), 20.7 (CH3), 20.6 (CH3), 20.5 (CH3).

1,2,3,4-Tetra-O-acetyl-α-L-rhamnopyranose (1e)

The starting material tetra-O-acetyl-α-L-rhamnopyranose 1e gave acceptable "H NMR spectra that matched the data reported in the literature. "H NMR (500 MHz, CDCl3): δ 6.01 (d, J1,2 = 1.9 Hz, 1H, H-1), 5.30 (dd, J3,4 = 10.0 Hz, 1H, H-3), 5.25 (dd, J2,3 = 3.5, 1H, H-2), 5.12 (t, J4,5 = 9.7 Hz, 1H, H-4), 3.94 (dq, 1H, H-5), 2.17 (s, 3H, -OAc), 2.15 (s, 3H, -OAc), 2.06 (s, 3H, -OAc), 2.00 (s, 3H, -OAc), 1.23 (d, J1,Me = 6.2 Hz, 3H, -CH3).

The starting material 1e (332 mg, 0.48 mmol) was photobrominated according to the general procedure (8 h). No bromide formation was observed during this time.

Tetra-O-acetyl-β-D-xylopyranose (1f)

D-Xylose (731 mg, 4.9 mmol, 1.0 equiv.) and NaOAc (606 mg, 7.3 mmol, 1.5 equiv.) were dissolved in Ac2O (20 ml) and heated under reflux for 1.5 h. The reaction mixture was then cooled to room temperature and treated with iced water (100 mL). The resulting precipitate was collected and
recrystallized from water to afford the tetraacetate 1f (1.1 g, 3.4 mmol, 71%) as white crystals, m.p. 126–127 °C (lit.8 120–122 °C), [α]D −32.7 (c. 2.6, CHCl3; lit.9 –25.2). The product gave acceptable 1H NMR spectra that matched the data reported in the literature.9 1H NMR (500 MHz, CDCl3): δ 5.72 (d, J1,2 = 6.9 Hz, 1H, H-1), 5.21 (dd, J2,3 = J3,4 =8 .3 Hz, 1H, H-3), 5.04 (dd, 1H, H-2), 4.98 (td, J4,5a = 5.0 Hz, 1H, H-4), 4.15 (dd, J5a,5b = 12.0 Hz, 1H, H-5a), 3.53 (dd, J4,5b = 8.4 Hz, 1H, H-5b), 2.11 (s, 3H, -OAc), 2.06 (s, 3H, -OAc), 2.05 (s, 6H, 2 × -OAc).

Methyl (2,3,4-tri-O-acetyl-5-C-bromo-β-D-glucopyranosyl fluoride)uronate 2f

The tetraacetate 1f (168 mg, 0.53 mmol) was photobrominated according to the general procedure (6 h) to afford 150 mg (50%) of the 5-C-bromide 2f as a white solid after purification by flash chromatography, m.p. 143–144 °C (lit.10 135–140 °C), [α]D −132.2 (c. 3.1, CHCl3; lit.10 –117), Rf = 0.3 (10:1 PhMe/EtOAc). 1H and 13C NMR spectra were consistent with literature values.10,11 1H NMR (500 MHz, CDCl3): δ 6.50 (d, J4,5 = 4.1 Hz, 1H, H-5), 6.25 (dd, J1,2 = 8.6 Hz, 1H, H-1), 5.62 (dd, J2,3 = J3,4 = 9.8 Hz, 1H, H-3), 5.19 (dd, 1H, H-2), 4.87 (dd, 1H, H-4), 2.11 (s, 3H, -OAc), 2.11 (s, 3H, -OAc), 2.05 (s, 3H, -OAc). 13C NMR (126 MHz, CDCl3): δ 169.7 (C=O), 169.5 (C=O), 168.5 (C=O), 90.0 (C-1), 82.2 (C-5), 70.5 (C-4), 69.8 (C-2), 69.4 (C-3), 20.8 (CH3), 20.8 (CH3), 20.7 (CH3), 20.7 (CH3).
\( R_f = 0.5 \) (5:1 PhMe/EtOAc). \(^1\)H and \(^{13}\)C NMR spectra were consistent with literature values. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 5.71 (dd, \( 1H, J_{1,F} = 51.2 \) Hz, \( J_{1,2} = 7.3 \) Hz, H-1), 5.49 (ddd, \( 1H, J_{3,4} = 9.5 \) Hz, \( J_{2,3} = 10.3 \) Hz, \( J_{3,F} = 0.7 \) Hz, H-3), 5.37 (d, \( 1H, H-4 \)), 5.24 (ddd, \( 1H, J_{2,F} = 23.2 \) Hz, H-2), 3.86 (s, \( 3H, OCH_3 \)), 2.10 (s, \( 3H, -OAc \)), 2.09 (s, \( 3H, -OAc \)), 2.02 (s, \( 3H, -OAc \)). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \( \delta \) 169.7 (C=O), 169.1 (C=O), 168.9 (C=O), 164.0 (C=O), 107.3 (d, \( J_{1,F} = 225 \) Hz, C-1), 87.9 (d, \( J_{5,F} = 8.0 \) Hz, C-5), 70.4 (d, \( J_{2,F} = 23.9 \) Hz, C-2), 70.1 (d, \( J_{3,F} = 10.6 \) Hz, C-3), 69.6 (C-4), 54.5 (OCH\(_3\)), 20.7 (CH\(_3\)), 20.58 (CH\(_3\)), 20.56 (CH\(_3\)).

