Supporting Information:

Scheme S1

Methyl 1-(4-formyl-2-nitrophenyl)-2,3,4-tri-O-acetyl-β-D-glucopyronuronate (6): Methyl 1-bromo-2,3,4-tri-O-acetyl-α-D-glucopyronuronate (10.75 g, 27.1 mmol) was dissolved in 250 ml anhydrous MeCN. 4-hydroxy-3-nitrobenzaldehyde (7.64 g, 45.7 mmol) was then added followed by 28.5 g (123 mmol) of Ag2O. The resulting slurry was stirred in the dark under N2 for 4h. The solution was filtered through Celite to remove solids and the filtrate concentrated in vacuo. The residue was brought up in EtOAc (400 ml) and washed with saturated NaHCO3 (6 x 200 ml), water and brine. The organic layer was dried over MgSO4, filtered and concentrated in vacuo. The beige solid was triturated with hexanes yielding 6 (12.52 g, 96%). 1H NMR (500 MHz, DMSO-d6) δ 2.01, 2.02, 2.03 (3s, 3 x 3H, OAc), 3.64 (s, 3H, COOCH3), 4.80 (d, 1H, H-5, J=10 Hz), 5.15 (m, 2H, H-2, H-4), 5.74 (m, 1H, H-3), 5.94 (d, 1H, H-1 J=8 Hz), 7.64 (d, 1H, ArH, J=9 Hz), 8.22 (dd, 1H, ArH, J=9 Hz, J’=1.5 Hz), 8.44 (d, 1H, ArH, J=1.5 Hz), 9.98 (s, 1H, CHO); 13C NMR (126 MHz, DMSO-d6) δ 20.17, 20.22, 20.26, 52.65, 68.49, 69.67, 70.43, 71.18, 97.25, 117.58, 126.23, 131.07, 134.74, 140.25, 152.10, 166.85, 168.72, 169.34, 169.49, 190.48; IR (KBr plate) ν 2956, 1756, 1700, 1612, 1538, 1368, 1235, 1074, 1039 cm⁻¹; ESI-MS m/z (M + Na)+ 506.1; Anal. Calcd for C20H21NO13: C 49.69, H 4.38, N 2.90; Found C 49.92, H 4.55, N 2.80.

