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Note

Koenigs–Knorr reaction of fusel alcohols with methyl (1-bromo-2,3,4-tri-*O*-acetyl-α-D-glucopyranosid)uronate leading to the protected alkyl glucuronides—crystal structures and high resolution ^{1}H and ^{13}C NMR data

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ABSTRACT

Crystal structures and high resolution ^{1}H and ^{13}C NMR spectral data for methyl (alkyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)uronates (alkyl = methyl, ethyl, *n*-propyl, *i*-propyl, *n*-butyl, *sec*-butyl, *i*-butyl, *n*-pentyl, 2-methyl-1-butyl and 3-methyl-1-butyl) are presented.

Glucuronidation is one of the main metabolic pathways to remove toxic substances from the human organism. By this means the elimination of lipophilic drugs or pollutants for example, morphine, paracetamol or some hydroxylated polychlorinated biphenyls (PCBs),[1] from the body after phase I oxidation is advanced by urine or faeces, as the water solubility of these substances is increased. To a lesser extent hydrophilic molecules are also metabolized through glucuronidation. For example, 0.02–0.06% of ingested ethanol is metabolised in this way,[2] and the conversion rates for longer chain alkyl alcohols are suspected to be higher than those of ethanol.[3] Because alcohol metabolites play a significant role in alcohol-abuse related analytical research.[2,4] the analysis of these glucuronic metabolites, including their synthesis and full characterisation is mandatory.

Several short-chain alkyl alcohols such as methanol, *n*-propanol, *n*-butanol, *i*-butanol, *sec*-butanol and 2- and 3-methylbutanol are found in alcoholic beverages as a result of fermentation processes.[5] These alcohols have significant importance as so-called fusel alcohols, and their glucuronides are interesting markers for the consumption of alcohol.[3] We herein report the synthesis, high-resolution NMR and X-ray analysis of several protected short-chain alkyl glucopyranuronates according to the reaction scheme given in Figure 1.

Treatment of D-glucurono-6,3-lactone (**1**) with sodium methoxide in methanol gave a mixture of α- and β-methyl-glucopyranuronates, which were then combined with acetic acid anhydride and catalytic perchloric acid to yield the anomeric acetates (**2,** Fig. 1). The crystalline product was subsequently reacted with hydrobromic acid to give the corresponding acetobromo-α-D-glucuronic acid methyl ester (**3**) as a crystalline product as reported earlier.[6]

The yields of the following Koenigs–Knorr reaction with the corresponding short chain alcohols to the fully protected glucopyranuronates could be increased compared to earlier procedures[7] by thorough exclusion of any traces of water. Full NMR- and single crystal structure characterisation were carried out for all products. To complete the synthesis of the protected glucuronides of fusel alcohols, the glucuronides of *i*-propanol and *n*-pentanol were also prepared.

Table 1 shows the ^{1}H NMR and ^{13}C NMR data of the anomeric centre of the synthesised glucuronides. It can be seen that the NMR shifts and coupling constants differ only slightly in all of the glucopyranuronates. The influence of the alkyl moiety on the shift and coupling constants of the anomeric centre is negligible.

From the coupling constant of the anomeric proton with the adjacent ring-proton a β-configuration can be deduced, which was confirmed by the X-ray structures. From this reaction, β-glucopyranuronates were obtained as anomerically pure products.[8] Noticeable in the proton NMR is an ABX-pattern of the diastereotopic protons of the CH_2-group at C-1′, which leads to a complex

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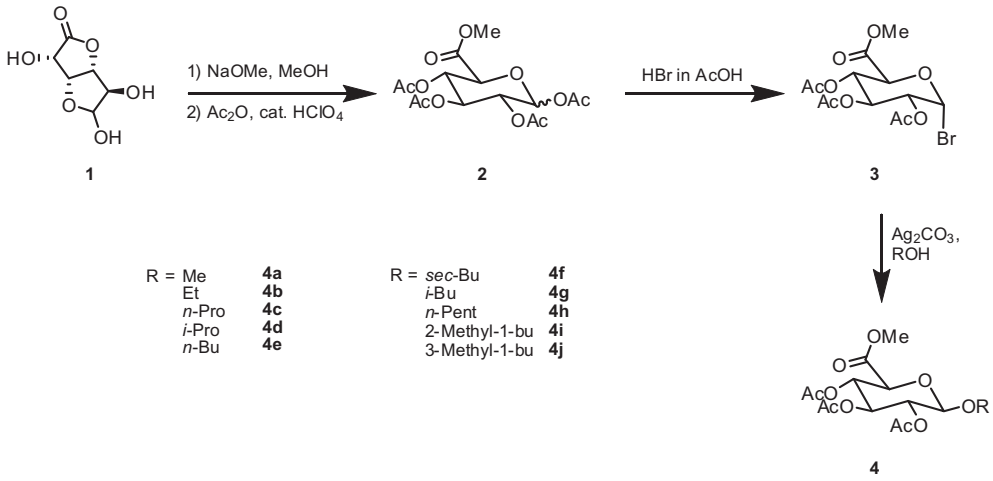

Figure 1. Reaction scheme for short chain alkyl alcohols.