**Methyl (2,3,4-tri-O-acetyl-5-C-bromo-\( \beta \)-D-mannopyranosyl fluoride)uronate (2h)**

Methyl (2,3,4-tri-O-acetyl-5-C-bromo-\( \beta \)-D-mannopyranosyl fluoride)uronate (1h)**

The fluoride 1h\(^{14}\) (194 mg, 0.58 mmol) was photobrominated according to the general procedure (1.5 h) to afford 217 mg (91%) of the 5-C-bromide 2h as a colorless syrup after purification by flash chromatography, [\( \alpha \)\(_D\)] = -124.0 (c. 2.7, CHCl\(_3\)), \( R_f \) = 0.3 (20:1 PhMe/EtOAc). \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 5.87 (dd, \( 1H, J_{1,F} = 46.9 \) Hz, \( J_{1,2} = 1.4 \) Hz, H-1), 5.70 (td, \( J_{2,F} = 2.9 \) Hz, \( J_{2,3} = 1.3 \) Hz, H-2), 5.53 (dd, \( J_{3,4} = 10.1 \) Hz, \( J_{4,F} = 0.5 \) Hz, \( 1H, H-4 \)), 5.38 (d, \( J_{3,F} = 1.0 \) Hz, \( 1H, H-3 \)), 3.88 (s, \( 3H, -\text{CO}_2\text{CH}_3 \)), 2.20 (s, \( 3H, -\text{OAc} \)), 2.12 (s, \( 3H, -\text{OAc} \)), 2.02 (s, \( 3H, -\text{OAc} \)). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \( \delta \) 169.8 (C=O), 169.7 (C=O), 169.2 (C=O), 164.2 (C=O), 104.1 (d, \( J_{1,F} = 224.8 \) Hz, C-1), 89.1 (d, \( J_{5,F} = 7.9 \) Hz, C-5), 68.5 (d, \( J_{3,F} = 8.3 \) Hz, C-3), 66.7 (d, \( J_{2,F} = 17.6 \) Hz, C-2), 66.5 (C-4), 54.4 (OCH\(_3\)), 20.9 (CH\(_3\)), 20.7 (CH\(_3\)), 20.6 (CH\(_3\)). \(^{19}\)F NMR (470 MHz, CDCl\(_3\)): \( \delta \) -153.9 (app. d, \( J_{1,F} = 47.0 \) Hz). HRMS: calcd for C\(_{13}\)H\(_{16}\)BrFO\(_9\)Na 436.9860 [M + Na]\(^+\); found 436.9836 [M + Na]\(^+\).

