Diastereoselective hydrogenations of α-alkyl α-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyloxy)methylene carbonyl compounds. New route to stereopure α-alkyl α-oxymethyl carbonyl compounds[1]

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Wittig condensation of the stabilised phosphoranes 9, 10 and 26 with 1-formyl-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose 11 leads to the vinylogous carbonates 12, 13 and 22. The salts 27–30 and 44, prepared from the corresponding carbonyl compounds, ethyl formate and sodium methoxide, react with acetobromoglucose 21 to give compounds 22–25 and 43.

The vinylogous esters/carbonates 12, 13, 22–25 and 43 undergo stereoselective catalytic hydrogenations under mild conditions to give mainly the dihydro derivatives 14, 15, 31–34 and 16. Although the selectivity for *re*-face addition is modest (ranging from 85:15 to 67:33), it is possible to isolate the dihydro derivatives 15 and 31–33 in acceptable yields (ranging from 71 to 49%) simply by fractional crystallisation. Acidic hydrolysis of compound 31 provides (α*S*)-α-hydroxymethyl-γ-butyrolactone 39 in high yield with an ee of ~96%.

A model to account for the role of the 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl unit in the stereoinduction process is presented.

Introduction

Processes in which stereogenic centres are introduced into prochiral substrates in a defined manner, through the influence of a temporarily attached stereodirector, are of continuing interest to the synthetic chemist. Moreover, models that facilitate the interpretation—and thence prediction—of such asymmetric inductions are of both mechanistic and theoretical relevance.[2]

Over the past few years, we have shown that the 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl auxiliary confers a useful degree of facial reactivity on dienes of type **1** in their reactions with dienophiles (under thermal conditions)[3–6] and heterodienophiles (under thermal conditions and in the presence of Lewis acids).[7,8] Notable features of the technology are its predictable stereochemical outcome (*e.g.*, with *N*-phenylmaleimide, cycloadducts of type **2** predominate) and its practicality (in almost all cases, the major cycloadducts can be isolated in a diastereopure state simply by fractional crystallisation). Moreover, after appropriate manipulation of the cycloadducts, the sugar auxiliary can be detached by hydrolysis under relatively mild acidic conditions. The methodology has been used to effect the synthesis of (+)-4-demethoxydaunomycinone,[9] (+)-daunomycinone,[10] (+)-bostrycin[11] and (3*S*)-2,3,4,6-tetrahydropyridazine-3-carboxylic acid.[8]

We have postulated[4–8] that dienes of type **1** react preferentially by way of conformers of type **3**, which are favoured through a combination of *exo*-anomeric and steric effects. *endo*-Additions of dienophiles to the less hindered 'top' faces (*i.e.*, *re*-faces†) of these conformers then lead to the observed major cycloadducts.

Based upon the afore-cited model, we reasoned that β-oxy-α,β-unsaturated carbonyl systems of type **4** would undergo diastereoselective additions to their olefinic bonds. Thus, on the assumption that hydrogen would be added in a *syn*-selective manner, compounds of type **5** were expected to predominate over compounds of type **6** in catalytic hydrogenation reactions. This expectation rested on the assumption that systems of type **4** would react by way of conformers of type **7** (and/or **8**) and that hydrogen would be delivered by the catalyst to the less hindered *re*-faces of the olefinic bonds. We now present results, involving vinylogous carbonates/esters of type **4**, that are consistent with our expectations.

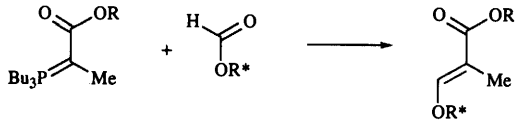
Results and discussion

The first vinylogous carbonate‡ to be subjected to catalytic hydrogenation studies was compound **12**. It was synthesised

† The stereodescriptor refers to the carbon atom of the diene bearing the 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyloxy unit.

‡ Surprisingly, the hydrogenation of such systems does not appear to have been widely studied. We are aware of only one asymmetric version of the reaction that is directed by a detachable auxiliary (ref. 12).

(79% yield after crystallisation) by Wittig condensation of the phosphorane **9** (prepared in 76% yield by sequential treatment of methyl 2-bromopropionate with Bu_3P and NaOH) with the formyl ester **11**[6,13] in boiling toluene (Scheme 1). The (*E*)-



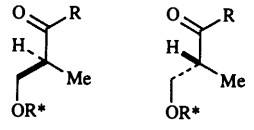
9 R = Me
10 R = Et

11

12 R = Me
13 R = Et

Scheme 1 *Conditions:* toluene, reflux

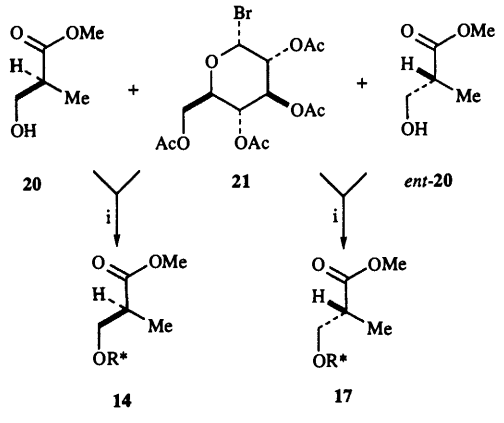
configuration of compound **12** was inferred from a nuclear Overhauser effect difference (NOED) spectroscopic experiment, in which no mutual enhancements were observed when the 2-methyl group and the olefinic hydrogen atom were irradiated. A brief survey of catalysts and solvents revealed that the hydrogenation of compound **12** was rapidly effected in ethyl acetate using hydrogen in the presence of 10% palladium–carbon; an 85:15 mixture of the dihydro derivatives **14** and **17** was produced in high yield. After three crystallisations, the major dihydro derivative **14** was obtained in a diastereopure state, albeit in only 15% yield.



14 R = OMe
15 R = OEt
16 R = Me

17 R = OMe
18 R = OEt
19 R = Me

That the major dihydro derivative possessed the stereostructure **14** was established by synthesis (Scheme 2). Thus, acetobromoglucose **21**[14] underwent condensation with methyl (2*S*)-3-hydroxy-2-methylpropionate **20** in the presence of silver(I) carbonate to give a material (40% yield after chromatography and crystallisation) that was identical to the major hydrogenation product of compound **12**. Similarly, the product obtained (25% yield after chromatography and crystallisation) from the corresponding reaction of acetobromoglucose **21** with methyl (2*R*)-3-hydroxy-2-methylpropionate *ent*-**20** matched the minor hydrogenation product of compound **12**.