Methyl 1-(4-hydroxymethyl-2-nitrophenyl)-2,3,4-tri-O-acetyl-β-D-glucopyronuronate (7): 1,3 1.41 g (37.3 mmol) NaBH4 were added to a stirring solution of 12.03 g (24.9 mmol) NaBH4 were added to a stirring solution of 12.03 g (24.9 mmol) 6 and 5 g silica gel at 0°C in 300 ml 1:5 IPA:CHCl3. After 45 min, the solution was poured into 300 ml ice water and filtered through Celite. The layers were separated and the organic fraction washed with brine, dried (MgSO4), concentrated in vacuo, and triturated with Et2O, yielding 7 as a white solid (11.65 g, 96%). 1H NMR (500 MHz, DMSO-d6) δ 1.99 (s, 3H, OAc), 2.02 (s, 6H, OAc), 3.33 (br
Methyl 1-(4-(2-bromoethylcarbamoyloxymethyl)-2-nitrophenyl)-2,3,4-tri-O-acetyl-\(\beta\)-D-glucopyranuronate (9): 3.75 g (7.73 mmol) sugar 7 and 189 mg (1.55 mmol) DMAP in 50 ml dry CH\(_2\)Cl\(_2\) under N\(_2\) were subjected to 2.51 g (15.5 mmol) 1,1'-carbonyl-diimidazole. When the reaction was complete by TLC (silica, 5% MeOH/CH\(_2\)Cl\(_2\)) (2.25 h), the solution was washed with water, 5% NaH\(_2\)PO\(_4\), sat. NaHCO\(_3\), and brine. The organic layer was dried (MgSO\(_4\)) and concentrated in vacuo to yield 4.19 g of the imidazolyl intermediate 8. 8 was dissolved in 65 ml anhydrous CH\(_2\)Cl\(_2\) under N\(_2\) and cooled to 0°C. 0.90 ml (7.95 mmol) MeOTf was added over 5 min. After 30 min, the reaction was diluted with 30 ml Et\(_2\)O and cooled to -20°C to allow all methylated product to precipitate. The white solid was collected by filtration, washed with Et\(_2\)O and dried in vacuo. The activated compound was suspended in 50 ml anhydrous CH\(_2\)Cl\(_2\) under N\(_2\) and 2.22 g (10.85 mmol) 2-bromoethylamine hydrobromide were added. The slurry was brought to 0°C and 1.51 ml (10.85 mmol) TEA added in one portion. The reaction stirred for 2 h and was then washed with water and brine. The organic layer was dried (MgSO\(_4\)), concentrated in vacuo and purified by chromatography (silica, 0-55% EtOAc in hexanes) to give 2.99 g (65%) 9 as a white solid. \(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) 2.00 (s, 3H, OAc), 2.02 (s, 6H, OAc), 3.39 (t, 2H, \(J=6\) Hz), 3.47 (t, 2H, \(J=6\) Hz), 3.64 (s, 3H, COOCH\(_3\)), 4.73 (t, 2H, \(J=6\) Hz), 3.64 (s, 3H, COOCH\(_3\)), 4.73 (d, 1H, H-5, \(J=10\) Hz), 5.06-5.14 (m, 4H, benzyllic C\(_2\)H, H-2, H-4), 6.46 (m, 1H, H-3), 5.74 (d, 1H, H-1, O\(\text{H}\)), 7.43 (d, 1H, ArH, \(J=9\) Hz), 7.67 (m, 2H, ArH, N\(\text{H}\)), 7.89 (s, 1H, ArH); \(^{13}\)C NMR (101 MHz, DMSO-\(d_6\)) \(\delta\) 20.22, 20.26, 20.31, 32.44, 42.34, 52.63, 63.81, 68.65, 69.83, 70.66, 71.01, 97.79, 117.72, 123.86, 132.77, 133.51, 139.99, 147.58, 155.70, 166.78, 168.62, 169.21, 169.38; ESI-MS \(m/z\) (M + Na)\(^+\) 657.0, 659.0 (Br isotope pattern); Anal. Calcd for C\(_{23}\)H\(_{27}\)BrN\(_2\)O\(_{14}\): C 43.48, H 4.28, N 4.41; Found C 43.74, H 4.20, N 4.34.

Methyl 1-(4-(2-bromoethylcarbamoyloxymethyl)-2-nitrophenyl)-\(\beta\)-D-glucopyranuronate (10): 2.84 g (4.47 mmol) 9 were suspended in 90 ml dry MeOH under N\(_2\) at 0°C. 650 \(\mu\)L 30% w/v NaOMe in MeOH were added and the solution stirred for 100 min. The reaction was quenched with 197 \(\mu\)L acetic acid. Removal of solvent was followed by purification on silica (10% MeOH/CH\(_2\)Cl\(_2\)). The resulting solid was dissolved in acetone and filtered through a 0.2 \(\mu\)m PTFE filter to remove any silica. The solution was concentrated in vacuo and triturated (Et\(_2\)O) to give 1.80 g (79%) 10. Data for 10 \(^1\)H NMR (500 MHz, DMSO-\(d_6\)) \(\delta\) 3.26-3.42 (m, 5H), 3.47 (t, 2H, \(J=6\) Hz), 3.65 (s, 3H, COOCH\(_3\)), 4.13 (d, 1H, H-5, \(J=10\) Hz), 5.04 (s, 2H, benzyllic C\(_2\)H), 5.31 (m, 2H, H-1, O\(\text{H}\)), 5.49 (d, 1H, O\(\text{H}\), \(J=6\) Hz), 5.54 (d, 1H, O\(\text{H}\), \(J=5\) Hz), 7.44 (d, 1H, ArH, \(J=9\) Hz), 7.63 (m, 2H, ArH, N\(\text{H}\)), 7.86 (s, 1H, ArH); \(^{13}\)C NMR (126 MHz, DMSO-\(d_6\)) \(\delta\) 32.44, 42.35, 52.02, 63.94, 71.19, 72.71, 75.17, 75.61, 99.76, 116.86, 124.09, 131.27, 133.54, 139.86, 148.58, 155.88, 169.06; ESI-MS \(m/z\) (M + Na)\(^+\) 530.9, 532.9 (Br isotope pattern);
Anal. Calcd for C$_{17}$H$_{21}$BrN$_2$O$_{11}$: C 40.09, H 4.16, N 5.50; Found C 40.32, H 4.46, N 5.39.