**Methyl (2,3,4-tri-O-acetyl-\( \beta \)-D-galactopyranosyl fluoride)uronate (1i)**

(a) To a stirred solution of HClO\(_4\) (2 drops) in excess Ac\(_2\)O (20 mL) at 0 °C was added D-galacturonic
acid (1.9 g, 9.9 mmol) in one portion. The suspension was stirred for 10 min under N₂(g) before it was warmed to r.t. and stirred for a further 3 h. Anhydrous MeOH (20 mL) was then added cautiously at 0 °C before the solution was once more warmed to r.t. and stirred o/n. The product mixture was diluted with EtOAc (100 mL) and washed with water (50 mL). The aqueous phase was then extracted with EtOAc (3 × 50 mL). The combined organic phases were then washed with brine (2 × 50 mL) before the product was dried (MgSO₄), filtered, and concentrated under reduced pressure. Acetic acid was removed azeotropically with anhydrous PhMe. The resulting white solid was briefly dried over P₂O₅ in vacuo before it was taken up in dry DMF (20 mL). Dried, finely powdered KHCO₃ (1.98 g, 19.8 mmol) and MeI (1.54 mL, 24.7 mmol) were then added, and the resulting suspension was stirred at r.t. in the dark o/n. The product mixture was diluted with EtOAc (100 mL) and water (50 mL). The phases were separated, and the aqueous phase was re-extracted with EtOAc (3 × 75 mL). The combined organic phases were washed with water (3 × 50 mL) and brine (3 × 50 mL). The product was dried (MgSO₄), filtered and concentrated under reduced pressure to furnish methyl 1,2,3,4-tetra-O-acetyl-α-D-galactopyranuronate as a white foam 3.5 g (95%). Rf = 0.28 (PhMe/EtOAc 6:1; stained brown with panisaldehyde/H₂SO₄ dip). [α]D + 106.5 (c. 0.44, CHCl₃). ¹H NMR (500 MHz, CDCl₃): δ 6.51 (d, 1H, J₁,₂ = 2.5 Hz, H-1), 5.82 (m, 1H, H-4), 5.39 (m, 2H, H-2, H-3), 4.75 (d, 1H, J₄,₅ = 1.6 Hz, H-5), 3.76 (s, 3H, -CO₂CH₃), 2.15 (s, 3H), 2.11 (s, 3H), 2.01 (s, 6H) (4 × CH₃). ¹³C NMR (125 MHz, CDCl₃): δ 170.0, 169.6, 168.5, 166.6 (4 × C=O), 89.5 (C-1), 70.8 (C-5), 68.6 (C-4), 66.9 (C-3), 66.0 (C-2), 52.9 (-CO₂CH₃), 20.8, 20.6, 20.4(9), 20.4(7) (4 × CH₃). LRMS: m/z 399.3 [M + Na]⁺. The ¹H and ¹³C NMR data were in agreement with the literature.¹⁵

(b) Methyl 1,2,3,4-tetra-O-acetyl-α-D-galactopyranuronate (1.8 g, 4.5 mmol) was suspended at 0 °C in 33% HBr in acetic acid (24 mL) under an Ar atmosphere. After stirring for 15 min at 0 °C, the reaction mixture was allowed to warm up to r.t. and stirred for a further 2 h. The acetic acid was then removed by evaporation with toluene under reduced pressure. The crude oil was diluted with EtOAc (50 mL) and washed with cold sat. NaHCO₃ (3 × 40 mL) until bubbling ceased. The organic layer was dried (MgSO₄) and concentrated under reduced pressure to give the bromide, methyl (2,3,4-tri-O-acetyl-α-D-galactopyranosyl bromide) uronate, as the light-yellow foam. The crude material was used in the next step without further purification. To a solution of the bromide in dry acetonitrile (20 mL) under an Ar atmosphere was added silver fluoride (2.9 g, 22.6 mmol). The reaction mixture was then
stirred overnight in the dark at r.t. The reaction mixture was then filtered and concentrated under reduced pressure. The crude material was purified by flash chromatography to give the fluoride 1i (1.2 g, 81%, two steps) as a white solid, m.p. 155–157 °C (lit.16 156 °C), [α]D + 40.3 (c. 0.79, CHCl3; lit.16 +46), Rf = 0.3 (3:1 PhMe/EtOAc). 1H NMR spectra that matched the data reported in the literature.17

1H NMR (500 MHz, CDCl3): δ 5.74 (app. s, 1H, H-4), 5.34 (ddd, 1H, J1,2 = 7.3 Hz, J2,3 = 10.8 Hz, J2,F = 12.9 Hz, H-2), 5.28 (dd, 1H, J1,F = 50.7 Hz, H-1), 5.09 (ddd, 1H, J3,4 = 3.5 Hz, J3,F = 1.0 Hz, H-3), 4.42 (app. s, 1H, H-5), 3.79 (s, 3H, -CO2CH3), 2.14 (s, 3H), 2.10 (s, 3H), 2.01 (s, 3H) (3 × -CH3).