20 **21** *ent*-**20**

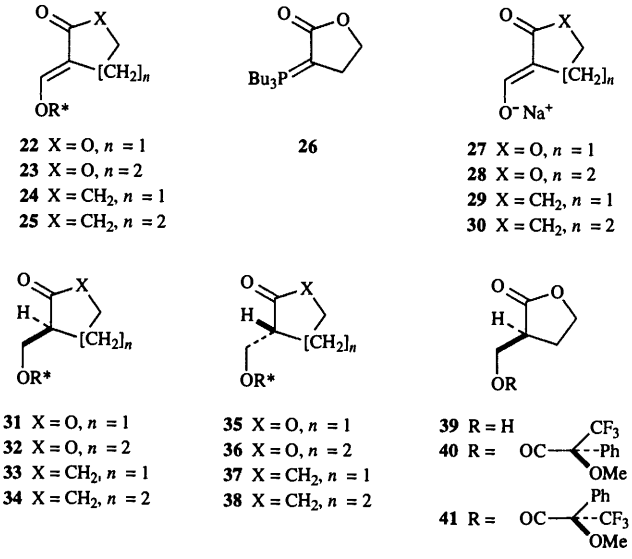
14 **17**

Scheme 2 *Reagent:* i, Ag_2CO_3

In the hope that the separation of the dihydro derivative **15** from its diastereomer **18** by fractional crystallisation would prove to be more efficient, the hydrogenation of the acrylate **13** was examined. The acrylate **13**, prepared (68% yield after crystallisation) as shown in Scheme 1, underwent hydrogenation to give an 84:16 mixture of the dihydro derivatives **15** and **18** in high yield. A single crystallisation provided the major dihydro derivative **15**§ in a diastereopure state in 68% yield.

To define further the scope of the hydrogenation reaction, the synthesis of the γ-butyrolactone **22** was undertaken. Initially, compound **22** was assembled using Wittig methodology. Thus, the phosphorane **26** (obtained in 87% yield by sequential treatment of α-bromo-γ-butyrolactone with PBu_3 and NaOH) underwent reaction with the formyl ester **11** in boiling toluene to give the γ-butyrolactone **22** in 70% yield after crystallisation. Subsequently, compound **22** was synthesised using enolate technology. Thus, the sodium salt **27**[16] underwent reaction with acetobromoglucose **21** in aq. acetone to give compound **22** in 39% yield after crystallisation.¶

Hydrogenation of the unsaturated lactone **22** proceeded rapidly in ethyl acetate in the presence of 10% palladium–carbon (0.5 mass equiv.) to give an 81:19 mixture of the dihydro derivatives **31** and **35** in high yield; a single crystallisation provided compound **31**‖ in a diastereopure state in 69% yield. A study of hydrogenation conditions revealed that the amount of catalyst employed could be substantially reduced. Thus, it was possible to hydrogenate compound **22** to an 83:17 mixture of the dihydro derivatives **31** and **35** using 1% palladium–carbon (0.1 mass equiv.) in a 1:1 mixture of ethyl acetate and ethanol over a period of 24 h on a 30 g scale; after crystallisation, compound **31** was isolated in a diastereopure state in 71% yield.



22 X = O, *n* = 1
23 X = O, *n* = 2
24 X = CH_2, *n* = 1
25 X = CH_2, *n* = 2

26

27 X = O, *n* = 1
28 X = O, *n* = 2
29 X = CH_2, *n* = 1
30 X = CH_2, *n* = 2

31 X = O, *n* = 1
32 X = O, *n* = 2
33 X = CH_2, *n* = 1
34 X = CH_2, *n* = 2

35 X = O, *n* = 1
36 X = O, *n* = 2
37 X = CH_2, *n* = 1
38 X = CH_2, *n* = 2

39 R = H
40 R =
41 R =

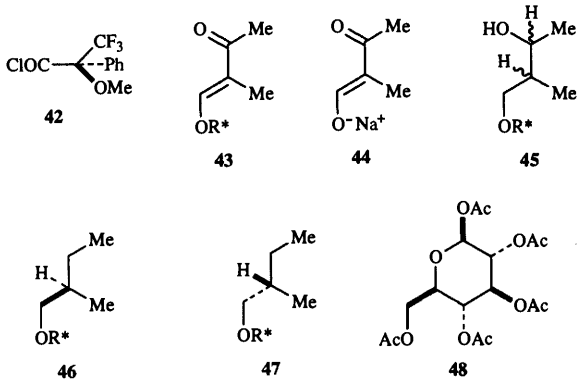
In the hope of corroborating its stereostructure and showing that its sugar auxiliary could be detached without compromising the stereochemical integrity of the γ-butyrolactone entity, we heated compound **31** under reflux in methanolic hydrochloric acid. Work-up gave compound **39**‖ as an essentially pure oil in 90% yield. On the basis of its optical rotation {$[\alpha]_D$ +20.3 ($CHCl_3$)}, compound **39** was considered to possess the (*S*)-configuration and to be of high enantiomeric purity {lit.,[19] $[\alpha]_D$ −21.1 ($CHCl_3$) for *ent*-**39**}. In accord with the latter notion, the alcohol **39** underwent reaction with the Mosher (*R*)-acid chloride **42** to give a 98:2 mixture of the esters **40** and *ent*-**41** (76% yield after chromatography) according to ^{19}F NMR spectroscopy. With the Mosher (*S*)-acid chloride *ent*-**42**, it afforded a 98:2 mixture of the esters **41** and *ent*-**40** (38% yield

§ For the synthesis and applications of 3-hydroxy-2-methylpropionic acid derivatives and related bifunctional C_4 chirons, see ref. 15.
¶ Recently, it has been reported that this reaction, when conducted in dimethyl sulfoxide, affords compound **22** in 55% yield after chromatography and crystallisation (ref. 17).
‖For the synthesis of 4-hydroxy-2-(hydroxymethyl)butyric acid derivatives and related trifunctional C_5 chirons, see refs. 18, 19.

after chromatography). Evidently, compound **39** possessed an enantiomeric purity of ~96%.