Table 1
NMR data of the anomeric centre at C-1

Anomeric centre C-1	^{1}H NMR		^{13}C NMR
	$\delta_{H\text{-}1}$	$J_{1,2}$ (Hz)	$\delta_{C\text{-}1}$
4a	4.47	7.7	101.7
4b	4.56	7.7	100.5
4c	4.52	7.7	100.7
4d	4.54	7.7	99.5
4e	4.53	7.7	100.8
4f	4.57	7.7	100.7
	4.58	7.5	99.1
4g	4.51	7.8	101.1
4h	4.54	7.8	100.8
4i	4.49	7.7	101.2
4j	4.51	7.7	100.8

spectrum if the alkyl alcohol itself carries an enantiomeric centre, like the *sec*-butyl rest in **4f** and the 2-methyl-1-butyl group in **4i**.

The crystal structures of the glucuronides **4a**–**j** are nearly in congruence with each other. As deduced from the NMR data, the alcohol attached to the sugar moiety has very little influence on the ring itself. Comparing the shortest alkyl chain (Me, **4a**) with the longest (Pent, **4h**) introduced, the plane of the sugar ring remains untwisted and the alkyl chains changes the cell volume by only 25%. Single crystal X-ray showed only one aberration of the unit cell, which is that the unit cell of **4i** (2-Me-1-Bu) contains two molecules. Figure 2 shows two examples of the measured crystal structures.

1. Experimental

1.1. General procedures

Melting points were determined on a Krüss melting point meter KSP I N and are uncorrected. The NMR spectra were recorded on a Bruker Avance II 500 instrument at 500 MHz with the $CHCl_3$ peak as internal standard. ^{13}C assignments were done on the basis of 2D-NMR spectra (C–H COSY) and chemical shifts. Optical rotations were measured with a Jasco Digital Polarimeter DIP-370 at room temperature. Mass spectra were recorded with an Exactive Benchtop Orbitrap™ from Thermo Fisher Scientific.

The single crystal X-ray data collection was carried out on a Bruker AXS SMART diffractometer at room temperature using Mo Ka radiation (l = 0.71073 Å), monochromatised by a graphite crystal. The crystals were measured at room temperature. Data reduction was performed by using Bruker AXS SAINT and SADABS packages. The structures were solved by direct methods and refined by full-matrix least-squares calculation using SHELX.[9] Anisotropic thermal parameters were employed for non-hydrogen atoms. The hydrogen atoms were treated isotropically with U_{iso} = 1.2 times the U_{eq} value of the parent atom. In the case of methyl groups U_{iso} = 1.5 times the U_{eq} value was chosen. Crystal data and selected refinement details for **4a**–**4j** are summarised in Table 2. CCDC-853961–853972 contain the supplementary crystallographic data for **2**–**4j** described in this paper. The data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.cdc.cam.ac.uk/data_request/cif.

1.2. General procedure for the synthesis of protected short-chain alkyl glucopyranuronates

To a stirred solution of methyl (2,3,4-tri-*O*-acetyl-α-D-glucopyranosyl)uronate bromide (**3**) in dry toluene under Argon atmosphere the corresponding dried alcohol was added and the solution was warmed to 75 °C. Subsequently, silver carbonate was added in three portions over a period of 3 h. Then the reaction was stirred at room temperature for 18 h. Afterwards, the suspension was filtered and the filtrate was evaporated to dryness. Purification by flash chromatography (silica gel, cyclohexane–ethyl acetate 1:1) or recrystallisation from *i*-propanol gave the product **4**.

1.2.1. Methyl (methyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)-uronate (4a)

According to the general procedure, 0.75 g (1.89 mmol, 1.0 equiv) **3**, 1.5 mL methanol (37.0 mmol, 19.6 equiv) and 0.75 g silver carbonate (2.72 mmol, 1.4 equiv) were reacted to yield **4a** after recrystallisation from *i*-propanol as colourless crystals (0.56 g, 1.61 mmol, 85.4%). Mp 154.1–154.4 °C; $[\alpha]_D^{20}$ −30.3 (*c* 10.4, $CHCl_3$); calcd for $C_{14}H_{20}O_{10}^+$ 349.1135; found 349.1108 $[M+H]^+$; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.95 (s, 3H, OAc), 1.96 (s, 3H, OAc), 1.98 (s, 3H, OAc), 3.45 (s, 3H, H-1′), 3.70 (s, 3H, OMe), 4.03 (d, $J_{5,4}$ = 9.5 Hz, 1H, H-5), 4.47 (d, $J_{1,2}$ = 7.7 Hz, 1H, H-1), 4.99 (dd, $J_{2,3}$ = 9.3, $J_{2,1}$ = 7.7 Hz, 1H, H-2), 5.23 (dd, J = 9.4, J = 9.3 Hz, 1H, H-4), 5.24 (dd, J = 9.3, J = 9.0 Hz, 1H, H-3); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 20.5 ((C═O)CH_3), 20.6 ((C═O)CH_3), 20.7 ((C═O)CH_3), 52.9 (OMe), 57.3 (C-1′), 69.5 (C-4), 71.2 (C-3), 72.1 (C-2), 72.6 (C-5), 101.7 (C-1), 167.3 (C-6), 169.3 ((*C*═O)CH_3), 169.4 ((*C*═O)CH_3), 170.1 ((*C*═O)CH_3).