13C NMR (125 MHz, CDCl3): δ 169.9, 169.6, 169.1, 165.5 (4 × C=O), 106.8 (d, J1,F = 223.3 Hz, C-1), 72.4 (d, J5,F = 6.2 Hz, C-5), 69.6 (d, J3,F = 9.2 Hz, C-3), 68.4 (d, J2,F = 27.2 Hz, C-2), 67.5 (C-4), 53.1 (-CO2CH3), 20.6, 20.4(9), 20.4(8) (3 × -CH3). 19F NMR (470 MHz, CDCl3): δ -142.3 (dd, J1,F = 50.7 Hz, J2,F = 12.9 Hz). LRMS: 359.2 [M + Na]+. HRMS: calcd for C13H17FO9Na 359.0755 found 359.0747 [M + Na]+.

Methyl (2,3,4-tri-O-acetyl-5-C-bromo-β-D-galactopyranosyl fluoride)uronate (2i)

Small scale: The fluoride 1i (155 mg, 0.34 mmol) was photobrominated according to the general procedure (1.5 h) to afford 138 mg (97%) of the 5-C-bromide 2i as white foam after purification by flash chromatography, Rf = 0.7 (3:1 PhMe/EtOAc), [α]D − 80.1 (c. 2.8, CHCl3).

Gram scale: The fluoride 1i (1.1 g, 3.3 mmol) was photobrominated according to the general procedure (6 h) to afford 1.3 g (95%) of the 5-C-bromide 2i as white foam after purification by flash chromatography, identical in all respects to that prepared above.

1H NMR (500 MHz, CDCl3): δ 5.91 (dd, J3,4 = 3.3 Hz, J4,F = 1.8 Hz, 1H, H-4), 5.73 (ddd, J2,3 = 10.6 Hz, J3,F = 0.9 Hz, 1H, H-3), 5.64 (dd, J1,F = 51.4 Hz, J1,2 = 7.6 Hz, 1H, H-1), 5.45 (ddd, J2,F = 13.7 Hz, 1H,H-2), 3.88 (s, 3H, -CO2CH3), 2.13 (s, 3H, -OAc), 2.11 (s, 3H, -OAc), 2.00 (s, 3H, -OAc). 13C NMR (126 MHz, CDCl3) δ 169.7 (C=O), 169.2 (C=O), 168.6 (C=O), 163.8 (C=O), 107.0 (d, J1,F = 224.9 Hz, C-1), 84.0 (d, J5,F = 7.1 Hz, C-5), 71.2 (C-4), 68.0 (d, J2,F = 23.3 Hz, C-2), 67.3 (d, J3,F = 11.1 Hz, C-
3), 54.3 (OCH<sub>3</sub>), 20.7 (CH<sub>3</sub>), 20.56 (CH<sub>3</sub>), 20.54 (CH<sub>3</sub>). <sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>): δ -150.8 (dd, J<sub>1,F</sub> = 51.5 Hz, J<sub>2,F</sub> = 12.4 Hz). LRMS: 437.9 [M + Na]<sup>+</sup>. HRMS: calcd for C<sub>13</sub>H<sub>16</sub>BrFO<sub>9</sub>Na 436.9860 found 436.9853 [M + Na]<sup>+</sup>.

2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl fluoride (1j)

β-D-Glucose pentaacetate 1a (1.1 g, 2.8 mmol) was suspended at 0 °C in 33% HBr in acetic acid (10 mL) under an Ar atmosphere. After stirring for 15 min at 0 °C, the reaction mixture was allowed to warm up to r.t. and stirred for a further 2 h. The acetic acid was then removed by evaporation with toluene under reduced pressure. The crude oil was diluted with EtOAc (40 mL) and washed with cold sat. NaHCO<sub>3</sub> (3 × 40 mL) until bubbling ceased. The organic layer was dried (MgSO<sub>4</sub>) and concentrated under reduced pressure to give crude 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide, as a light-yellow foam, used in the next step without further purification. To a solution of the bromide in dry acetonitrile (15 mL) under an Ar atmosphere was added silver fluoride (1.8 g, 14.4 mmol). The reaction mixture was then stirred overnight in the dark at r.t. The reaction mixture was then filtered and concentrated under reduced pressure. The crude material was purified by flash chromatography to give the fluoride 1j (967 mg, 98%, two steps) as a white solid, m.p. 90–91 °C (lit. 87–88 °C), [α]<sub>D</sub> +20.1 (c 2.7, CHCl<sub>3</sub>; lit. +20.8), R<sub>f</sub> = 0.3 (10:1 PhMe/EtOAc). <sup>1</sup>H NMR spectra that matched the data reported in the literature.

2,3,4,6-Tetra-O-acetyl-5-C-bromo-β-D-glucopyranosyl fluoride (2j)

2,3,4,6-Tetra-O-acetyl-5-C-bromo-β-D-glucopyranosyl fluoride (2j)
The fluoride 1j (145 mg, 0.41 mmol) was photobrominated according to the general procedure (4.5 h) to afford 132 mg (75%) of the 5-C-bromide 2j as colorless syrup, after purification by flash chromatography, [α]D −103.8 (c. 1.4, CHCl3; lit.20 −109), Rf = 0.5 (10:1 PhMe/EtOAc). 1H and 13C NMR spectra that matched the data reported in the literature.19 1H NMR (500 MHz, CDCl3) δ 5.68 (dd, J1,F = 51.8 Hz, J1,2 = 7.4 Hz, 1H, H-1), 5.53 (td, J2,3 = 9.6 Hz, J3,F = 0.7 Hz, 1H, H-3), 5.29 (d, J3,4 = 9.6 Hz, 1H, H-4), 5.27 (ddd, J2,F =14.3 Hz, 1H, H-2), 4.55 (dd, J6a,6b = 12.3 Hz, 1H, 6a,F = 0.9 Hz, 1H, H-6a), 4.40 (d, 1H, H-6b), 2.13 (s, 3H, -OAc), 2.11 (s, 3H, -OAc), 2.08 (s, 3H, -OAc), 2.02 (s, 3H, -OAc). 13C NMR (126 MHz, CDCl3) δ 169.9 (C=O), 169.8 (C=O), 169.3 (C=O), 169.1 (C=O), 106.9 (d, J1,F = 222.8 Hz, C-1), 94.9 (d, J5,F = 7.3 Hz, C-5), 70.7 (d, J3,F = 6.0 Hz, C-3), 70.6 (d, J2,F = 7.8 Hz, C-2), 68.2 (C-4), 65.8 (C-6), 20.7 (CH3), 20.6 (CH3), 20.6 (CH3), 20.6 (CH3).

2-Acetamido-1,3,4,6-tetra-O-acetyl-2-deoxy-β-D-glucopyranose (1k)

The starting material 2-acetamido-1,3,4,6-tetra-O-acetyl-2-deoxy-β-D-glucopyranose 1k gave acceptable 1H NMR spectra that matched the data reported in the literature.21 1H NMR (500 MHz, CDCl3) δ 6.17 (d, J2,NH = 3.6 Hz, 1H, NH), 5.53 (d, J1,2 = 9.0 Hz, 1H, H-1), 5.31 – 5.14 (m, 2H, H-3, H-4), 4.49 (ddd, J2,3 = 10.7 Hz, 1H, H-2), 4.25 (dd, J6a,6b = 12.5 Hz, J5,6a = 4.1 Hz, 1H, H-6a), 4.07 (dd, J5,6b = 12.5, 2.4 Hz, 1H, H-6b), 3.99 (ddd, J4,5 = 9.8 Hz, 1H, H-5), 2.20 (s, 3H, -OAc), 2.09 (s, 3H, -OAc), 2.06 (s, 3H, -OAc), 2.05 (s, 3H, -OAc), 1.94 (s, 3H, -OAc).