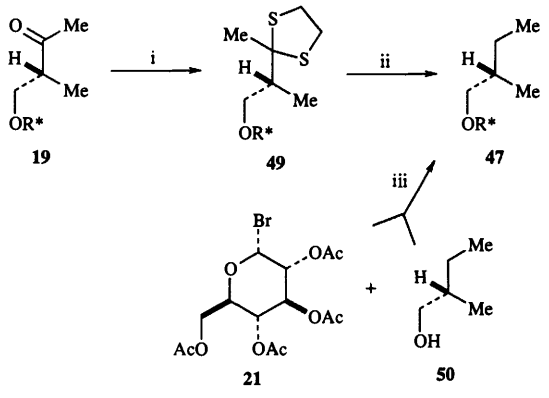
The δ-valerolactone **23**—the final example of a vinylogous carbonate to be studied—was prepared (44% yield after crystallisation) from the reaction of the sodium salt **28**[20] with acetobromoglucose **21** in aq. acetone. Hydrogenation of compound **23** gave a 75:25 mixture of the dihydro derivatives **32** and **36** in high yield; two crystallisations of the product provided compound **32**** in a diastereopure state in 49% yield.

It was of interest to extend the hydrogenation study to vinylogous esters†† to determine if it would be possible to reduce the olefinic linkage chemoselectively. Compound **43**,[5] prepared in improved yield (47% after crystallisation) by conducting the reaction of the sodium salt **44**[6,22] with acetobromoglucose **21** in aq. acetone rather than dimethyl sulfoxide, was selected for an initial study.



The butenone **43** underwent hydrogenation in ethyl acetate in the presence of 10% palladium–carbon to give mainly a 3:1:1 mixture of compounds **16**, **19** and **45**. Column chromatography led to the isolation of a 4:1 mixture of compounds **46** and **47** (1% yield), 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose **48** (5% yield), the butanone **16** (9% yield after crystallisation), mixtures of the butanones **16** and **19** (54% combined yield) and a 2:1 mixture of materials with the structure **45** (20% yield). 'Over-reduction' of the butenone **43** could be suppressed by conducting the hydrogenation reaction in propan-2-ol in the presence of 3% palladium–carbon; an 83:17 mixture of the butanones **16** and **19** was produced in high yield. Unfortunately, the mixture was not separable by fractional crystallisation.

It was envisaged that the stereostructures of the butanones **16** and **19** could be established by the chemical correlation outlined in Scheme 3. Thus, the presumed minor butanone **19**



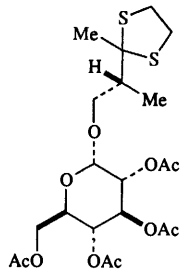
Scheme 3 *Reagents:* i, $(CH_2SH)_2$, $TiCL_4$; ii, Ra–Ni; iii, Ag_2CO_3

** We are unaware of any related trifunctional C_6 chirons.

†† Seemingly, little is known about the reduction of such systems (see ref. 21). We have not encountered any asymmetric versions of the reaction that are directed by a detachable auxiliary.

was expected to be convertible into the dithioketal **49** and thence the butane **47**. Hopefully, the last-cited compound would be independently available from the reaction of (*S*)-2-methylbutan-1-ol **50** with acetobromoglucose **21**. Clearly, a pure sample of the butanone **19** was required in order for us to undertake the correlation.

The butanones **16** and **19** were separable by preparative HPLC and pure samples of each were obtained after crystallisation; the recoveries were 52% for the butanone **16** and 11% for the butanone **19**. Mainly two products resulted when the butanone **19** was subjected to the action of ethane-1,2-dithiol and titanium(IV) chloride in dichloromethane and it was necessary to resort to preparative HPLC to effect their separation. The first fraction (22% yield) was identified as compound **51** and the second fraction (33% yield) as the required product **49**. The structural assignments rested upon the appearance of the 1′- and 2′-hydrogen signals in the ^1H NMR spectra [resonating as a doublet (*J* 3.5 Hz) at δ 5.06 and a double doublet (*J* 10 and 3.5 Hz) at δ 4.87 in the case of the α-anomer **51** and as a doublet (*J* 8 Hz) at δ 4.49 and a double doublet (*J* 9.5 and 8 Hz) at δ 5.01 in the case of the β-anomer **49**]. Evidently, in addition to promoting the desired dithioketalisation, the Lewis acid had induced an unwanted anomerisation process [presumably by effecting a cleavage and reformation of the C(1′)–O(5′) bond].



In the presence of hydrogen and Raney nickel in ethanol, the dithioketal **49** underwent reductive desulfurisation to give the butane **47** in 77% yield. The last-cited compound was also produced (50% yield after crystallisation) from the reaction of acetobromoglucose **21** with (*S*)-2-methylbutan-1-ol **50** and silver(I) carbonate. Clearly, as anticipated, hydrogenation of the butenone **43** had led to the butanone **16** as the major product and the butanone **19** as the minor product.

It was of interest to extend the hydrogenation study to the cyclic vinylogous ester **24**. Compound **24** was prepared (30% yield after crystallisation) from the reaction of the salt **29**[23] with acetobromoglucose **21** in aq. acetone. An 80:20 mixture of the dihydro derivatives **33** and **37** resulted when the methylenecyclopentanone **24** was hydrogenated. Crystallisation of the mixture provided the major dihydro derivative **33** in 50% yield. The configuration of the last-cited compound was not rigorously determined but was assigned by analogy with the earlier results.

Perhaps not surprisingly, because of the likely increased propensity to β-elimination, compound **33** was not converted into 2-(hydroxymethyl)cyclopentanone under the acidic hydrolytic conditions that effected the **31**⟶**39** transformation.

In a final study, the hydrogenation of compound **25** was examined. The methylenecyclohexanone **25**, prepared (27% yield after crystallisation) by treatment of acetobromoglucose **21** with the salt **30**[24] in aq. acetone, underwent hydrogenation to give a 67:33 mixture of the dihydro derivatives **34** and **38** (43% yield after chromatography and crystallisation). Attempts to fractionate the mixture by further crystallisation were unproductive.