The major byproduct of this reaction was $\alpha,\beta$-unsaturated compound 11, resulting from base-catalyzed $\beta$-acetate elimination. Data for 11

$^1$H NMR (500 MHz, CD$_3$OD) $\delta$ 3.23 (t, 2H, $J$=5 Hz), 3.45 (t, 2H, $J$=5 Hz), 3.77 (s, 3H, COOCH$_3$), 4.09 (m, 2H), 5.09 (s, 2H, benzylic CH$_2$), 5.90 (br. s, 1H, H-4), 6.28 (d, 1H, H-1 $J$=2.5 Hz), 7.57 (d, 1H, ArH, $J$=9 Hz), 7.66 (d, 1H, ArH, $J$=9 Hz), 7.92 (s, 1H, ArH); $^{13}$C NMR (126 MHz, CD$_3$OD) $\delta$ 33.67, 44.41, 53.12, 65.83, 66.77, 70.58, 100.08, 114.14, 120.19, 126.04, 134.37, 135.11, 141.05, 142.02, 150.24, 158.73, 163.96.

Methyl 1-(4-(2-hydroxy-ethylcarbamoyloxymethyl)-2-nitrophenyl)-2,3,4-tri-O-acetyl-$\beta$-D-glucopyronuronate (15): 1.05 ml (9.25 mmol) MeOTf were added over 5 min to a solution of 4.87 g (8.41 mmol) 8 in 60 ml anhydrous CH$_2$Cl$_2$ under N$_2$ at 0°C. After 30 min, the reaction was diluted with 30 ml Et$_2$O and cooled to -20°C to allow all methylated product to precipitate. The white solid was collected by filtration, washed with Et$_2$O and dried in vacuo. The activated compound was suspended in 60 ml anhydrous CH$_2$Cl$_2$ under N$_2$ and brought to 0°C. 761 µl (12.6 mmol) 2-hydroxyethylamine were added and the solution was allowed to warm to room temperature over 2 h and was then washed with water, 5% NaH$_2$PO$_4$, sat. bicarbonate and brine. The organic layer was dried (MgSO$_4$), concentrated in vacuo and purified by chromatography (silica, 0-5% MeOH in CH$_2$Cl$_2$) to give 3.68 g (77%) 15 as a white solid.

$^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 1.99 (s, 3H, OAc), 2.02 (s, 6H, OAc), 3.05 (q, 2H, $J$=6 Hz), 3.33 (s, 1H, O$_H$), 3.38 (q, 2H, $J$=6 Hz), 3.64 (s, 3H, COOCH$_3$), 4.64 (t, 0.5H, NH, $J$=6 Hz), 4.74 (d, 1H, H-5, $J$=10 Hz), 5.02 (s, 2H, benzylic CH$_2$), 5.10 (m, 2H), 5.46 (t, 1H, $J$=10 Hz), 5.46 (d, 1H, H-1, $J$=8 Hz), 7.27 (t, 0.5H, NH, $J$=6 Hz), 7.43 (d, 1H, ArH, $J$=9 Hz), 7.67 (d, 1H, ArH, $J$=9Hz), 7.88 (s, 1H, ArH); $^{13}$C NMR (126 MHz, DMSO-d$_6$) $\delta$ 20.20, 20.23, 20.28, 43.09, 52.64, 59.86, 63.59, 68.69, 69.87, 70.71, 71.05, 97.89, 117.80, 123.89, 133.12, 133.55, 140.11, 147.63, 155.93, 166.90, 168.74, 169.33, 169.51; IR (KBr plate) v 3394, 2962, 1756, 1708, 1535, 1366, 1235, 1073, 1039 cm$^{-1}$; ESI-MS $m/z$ (M + Na)$^+$ 595.3; Anal. Calcd for C$_{23}$H$_{28}$N$_2$O$_{15}$: C 48.25, H 4.93, N 4.89; Found C 47.96, H 5.14, N 4.91.