The starting material 1k (285mg, 0.73mmol) was photobrominated according to the general procedure (8 h). No bromide formation was observed during this time.
Tetra-O-acetyl-2-phthalimido-2-deoxy-β-D-glucopyranose (1I)

The starting material tetra-O-acetyl-2-phthalimido-2-deoxy-β-D-glucopyranose 1I gave acceptable $^1$H NMR spectra that matched the data reported in the literature. $^{22}$ $^1$H NMR (500 MHz, CDCl$_3$) δ 7.86 (dd, $J = 5.5$, 3.1 Hz, 2H, Ph), 7.75 (dd, 2H, Ph), 6.51 (d, $J_{1,2} = 8.9$ Hz, 1H, H-1), 5.88 (dd, $J_{3,4} = 9.1$ Hz, 1H, H-3), 5.21 (dd, $J_{4,5} = 10.2$, Hz, 1H, H-4), 4.47 (dd, $J_{2,3} = 10.6$ Hz, 1H, H-2), 4.37 (dd, $J_{6a,6b} = 12.4$ Hz, 1H, H-6a), 4.15 (dd, 1H, H-6b), 4.02 (ddd, $J_{5,6a} = 4.5$ Hz, $J_{5,6a} = 2.1$ Hz, 1H, H-5), 2.11 (s, 3H, -OAc), 2.04 (s, 3H, -OAc), 2.00 (s, 3H, -OAc), 1.86 (s, 3H, -OAc).

1,3,4,6-Tetra-O-acetyl-5-C-bromo-2-deoxy-2-phthalimido-β-D-glucopyranose (2I)

The starting material 1I (212 mg, 0.44 mmol) was photobrominated according to the general procedure (8 h) to afford 96 mg (39%) of the 5C-bromide 2I as white solid, after purification by flash chromatography, m.p. 156–158 °C (lit.$^{23}$ 158 °C); $[\alpha]_D = -12.6$ (c.1.4, CHCl$_3$); $R_f = 0.2$ (10:1 PhMe/EtOAc), along with unreacted starting material 1I (37%). $^1$H and $^{13}$C NMR spectra matched the data reported in the literature.$^{23}$ $^1$H NMR (500 MHz, CDCl$_3$) δ 7.88 (dd, $J = 5.4$, 3.1 Hz, 2H, Ph), 7.77 (dd, 2H, Ph), 7.01 (d, $J_{1,2} = 9.2$ Hz, 1H, H-1), 6.16 (dd, $J_{3,4} = 9.4$ Hz, 1H, H-3), 5.33 (d, 1H, H-4), 4.65 (d, $J_{6a,6b} = 12.3$ Hz, 1H, H-6a), 4.58 (dd, $J_{2,3} = 10.6$ Hz, 1H, H-2), 4.35 (d, 1H, H-6b), 2.15 (s, 3H, -OAc), 2.09 (s, 3H, -OAc), 2.02 (s, 3H, -OAc), 1.86 (s, 3H, -OAc). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 169.9 (C=O), 169.7 (C=O), 169.3 (C=O), 168.2 (C=O), 167.3 (2×C=O), 134.7 (Ph), 124.0 (Ph), 95.4 (C-5), 89.9 (C-1), 69.3 (C-3), 69.2 (C-4), 66.0 (C-6), 52.8 (C-2), 20.8 (CH$_3$), 20.8 (CH$_3$), 20.7 (CH$_3$), 20.5 (CH$_3$).
1,2,2',3,3',4',6,6'-Octa-\(O\)-acetyl-\(\beta\)-maltose (1m)