The afore-cited results are of interest in several respects. They reveal that the model proposed to account for the preferential

re-face reactivity of dienes of type **1** in cycloadditions can be extended to accommodate the preferential *re*-face reactivity of systems of type **4** in catalytic hydrogenation reactions. They expand the role of the 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl unit as a cheap and practical auxiliary in asymmetric synthesis. *In illustrating* the ease with which systems of type **4** undergo catalytic hydrogenations, they expose a little-exploited reactivity of vinylogous carbonates/esters. They exemplify new methodology for effecting the stereoselective α-oxymethylation of α-methylene esters, lactones and ketones. Hitherto, such processes have been brought about by the alkylation of chiral enolates with benzyl chloromethyl ether;[25] microbiological reduction has also been used to convert 3-hydroxy-2-methylpropenoates into 3-hydroxy-2-methylpropionates.[26] Finally, it is worth noting that compounds **15**, **31**, **32**, **33** and **39** are of interest as chirons in stereoselective synthesis. The processes described herein render them accessible in multigram quantities by chromatography-free routes.

Experimental

Dry solvents, referred to in the ensuing experiments, were prepared as follows: toluene and dichloromethane were distilled from calcium chloride granules; methanol was distilled from magnesium turnings and iodine; diethyl ether was stored over sodium wire. Unless otherwise stated, light petroleum refers to that fraction boiling in the range 40–60 °C.

TLC was performed on Merck plastic or aluminium plates coated with silica gel (60 F_{254}); chromatograms were initially examined under UV light (Mineralight UVG2-58 lamp) and visualised with either iodine vapour or a *p*-anisaldehyde stain [plates were sprayed with *p*-$MeOC_6H_4CHO$–conc. H_2SO_4–EtOH (1:4:95) and heated]. Column chromatography was effected, under positive pressure from a compressed air line, employing Crossfield Sorbsil C60 flash silica. Preparative HPLC was carried out using a column (25 × 0.8 cm) of Spherisorb S10 silica, a Kontron 420 pump, and Kontron 742 UV and ERC-7515A RI detectors.

Evaporations were conducted under reduced pressure (using a water-pump or an oil-pump) at ≤40 °C with a Buchi rotary evaporator. Mps were determined with a Buchi 512 melting point apparatus. Optical rotations, given in 10^{-1} deg cm^2 g^{-1}, were measured at ~20 °C using a Thorn Automation Type 243 or an Optical Activity 1000 polarimeter. IR spectra were recorded using a Perkin-Elmer 783 spectrometer. A Perkin-Elmer Lambda 15 spectrometer was used to determine UV spectra; extinction coefficients (ε) are presented in cm^2 $mmol^{-1}$. NMR spectra were measured using a Bruker AC 300 {for ^1H and ^{13}C [with distortionless enhancement by polarisation transfer (DEPT) editing]} or a Bruker AC 200 spectrometer (for ^1H and ^{19}F); *J*-values and separations are given in Hz. FAB mass spectra (*p*-$NO_2C_6H_4CH_2OH$ as matrix) were measured using a Kratos MS 50 spectrometer; EI mass spectra were determined using a VG 7070 instrument. Elemental analyses were performed with a Carlo-Erba Model 1108 analyser.

Methyl (*E*)-2-methyl-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)acrylate 12

A mixture of tributylphosphine (1.25 cm^3, 5.02 mmol) and methyl 2-bromopropionate (0.56 cm^3, 5.02 mmol) in dry toluene (5 cm^3) was stirred for 15 h. Evaporation of the mixture left a syrup, which was dissolved in dichloromethane (10 cm^3). The solution was washed with 10% aq. sodium hydroxide (30 cm^3), dried ($MgSO_4$), and concentrated to leave the phosphorane **9** (1.10 g, 76%) as a clear syrup which was used immediately.

A solution of the formyl ester **11** (1.00 g, 2.66 mmol) and the phosphorane **9** (1.00 g, 3.47 mmol) in dry toluene (20 cm^3) was heated under reflux for 25 min. Evaporation of the mixture left a residue which, after having been washed with light petroleum (2 × 50 cm^3), was crystallised from dichloromethane–diethyl ether to give the *title compound* **12** (0.935 g, 79%); mp 161–163 °C; $[\alpha]_D$ −19 (*c* 0.8, CH_2Cl_2) (Found: C, 50.9; H, 6.1. $C_{19}H_{26}O_{12}$ requires C, 51.1; H, 5.85%); λ_{max}(EtOH)/nm 229 (ε 15 600); ν_{max}(KBr)/cm^{-1} 1750 (ester C=O), 1705 (vinylogous carbonate C=O) and 1660 (C=C); δ_H(300 MHz; $CDCl_3$) 1.73 (3 H, d, *J* 1.5, 2-Me), 2.02, 2.04, 2.05 and 2.09 (each 3 H, s, 4 × $MeCO_2$), 3.72 (3 H, s, MeO_2C), 3.80 (1 H, ddd, *J* 10, 4.5 and 2.5, 5′-H), 4.14 and 4.30 [each 1 H, dd (*J* 12.5 and 2.5) and dd (*J* 12.5 and 4.5), 6′-H_2], 4.87 (1 H, d, *J* 7.5, 1′-H), 5.11–5.29 (3 H, m, 2′-, 3′- and 4′-H) and 7.41 (1 H, q, *J* 1.5, 3-H) (in an NOED spectroscopic experiment, irradiation at δ 7.41 enhanced the d at δ 4.87 by 13%; irradiation at δ 1.73 caused no enhancement); *m*/*z* (FAB) 447 (MH^+, 20%), 331 ($C_{14}H_{19}O_9^+$, 80) and 169 (100).

Hydrogenation of the methyl acrylate 12

(With W. C. Ding.) A mixture of the methyl acrylate **12** (0.900 g, 2.02 mmol) and 10% palladium–carbon (0.450 g, 0.5 mass equiv.) in ethyl acetate (20 cm^3) was stirred under hydrogen for 1 h. The mixture was filtered through a pad of Celite and the filtrate was concentrated to leave an 85:15 mixture of the dihydro derivatives **14** and **17** [the ratio was estimated from the integrals of the ds (*J* 7) at δ 1.13 and 1.17, attributed to the 2-Me groups of products **14** and **17**]. Three crystallisations of the material from methanol gave *methyl* (2S)-2-*methyl*-3-(2′,3′,4′,6′-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)*propionate* **14** (0.136 g, 15%); mp 62–64 °C; $[\alpha]_D$ −15 (*c* 0.54, CH_2Cl_2) (Found: C, 50.6; H, 6.2. $C_{19}H_{28}O_{12}$ requires C, 50.9; H, 6.3%); λ_{max}(EtOH)/nm 208 (ε 400) and 260 (150); ν_{max}(KBr)/cm^{-1} 1745 (ester C=O); δ_H(300 MHz; $CDCl_3$) 1.13 (3 H, d, *J* 7, 2-Me), 2.00, 2.02, 2.04 and 2.09 (each 3 H, s, 4 × $MeCO_2$), 2.69–2.82 (1 H, m, 2-H), 3.65–3.73 (2 H, m, 3- and 5′-H), 3.68 (3 H, s, MeO_2C), 3.87 (1 H, dd, *J* 9.5 and 5.5, 3-H), 4.13 and 4.26 [each 1 H, dd (*J* 12.5 and 2.5) and dd (*J* 12.5 and 4.5), 6′-H_2], 4.49 (1 H, d, *J* 8, 1′-H), 4.96 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.07 (1 H, t, *J* 9.5, 4′-H) and 5.19 (1 H, t, *J* 9.5, 3′-H); *m*/*z* (FAB) 449 (MH^+, 6%), 331 ($C_{14}H_{19}O_9^+$, 100) and 169 (80).

Reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide 21 with the alcohols 20 and *ent*-20

(a) A mixture of acetobromoglucose **21** (0.388 g, 0.94 mmol), silver(I) carbonate (0.310 g, 1.12 mmol) and methyl (2*S*)-3-hydroxy-2-methylpropionate **20** (3 cm^3) was stirred in the dark. After 6 h, the mixture was diluted with dichloromethane and filtered through a pad of Celite. After having been washed successively with water and brine, the filtrate was dried ($MgSO_4$) and concentrated. Subjection of the residue to column chromatography [light petroleum–Et_2O (1:1) as eluent] led to the isolation of an oil, which was crystallised from diethyl ether–light petroleum to give compound **14** (0.168 g, 40%), mp 64–66 °C; $[\alpha]_D$ −19 (*c* 0.6, CH_2Cl_2). The IR and ^1H NMR spectra of the material matched those of the major product obtained by hydrogenation of the methyl acrylate **12**.

(b) A mixture of acetobromoglucose **21** (0.466 g, 1.13 mmol), silver(I) carbonate (0.393 g, 1.43 mmol) and methyl (2*R*)-3-hydroxy-2-methylpropionate *ent*-**20** (3 cm^3) was stirred in the dark for 15 h. Work-up and purification of the product as described above gave *methyl* (2R)-2-*methyl*-3-(2′,3′,4′,6′-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)*propionate* **17** (0.128 g, 25%); mp 92–94 °C; $[\alpha]_D$ −24 (*c* 0.3, CH_2Cl_2) (Found: C, 50.8; H, 6.0. $C_{19}H_{28}O_{12}$ requires C, 50.9; H, 6.3%); λ_{max}(EtOH)/nm 209 (ε 250); ν_{max}(KBr)/cm^{-1} 1750 (ester C=O); δ_H(300 MHz; $CDCl_3$) 1.17 (3 H, d, *J* 7, 2-Me), 2.00, 2.02, 2.04 and 2.09 (each 3 H, s, 4 × $MeCO_2$), 2.67–2.79 (1 H, m, 2-H), 3.58 and 4.06 [each 1 H, dd (*J* 10 and 6.5) and dd (*J* 10 and 5.5), 3-H_2], 3.67 (3 H, s, MeO_2C), 3.68 (1 H, ddd, *J* 10, 4.5 and 2.5, 5′-H), 4.12 and 4.26 [each 1 H, dd (*J* 12.5 and 2.5) and dd (*J* 12.5 and 4.5), 6′-H_2], 4.50 (1 H, d, *J* 8, 1′-H), 4.97 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.07 (1 H, t, *J* 9.5, 4′-H) and 5.19 (1 H, t, *J* 9.5, 3′-H); *m*/*z* (FAB) 581

(MCs$^+$, 20%), 471 (MNa$^+$, 15), 331 ($C_{14}H_{19}O_9^+$, 100) and 169 (50).

Ethyl (*E*)-2-methyl-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)acrylate 13

A mixture of tributylphosphine (25.0 cm^3, 0.100 mol) and ethyl 2-bromopropionate (13.0 cm^3, 0.100 mol) in dry toluene (25 cm^3) was stirred for 15 h. Evaporation of the mixture left a syrup, which was dissolved in dichloromethane (50 cm^3). The solution was washed with 10% aq. sodium hydroxide (200 cm^3), dried ($MgSO_4$), and concentrated to leave the phosphorane **10** (25.8 g, 85%) as a clear syrup which was used immediately.

A solution of the formyl ester **11** (10.6 g, 0.028 mol) and the phosphorane **10** (25.8 g, 0.085 mol) in dry toluene (150 cm^3) was heated under reflux for 8 h; an intense maroon colour developed. Evaporation of the solvent left a residue, which was dissolved in hot dichloromethane (50 cm^3), the solution was treated with a 1:1 mixture of dichloromethane and light petroleum (distilled 30–40 °C) (100 cm^3) followed by light petroleum (distilled 30–40 °C) (100 cm^3) and allowed to crystallise. Filtration gave the *title compound* **13** (8.82 g, 68%); mp 139–142 °C (with softening at 136 °C); $[\alpha]_D$ −11 (*c* 1.5, CH_2Cl_2) (Found: C, 52.0; H, 6.2. $C_{20}H_{28}O_{12}$ requires C, 52.15; H, 6.15%); λ_{max}(EtOH)/nm 229 (ε 15 800); ν_{max}(KBr)/cm^{-1} 1760 and 1740 (ester C=O), 1710 (vinylogous carbonate C=O) and 1650 (C=C); δ_H(300 MHz; $CDCl_3$) 1.28 (3 H, t, *J* 7, *Me*CH_2), 1.73 (3 H, d, *J* 1.5, 2-Me), 2.03, 2.04, 2.05 and 2.09 (each 3 H, s, 4 × $MeCO_2$), 3.81 (1 H, ddd, *J* 10, 4.5 and 2.5, 5′-H), 4.15 and 4.30 [each 1 H, dd (*J* 12.5 and 2.5) and dd (*J* 12.5 and 4.5), 6′-H_2], 4.18 (2 H, q, *J* 7, MeCH_2), 4.87 (1 H, d, *J* 7.5, 1′-H), 5.11–5.29 (3 H, m, 2′-, 3′- and 4′-H) and 7.39 (1 H, q, *J* 1.5, 3-H) (in an NOED spectroscopic experiment, irradiation at δ 7.39 enhanced the d at δ 4.87 by 13%; irradiation at δ 1.73 caused no enhancement); δ_C(75 Hz; $CDCl_3$) 9.15 (*C*H_3CH_2), 14.15 (2-CH_3), 20.31, 20.35 and 20.48 (4 × *C*H_3CO), 60.06 (*C*H_2CH_3), 61.37 (6′-CH_2), 67.66, 70.51, 72.06 and 72.30 (2′-, 3′-, 4′- and 5′-CH), 100.4 (1′-CH), 110.4 (2-C), 152.3 (3-CH) and 167.8, 168.8, 169.1, 169.9 and 170.4 (4 × CH_3*C*O and 1-CO); *m*/*z* (FAB) 461 (MH^+, 20%), 331 ($C_{14}H_{19}O_9^+$, 65) and 169 (100).

Hydrogenation of the ethyl acrylate 13

A mixture of the ethyl acrylate **13** (0.564 g, 1.23 mmol), 10% palladium–charcoal (0.227 g, 0.4 mass equiv.) and ethyl acetate (50 cm^3) was stirred under hydrogen for 24 h. The mixture was filtered through a pad of Celite and the filtrate was concentrated to leave an 84:16 mixture of the dihydro derivatives **15** and **18** [the ratio was estimated from the integrals of the ds (*J* 7) at δ 1.13 and 1.17, ascribed to the 2-Me groups of compounds **15** and **18**]. Crystallisation of the mixture from ethyl acetate–light petroleum gave *ethyl* (2S)-2-*methyl*-3-(2′,3′,4′,6′-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)*propionate* **15** (0.384 g, 68%); mp 79–81 °C; $[\alpha]_D$ −13 (*c* 0.9, CH_2Cl_2) (Found: C, 51.6; H, 6.7. $C_{20}H_{30}O_{12}$ requires C, 51.95; H, 6.55%); λ_{max}(EtOH)/nm 210 (ε 280); ν_{max}(KBr)/cm^{-1} 1760, 1745 and 1735 (ester C=O); δ_H(300 MHz; $CDCl_3$) 1.13 (3 H, d, *J* 7, 2-Me), 1.26 (3 H, t, *J* 7, *Me*CH_2), 2.00, 2.02, 2.03 and 2.09 (each 3 H, s, 4 × $MeCO_2$), 2.67–2.79 (1 H, m, 2-H), 3.69 (1 H, ddd, *J* 10, 4.5 and 2.5, 5′-H), 3.70 and 3.86 [each 1 H, dd (*J* 9.5 and 8.5) and dd (*J* 9.5 and 5.5), 3-H_2], 4.07–4.19 (3 H, m, MeCH_2 and 6′-H), 4.26 (1 H, dd, *J* 12.5 and 4.5, 6′-H), 4.50 (1 H, d, *J* 8, 1′-H), 4.96 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.07 (1 H, t, *J* 9.5, 4′-H) and 5.19 (1 H, t, *J* 9.5, 3′-H); δ_C(75 MHz; $CDCl_3$) 13.79 and 14.13 (2 × CH_3), 20.56 and 20.70 (4 × *C*H_3CO), 40.02 (2-CH), 60.46 (*C*H_2CH_3), 61.64 (6′-CH_2), 68.34, 71.04, 71.73 and 72.67 (2′-, 3′-, 4′- and 5′-CH), 71.41 (3-CH_2), 101.0 (1′-CH), 169.3, 169.4, 170.2 and 170.6 (4 × CH_3*C*O), and 174.4 (1-CO); *m*/*z* (FAB) 463 (MH^+, 7%), 331 ($C_{14}H_{19}O_9^+$, 90) and 169 (100).

(*E*)-α-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyloxymethylene)-γ-butyrolactone 22

(**a**) A mixture of tributylphosphine (1.89 cm^3, 7.59 mmol) and α-bromo-γ-butyrolactone (0.63 cm^3, 7.60 mmol) in dry toluene (5 cm^3) was stirred for 15 h. Evaporation of the mixture left a syrup, which was dissolved in dichloromethane (15 cm^3). The solution was washed with 10% aq. sodium hydroxide (50 cm^3), dried ($MgSO_4$) and concentrated to leave the phosphorane **26** (1.89 g, 87%) as a clear syrup which was used immediately.

A solution of the formyl ester **11** (2.00 g, 5.31 mmol) and the phosphorane **26** (1.83 g, 6.38 mmol) in dry toluene (20 cm^3) was heated under reflux for 1 h. Evaporation of the mixture left a dark residue which, after having been washed with light petroleum (100 cm^3), was dissolved in dichloromethane. Activated carbon was added and the mixture was filtered through a pad of Celite. Addition of diethyl ether to the filtrate induced crystallisation of the *title compound* **22** (1.65 g, 70%). A sample, recrystallised from methanol, showed mp 167–69 °C; $[\alpha]_D$ −12 (*c* 0.5, CH_2Cl_2) (Found: C, 51.7; H, 5.7. $C_{19}H_{24}O_{12}$ requires C, 51.35; H, 5.45%); λ_{max}(EtOH)/nm 234 (ε 15 600); ν_{max}(KBr)/cm^{-1} 1755, 1740 and 1730 (γ-lactone and ester C=O) and 1685 (C=C); δ_H(300 MHz; $CDCl_3$) 2.02, 2.03, 2.05 and 2.09 (each 3 H, s, 4 × $MeCO_2$), 2.76–2.99 (2 H, m, β-H_2), 3.82 (1 H, ddd, *J* 10, 5 and 2, 5-H), 4.13 and 4.29 [each 1 H, dd (*J* 12.5 and 2) and dd (*J* 12.5 and 5), 6-H_2], 4.36 (2 H, t, separation 7.5, γ-H_2), 4.91 (1 H, d, *J* 7.5, 1-H), 5.08–5.18 (2 H, m, 2- and 4-H), 5.25 (1 H, t, *J* 9.5, 3-H) and 7.42 (1 H, t, *J* 2.5, C=CH) (in an NOED spectroscopic experiment, irradiation at δ 7.42 enhanced the d at δ 4.91 by 14%); δ_C(75 MHz; $CDCl_3$) 20.54 and 20.71 (4 × *C*H_3CO), 23.76 (β-CH_2), 61.50 (6-CH_2), 65.97 (γ-CH_2), 67.67, 70.71, 72.22 and 72.69 (2-, 3-, 4- and 5-CH), 101.1 (1-CH), 106.9 (α-C), 151.0 (C=*C*H), 169.1, 169.3, 170.1 and 170.6 (4 × CH_3*C*O) and 172.1 (γ-lactone CO); *m*/*z* (FAB) 445 (MH^+, 40%), 331 ($C_{14}H_{19}O_9^+$, 90) and 169 (100).

(**b**) A mixture of ethyl formate (80.0 cm^3, 0.99 mol) and γ-butyrolactone (65.0 cm^3, 0.797 mol) was added in drops over a period of 15 min to a stirred slurry of sodium methoxide [prepared by the addition of Na (18.4 g, 0.8 mol) in small pieces to ice-cold, dry MeOH (400 cm^3) followed, after the reaction was complete, by evaporation] in dry diethyl ether (280 cm^3). After 12 h, the mixture was filtered under argon and the filtered material was washed well with diethyl ether to give the salt **27** (74.9 g, 69%); δ_H(300 MHz; D_2O) 2.60 (2 H, dt, *J* 8, 8 and 1.5, β-H_2), 4.15 (2 H, t, *J* 8, γ-H_2), 4.65 (HOD) and 8.25 (1 H, t, *J* 1.5, C=CH).

A solution of the salt **27** (74.5 g, 0.547 mol) in water (240 cm^3) was added to a stirred solution of acetobromoglucose **21** (113 g, 0.275 mol) in acetone (480 cm^3). After 20 h, the mixture was partially concentrated (to remove Me_2CO), and partitioned between dichloromethane and water. Evaporation of the dried ($MgSO_4$) organic phase, and crystallisation of the residue from dichloromethane–diethyl ether, gave the title compound **22** (47.5 g, 39%); mp 158–160 °C; $[\alpha]_D$ −14 (*c* 0.8, CH_2Cl_2). The ^{1}H NMR spectrum of the material matched that of the sample obtained in the above experiment.

Hydrogenation of the methylenebutyrolactone 22

(**a**) A mixture of compound **22** (1.00 g, 2.25 mmol), 10% palladium–carbon (0.500 g, 0.5 mass equiv.) and ethyl acetate (20 cm^3) was stirred under hydrogen for 1 h. The mixture was filtered through a pad of Celite and the filtrate was concentrated to leave an 81:19 mixture of the dihydro derivatives **31** and **35** [the ratio was estimated from the integrals of the dds at δ 3.94 (*J* 11 and 4.5) and 3.84 (*J* 10 and 4), attributed to a γ-H atom of compounds **31** and **35**]. Crystallisation of the mixture from dichloromethane–diethyl ether gave (αS)-α-(2,3,4,6-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxymethyl*)-γ-*butyrolactone* **31** (0.690 g, 69%); mp 150–152 °C; $[\alpha]_D$ −9 (*c* 1.6, CH_2Cl_2) (Found: C, 51.0; H, 6.0. $C_{19}H_{26}O_{12}$ requires C, 51.1; H, 5.85%); λ_{max}(EtOH)/nm 206 (ε 240);

ν_{max}(KBr)/cm^{-1} 1760, 1750, 1745 and 1730 (γ-lactone and ester C=O); δ_H(300 MHz; $CDCl_3$) 2.00, 2.01, 2.05 and 2.09 (each 3 H, s, 4 × $MeCO_2$), 2.26–2.38 (2 H, m, β-H_2), 2.74 (1 H, apparent septet, separation 5, α-H), 3.66 (1 H, ddd, *J* 10, 4 and 2.5, 5-H), 3.94 and 4.07 [each 1 H, dd (*J* 11 and 4.5) and dd (*J* 11 and 5), α-CH_2O], 4.17 (1 H, dd, *J* 12.5 and 2.5, 6-H), 4.21–4.28 (2 H, m, 6- and γ-H), 4.37 (1 H, ddd, *J* 12, 7.5 and 4.5, γ-H), 4.52 (1 H, d, *J* 8, 1-H), 4.99 (1 H, dd, *J* 9.5 and 8, 2-H),5.08 (1 H, t, *J* 9.5, 4-H) and 5.18 (1 H, t, *J* 9.5, 3-H); δ_C(75 MHz; $CDCl_3$) 20.64, 20.72 and 20.79 (4 × CH_3CO), 25.11 (β-CH_2), 40.47 (α-CH), 61.57 (6-CH_2), 66.95 and 68.70 (α-CH_2O and γ-CH_2), 68.12, 71.11, 71.79 and 72.79 (2-, 3-, 4- and 5-CH), 101.3 (1-CH), 169.4, 170.2 and 170.7 (4 × CH_3CO) and 177.2 (γ-lactone CO); *m/z* (FAB) 469 (MNa^+, 10%), 447 (MH^+, 2), 331 ($C_{14}H_{19}O_9^+$, 75) and 169 (100).

(b) Hydrogen was bubbled into a stirred solution of compound **22** (30.0 g, 6.75 mmol) in a 1:1 mixture of ethyl acetate and ethanol (1200 cm^3) in the presence of 1% palladium–carbon (3.0 g, 0.1 mass equiv.). When the reaction was complete (TLC monitoring; *ca.* 24 h), the mixture was filtered through a pad of Celite and the filtrate was concentrated to give an 83:17 mixture of the dihydro derivatives **31** and **35**. Crystallisation of the mixture from dichloromethane–diethyl ether gave the dihydro derivative **31** (21.3 g, 71%); $[\alpha]_D$ −11 (*c* 0.8, CH_2Cl_2), identified by its ^{1}H NMR spectrum.