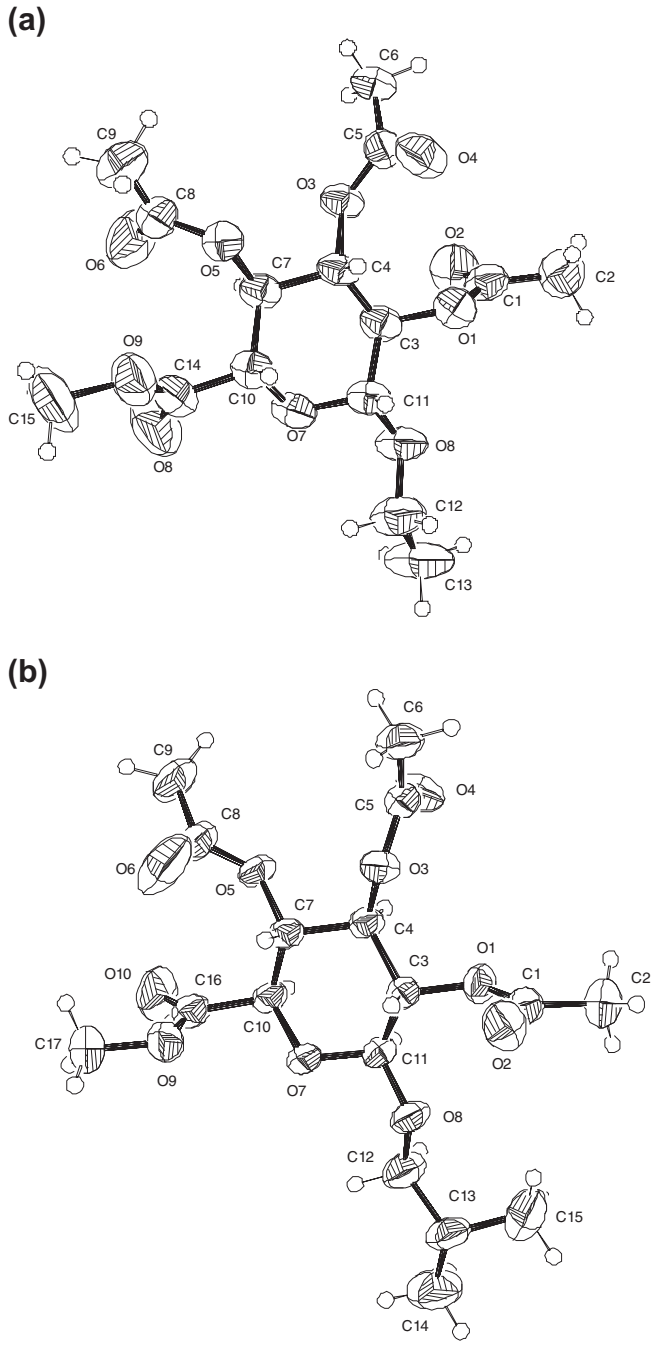

Figure 2. Molecular structure of **4b** (a) and **4g** (b), with displacement ellipsoids drawn at the 50% probability level.

1.2.2. Methyl (ethyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid) urona te (4b)

According to the general procedure, 0.9 g **3** (2.27 mmol, 1.0 equiv), 0.8 mL ethanol (13.7 mmol, 6.1 equiv) and 0.81 g silver carbonate (2.95 mmol, 1.3 equiv) were reacted to yield **4b** after recrystallisation from *i*-propanol as colourless crystals (0.68 g, 1.88 mmol, 83%). Mp 150.3–151.0 °C; $[\alpha]_D^{20}$ −35.4 (*c* 10.3, $CHCl_3$); calcd for $C_{15}H_{22}O_{10}^{+}$ 363.1291; found 363.1264 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$) δ = 1.19 (t, $J_{2',1'}$ = 7.0 Hz, 3H, H-2′), 2.01 (s, 3H, OAc), 2.02 (s, 3H, OAc), 2.04 (s, 3H, OAc), 3.58 (dq, $J_{1'A,1'B}$ = 9.9, $J_{1'A,2'}$ = 7.1 Hz, 1H, H-$1'_A$), 3.75 (s, 3H, OMe), 3.93 (dq, $J_{1'B,1'A}$ = 9.9, $J_{1'B,2'}$ 7.1 Hz, 1H, H-$1'_B$), 4.04 (d, $J_{5,4}$ = 9.6 Hz, 1H, H-5), 4.56 (d, $J_{1,2}$ = 7.7 Hz, 1H, H-1), 4.88 (dd, $J_{2,3}$ = 9.2, $J_{2,1}$ = 7.8 Hz, 1H, H-2), 5.23 (dd, *J* = 9.5, *J* = 9.4 Hz, 1H, H-3), 5.24 (dd, *J* = 9.4, *J* = 9.1 Hz, 1H, H-4); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 14.9 (C-2′), 20.5 ((C=O)CH_3), 20.6 ((C=O)CH_3), 20.6 ((C=O)CH_3), 52.8 (OMe), 65.8 (C-1′), 69.5 (C-4), 71.3 (C-3), 72.1 (C-2), 72.6 (C-5), 100.5 (C-1), 167.3 (C-6), 169.2 ((*C*=O)CH_3), 169.3 ((*C*=O)CH_3), 170.1 ((*C*=O)CH_3).

1.2.3. Methyl (*n*-propyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)-uronate (4c)

According to the general procedure, 0.75 g (1.89 mmol, 1.0 equiv) **3**, 1.5 mL *n*-propanol (20.0 mmol, 10.6 equiv) and 0.75 g silver carbonate (2.72 mmol, 1.4 equiv) were reacted to yield **4c** after recrystallisation from *i*-propanol as colourless crystals (0.50 g, 1.33 mmol, 71%). Mp 113.5–113.8 °C; $[\alpha]_D^{20}$ −35.7 (*c* 10.5, $CHCl_3$); calcd for $C_{16}H_{24}Om_{10}^{=}$ 377.1448; found 377.1417 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$) δ = 0.87 (t, $J_{3',2'}$ = 7.5 Hz, 3H, H-3′), 1.52–1.61 (m, 2H, H-2′), 2.00 (s, 3H, OAc), 2.02 (s, 3H, OAc), 2.04 (s, 3H, OAc), 3.41 (dt, $J_{1'A,1'B'}$ = 9.4, $J_{1'A,2'}$ = 6.8 Hz, 1H, H-$1'_A$), 3.73 (s, 3H, OMe), 3.84 (dt, $J_{1'B,\ 1'A}$ = 9.5, $J_{1'B,2'}$ = 6.4 Hz, 1H, H-$'_B$), 4.01 (d, $J_{5,4}$ = 9.3 Hz, 1H, H-5), 4.52 (d, $J_{1,2}$ = 7.7 Hz, 1H, H-1), 4.98 (dd, $J_{2,3}$ = 8.6, $J_{2,1}$ = 7.7 Hz, 1H, H-2), 5.20 (dd, *J* = 9.6, *J* = 8.7 Hz, 1H, H-3), 5.24 (dd, *J* = 9.6, *J* = 9.3 Hz, 1H, H-4); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 10.2 (C-3′), 20.5 ((C=O)CH_3), 20.5 ((C=O)CH_3), 20.6 ((C=O)CH_3), 22.5 (C-2′), 52.8 (OMe), 69.5 (C-4), 71.2 (C-3), 71.9 (C-1′), 72.1 (C-2), 72.6 (C-5), 100.7 (C-1), 167.3 (C-6), 169.2 ((*C*=O)CH_3), 169.4 ((*C*=O)CH_3), 170.2 ((*C*=O)CH_3).

1.2.4. Methyl (*i*-propyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)-uronate (4d)

According to the general procedure, 0.9 g **3** (2.27 mmol, 1.0 equiv), 1.8 mL *i*-propanol (23.4 mmol, 10.3 equiv) and 0.81 g silver carbonate (2.95 mmol, 1.3 equiv) were reacted to yield **4d** after purification by flash chromatography (silica gel, cyclohexane/ethyl acetate 1:1) as colourless crystals (0.49 g, 1.31 mmol, 58%). Mp 129.2–129.4 °C; $[\alpha]_D^{20}$ −31.4 (*c* 9.7, $CHCl_3$); calcd for $C_{18}H_{28}O_{10}^{+}$ 375.1291; found 375.1301 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$) δ = 1.12 (d, $J_{3',1'}$ = 6.3 Hz, 3H, H-3′), 1.20 (d, $J_{2',1'}$ = 6.2 Hz, 3H, H-2′), 2.00 (s, 6H, OAc), 2.02 (s, 3H, OAc), 3.73 (s, 3H, OMe), 3.93 (sept, *J* = 6.2 Hz, 1H, H-1′), 4.01 (d, $J_{5,4}$ = 9.5 Hz, 1H, H-5), 4.54 (d, $J_{1,2}$ = 7.7 Hz, 1H, H-1), 4.94 (dd, $J_{2,3}$ = 8.8, $J_{2,1}$ = 7.7 Hz, 1H, H-2), 5.20 (dd, *J* = 9.6, *J* = 9.5 Hz, 1H, H-3), 5.23 (dd, *J* = 9.5, *J* = 9.3 Hz, 1H, H-4); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 20.5 ((C=O)CH_3), 20.6 ((C=O)CH_3), 20.6 ((C=O)CH_3), 21.7 (C-2′), 23.2 (C-2′Me), 52.8 (OMe), 69.5 (C-4), 71.5 (C-3), 72.2 (C-2), 72.6 (C-5), 72.9 (C-1′), 99.5 (C-1), 167.3 (C-6), 169.2 ((*C*=O)CH_3), 169.4 ((*C*=O)CH_3), 170.2 ((*C*=O)CH_3).

1.2.5. Methyl (*n*-butyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)-uronate (4e)

According to the general procedure 0.47 g (1.18 mmol, 1.0 equiv) **3**, 9.5 mL *n*-butanol (103.8 mmol, 87.7 equiv) and 0.42 g silver carbonate (1.54 mmol, 1.3 equiv) were reacted to yield **4e** after purification with flash chromatography (silica gel, cyclohexan/ethyl acetate 1:1) as colourless crystals (0.28 g, 0.72 mmol, 61%). Mp 88.8–90.7 °C; $[\alpha]_D^{20}$ −25.8 (*c* 9.58, $CHCl_3$); calcd for $C_{17}H_{26}O_{10}^{+}$ 391.1604; found 391.1572 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$) δ = 0.87 (t, $J_{4',3'}$ = 7.2 Hz, 3H, H-4′), 1.29–1.38 (m, 2H, H-3′), 1.48–1.60 (m, 2H, H-2′), 2.01 (s, 6H, OAc), 2.03 (s, 3H, OAc),3.47 (dt, $J_{1'A,1'B}$ = 9.6, $J_{1'A,2'}$ = 6.4 Hz, 1H, H-$1'_A$), 3.75 (s, 3H, OMe), 3.89 (dt, $J_{1'B,1'A}$ = 9.6, $J_{1'B,2'}$ = 6.5 Hz, 1H, H-$'_B$), 4.02 (d, $J_{5,4}$ = 9.5 Hz, 1H, H-5), 4.53 (d, $J_{1,2}$ = 7.7 Hz, 1H, H-1), 4.99 (dd, $J_{2,3}$ = 9.2, $J_{2,1}$ = 8.0 Hz, 1H, H-2), 5.21 (dd, *J* = 9.3, *J* = 9.2 Hz, 1H, H-3), 5.24 (dd, *J* = 9.4, *J* = 9.3 Hz, 1H, H-4); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.3 (C-4′), 18.9 (C-3′), 20.5 ((C=O)CH_3), 20.5 ((C=O)CH_3), 20.6 ((C=O)CH_3), 31.3 (C-2′), 52.8 (OMe), 69.5 (C-4), 70.1 (C-1′), 71.2 (C-3), 72.1 (C-2), 72.6 (C-5), 101.1 (C-1), 167.3 (C-6), 169.1 ((*C*=O)CH_3), 169.3 ((*C*=O)CH_3), 170.1 ((*C*=O)CH_3).

Table 2
Crystal data and structure refinement of protected glucuronides **4a–j**

Alkyl moiety Compound	**4a** Me	**4b** Mt	**4c** *n*Pro	**4d** *i*Pro	**4e** *n*Bu	**4f** *s*Bu	**4g** *i*Bu	**4h** *n*Pent	**4i** 2-Me-1-bu	**4j** 3-Me-1-bu
Molecular formula	$C_{14}H_{20}O_{10}$	$C_{15}H_{22}O_{10}$	$C_{16}H_{24}O_{10}$	$C_{16}H_{24}O_{10}$	$C_{17}H_{26}O_{10}$	$C_{17}H_{26}O_{10}$	$C_{17}H_{26}O_{10}$	$C_{18}H_{28}O_{10}$	$C_{18}H_{28}O_{10}$	$C_{18}H_{28}O_{10}$
Crystal system	Ortho-rhombic	Ortho-rhombic	Ortho-rhombic	Ortho-rhombic	Ortho-rhombic	Ortho-rhombic	Ortho-rhombic	Ortho-rhombic	Ortho-rhombic	Ortho-rhombic
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
a (Å)	7.260(4)	7.4822(6)	7.6044(17)	6.0479(13)	5.7486(14)	6.947(3)	9.0667(7)	9.5511(12)	14.4629(17)	9.4748(11)
b (Å)	13.605(7)	14.2337(13)	14.533(4)	16.774(3)	16.217(5)	14.829(6)	14.0702(9)	13.5932(16)	14.9085(16)	13.2024(15)
c (Å)	18.070(9)	17.7818(16)	17.244(4)	19.097(5)	22.957(6)	20.445(8)	16.3679(10)	17.349(2)	21.127(2)	17.841(3)
Cell volume (Å^3)	1784.8(16)	1893.8(3)	1905.7(8)	1937.3(7)	2140.2(10)	2106.2(15)	2088.1(2)	2252.4(5)	4555.4(8)	2231.7(5)
Unit cell *Z*	4	4	4	4	4	4	4	4	8	4
Final *R* indices	0.0389	0.0626	0.0472	0.0441	0.0508	0.0620	0.0474	0.0573	0.0455	0.0471
Final *R* indices (all data)	0.0499	0.1104	0.1637	0.1737	0.2308	0.0964	0.1036	0.1108	0.2126	0.1483
Goodness of fit on F^2	0.961	0.894	0.579	0.640	0.696	0.985	0.818	0.898	0.701	0.748

1.2.6. Methyl (*sec*-butyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)-uronate (4f)

According to the general procedure 1.00 g (2.52 mmol, 1.0 equiv) **3**, 3.7 mL *sec*-butanol (40.43 mmol, 16.05 equiv) and 0.90 g silver carbonate (3.28 mmol, 1.3 equiv) were reacted to yield **4f** after purification with flash chromatography (silica gel, cyclohexan/ethyl acetate 1:1) as colourless crystals (0.39 g, 1.00 mmol, 40%). Mp 111.1–111.9 °C; $[\alpha]_D^{20}$ −34.7 (*c* 10.69, $CHCl_3$); calcd for $C_{17}H_{26}O_{10}^+$ 391.1604; found 391.1567 $[M+H]^+$; ^{1}H NMR (500 MHz, $CDCl_3$) diastereomer A: δ = 0.86 (t, $J_{3',2'}$ = 7.4 Hz, 3H, H-3′), 1.19 (d, $J_{4',1'}$ = 6.5 Hz, 3H, H-4′), 1.53–1.60 (m, 2H, H-2′), 1.99 (s, 3H, OAc), 2.01 (s, 6H, OAc), 3.64 (dq, *J* = 6.5, *J* = 5.5 Hz, 1H, H-1′), 3.73 (s, 3H, OMe), 4.00 (d, $J_{5,4}$ = 9.4 Hz, 1H, H-5), 4.58 (d, $J_{1,2}$ = 7.5 Hz, 1H, H-1), 4.97 (dd, *J* = 9.0, *J* = 8.3 Hz, 1H, H-2), 5.18 (dd, *J* = 9.7, *J* = 9.7 Hz, 1H, H-3), 5.23 (dd, *J* = 9.6, *J* = 9.6 Hz, 1H, H-4), diastereomer B: δ = 0.84 (t, $J_{3',2'}$ = 7.1 Hz, 3H, H-3′), 1.08 (d, $J_{4',1'}$ = 6.2 Hz, 3H, H-4′), 1.54–1.53 (m, 2H, H-2′), 1.99 (s, 3H, OAc), 2.01 (s, 6H, OAc), 3.70 (dq, *J* = 6.2, *J* = 6.2 Hz, 1H, H-1′), 3.72 (s, 3H, OMe), 3.99 (d, $J_{5,4}$ = 9.3 Hz, 1H, H-5), 4.57 (d, $J_{1,2}$ = 7.7 Hz, 1H, H-1), 4.97 (dd, *J* = 9.1, *J* = 8.4 Hz, 1H, H-2), 5.17 (dd, *J* = 9.6, *J* = 9.3 Hz, 1H, H-3), 5.23 (dd, *J* = 9.6, *J* = 9.6 Hz, 1H, H-4); ^{13}C NMR (125 MHz, $CDCl_3$) diastereomer A: δ = 9.4 (C-3′), 20.9 (C-1′Me), 20.4 ((C=O)CH_3), 20.5 ((C=O)CH_3), 20.9 ((C=O)CH_3), 29.6 (C-2′), 52.7 (OMe), 69.5 (C-4), 71.4 (C-3), 72.2 (C-2), 72.4 (C-5), 79.2 (C-1′), 100.7 (C-1), 167.3 (C-6), 169.1 ((*C*=O)CH_3), 169.3 ((*C*=O)CH_3), 170.2 ((*C*=O)CH_3), diastereomer B: δ = 9.4 (C-3′), 18.9 (C-1′Me), 20.4 ((C=O)CH_3), 20.5 ((C=O)CH_3), 20.9 ((C=O)CH_3), 29.0 (C-2′), 52.7 (OMe), 69.4 (C-4), 71.3 (C-3), 72.2 (C-2), 72.4 (C-5), 79.2 (C-1′), 99.1 (C-1), 167.2 (C-6), 169.1 ((*C*=O)CH_3), 169.3 ((*C*=O)CH_3), 170.3 ((*C*=O)CH_3).

1.2.7. Methyl (*i*-butyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)-uronate (4g)

According to the general rocedure 0.71 g **3** (1.79 mmol, 1.0 equiv), 1.5 mL *i*-butanol (16.2 mmol, 9.1 equiv) and 0.71 g silver carbonate (2.57 mmol, 1.4 equiv) were reacted to yield **4g** as colourless crystals after recrystallisation from *i*-propanol (0.52 g, 1.3 mmol, 75%). Mp 144.2–144.4 °C; $[\alpha]_D^{20}$ −27.1 (*c* 10.3, $CHCl_3$); calcd for $C_{17}H_{26}O_{10}^+$ 391.1604; found 391.1574 $[M+H]^+$; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.86 (t, *J* = 6.5 Hz, 6H, H-3′ and H-4′), 1.84 (sept, *J* = 6.6 Hz, 1H, H-2′), 2.00 (s, 6H, OAc), 2.03 (s, 3H, OAc), 3.18 (dd, $J_{1'A,1'B}$ = 9.3, $J_{1'A,2'}$ = 7.1 Hz, 1H, H-1′$_A$), 3.71 (dd, $J_{1'B,1'A}$ = 9.3, $J_{1'B,2'}$ = 6.2 Hz, 1H, H-′$_B$), 3.74 (s, 3H, OMe), 4.01 (d, $J_{5,4}$ = 9.5 Hz, 1H, H-5), 4.51 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1), 5.01 (dd, $J_{2,3}$ = 9.6, $J_{2,1}$ = 7.6 Hz, 1H, H-2), 5.21 (dd, *J* = 9.3, *J* = 9.2 Hz, 1H, H-3), 5.24 (dd, *J* = 9.6, *J* = 9.3 Hz, 1H, H-4); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 18.8 (C-3′), 18.9 (C-2′Me), 20.5 ((C=O)CH_3), 20.5 ((C=O)CH_3), 20.6 ((C=O)CH_3), 28.2 (C-2′), 52.8 (OMe), 69.5 (C-4), 71.2 (C-3), 72.1 (C-2), 72.6 (C-5), 76.9 (C-1′), 101.1 (C-1), 167.3 (C-6), 169.1 ((*C*=O)CH_3), 169.3 ((*C*=O)CH_3), 170.1 ((*C*=O)CH_3).

1.2.8. Methyl (*n*-pentyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)-uronate (4h)

According to the general procedure 0.9 g **3** (2.27 mmol, 1.0 equiv), 1.4 mL *n*-pentanol (12.9 mmol, 5.7 equiv) and 0.81 g silver carbonate (2.95 mmol, 1.3 equiv) were reacted to yield **4h** as colourless crystals after recrystallisation from *i*-propanol (0.62 g, 1.55 mmol, 68%). Mp 99.5–100.2 °C; $[\alpha]_D^{20}$ −33.0 (*c* 10.5, $CHCl_3$); calcd for $C_{18}H_{28}O_{10}^+$ 405.1761; found 405.1731 $[M+H]^+$; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.87 (t, $J_{5',4'}$ = 7.2 Hz, 3H, H-5′), 1.25–1.34 (m, 4H, H-3′ and H-4′), 1.52–1.61 (m, 2H, H-2′), 2.01 (s, 6H, OAc), 2.03 (s, 3H, OAc), 3.56 (dt, *J* = 6.8, *J* = 6.4 Hz, 1H, H-1′$_A$), 3.74 (s, 3H, OMe), 3.89 (dt, *J* = 6.8, *J* = 6.4 Hz, 1H, H-′$_B$), 4.01 (d, $J_{5,4}$ = 9.4 Hz, 1H, H-5), 4.54 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1), 4.99 (dd, $J_{2,3}$ = 9.0, $J_{2,1}$ = 7.9 Hz, 1H, H-2), 5.21 (dd, *J* = 9.9, *J* = 9.4 Hz, 1H, H-3), 5.25 (dd, *J* = 9.9, *J* = 9.4 Hz, 1H, H-4); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.9 (C-5′), 20.5 ((C=O)CH_3), 20.6 ((C=O)CH_3), 20.6 ((C=O)CH_3), 22.3 (C-4′), 27.9 (C-3′), 28.9 (C-2′), 52.8 (OMe), 69.5 (C-4), 70.4 (C-1′), 71.3 (C-3), 72.1 (C-2), 72.6 (C-5), 100.8 (C-1), 167.3 (C-6), 169.1 ((*C*=O)CH_3), 169.3 ((*C*=O)CH_3), 170.2 ((*C*=O)CH_3).

1.2.9. Methyl (2-methyl-1-butyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)uronate (4i)

According to the general procedure 2.00 g **3** (5.04 mmol, 1.0 equiv), 8.7 mL 2-methyl-1-butanol (79.9 mmol, 15.9 equiv) and 2.2 g silver carbonate (7.98 mmol, 1.6 equiv) were reacted to yield **4i** as purple crystals after recrystallisation from *i*-propanol (0.61 g, 1.51 mmol, 30%). Mp 111.3–112.4 °C; $[\alpha]_D^{20}$ −32.7 (*c* 10.2, $CHCl_3$); calcd for $C_{18}H_{28}O_{10}^+$ 405.1761; found 405.1734 $[M+H]^+$; *Distinguishable diastereomers given in brackets*; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.82 (d, $J_{4',3'}$ = 8.6 Hz, 3H, H-4′), 0.85 (d, $J_{5',2'}$ = 7.5 Hz, 3H, H-5′), 1.08–1.14 (m, 1H, H-2′), 1.33–1.43 (m,2H, H-3′), [1.59–1.67 (m, 2H, H-3′)], 1.98 (s, 6H, OAc), 2.00 (s, 3H, OAc), 3.18 (dd, *J* = 9.3, *J* = 7.1 Hz, 1H, H-1′$_A$), [3.26 (dd, *J* = 9.3, *J* = 6.8 Hz, 1H, H-1′$_A$)], 3.70 (dd, *J* = 9.6, *J* = 6.2 Hz, 1H, H-′$_B$), [3.79 (dd, *J* = 9.3, *J* = 5.6 Hz, 1H, H-′$_B$)], 3.74 (s, 3H, OMe), 4.00 (d, $J_{5,4}$ = 9.5 Hz, 1H, H-5), 4.49 (d, $J_{1,2}$ = 7.7 Hz, 1H, H-1), 4.99 (dd, $J_{2,3}$ = 8.6, $J_{2,1}$ = 7.7 Hz, 1H, H-2), 5.18 (dd, *J* = 9.6, *J* = 9.3 Hz, 1H, H-3), 5.23 (dd, *J* = 9.6, *J* = 9.3 Hz, 1H, H-4); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 11.0 (C-4′), [11.1 (C-4′)], 16.0 (C-2′Me), [16.3 (C-2′Me)], 20.5 ((C=O)CH_3), 20.5 ((C=O)CH_3), 20.6 ((C=O)CH_3), 25.7 (C-3′), [25.8 (C-3′)], 34.7 (C-2′), 52.8 (OMe), 69.5 (C-4), 71.2 (C-3), 72.1 (C-2), 72.6 (C-5), 75.2 (C-1′), [75.4 (C-1′)], 101.2 (C-1), 167.3 (C-6), 169.1 ((*C*=O)CH_3), 169.3 ((*C*=O)CH_3), 170.1 ((*C*=O)CH_3).

1.2.10. Methyl (3-methyl-1-butyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)uronate (4j)

According to the general procedure 2.00 g (5.04 mmol, 1.0 equiv) **3**, 8.7 mL 3-methyl-1-butanol (79.9 mmol, 15.9 equiv) and 2.2 g silver carbonate (7.98 mmol, 1.6 equiv) were reacted to yield **4j** after recrystallisation from *i*-propanol as yellow crystals (0.76 g, 1.89 mmol, 37%). Mp 106.4–107.7 °C; $[\alpha]_D^{20}$ −33.4 (*c* 10.6, $CHCl_3$); calcd for $C_{18}H_{28}O_{10}^{+}$ 405.1761; found 405.1737 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$); δ = 0.87 (d, $J_{4',3'}$ = 6.6 Hz, 3H, H-4′), 0.88 (d, $J_{5',3'}$ = 6.6 Hz, 3H, H-5′), 1.32–1.51 (m, 2H, H-2′), 1.64 (tsept, *J* = 6.9; 6.7 Hz, 3H, H-3′), 2.01 (s, 3H, OAc), 2.02 (s, 3H, OAc), 2.03 (s, 3H, OAc), 3.51 (dt, *J* = 7.2, *J* = 6.9 Hz, 1H, H-$1'_A$), 3.76 (s, 3H, OMe), 3.93 (dt, *J* = 7.2, *J* = 6.9 Hz, 1H, H-$1'_B$), 4.01 (d, $J_{5,4}$ = 9.3 Hz, 1H, H-5), 4.51 (d, $J_{1,2}$ = 7.7 Hz, 1H, H-1), 4.97 (dd, $J_{2,3}$ = 9.3, $J_{2,1}$ = 7.8 Hz, 1H, H-2), 5.19 (dd, *J* = 9.9, *J* = 9.2 Hz, 1H, H-3), 5.23 (dd, *J* = 9.3, *J* = 9.2 Hz, 1H, H-4); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 20.5 ((C=O)CH_3), 20.6 ((C=O)CH_3), 20.6 ((C=O)CH_3), 22.2 (C-4′), 22.6 (C-3′Me), 24.7 (C-3′), 38.0 (C-2′), 52.8 (OMe), 68.8 (C-1′), 69.5 (C-4), 71.3 (C-3), 72.1 (C-2), 72.6 (C-5), 100.8 (C-1), 167.3 (C-6), 169.2 ((*C*=O)CH_3), 169.3 ((*C*=O)CH_3), 170.1 ((*C*=O)CH_3).

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