D-Maltose (2.2 g, 6.4 mmol, 1.0 equiv.) and NaOAc (630 mg, 7.7 mmol, 1.2 equiv.) were dissolved in Ac\(_2\)O (20 ml) and heated at 1.5 h under reflux. Afterwards the reaction mixture was cooled to room temperature and treated with iced water (100 ml). The resulting precipitate was collected and recrystallized from water to afford the desired peracetate as a mixture of anomers (\(\alpha: \beta = 5: 95\)), (4.0 g, 92%) as colorless crystals. Subsequently, pure \(\beta\)-maltose octaacetate \(1m\) (82%) was obtained through a second recrystallization from EtOAc and hexane, m.p. 160.1–160.6 °C (lit. 24159–160 °C), [\(\alpha\)]\(_D\) +59.2 (c 2.1, CHCl\(_3\), lit. 24 +64). The product gave acceptable \(^1\)H NMR spectra that matched the data reported in the literature. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 5.74 (d, \(J_{1,2} = 8.2\) Hz, 1H, H-1\(\text{I}\)), 5.40 (d, \(J_{1,2} = 4.0\) Hz, 1H, H-1\(\text{II}\)), 5.35 (dd, \(J_{2,3} = 10.5\) Hz, \(J_{3,4} = 9.7\) Hz, 1H, H-3\(\text{II}\)), 5.29 (dd, \(J_{2,3} = 9.1\) Hz, \(J_{1,2} = 8.2\) Hz, 1H, H-2\(\text{I}\)), 4.86 (dd, \(J_{2,3} = 10.5\) Hz, \(J_{1,2} = 4.0\) Hz, 1H, H-2\(\text{II}\)), 4.45 (dd, \(J_{6a,6b} = 12.3\) Hz, \(J_{5,6a} = 2.5\) Hz, 1H, H-6\(\text{aI}\)), 4.24 (dd, \(J_{6a,6b} = 12.4\) Hz, \(J_{5,6a} = 3.7\) Hz, 1H, H-6\(\text{aII}\)), 4.23 (dd, \(J_{6a,6b} = 12.3\) Hz, \(J_{5,6b} = 4.4\) Hz, 1H, H-6\(\text{bI}\)), 4.03 (dd, \(J_{6a,6b} = 12.4\) Hz, \(J_{5,6b} = 2.4\) Hz, 1H, H-6\(\text{bII}\)), 4.02 (dd, \(J_{4,5} = 9.6\) Hz, \(J_{3,4} = 8.7\) Hz, 1H, H-4\(\text{I}\)), 3.94 (ddd, \(J_{4,5} = 10.2\) Hz, \(J_{5,6a} = 3.7\) Hz, \(J_{5,6b} = 2.4\) Hz, 1H, H-5\(\text{II}\)), 3.84 (ddd, \(J_{4,5} = 9.6\) Hz, \(J_{5,6a} = 4.4\) Hz, \(J_{5,6b} = 2.5\) Hz, 1H, H-5\(\text{I}\)), 2.14 (s, 3H, -OAc), 2.10 (s, 3H, -OAc), 2.09 (s, 3H, -OAc), 2.05 (s, 3H, -OAc), 2.03 (s, 3H, -OAc), 2.02 (s, 3H, -OAc), 2.01 (s, 3H, -OAc), 2.00 (s, 3H, -OAc).

\(1,2,2',3,3',4',6,6'\)-Octa-\(O\)-acetyl-5-C-bromo-\(\beta\)-maltose (2m)

\(\beta\)-Maltose octaacetate \(1m\) (172 mg, 0.25 mmol) was photobrominated according to the general
procedure (1 h) to afford, after purification by flash chromatography, $R_f = 0.3$ (2:1 PhMe/EtOAc), 151 mg of an inseparable mixture of the bromide 2m (45%) and unreacted starting material 1m (38%) as a colorless oil. Key data for 2m: $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 6.18 (d, $J_{1,2} = 8.7$ Hz, 1H, H-1$^1$), 5.65 (t, $J_{3,4} = 9.7$ Hz, 1H, H-3$^1$), 5.14 (dd, $J_{2,3} = 9.9$ Hz, 1H, H-2$^1$), 3.93 (d, 1H, H-4$^1$). $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 91.4 (C-1$^1$), 71.9 (C-3$^1$), 68.7 (C-2$^1$), 68.1 (C-4$^1$).
NMR Spectra
$^{13}$C NMR (125 MHz, CDCl$_3$)

COSY NMR (500 MHz, CDCl$_3$)
**1e**

$^1$H NMR (500 MHz, CDCl$_3$)

![NMR Spectrum 1e](image)

**1f**

$^1$H NMR (500 MHz, CDCl$_3$)

![NMR Spectrum 1f](image)
References