Methyl 1-(4-(2-hydroxy-ethylcarbamoyloxymethyl)-2-nitrophenyl)-$\beta$-D-glucopyronuronate (16): 3.49 g (6.10 mmol) 15 in 100 ml anhydrous MeOH were cooled to 0°C under N$_2$. 776 µl (4.27 mmol) 30% NaOMe in MeOH were added and the solution allowed to stir for 1 h. 210 µl acetic acid were added and the volatiles removed in vacuo. The resulting solid was purified by chromatography (silica, 10-15% MeOH in CH$_2$Cl$_2$) and excess silica removed by filtration of an acetone solution through a 0.2 µm PTFE filter. Trituration of the solid with Et$_2$O yielded 2.15 g (79%) 16 as a white solid.

$^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 3.05 (q, 2H, $J$=6 Hz), 3.25-3.44 (m, 6H), 3.66 (s, 3H, COOCH$_3$), 4.12 (d, 1H, H-5, $J$=10 Hz), 4.63 (t, 0.5H, NH, $J$=5.5 Hz), 5.00 (s, 2H, benzylic CH$_2$), 5.31 (d, 2H, H-1, OH), 5.49 (d, 1H, OH, $J$= 5.5 Hz), 5.54 (d, 1H, OH, $J$=4.5 Hz), 7.25 (t, 0.5H, NH, $J$=6 Hz), 7.44 (d, 1H, ArH, $J$=9 Hz), 7.63 (d, 1H, ArH, $J$=9Hz), 7.85 (s, 1H, ArH); $^{13}$C NMR (126 MHz, DMSO-d$_6$) $\delta$ 43.10, 52.03, 59.88, 63.70, 71.20, 72.72, 75.17, 75.61, 99.80, 116.86, 124.05, 133.51, 133.51, 139.87, 148.53, 155.99, 169.07; IR (KBr plate) v 3394, 2962, 1757, 1705, 1535, 1533, 1354, 1252, 1083, 1060,
1019 cm⁻¹; ESI-MS m/z (M + Na)⁺ 469.2; Anal. Calcd for C₁₇H₂₂N₂O₁₂: C 45.74, H 4.97, N 6.28; Found C 47.92, H 5.06, N 5.98.

Methyl 1-(4-(2-methanesulfonyloxy-ethylcarbamoyloxymethyl)-2-nitrophenyl)-β-D-glucopyranuronate (14): 950 µl (6.81 mmol) NEt₃, 100mg (0.85 mmol) DMAP and 1.90 g (4.26 mmol) 16 were dissolved in 50 ml anhydrous pyridine and cooled to 0°C. 529 µl (6.81 mmol) methanesulfonyl chloride were added and the reaction checked by TLC (10% MeOH/CH₂Cl₂). After 1 h an additional 0.5 eq (2.13 mmol) of NEt₃ and MsCl were added and the solution was allowed to stir for 1 h more. The volatiles were then removed in vacuo and the resulting oil purified by chromatography (silica, 10% MeOH/CH₂Cl₂). The solid was dissolved in acetone, filtered as in 16, concentrated and triturated with hexanes to give 1.60 g (72%) 14. The compound decomposes upon prolonged storage at ambient temperature even desiccated under N₂. ¹H NMR (500 MHz, CD₃OD) δ 3.03 (s, 3H), 3.44 (m, 2H), 3.48-3.66 (m, 3H, H-2-4), 3.76 (s, 3H, COOCH₃), 4.09 (d, 1H, H-5, J=10 Hz), 4.25 (m, 2H), 5.09 (s, 2H, benzylic CH₂), 5.19 (d, 1H, H-1), 7.37 (d, 1H, ArH, J=8 Hz), 7.59 (d, 1H, ArH, J=8 Hz), 7.83 (s, 1H, ArH); ¹³C NMR (126 MHz, CD₃OD) δ 37.32, 41.37, 53.11, 66.06, 69.95, 72.77, 74.48, 76.89, 77.25, 102.44, 118.94, 125.64, 133.44, 134.52, 142.24, 150.61, 158.62, 170.81; Anal. Calcd for C₁₈H₂₄N₂O₁₄S: C 41.22, H 4.61, N 5.34; Found C 41.52, H 4.55, N 5.24.

References: