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SYNTHESIS OF 1,2-*O*-CYANOETHYLIDENE DERIVATIVES OF ALKYL GLYCOPYRANURONATES BY OXIDATION OF THE 6-TRITYL ETHERS OF THEIR HEXOSE ANALOGUES*†

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ABSTRACT

The synthesis of 1,2-*O*-cyanoethylidene derivatives (CED) of alkyl glycopyranuronates with the D-Glc, D-Gal, and D-Man configurations is described by oxidation of the 3,4-di-*O*-acetyl-6-*O*-trityl-CED-hexose analogues with the Jones reagent [chromium(VI) oxide–sulfuric acid]. The isopropylidenation of hydroxyl-containing triphenylmethyl ethers is demonstrated.

INTRODUCTION

Uronic acids are widely encountered in many important biopolymers of plant and animal origin in the form of glycosiduronic acids. The methods for the chemical synthesis of these compounds developed so far are inadequate. The 1,2-*O*-cyanoethylidene derivatives of methyl D-gluco- and D-galacto-pyranuronates have been synthesised and shown to be stereospecific glycosylating reagents in the synthesis of derivatives of aldobiouronic acids[2] and homo- and hetero-glycuronans[3]. The synthesis of CED of uronic acids involved the sequence[2] uronic acid → methyl pyranuronate tetra-acetate → glycosyl bromide → 1,2-*O*-(1-cyanoethylidene) derivative. This approach is limited by the availability of the starting uronic acid and, moreover, yields methyl esters, which restricts the scope of further conversions. We now report a new route to the synthesis of CED of uronic acid esters by oxidation of the 6-*O*-trityl-CED of the corresponding neutral sugars.

RESULTS AND DISCUSSION

The 3,4,6-tri-*O*-acetyl-1,2-*O*-(1-cyanoethylidene) derivatives **1** and **7** *(manno)*, **15** and **18** *(gluco)*, and **21** and **24** *(galacto)*, prepared[4] in high yields (90 ±5%), were subjected to Zemplén deacetylation in methanol–pyridine as described for thio-orthoesters[5]. The resulting triols of type **2** were treated conventionally with

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trityl chloride and then acetic anhydride in pyridine to give the trityl di-acetates **4, 6, 8, 16, 19, 22,** and **25,** respectively. These compounds could be obtained (in yields of ≥80%) by a "one-pot" procedure without isolation of the intermediate triol and its trityl ether. Oxidation of the aforementioned trityl ethers to the corresponding CED uronic acid (*e.g.*, **11, 12,** and **20**) with the Jones reagent[6] and interphase alkylation of the resulting acid, as described for the synthesis of amino acid esters[7], proceeded with yields of 70–80% for each step.

The first experiments with the Jones reagent involved **6**, and the resulting mixture of products (primary alcohol **5** and acid **11**) was treated with diazomethane to give the methyl ester **9**, as described for the synthesis of methyl pyranuronates starting from partially acetylated glycosides containing an unsubstituted primary alcohol function[8]. The yields of **9** were 30 ±2%, and ~30% of **6** was recovered together with ~15% of **5**. The molar ratios of **6**, CrO_3, and H_2SO_4 were 1:2.4:3.8.

In seeking to optimise the synthesis of **9**, the oxidation of the more acid-labile monomethoxytrityl ether **4** and the primary alcohol **5**, obtained from **4**, were studied. The substrate–reagents ratios were 1:2.7:5 (oxidation *A*, see Experimental) and the yields of **9** were increased to 46 and 41%, respectively. Also, the previously described[2] methyl CED-glycuronates (**17, 23,** and **26**) were re-synthesised by method *A* in yields of 31, 45, and 33%, respectively.

In order to improve further the synthesis of **9**, a large excess of the Jones reagent was used (substrate–reagents ratios, 1:5:7.5; oxidation *B*) and another method of isolating the uronic acid CED was used (see Experimental). The oxidation was carried out in 2:3 dichloromethane–acetone, which is better than the use of acetone alone, since it is a better solvent for all trityl ethers studied so far. The yields of the uronic acid CED **20, 11,** and **12** (from **19, 6,** and **8**, respectively) were 55, 61, and 77%, whereas the overall yields for the detritylation–oxidation–esterification sequence increased to >50% (with the exception of benzyl uronate **10**). In this way, the methyl esters of the D-mannuronic (**9** and **13**), D-glucuronic (**17**), and D-galacturonic (**23** and **26**) acid CED were synthesised as well as the benzyl esters **10** and **14**.

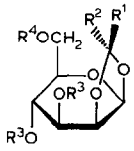
The sequence primary trityl ether → primary alcohol → acid → ester can be carried out also with derivatives of alkyl glycosides of the type **28** and **34**. On attempted oxidation of the trityl isopropylidene derivative **32** using conditions *A* and *B*, detritylation was accompanied by loss of the isopropylidene group. However, the required methyl galactopyranuronate derivative **35** was synthesised without isolation of the corresponding acid, in a yield of 71%, by using the more acid-labile dimethoxytrityl ether **34** and substrate–reagents ratios of 1:2.5:3.3 (oxidation *C*).

Thus, when the substrate contains acid-labile groups (*e.g.*, isopropylidene), the Jones oxidation can be performed by increasing the acid lability of the trityl ether function (*e.g.*, trityl → monomethoxytrityl → dimethoxytrityl).

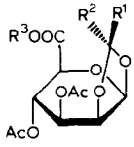
The trityl ether of the isopropylidene derivative **31** was synthesised by (*a*) isopropylidenation of methyl β-D-galactopyranoside followed by tritylation (the di-

methoxytrityl ether **33** was prepared also in this way), and (*b*) by isopropylidenation of the trityl ether **27** with acetone–2,2-dimethoxypropane in the presence of copper(II) sulphate. This exemplifies the possibility of isopropylidenation of primary trityl ethers of polyhydroxyl compounds.

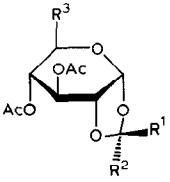
The structures of all the compounds obtained were supported by ^{1}H- and ^{13}C-n.m.r. data.



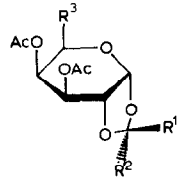
1 R^1 = CN, R^2 = Me, R^3 = R^4 = Ac
2 R^1 = CN, R^2 = Me, R^3 = R^4 = H
3 R^1 = CN, R^2 = Me, R^3 = H, R^4 = $C(Ph)_2C_6H_4$-*p*-OMe
4 R^1 = CN, R^2 = Me, R^3 = Ac, R^4 = $C(Ph)_2C_6H_4$-*p*-OMe
5 R^1 = CN, R^2 = Me, R^3 = Ac, R^4 = H
6 R^1 = CN, R^2 = Me, R^3 = Ac, R^4 = Tr
7 R^1 = Me, R^2 = CN, R^3 = R^4 = Ac
8 R^1 = Me, R^2 = CN, R^3 = Ac, R^4 = Tr



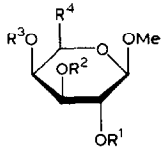
9 R^1 = CN, R^2 = Me, R^3 = Me
10 R^1 = CN, R^2 = Me, R^3 = Bn
11 R^1 = CN, R^2 = Me, R^3 = H
12 R^1 = Me, R^2 = CN, R^3 = H
13 R^1 = Me, R^2 = CN, R^3 = Me
14 R^1 = Me, R^2 = CN, R^3 = Bn



15 R^1 = CN, R^2 = Me, R^3 = CH_2OAc
16 R^1 = CN, R^2 = Me, R^3 = CH_2OTr
17 R^1 = CN, R^2 = Me, R^3 = COOMe
18 R^1 = Me, R^2 = CN, R^3 = CH_2OAc
19 R^1 = Me, R^2 = CN, R^3 = CH_2OTr
20 R^1 = Me, R^2 = CN, R^3 = COOH
R^1 = Me, R^2 = CN, R^3 = COOMe



21 **22** **23** **24** **25** **26**



27 R^1 = R^2 = R^3 = H, R^4 = CH_2OTr
28 R^1 = R^2 = R^3 = Ac, R^4 = CH_2OTr
29 R^1 = R^2 = R^3 = Ac, R^4 = COOMe
30 R^1 = H, R^2 and R^3 = $C(Me)_2$, R^4 = CH_2OH
31 R^1 = H, R^2 and R^3 = $C(Me)_2$, R^4 = CH_2OTr
32 R^1 = Ac, R^2 and R^3 = $C(Me)_2$, R^4 = CH_2OTr
33 R^1 = H, R^2 and R^3 = $C(Me)_2$, R^4 = $CH_2OC(C_6H_4$-*p*-$OMe)_2Ph$
34 R^1 = Ac, R^2 and R^3 = $C(Me)_2$, R^4 = $CH_2OC(C_6H_4$-*p*-$OMe)_2Ph$
35 R^1 = Ac, R^2 and R^3 = $C(Me)_2$, R^4 = COOMe

EXPERIMENTAL

When previously described crystalline compounds contained, according to the ^{1}H- and ^{13}C-n.m.r. data, no impurities and showed correct $[\alpha]_D$ values, no attempts were made to crystallise to constant m.p. In order not to decrease preparative yields of these analytically pure compounds, they were characterised in the form (solid, foam, *etc.*) isolated initially.

Optical rotations were determined with an Al-EPO polarimeter (U.S.S.R.) at 20 ±2° for solutions in chloroform unless otherwise specified. Melting points were determined with a Kofler apparatus and are uncorrected.

N.m.r. spectra were recorded at room temperature for solutions in $CDCl_3$

(internal Me_4Si), unless otherwise specified, with Bruker WM-250 and AM-300 instruments (250 and 300 MHz for ^1H, and 62.89 and 75 MHz for ^{13}C). Key ^1H resonances were assigned by using selective homonuclear resonance, and ^{13}C resonances by using selective heteronuclear resonance.

Column chromatography was performed on Silica Gel L (40–100, 100–160, or 100–250 μm, Č.S.S.R.). T.l.c. was performed on Silica Gel L (5–40 μm, Č.S.S.R.) with detection by charring with sulfuric acid. Prior to charring, trityl derivatives gave bright-yellow spots, whereas mono- and di-methoxytrityl derivatives gave bright-orange spots.

Solvents were prepared as described previously[2–5]. Organic solutions were dried by filtration through cotton and then concentrated *in vacuo* at ≤40°. All procedures were carried out at ambient temperature unless otherwise stated.

*1,2-*O*-[1-(*exo*-Cyano)ethylidene]-β-*D*-mannopyranose* (**2**). — To a solution of the triacetate **1** (4.66 g, 11.3 mmol) in dry pyridine (59 mL) was added dry methanol (15 mL) and methanolic M sodium methoxide (0.6 mL). After 5 min, M acetic acid in toluene (0.8 mL) was added and the mixture was concentrated. Column chromatography (chloroform → chloroform–ethanol, 9:1) of the syrupy residue gave **2** (R_F 0.4; chloroform–methanol, 4:1), which crystallised from acetone to give a product (2.38 g, 77%) having m.p. 61°, $[\alpha]_D$ +22.3° (*c* 1.0, methanol). N.m.r. data (CD_3OD): ^1H, δ 1.86 [s, 3 H, Me(CN)C], 3.29 (m, 1 H, $J_{5,6}$ 2.3, $J_{5,6'}$ 5.6 Hz, H-5), 3.59 (t, 1 H, $J_{4,5}$ 9.1 Hz, H-4), 3.66 (dd, 1 H, $J_{6',6}$ 11.6 Hz, H-6'), 3.82 (dd, 1 H, H-6), 3.86 (dd, 1 H, $J_{3,4}$ 9.1 Hz, H-3), 4.45 (dd, 1 H, $J_{2,3}$ 3.8 Hz, H-2), 5.45 (d, 1 H, $J_{1,2}$ 2.1 Hz, H-1); ^{13}C, δ 25.8 [CH_3(CN)C], 61.4 (C-6), 67.0 (C-4), 70.6 (C-3), 75.8 (C-5), 80.6 (C-2), 97.0 (C-1), 101.0 [*C*(CN)CH_3], 116.7 (CN).

Anal. Calc. for $C_9H_{13}NO_6$: C, 46.75; H, 5.61; N, 6.06. Found: C, 47.32; H, 5.62; N, 6.10.

*1,2-*O*-[1-(*exo*-Cyano)ethylidene]-6-*O*-(4-methoxytrityl)-β-*D*-mannopyranose* (**3**). — A solution of **2** (3.3 g, 14.3 mmol) and 4-methoxytrityl chloride (3.96 g, 14.5 mmol) in dry pyridine (75 mL) was kept for 15 h, then poured into ice–water (900 mL), and extracted with chloroform (300 mL). The organic layer was washed with water (3 × 100 mL), dried, and concentrated to dryness. Column chromatography (benzene → 30% ether in benzene) of the residue afforded **3** (6.5 g, 90%) as a syrup, R_F 0.2 (benzene–ether, 3:2), $[\alpha]_D$ +10.4° (*c* 5.0). N.m.r. data: ^1H, δ 1.96 [s, 3 H, Me(CN)C], 3.43 (m, 3 H, H-5,6,6'), 3.88 (dd, 1 H, $J_{3,4}$ 9.0 Hz, H-3), 3.98 (t, 1 H, $J_{4,5}$ 9.0 Hz, H-4), 4.55 (dd, 1 H, $J_{2,3}$ 3.7 Hz, H-2), 5.42 (d, 1 H, $J_{1,2}$ 2.2 Hz, H-1), 6.90 (d, 2 H, aromatic), 7.2–7.5 (m, 12 H, aromatic); ^{13}C, δ 26.5 [CH_3(CN)C], 55.2 (OMe), 63.5 (C-6), 69.0 (C-4), 71.3 (C-3), 74.1 (C-5), 79.8 (C-2), 87.0 (CPh_3), 97.3 (C-1), 101.3 [*C*(CN)CH_3], 113.4, 127.1, 127.95, 128.3, 130.3, 135.2, 144.1, and 158.9 (aromatic), 116.8 (CN).

*3,4-Di-*O*-acetyl-1,2-*O*-[1-(*exo*-cyano)ethylidene]-6-*O*-(4-methoxytrityl)-β-*D*-mannopyranose* (**4**). — To a solution of **3** (6.0 g, 12 mmol) in pyridine (20 mL) was added acetic anhydride (7 mL). The mixture was kept overnight, then poured into ice–water (250 mL), and treated as described above. Column chromatography

(benzene → 4% ether in benzene) of the residue gave **4** (6.1 g, 87%) as a chromatographically homogeneous solid, R_3 2.0 (benzene–ether, 9:1), which was used in all subsequent syntheses. A crystalline analytical sample of **4** had m.p. 146° (from ethanol), $[\alpha]_D$ +43.4° (*c* 2.3). N.m.r. data: ^1H, δ 1.86 (s, 3 H, Ac), 1.97 [s, 3 H, Me(CN)C], 2.12 (s, 3 H, Ac), 3.07 (dd, 1 H, $J_{6',6}$ 10.5 Hz, H-6'), 3.28 (dd, 1 H, H-6), 3.58 (m, 1 H, $J_{5,6}$ 2.5, $J_{5,6'}$ 4.0 Hz, H-5), 4.58 (dd, 1 H, $J_{2,3}$ 4.0 Hz, H-2), 5.22 (dd, 1 H, $J_{3,4}$ 10.0 Hz, H-3), 5.48 (d, 1 H, $J_{1,2}$ 2.3 Hz, H-1), 5.49 (t, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 6.81 (d, 2 H, aromatic), 7.2–7.5 (m, 12 H, aromatic); ^{13}C, δ 20.3 and 20.5 (CH_3CO), 26.5 [$CH_3(CN)C$], 55.15 (OMe), 62.1 (C-6), 65.8 (C-4), 69.7 (C-3), 73.4 (C-5), 78.3 (C-2), 86.4 (CPh_3), 97.1 (C-1), 101.6 [$C(CN)CH_3$], 113.1, 126.9, 127.7, 128.4, 130.3, 135.3, 144.0, and 158.9 (aromatic), 116.1 (CN), 168.9 and 170.0 (CH_3CO).

Anal. Calc. for $C_{33}H_{33}NO_9$: C, 67.45; H, 5.66; N, 2.38. Found: C, 67.42; H, 5.56; N, 2.37.

3,4-Di-O-acetyl-1,2-O-[1-(exo-cyano)ethylidene]-β-D-mannopyranose (**5**). — A solution of **4** (1.2 g, 2 mmol) in aqueous 80% acetic acid (20 mL) was kept for 20 min at 50°, then poured into ice–water (100 mL), and extracted with chloroform (100 mL). The organic layer was washed with water to pH 7, dried, concentrated to 2–3 mL, and diluted with hexane to give **5** (0.5 g, 77%), R_F 0.15 (benzene–ether, 1:1), m.p. 151°, $[\alpha]_D$ −5.1° (*c* 2.0). N.m.r. data: ^1H, δ 1.94 [s, 3 H, Me(CN)C], 2.08 and 2.15 (2 s, each 3 H, Ac), 2.31 (m, 1 H, OH), 3.54 (m, 1 H, H-5), 3.63 (m, 1 H, H-6'), 3.70 (m, 1 H, H-6), 4.62 (dd, 1 H, $J_{2,3}$ 3.7 Hz, H-2), 5.23 (t, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 5.32 (dd, 1 H, $J_{3,4}$ 9.7 Hz, H-3), 5.50 (d, 1 H, $J_{1,2}$ 2.4 Hz, H-1); ^{13}C, δ 20.6 (2 C, CH_3CO), 26.4 [$CH_3(CN)C$], 61.5 (C-6), 66.0 (C-4), 69.3 (C-3), 74.7 (C-5), 78.1 (C-2), 97.2 (C-1), 101.6 [$C(CN)CH_3$], 116.5 (CN), 170.0 and 170.2 (CH_3CO).

Anal. Calc. for $C_{13}H_{17}NO_8$: C, 49.52; H, 5.44; N, 4.44. Found: C, 49.57; H, 5.43; N, 4.37.

3,4-Di-O-acetyl-1,2-O-[1-(exo-cyano)ethylidene]-6-O-trityl-β-D-mannopyranose (**6**). — Triacetate **1** (3.57 g, 10 mmol) was deacetylated as described for **2**. The syrup obtained after the addition of acetic acid was co-concentrated with dry pyridine (3 × 15 mL) and, to a solution in dry pyridine (70 mL), trityl chloride (4.16 g, 14.7 mmol) was added. The mixture was kept for several hours at 50–60° (t.l.c. control) and then chilled to ~0°, acetic anhydride (15 mL) was added, and, after 1–2 h at 40–50° (t.l.c. control), the mixture was poured into ice–water (400 mL). The precipitate was collected, the aqueous layer was extracted with chloroform (3 × 20 mL), the precipitate was dissolved in the combined extracts, and hexane (120 mL) was added. The organic solution was washed successively with 50-mL portions of cold water, aqueous 10% sodium hydrogensulphate (to pH <7), saturated aqueous sodium hydrogencarbonate, and water, then dried, and concentrated to dryness. Column chromatography (benzene → 5% ethyl acetate in benzene) of the residue afforded **6** (4.48 g, 80%), R_1 2.0 (benzene–ethyl acetate, 2:1), m.p. 165.5° (from ether–heptane), $[\alpha]_D$ +46.0° (*c* 2.0); lit.[9] m.p. 161–163°

(ethanol), $[\alpha]_D$ +44° (chloroform). N.m.r. data: ^1H, δ 1.78 (s, 3 H, Ac), 1.98 [s, 3 H, Me(CN)C], 2.15 (s, 3 H, Ac), 3.10 (dd, 1 H, $J_{6',6}$ 10.2 Hz, H-6'), 3.31 (dd, 1 H, H-6), 3.60 (ddd, 1 H, $J_{5,6}$ 2.8, $J_{5,6'}$ 4.2 Hz, H-5), 4.60 (dd, 1 H, $J_{2,3}$ 3.7 Hz, H-2), 5.25 (dd, 1 H, $J_{3,4}$ 9.9 Hz, H-3), 5.49 (d, 1 H, $J_{1,2}$ 2.2 Hz, H-1), 5.50 (dd, 1 H, $J_{4,5}$ 9.3 Hz, H-4), 7.2–7.5 (m, 15 H, Ph); ^{13}C, δ 20.5 and 20.75 (CH_3CO), 26.7 [CH_3(CN)C], 62.25 (C-6), 65.7 (C-4), 69.85 (C-3), 73.5 (C-5), 78.5 (C-2), 86.8 (CPh_3), 97.2 (C-1), 101.8 [C(CN)CH_3], 116.8 (CN), 127.2, 127.9, 128.8, and 143.65 (Ph), 169.0 and 170.2 (CH_3CO).

3,4-Di-O-acetyl-1,2-O-[1-(endo-cyano)ethylidene]-6-O-trityl-β-D-mannopyranose (**8**). — Treatment of **7** (1.20 g), as described above for **1**, and crystallisation of the product from chloroform–ether gave **8** (1.40 g), m.p. 215.5°, $[\alpha]_D$ −0.2° (*c* 4.0). Column chromatography of the mother liquor gave more (0.30 g) **8** (total yield, 91%). N.m.r. data: ^1H, δ 1.74 (s, 3 H, Ac), 1.82 [s, 3 H, Me(CN)C], 2.09 (s, 3 H, Ac), 3.24 (m, 2 H, $J_{6,6'}$ 10.4 Hz, H-6,6'), 3.59 (ddd, 1 H, $J_{5,6}$ 2.8, $J_{5,6'}$ 4.1 Hz, H-5), 4.43 (dd, 1 H, $J_{2,3}$ 3.7 Hz, H-2), 5.13 (dd, 1 H, $J_{3,4}$ 9.4 Hz, H-3), 5.42 (t, 1 H, $J_{4,5}$ 9.4 Hz, H-4), 5.53 (d, 1 H, $J_{1,2}$ 1.9 Hz, H-1), 7.2–7.5 (m, 15 H, Ph); ^{13}C, δ 20.5 and 20.7 (CH_3CO), 26.65 [CH_3(CN)C], 62.5 (C-6), 66.1 (C-4), 70.25 (C-3), 73.7 (C-5), 77.8 (C-2), 87.0 (-CPh_3), 98.3 (C-1), 101.1 [C(CN)CH_3], 117.1 (CN), 127.1, 127.9, 128.9, and 143.7 (Ph), 168.9 and 170.4 (CH_3CO).

Anal. Calc. for $C_{32}H_{31}NO_8$: C, 68.93; H, 5.58; N, 2.51. Found: C, 68.88; H, 5.57; N, 2.73.

3,4-Di-O-acetyl-1,2-O-[1-(exo-cyano)ethylidene]-6-O-trityl-α-D-glucopyranose (**16**). — Treatment of **15** (1.97 g), as described for **6**, afforded **16** (2.60 g, 84%), m.p. 132° (from ether–hexane), $[\alpha]_D$ +32.7° (*c* 4.0); lit.[10] m.p. 130–131°, $[\alpha]_D$ +33° (chloroform). N.m.r. data: ^1H, δ 1.86 (s, 3 H, Ac), 1.89 [s, 3 H, Me(CN)C], 2.14 (s, 3 H, Ac), 3.14 (dd, 1 H, $J_{6',6}$ 10.4 Hz, H-6'), 3.33 (dd, 1 H, $J_{6,5}$ 4.5 Hz, H-6), 3.81 (ddd, 1 H, $J_{5,6'}$ 2.4 Hz, H-5), 4.39 (ddd, 1 H, $J_{2,3}$ 2.8, $J_{2,4}$ 0.8 Hz, H-2), 5.07 (ddd, 1 H, $J_{4,5}$ 9.2 Hz, H-4), 5.20 (t, 1 H, $J_{3,4}$ 2.8 Hz, H-3), 5.88 (d, 1 H, $J_{1,2}$ 5.0 Hz, H-1), 7.2–7.5 (m, 15 H, Ph); ^{13}C, δ 20.7 (2 C, CH_3CO), 24.5 [CH_3(CN)C], 62.6 (C-6), 68.1 (C-4), 69.0 (C-5), 69.7 (C-3), 74.3 (C-2), 86.8 (-CPh_3), 97.9 (C-1), 98.7 [C(CN)CH_3], 116.7 (CN), 127.2, 127.9, 128.8, and 143.75 (Ph), 169.1 and 169.2 (CH_3CO).

3,4-Di-O-acetyl-1,2-O-[1-(endo-cyano)ethylidene]-6-O-trityl-α-D-glucopyranose (**19**). — Treatment of **18** (913 mg), as described for **6**, gave **19** (1.20 g, 81%), m.p. 142° (from ether), $[\alpha]_D$ +81.7° (*c* 4.5). N.m.r. data: ^1H, δ 1.77 [s, 3 H, Me(CN)C], 1.84 and 2.09 (2 s, each 3 H, Ac), 3.14 (dd, 1 H, $J_{6',6}$ 10.3, $J_{6',5}$ 2.4 Hz, H-6'), 3.42 (dd, 1 H, $J_{6,5}$ 3.8 Hz, H-6), 4.16 (ddd, 1 H, H-5), 4.38 (t, 1 H, $J_{2,3}$ 4.3 Hz, H-2), 5.22 (dd, 1 H, $J_{4,5}$ 9.1 Hz, H-4), 5.48 (dd, 1 H, $J_{3,4}$ 6.7 Hz, H-3), 5.82 (d, 1 H, $J_{1,2}$ 4.8 Hz, H-1), 7.2–7.5 (m, 15 H, Ph); ^{13}C, δ 20.7 (2 C, CH_3CO), 27.3 [CH_3(CN)C], 62.1 (C-6), 67.2 (C-4), 71.0 (C-5), 71.5 (C-3), 76.8 (C-2), 86.8 (CPh_3), 98.7 (C-1), 99.9 [C(CN)CH_3], 117.3 (CN), 127.2, 127.95, 128.9, and 143.65 (Ph), 169.3 and 169.4 (CH_3CO).

Anal. Calc. for $C_{32}H_{31}NO_8$: C, 68.93; H, 5.58; N, 2.51. Found: C, 69.84; H, 5.81; N, 2.53.

3,4-Di-O-*acetyl-1,2*-O-[*1*-(exo-*cyano*)*ethylidene*]-*6*-O-*trityl*-α-D-*galactopyranose* (**22**). — Treatment of **21** (880 mg), as described for **6**, and crystallisation of product from methanol (25 mL) gave **22** (940 mg). Column chromatography of the mother liquor gave more (175 mg) of **22** (total yield, 84%), m.p. and mixture m.p. 214°; lit.[11] m.p. 214°, $[\alpha]_D$ +28.5° (chloroform). N.m.r. data: ^{1}H, δ 1.86 [s, 3 H, Me(CN)C], 1.88 and 2.06 (2 s, each 3 H, Ac), 3.07 (dd, 1 H, $J_{6',6}$ 9.1 Hz, H-6'), 3.37 (dd, 1 H, $J_{6,5}$ 5.6 Hz, H-6), 4.20 (m, 1 H, $J_{5,6'}$ 7.8 Hz, H-5), 4.22 (dd, 1 H, $J_{2,3}$ 7.0 Hz, H-2), 4.95 (dd, 1 H, $J_{3,4}$ 3.5 Hz, H-3), 5.56 (dd, 1 H, $J_{4,5}$ 2.0 Hz, H-4), 5.77 (d, 1 H, $J_{1,2}$ 5.0 Hz, H-1), 7.2–7.4 (m, 15 H, Ph); ^{13}C, δ 20.3 (2 C, CH_3CO), 26.05 [CH_3(CN)C], 60.85 (C-6), 65.8 (C-4), 71.4 (C-5), 71.9 (C-3), 73.0 (C-2), 87.1 (CPh_3), 97.15 [C(CN)CH_3], 99.25 (C-1), 117.0 (CN), 127.25, 127.9, 128.65, and 143.3 (Ph), 169.3 and 169.8 (CH_3CO).

3,4-Di-O-*acetyl-1,2*-O-[*1*-(endo-*cyano*)*ethylidene*]-*6*-O-*trityl*-α-D-*galactopyranose* (**25**). — Treatment of **24** (690 mg), as described for **6**, gave **25** (860 mg, 80%), m.p. 150° (from ether–hexane), $[\alpha]_D$ +25.8° (*c* 5.6). N.m.r. data: ^{1}H, δ 1.76 [s, 3 H, Me(CN)C], 1.88 and 2.06 (2 s, each 3 H, Ac), 3.07 (dd, 1 H, $J_{6',6}$ 9.2 Hz, H-6'), 3.38 (dd, 1 H, $J_{6,5}$ 7.7 Hz, H-6), 4.30 (dd, 1 H, $J_{2,3}$ 7.3 Hz, H-2), 4.31 (ddd, 1 H, $J_{5,6'}$ 5.4 Hz, H-5), 5.42 (dd, 1 H, $J_{3,4}$ 3.1 Hz, H-3), 5.61 (d, 1 H, $J_{1,2}$ 4.3 Hz, H-1), 5.67 (dd, 1 H, $J_{4,5}$ 2.1 Hz, H-4), 7.2–7.4 (m, 15 H, Ph); ^{13}C, δ 20.5 and 20.65 (CH_3CO), 27.2 [CH_3(CN)C], 61.0 (C-6), 66.55 (C-4), 69.9 (C-3), 71.5 (C-5), 76.4 (C-2), 87.3 (CPh_3), 98.9 (C-1), 98.55 [C(CN)CH_3], 117.7 (CN), 127.3, 128.0, 128.8, and 143.5 (Ph), 169.2 and 169.4 (CH_3CO).

Anal. Calc. for $C_{32}H_{31}NO_8$: C, 68.93; H, 5.58; N, 2.51. Found: C, 69.42; H, 5.57; N, 2.45.

Methyl 3,4-di-O-*acetyl-1,2*-O-[1-(exo-*cyano*)*ethylidene*]-β-D-*mannopyranuronate* (**9**). — *Oxidation* A. To a solution of **4** (0.90 g, 1.5 mmol) in acetone (7.5 mL) was added, at 0°, 2.2 mL of Jones reagent [0.4 g of chromium(VI) oxide was dissolved in 1.6 mL of water and 0.4 mL of conc. sulphuric acid was added], and the mixture was stirred for 1 h at room temperature. Ethanol (3 mL) was then added, the mixture was filtered, and sodium hydrogencarbonate (1.5 g) was stirred with the filtrate, which was then filtered and concentrated to dryness. A solution of the residue in chloroform (10 mL) was stirred with KU-2 (H^+) resin (2–3 mL) to pH 2–3, then filtered, and concentrated to dryness. The residue was treated with a solution (7.5 mL) of diazomethane in dichloromethane[12] for 30 min and then concentrated to dryness. Column chromatography (hexane → ethyl acetate–hexane, 1:2) of the residue gave **9** (0.24 g, 46%), R_F 0.7 (benzene–ethyl acetate, 1:1).

Likewise, **5** (100 mg) was converted into **9** (45 mg, 41%).

Oxidation B. To a solution of **6** (560 mg, 1 mmol) in dichloromethane (2 mL) and acetone (3 mL) was added, with stirring and chilling to ≤5°, 2 mL of Jones reagent [0.5 g of chromium(VI) oxide was dissolved in 1.5 mL of water and 0.4 mL of conc. sulphuric acid was added], chilling was terminated, and the mixture was stirred for 1–1.5 h, then poured into ice–water (30 mL), and extracted with chloroform (3 × 10 mL). The combined extracts were washed with water (2 × 15

mL) and concentrated, and to the residue was added saturated aqueous sodium hydrogencarbonate (2 mL), tetrabutylammonium iodide (370 mg, 1 mmol), and a solution of methyl iodide (0.5 mL, 7 mmol) in dichloromethane (1 mL). The mixture was stirred vigorously for 4–5 h (t.l.c. control) and then diluted with 1:2 chloroform–hexane (30 mL), and the organic layer was washed with water (5 × 10 mL), dried, and concentrated to dryness. Column chromatography of the residue gave **9** (180 mg, 53%), m.p. 127.5° (from ether–hexane), $[\alpha]_D$ −14.3° (*c* 4.4). N.m.r. data: ^{1}H, δ 1.91 [s, 3 H, Me(CN)C], 2.06 and 2.16 (2 s, each 3 H, Ac), 3.77 (s, 3 H, OMe), 4.19 (d, 1 H, $J_{5,4}$ 7.1 Hz, H-5), 4.66 (t, 1 H, $J_{2,3}$ 3.7 Hz, H-2), 5.28 (dd, 1 H, $J_{3,4}$ 9.9 Hz, H-3), 5.64 (dd, 1 H, $J_{4,5}$ 7.1 Hz, H-4), 5.68 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1); ^{13}C, δ 20.6 (2 C, CH_3CO), 24.7 [CH_3(CN)C], 52.5 (OMe), 66.2 (C-4), 68.5 (C-3), 73.7 (C-5), 76.1 (C-2), 98.1 (C-1), 100.6 [C(CN)CH_3], 116.3 (CN), 167.7 (C-6), 169.4 and 170.1 (CH_3CO).

Anal. Calc. for $C_{14}H_{17}NO_9$: C, 48.98; H, 4.96; N, 4.08. Found: C, 50.33; H, 4.87; N, 4.04.

*Methyl 3,4-di-*O*-acetyl-1,2-*O*-[1-(*exo*-cyano)ethylidene]-*α*-*D*-glucopyranuronate* (**17**). — Application of oxidation *A* to **16** (270 mg) gave syrupy **17** (50 mg, 31%), $[\alpha]_D$ −6.8° (*c* 4.3); lit.[2] $[\alpha]_D^{23}$ −7.0° (chloroform). N.m.r. data: ^{1}H, δ 1.96 [s, 3 H, Me(CN)C], 2.12 and 2.14 (2 s, each 3 H, Ac), 3.79 (s, 3 H, OMe), 4.24 (d, 1 H, $J_{5,4}$ 8.0 Hz, H-5), 4.42 (ddd, 1 H, $J_{2,3}$ 2.5, $J_{2,4}$ 1.0 Hz, H-2), 5.17 (ddd, 1 H, H-4), 5.28 (dd, 1 H, $J_{3,4}$ 1.8 Hz, H-3), 5.93 (d, 1 H, $J_{1,2}$ 4.6 Hz, H-1); ^{13}C, δ 20.6 (2 C, CH_3CO), 24.7 [CH_3(CN)C], 52.9 (OMe), 68.1 (2 C, C-4,5), 69.2 (C-3), 74.3 (C-2), 99.6 (C-1), 99.7 [C(CN)CH_3], 116.4 (CN), 168.3, 168.8, and 169.2 (C-6 and CH_3CO).

*Methyl 3,4-di-*O*-acetyl-1,2-*O*-[1-(*exo*-cyano)ethylidene]-*α*-*D*-galactopyranuronate* (**23**). — Application of oxidation *A* to **22** (345 mg) gave syrupy **23** (155 mg, 45%), $[\alpha]_D$ +91.5° (*c* 1.4); lit.[2] $[\alpha]_D^{23}$ +89.0° (chloroform). N.m.r. data: ^{1}H, δ 1.91 [s, 3 H, Me(CN)C], 2.10 and 2.12 (2 s, each 3 H, Ac), 3.78 (s, 3 H, OMe), 4.44 (dd, 1 H, $J_{2,3}$ 5.7 Hz, H-2), 4.77 (d, 1 H, $J_{5,4}$ 4.0 Hz, H-5), 5.10 (dd, 1 H, $J_{3,4}$ 2.7 Hz, H-3), 5.77 (dd, 1 H, H-4), 5.95 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1); ^{13}C, δ 20.4 and 20.55 (CH_3CO), 25.8 [CH_3(CN)C], 52.55 (OMe), 66.3 (C-4), 70.7 (C-3), 72.1 (C-5), 76.65 (C-2), 97.7 (C-1), 99.6 [C(CN)CH_3], 116.7 (CN), 167.1 (C-6), 169.0 and 169.65 (CH_3CO).

*Methyl 3,4-di-*O*-acetyl-1,2-*O*-[1-(*endo*-cyano)ethylidene]-*α*-*D*-galactopyranuronate* (**26**). — Application of oxidation *A* to **25** (840 mg) gave **26** (170 mg, 33%), m.p. 135–137° (from ether–hexane), $[\alpha]_D$ +153° (*c* 1.0); lit.[2] syrup, $[\alpha]_D^{23}$ +119.5° (chloroform). N.m.r. data: ^{1}H, δ 1.84 [s, 3 H, Me(CN)C], 2.08 and 2.09 (2 s, each 3 H, Ac), 3.77 (s, 3 H, OMe), 4.46 (dd, 1 H, $J_{2,3}$ 6.7 Hz, H-2), 4.94 (d, 1 H, $J_{5,4}$ 4.5 Hz, H-5), 5.32 (dd, 1 H, $J_{3,4}$ 2.6 Hz, H-3), 5.87 (dd, 1 H, H-4), 6.06 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1); ^{13}C, δ 20.4 and 20.5 (2 C, CH_3CO), 26.2 [CH_3(CN)C], 52.4 (OMe), 66.8 (C-4), 70.4 (C-3), 72.5 (C-5), 79.0 (C-2), 98.4 (C-1), 99.9 [C(CN)CH_3], 117.55 (CN), 167.65 (C-6), 168.8 and 169.55 (CH_3CO).

Anal. Calc. for $C_{14}H_{17}NO_9$: C, 48.98; H, 4.96; N, 4.08. Found: C, 49.66; H, 4.33; N, 4.05.

*Benzyl 3,4-di-*O*-acetyl-1,2-*O*-[1-(exo-cyano)ethylidene]-β-*D*-mannopyranuronate* (**10**). — Application of oxidation *B* to **6** (560 mg), then alkylation with benzyl bromide (0.14 mL, 1.2 mmol), and column chromatography (benzene → 25% ether in benzene) of the product afforded **10** (200 mg, 48%), R_F 0.6 (benzene–ethyl acetate, 3:2), m.p. 117° (from methanol), $[\alpha]_D$ +8.0° (*c* 0.8). N.m.r. data: ^{1}H, δ 1.77 [s, 3 H, Me(CN)C], 1.91 and 2.12 (2 s, each 3 H, Ac), 4.23 (dd, 1 H, $J_{5,4}$ 7.4 Hz, H-5), 4.63 (t, 1 H, $J_{2,3}$ 3.4 Hz, H-2), 5.16 (s, 2 H, CH_2Ph), 5.26 (dd, 1 H, $J_{3,4}$ 10.0 Hz, H-3), 5.65 (dd, 1 H, H-4), 5.67 (d, 1 H, $J_{1,2}$ 4.2 Hz, H-1), 7.37 (s, 5 H, Ph); ^{13}C, δ 20.4 and 20.5 (CH_3CO), 24.7 [CH_3(CN)C], 66.2 (C-4), 67.0 (CH_2Ph), 68.6 (C-3), 78.8 (C-5), 76.2 (C-2), 98.0 (C-1), 100.6 [C(CN)CH_3], 116.2 (CN), 128.7 and 135.0 (Ph), 167.1 (C-6), 169.2 and 169.1 (CH_3CO).

Anal. Calc. for $C_{20}H_{21}NO_9$: C, 57.28; H, 5.01; N, 3.34. Found: C, 57.00; H, 5.20; N, 3.28.

Similarly, application of oxidation *B* to **8** (880 mg), followed by esterification with benzyl bromide, gave **14** (370 mg, 56%), R_F 0.6 (benzene–ethyl acetate, 7:3).

*3,4-Di-*O*-acetyl-1,2-*O*-[1-(endo-cyano)ethylidene]-β-*D*-mannopyranuronic acid* (**12**). — Application of oxidation *B* to **8** (880 mg) gave a product, a solution of which in chloroform (2–3 mL) was diluted with an excess of hexane to give **12** which was re-precipitated 2–3 times to give material (400 mg, 77%) having R_F 0.3 (benzene–ethyl acetate, 1:1). An analytical sample of **12**, prepared by recrystallisation from chloroform–hexane–ether, had m.p. 101°, $[\alpha]_D$ −45.5° (*c* 1.8, acetone). N.m.r. data: ^{1}H, δ 1.85 [s, 3 H, Me(CN)C], 2.11 and 2.17 (2 s, each 3 H, Ac), 4.32 (d, 1 H, $J_{5,4}$ 6.0 Hz, H-5), 4.54 (dd, 1 H, $J_{2,3}$ 4.4 Hz, H-2), 5.42 (dd, 1 H, $J_{3,4}$ 8.0 Hz, H-3), 5.52 (t, 1 H, H-4), 5.74 (d, 1 H, $J_{1,2}$ 2.4 Hz, H-1), 8.1 (broad s, 1 H, OH); ^{13}C, δ 20.65 (2 C, CH_3CO), 26.05 [CH_3(CN)C], 66.4 (C-4), 67.1 (C-3), 73.2 (C-5), 76.95 (C-2), 98.2 (C-1), 101.65 [C(CN)CH_3], 117.7 (CN), 167.45 (C-6), 168.9 and 169.8 (CH_3CO).

Anal. Calc. for $C_{13}H_{15}NO_9$: C, 47.42; H, 4.56; N, 4.25. Found: C, 47.61; H, 4.70; N, 4.05.

*3,4-Di-*O*-acetyl-1,2-*O*-[1-(exo-cyano)ethylidene]-β-*D*-mannopyranuronic acid* (**11**). — Application of oxidation *B* to **6** (560 mg) gave a product, R_F 0.3, R_5 1.8 (benzene–ethyl acetate, 3:2), which was crystallised from ~3 mL of chloroform–hexane (~2:1) to give **11** (200 mg, 61%), m.p. 123°, $[\alpha]_D$ −8.5° (*c* 2.5). N.m.r. data: ^{1}H, δ 1.91 [s, 3 H, Me(CN)C], 2.08 and 2.16 (2 s, each 3 H, Ac), 4.24 (d, 1 H, $J_{5,4}$ 7.3 Hz, H-5), 4.68 (dd, 1 H, $J_{2,3}$ 3.1 Hz, H-2), 5.30 (dd, 1 H, $J_{3,4}$ 9.0 Hz, H-3), 5.60 (dd, 1 H, H-4), 5.70 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 8.69 (broad s, 1 H, OH); ^{13}C, δ 20.6 (2 C, CH_3CO), 24.9 [CH_3(CN)C], 66.05 (C-4), 68.5 (C-3), 73.1 (C-5), 76.2 (C-2), 97.9 (C-1), 100.7 [C(CN)CH_3], 116.2 (CN), 169.8* (C-6), 170.2* and 170.6 (CH_3CO) (* indicates that the assignments may be interchanged).

Anal. Calc. for $C_{13}H_{15}NO_9$: C, 47.42; H, 4.56; N, 4.25. Found: C, 47.52; H, 4.76; N, 4.34.

*3,4-Di-*O*-acetyl-1,2-*O*-[1-(endo-cyano)ethylidene]-α-*D*-glucopyranuronic acid* (**20**). — Application of oxidation *B* to **19** (560 mg) gave a product, R_F 0.3 (benzene–

ethyl acetate, 1:1), which was crystallised from chloroform to give **20** (180 mg, 55%), m.p. 171°, $[\alpha]_D$ +118° (*c* 2.0, acetone). N.m.r. data [$CDCl_3$ + $(CD_3)_2CO$]: ^1H, δ 1.80 [s, 3 H, Me(CN)C], 2.04 and 2.13 (2 s, each 3 H, Ac), 4.31 (t, 1 H, $J_{2,3}$ 3.5 Hz, H-2), 4.75 (d, 1 H, $J_{5,4}$ 3.5 Hz, H-5), 5.24 (t, 1 H, H-4), 5.32 (t, 1 H, $J_{3,4}$ 3.5 Hz, H-3), 6.20 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1); ^{13}C, δ 20.4 and 20.6 (CH_3CO), 26.0 [CH_3(CN)C], 66.7 (2 C, C-3,4), 73.2 (C-5), 76.2 (C-2), 95.95 (C-1), 100.6 [*C*(CN)CH_3], 118.0 (CN), 169.5 (C-6), 169.9 (2 C, CH_3CO).

Anal. Calc. for $C_{13}H_{15}NO_9$: C, 47.42; H, 4.56; N, 4.25. Found: C, 48.57; H, 4.66; N, 4.42.

Benzyl 3,4-di-O-acetyl-1,2-O-[1-(endo-cyano)ethylidene]-β-D-mannopyranuronate (**14**). — To **12** (400 mg, 1.2 mmol) was added saturated aqueous sodium hydrogencarbonate (1.2 mL), tetrabutylammonium iodide (450 mg, 1.2 mmol), dichloromethane (1.2 mL), and benzyl bromide (0.17 mL, 1.4 mmol). The mixture was stirred vigorously for 3 h (t.l.c. control) and then processed as described for **9**. Chromatography of the product, as described for **10**, gave syrupy **14** (370 mg, 74%), $[\alpha]_D$ −29.0° (*c* 2.5). N.m.r. data: ^1H, δ 1.81 [s, 3 H, Me(CN)C], 1.85 and 2.08 (2 s, each 3 H, Ac), 4.14 (d, 1 H, $J_{5,4}$ 8.6 Hz, H-5), 4.47 (dd, 1 H, $J_{2,3}$ 4.2 Hz, H-2), 5.20 (d, 2 H, *J* 2.7 Hz, CH_2Ph), 5.26 (dd, 1 H, $J_{3,4}$ 9.2 Hz, H-3), 5.53 (t, 1 H, H-4), 5.60 (d, 1 H, $J_{1,2}$ 2.4 Hz, H-1), 7.3–7.4 (m, 5 H, Ph); ^{13}C, δ 20.3 and 20.6 (CH_3CO), 26.5 [CH_3(CN)C], 66.5 (C-4), 67.7 (CH_2Ph), 68.7 (C-3), 72.85 (C-5), 77.2 (C-2), 98.1 (C-1), 101.25 [*C*(CN)CH_3], 116.7 (CN), 128.4, 128.5, and 135.0 (Ph), 165.9 (C-6), 168.9 and 170.0 (CH_3CO).

Methyl 3,4-di-O-acetyl-1,2-O-[1-(endo-cyano)ethylidene]-β-D-mannopyranuronate (**13**). — *endo*-Acid **12** (75 mg) was alkylated with methyl iodide (0.3 mL) for 28 h, as described above. Treatment of the reaction mixture, as described for **9** (oxidation *B*), afforded **13** (58 mg, 72%), m.p. 172° (from ethyl acetate–ether–heptane), $[\alpha]_D$ −63.5° (*c* 0.9). N.m.r. data: ^1H, δ 1.83 [s, 3 H, Me(CN)C], 2.07 and 2.15 (2 s, each 3 H, Ac), 3.80 (s, 3 H, OMe), 4.11 (d, 1 H, $J_{5,4}$ 8.5 Hz, H-5), 4.50 (dd, 1 H, $J_{2,3}$ 4.2 Hz, H-2), 5.26 (dd, 1 H, $J_{3,4}$ 9.2 Hz, H-3), 5.44 (dd, 1 H, H-4), 5.61 (d, 1 H, $J_{1,2}$ 2.5 Hz, H-1); ^{13}C, δ 20.7 (2 C, CH_3CO), 26.6 [CH_3(CN)C], 53.0 (OMe), 66.6 (C-4), 68.75 (C-3), 73.05 (C-5), 77.1 (C-2), 98.1 (C-1), 101.1 [*C*(CN)CH_3], 166.6 (C-6), 169.0 and 170.1 (CH_3CO).

Anal. Calc. for $C_{14}H_{17}NO_9$: C, 48.98; H, 4.96; N, 4.08. Found: C, 48.96; H, 5.44; N, 4.75.

Methyl 6-O-trityl-β-D-galactopyranoside (**27**). — A solution of methyl β-D-galactopyranoside {400 mg, 2 mmol, m.p. 180° (from methanol), $[\alpha]_D$ −0.6° (*c* 2.8, water), −14.2° (*c* 2.6, methanol)} and trityl chloride (700 mg, 2.5 mmol) in dry pyridine (5 mL) was kept for a few h at 50° (t.l.c. control). Methanol (2 mL) was then added, and the solution was concentrated to 1/3 volume and co-evaporated with 5:1:1 toluene–ethanol–heptane (3 × 10 mL). Column chromatography (hexane → ethyl acetate) of the residue gave **27** (680 mg, 74%), R_F 0.8 (benzene–ethyl acetate–methanol, 5:5:1), m.p. 179° (from ethyl acetate–hexane), $[\alpha]_D$ −37.5° (*c* 1.5); lit.[13] m.p. 184–185°, $[\alpha]_D^{25}$ −38° (chloroform). N.m.r. data ($CDCl_3$ + D_2O): ^1H, δ 3.28 (d, 1 H, $J_{6',5}$ 5.4 Hz, H-6'), 3.43 (d, 1 H, $J_{6,5}$ 6.2, $J_{6,6'}$ 9.2 Hz,

H-6), 3.48 (dd, 1 H, $J_{3,4}$ 3.4 Hz, H-3), 3.48 (m, 1 H, H-5), 3.50 (s, 3 H, OMe), 3.58 (dd, 1 H, $J_{2,3}$ 9.6 Hz, H-2), 3.85 (d, 1 H, $J_{4,5}$ 3.4 Hz, H-4), 4.10 (d, 1 H, $J_{1,2}$ 7.4 Hz, H-1), 7.2–7.5 (m, 15 H, Ph); ^{13}C, δ 56.9 (OMe), 62.9 (C-6), 69.3 (C-4), 71.9 (C-2), 73.9 (2 C, C-3,5), 87.1 (CPh_3), 104.1 (C-1), 127.2, 128.0, 128.8, and 143.9 (Ph).

*Methyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-β-*D*-galactopyranoside* (**28**). — Methyl β-D-galactopyranoside (3.7 g) was tritylated and acetylated, and the resulting mixture was treated as described for **6**. Column chromatography (hexane → 10% ethyl acetate in hexane) gave **28** (7.9 g, 78%) as a chromatographically homogeneous white solid, R_F 0.7 (benzene–ethyl acetate, 9:1), $[\alpha]_D$ −50.7° (*c* 2.1); lit.[13] m.p. 143–145°, $[\alpha]_D^{25}$ −52.7° (chloroform). N.m.r. data: ^{1}H, δ 1.90, 2.00, and 2.07 (3 s, each 3 H, Ac), 3.13 (dd, 1 H, $J_{6',6}$ 8.5 Hz, H-6'), 3.43 (dd, 1 H, $J_{6,5}$ 5.4 Hz, H-6), 3.50 (s, 3 H, OMe), 3.86 (ddd, 1 H, $J_{5,6'}$ 7.9 Hz, H-5), 4.40 (d, 1 H, $J_{1,2}$ 7.3 Hz, H-1), 5.09 (dd, 1 H, $J_{3,4}$ 3.1 Hz, H-3), 5.17 (dd, 1 H, $J_{2,3}$ 10.1 Hz, H-2), 5.61 (dd, 1 H, $J_{4,5}$ 1.1 Hz, H-4), 7.25–7.45 (m, 15 H, Ph); ^{13}C, δ 20.5, 20.6, and 20.8 (3 C, CH_3CO), 56.9 (OMe), 60.9 (C-6), 67.4 (C-4), 69.2 (C-2), 71.3 (C-3), 72.1 (C-5), 86.9 (CPh_3), 102.1 (C-1), 127.2, 127.9, 128.9, and 143.4 (Ph), 169.2, 169.5, and 170.2 (CH_3CO).

*Methyl (methyl 2,3,4-tri-*O*-acetyl-β-*D*-galactopyranosid)uronate* (**29**). — Trityl ether **28** (6.6 g) was oxidised and methylated as described for **9** (oxidation *B*). A solution of the reaction mixture in chloroform (150 mL) was washed with water (3 × 50 mL), concentrated to ~5 mL, diluted with ether (~25 mL), filtered, and concentrated. Column chromatography (benzene–ethyl acetate) of the residue gave **29** (1.9 g, 45%), as a white foam, R_F 0.46 (benzene–ether, 1:1), $[\alpha]_D$ +15.2° (*c* 3.0); lit.[14] m.p. 118–120°, $[\alpha]_D^{25}$ +15.3° (chloroform). N.m.r. data: ^{1}H, δ 1.96, 2.04, and 2.09 (3 s, each 3 H, Ac), 3.54 (s, 3 H, OMe), 3.74 (s, 3 H, MeOOC), 4.32 (d, 1 H, $J_{5,4}$ 1.4 Hz, H-5), 4.41 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 5.05 (dd, 1 H, $J_{3,4}$ 3.2 Hz, H-3), 5.22 (dd, 1 H, $J_{2,3}$ 10.2 Hz, H-2), 5.68 (dd, 1 H, H-4); lit.[15], ^{13}C, δ 20.5 and 20.7 (CH_3CO), 52.7 (CH_3OOC), 57.2 (OMe), 68.4 (C-4), 68.5 (C-2), 70.6 (C-3), 72.4 (C-5), 101.9 (C-1), 166.5 (C-6), 169.3, 169.8, and 170.0 (CH_3CO).

*Methyl 3,4-*O*-isopropylidene-β-*D*-galactopyranoside* (**30**). — Methyl β-D-galactopyranoside (2.6 g) was stirred with acetone (80 mL) and 2,2-dimethoxypropane (8 mL) in the presence of toluene-*p*-sulphonic acid monohydrate (400 mg) for 16 h (t.l.c. control). The mixture was then passed through a layer of alumina (2 × 3 cm) and concentrated, and the syrupy residue (3.1 g) was crystallised from acetone (50 mL) and hexane (50 mL) to give **30** (1.83 g, 50%), m.p. 136.5°, $[\alpha]_D$ +17.5° (*c* 4.0); lit.[16] m.p. 132–134°, $[\alpha]_D^{24}$ +21° (water). N.m.r. data ($CDCl_3$ + D_2O): ^{1}H, δ 1.36 and 1.52 (2 s, each 3 H, Me_2C), 3.53 (dd, 1 H, $J_{2,3}$ 7.2 Hz, H-2), 3.58 (s, 3 H, OMe), 3.85 (dd, 1 H, $J_{6',6}$ 8.8 Hz, H-6'), 3.89 (dd, 1 H, $J_{5,6'}$ 3.8 Hz, H-5), 3.99 (dd, 1 H, $J_{6,5}$ 3.8 Hz, H-6), 4.10 (t, 1 H, $J_{3,4}$ 5.6 Hz, H-3), 4.12 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 4.17 (dd, 1 H, $J_{4,5}$ 2.0 Hz, H-4); ^{13}C, δ 26.4 and 28.1 [$C(CH_3)_2$], 57.1 (OMe), 62.4 (C-6), 73.6 (C-5), 73.7 (C-2), 74.1 (C-4), 79.1 (C-3), 103.5 (C-1), 110.6 [$C(CH_3)_2$].

*Methyl 3,4-*O*-isopropylidene-6-*O*-trityl-β-*D*-galactopyranoside* (**31**). — A

solution of **27** (2.2 g, 5 mmol) in acetone (50 mL), containing 2,2-dimethoxypropane (2.5 mL), was stirred with anhydrous copper(II) sulphate (12.5 g) for 3.5 h (t.l.c. control), then decanted, and concentrated, and a solution of the residue in chloroform (120 mL) was washed with water (40 mL) and concentrated. Column chromatography (hexane → ethyl acetate) of the residue gave **31** (1.9 g, 86%), m.p. 160° (from ether–hexane), $[\alpha]_D$ −20.5° (*c* 1.0); lit.[16] m.p. 162–164°, $[\alpha]_D^{25}$ −20.4° (chloroform). N.m.r. data: ^{1}H, δ 1.40 and 1.52 (2 s, each 3 H, Me_2C), 2.73 (s, 1 H, OH), 3.51 (m, 2 H, $J_{6,6'}$ 9.2 Hz, H-6,6'), 3.57 (s, 3 H, OMe), 3.57 (d, 1 H, $J_{2,3}$ 7.2 Hz, H-2), 3.84 (ddd, 1 H, $J_{5,6} = J_{5,6'}$ 6.3 Hz, H-5), 4.09 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1), 4.09 (dd, 1 H, $J_{3,4}$ 5.4 Hz, H-3), 4.28 (dd, 1 H, $J_{4,5}$ 2.1 Hz, H-4), 7.3–7.5 (m, 15 H, Ph); ^{13}C, δ 26.4 and 28.2 [$C(CH_3)_2$], 56.8 (OMe), 62.8 (C-6), 72.6 (C-5), 73.8 (C-4), 73.95 (C-2), 78.9 (C-3), 86.9 (CPh_3), 103.5 (C-1), 110.1 [$C(CH_3)_2$], 127.1, 127.9, 128.9, and 144.1 (Ph).

Methyl 2-O-acetyl-3,4-O-isopropylidene-6-O-trityl-β-D-galactopyranoside (**32**). — Treatment of **31** (1.44 g) with pyridine (6 mL) and acetic anhydride (1.5 mL), as described for **6**, gave chromatographically homogeneous, syrupy **32** (1.5 g), R_F 0.55 (benzene–ethyl acetate, 9:1). Crystallisation from ether–hexane afforded **32** (1.1 g, 70%), m.p. 159°, $[\alpha]_D$ −12.0° (*c* 4.3). N.m.r. data: ^{1}H, δ 1.38 and 1.56 (2 s, each 3 H, Me_2C), 2.13 (s, 3 H, Ac), 3.51 (s, 3 H, OMe), 3.46 (dd, 1 H, H-6'), 3.54 (dd, 1 H, $J_{6,6'}$ 9.3 Hz, H-6), 3.85 (ddd, 1 H, $J_{5,6'} = J_{5,6}$ = 6.1 Hz, H-5), 4.17 (dd, 1 H, $J_{3,4}$ 5.2 Hz, H-3), 4.24 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1), 4.28 (dd, 1 H, $J_{4,5}$ 2.0 Hz, H-4), 4.99 (dd, 1 H, $J_{2,3}$ 7.4 Hz, H-2), 7.25–7.5 (m, 15 H, Ph); ^{13}C, δ 21.1 (CH_3CO), 26.4 and 27.7 [$C(CH_3)_2$], 56.4 (OMe), 62.7 (C-6), 72.4 (C-5), 73.1 (C-2), 73.9 (C-4), 77.2 (C-3), 86.8 (CPh_3), 101.4 (C-1), 110.4 [$C(CH_3)_2$], 127.1, 127.8, 128.8, and 143.95 (Ph), 169.7 (CH_3CO).

Anal. Calc. for $C_{31}H_{34}O_7$: C, 71.81; H, 6.56. Found: C, 71.66; H, 6.79.

Methyl 6-O-(4,4'-dimethoxytrityl)-3,4-O-isopropylidene-β-D-galactopyranoside (**33**). — To a solution of **30** (6.3 g, 27 mmol) in dry pyridine (20 mL) was added a solution of 4,4'-dimethoxytrityl chloride (13.5 g, 40 mmol) in dry pyridine (50 mL). The mixture was kept overnight, methanol (2 mL) was then added, and, after 30 min, the mixture was poured with vigorous stirring into ice–water (1 L). The precipitate was collected and dried, and a solution in chloroform (250 mL) was washed with cold aqueous 5% potassium hydrogensulphate (2 × 75 mL), dried, and concentrated to give **33** (20.2 g; R_F 0.7, R_{30} 6.6, benzene–ethyl acetate, 1:1). The product, which contained a non-carbohydrate impurity with R_F >0.9, was used in the next step. A syrupy analytical sample, prepared by column chromatography (hexane → 50% ethyl acetate in hexane), had $[\alpha]_D$ −17.7° (*c* 2.5). N.m.r. data: ^{1}H, δ 1.38 and 1.50 (2 s, each 3 H, Me_2C), 2.80 (s, 1 H, OH), 3.46 (m, 2 H, $J_{6,6'}$ 9.1 Hz, H-6,6'), 3.54 (dd, 1 H, $J_{2,3}$ 7.2 Hz, H-2), 3.56 (s, 3 H, OMe), 3.80 (s, 6 H, 4,4'-OMe), 3.84 (ddd, 1 H, $J_{5,6'} = J_{5,6}$ = 6.6 Hz, H-5), 4.08 (dd, 1 H, $J_{3,4}$ 5.3 Hz, H-3), 4.09 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 4.26 (dd, 1 H, $J_{4,5}$ 1.9 Hz, H-4), 6.84 (d, 4 H, aromatic), 7.25–7.5 (m, 9 H, aromatic); ^{13}C, δ 26.4 and 28.2 [$C(CH_3)_2$], 55.3 (4,4'-OMe), 56.8 (OMe), 62.7 (C-6), 72.8 (C-5), 73.9 (C-4), 74.0 (C-2), 79.0 (C-3), 86.3

(CPh_3), 103.5 (C-1), 110.1 [$C(CH_3)_2$], 113.2, 126.8, 127.8, 130.3, 136.3, 145.1, and 158.7 (aromatic).

Methyl 2-O-acetyl-6-O-(4,4'-dimethoxytrityl)-3,4-O-isopropylidene-β-D-galactopyranoside (**34**). — Conventional treatment of **33** (20 g) with pyridine (50 mL) and acetic anhydride (5 mL) and column chromatography (toluene → 50% ethyl acetate in hexane) of the product gave **34** (15.0 g, 95% from **30**), as a syrup, R_F 0.5 (benzene–ethyl acetate, 9:1), $[\alpha]_D$ −8.0° (*c* 0.6). N.m.r. data: ^1H, δ 1.37 and 1.54 (2 s, each 3 H, Me_2C), 2.12 (s, 3 H, Ac), 3.41 (dd, 1 H, $J_{6',6}$ 9.2 Hz, H-6'), 3.50 (dd, 1 H, $J_{6,5}$ 6.3 Hz, H-6), 3.50 (s, 3 H, OMe), 3.82 (ddd, 1 H, $J_{5,6'} = J_{5,6} = 6.3$ Hz, H-5), 3.82 (s, 6 H, 4,4'-OMe), 4.16 (dd, 1 H, $J_{3,4}$ 5.2 Hz, H-3), 4.24 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1), 4.26 (dd, 1 H, $J_{4,5}$ 1.8 Hz, H-4), 4.97 (dd, 1 H, $J_{2,3}$ 7.4 Hz, H-2), 6.85 (d, 4 H, aromatic), 7.25–7.5 (m, 9 H, aromatic); ^{13}C, δ 21.1 (CH_3CO), 26.5 and 27.8 [$C(CH_3)_2$], 55.3 (4,4'-OMe), 56.4 (OMe), 62.65 (C-6), 72.6 (C-5), 73.2 (C-2), 74.0 (C-4), 77.3 (C-3), 86.4 (CPh_3), 101.5 (C-1), 110.5 [$C(CH_3)_2$], 113.3, 126.9, 127.9, 128.4, 130.3, 136.3, 145.1, 158.7 (aromatic).

Methyl (methyl 2-O-acetyl-3,4-O-isopropylidene-β-D-galactopyranosid)uronate (**35**). — *Oxidation* C. To a solution of **34** (1.8 g, 3 mmol) in 2:3 dichloromethane–acetone (27 mL) was added, dropwise at ~0°, 3 mL of Jones reagent [0.75 g of chromium(VI) oxide was dissolved in 3 mL of 3.5M sulphuric acid]. The chilling was terminated, and the mixture was stirred for 1.5 h (t.l.c. control); the temperature rose to 15°. Ethanol (6 mL) was added, and, after 0.5 h, the precipitate was collected and washed with acetone (10 mL). Saturated aqueous sodium hydrogencarbonate (30 mL) was added to the combined filtrate and washings, and the mixture was concentrated to 30 mL and extracted with chloroform (3 × 30 mL). The aqueous layer was concentrated to 10 mL, dichloromethane (3 mL), methyl iodide (1.5 mL), and tetrabutylammonium bromide (1 g) were added, and the mixture was stirred vigorously for 20 h (t.l.c. control) and then extracted with chloroform (3 × 20 mL). The combined extracts were washed with water (3 × 20 mL) and concentrated. Column chromatography (7% ethyl acetate in hexane → 30% ethyl acetate in hexane) of the residue gave **35** (570 mg), R_F 0.5 (benzene–ethyl acetate 4:1), which crystallised on concentration of the fractions. More (100 mg) **35** was obtained from the mother liquor (total yield, 71%), m.p. 148°/170.5° (from ethyl acetate–hexane), $[\alpha]_D$ −17.1° (*c* 5.1). N.m.r. data: ^1H, δ 1.33 and 1.54 (2 s, each 3 H, Me_2C), 2.09 (s, 3 H, Ac), 3.51 (s, 3 H, OMe), 3.85 (s, 3 H, MeOOC), 4.24 (dd, 1 H, $J_{3,4}$ 5.4 Hz, H-3), 4.33 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.43 (d, 1 H, $J_{5,4}$ 2.2 Hz, H-5), 4.50 (dd, 1 H, H-4), 5.01 (dd, 1 H, $J_{2,3}$ 7.0 Hz, H-2); ^{13}C, δ 20.95 (CH_3CO), 26.3 and 27.3 [$C(CH_3)_2$], 52.55 (CH_3OOC), 56.8 (OMe), 72.2 (2 C, C-2,5), 73.9 (C-4), 76.6 (C-3), 101.5 (C-1), 111.1 [$C(CH_3)_2$], 167.5 (C-6), 169.5 (CH_3CO).

Anal. Calc. for $C_{13}H_{20}O_8$: C, 51.32; H, 6.58. Found: C, 50.39; H, 7.02.

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