(*S*)-α-Hydroxymethyl-γ-butyrolactone 39

A mixture of compound **31** (15.0 g, 33.6 mmol), methanol (500 cm^3) and hydrochloric acid (5 mol dm^3; 500 cm^3) was heated under reflux for 3 h. The solution was concentrated (to ~500 cm^3) and continuously extracted with dichloromethane for 48 h. Evaporation of the dried ($MgSO_4$) organic extract left the title compound **39** (3.52 g, 90%) in an essentially pure state as a pale yellow oil; $[\alpha]_D$ +20.3 (*c* 1.9, $CHCl_3$) [lit.,[19] −21.1 (*c* 4.2, $CHCl_3$) for *ent*-**39**]; λ_{max}(EtOH)/nm no significant absorption; ν_{max}(film)/cm^{-1} 3400br (OH) and 1760 (γ-lactone C=O); δ_H(300 MHz; $CDCl_3$) 2.15–2.40 (2 H, m, β-H_2), 2.74 (1 H, apparent septet, separation 5, α-H), 3.1 (1 H, br s, OH), 3.77 and 3.91 (each 1 H, dd, *J* 11 and 5, α-CH_2O) and 4.22 and 4.37 [each 1 H, dt (*J* 9, 9 and 7) and dt (*J* 9, 9 and 3.5), γ-H_2]; δ_C(75 MHz; $CDCl_3$) 24.81 (β-CH_2), 41.80 (α-CH), 60.84 and 67.48 (α-CH_2O and γ-CH_2), and 179.1 (γ-lactone CO); *m/z* (EI) 117 (MH^+, 40%), 86 ($C_4H_6O_2^+$, 67), 57 ($C_3H_5O^+$, 100) and 55 (60). A *sample*, after Kugelrohr distillation, showed $[\alpha]_D$ +21.2 (*c* 0.85, $CHCl_3$) (Found: C, 51.4; H, 7.2. $C_5H_8O_3$ requires C, 51.75; H, 6.95%).

Mosher esters 40 and 41

(a) Pyridine (0.5 cm^3) was added in drops to a stirred mixture of the alcohol **39** (0.028 g, 0.24 mmol) and the (*R*)-acid chloride **42** (0.119 g, 0.47 mmol) in dry dichloromethane (2 cm^3). The solution was left overnight and then partitioned between dichloromethane and dil. hydrochloric acid. After having been washed successively with aq. sodium hydrogen carbonate and brine, the organic phase was dried ($MgSO_4$) and concentrated to leave mainly the Mosher ester **40**. The sample was subjected to column chromatography (light petroleum–EtOAc; gradient elution) to give a 98:2 mixture of (αS)-α-[(1S)-1-*methoxy*-1-(*trifluoromethyl*)(*phenyl*)*acetoxymethyl*]-γ-*butyrolactone* **40** and (αR)-α-[(1S)-1-*methoxy*-1-(*trifluoromethyl*)(*phenyl*)*acetoxymethyl*]-γ-*butyrolactone* ent-**41** (0.061 g, 76%) as a crystalline solid; mp 69 °C; $[\alpha]_D$ −32 (*c* 0.76, CH_2Cl_2) (Found: C, 54.5; H, 4.3; F, 17.5. $C_{15}H_{15}F_3O_5$ requires C, 54.2; H, 4.55; F, 17.15%); λ_{max}(EtOH)/nm 205 (ε 11 700), 250 (310), 256 (400), 261 (440) and 267 (300); ν_{max}(KBr)/cm^{-1} 1775 and 1765 (γ-lactone and ester C=O); δ_H(300 MHz; $CDCl_3$) (for **40**) 2.07–2.21 and 2.33–2.45 (each 1 H, m, β-H_2), 2.92–3.02 (1 H, m, α-H), 3.50 (3 H, d, *J* 1, MeO), 4.21 and 4.32 [each 1 H, dt (*J* 9, 9 and 7) and dt (*J* 9, 9 and 3), γ-H_2], 4.55 and 4.63 [each 1 H, dd (*J* 11 and 3) and dd (*J* 11 and 6), α-CH_2O] and 7.37–7.45 and 7.48–7.52 (3 and 2 H, each m, Ph); δ_F(188 MHz; $CDCl_3$) 5.89 and 6.07 (ratio 98:2) (CF_3CO_2H as external standard); *m/z* (FAB) 355 (MNa^+, 45%), 333 (MH^+, 75), 281 (50) and 189 (100).

(b) The afore-cited experiment was repeated using the (*S*)-acid chloride *ent*-**42** in place of its enantiomer. Work-up and purification as before gave a 98:2 mixture of (α*S*)-α-[(1*R*)-1-methoxy-1-(trifluoromethyl)(phenyl)acetoxymethyl]-γ-butyrolactone **41** and (α*R*)-α-[(1*R*)-1-methoxy-1- (trifluoromethyl)-(phenyl)acetoxymethyl]-γ-butyrolactone *ent*-**40** (0.030 g, 38%) as an oil; $[\alpha]_D$ +39 (*c* 0.5, CH_2Cl_2); λ_{max}(EtOH)/nm 206 (ε 8300), 250 (290), 256 (350), 261 (370) and 267 (270); ν_{max}(film)/cm^{-1} 1775 and 1760 (γ-lactone and ester C=O); δ_H(300 MHz; $CDCl_3$) (for **41**) 2.00–2.14 and 2.29–2.41 (each 1 H, m, β-H_2), 2.91–3.01 (1 H, m, α-H), 3.53 (3 H, s, MeO), 4.13–4.27 (2 H, m, γ-H_2), 4.54 and 4.62 [each 1 H, dd (*J* 11 and 3.5) and dd (*J* 11 and 5), α-CH_2O] and 7.38–7.44 and 7.47–7.51 (3 and 2 H, each m, Ph); δ_F(188 MHz; $CDCl_3$) 5.89 and 6.07 (ratio 2:98) (CF_3CO_2H as external standard); *m/z* (FAB) 355 (MNa^+, 5%), 333 (MH^+, 20), 281 (25) and 189 (100).

(*E*)-α-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyloxymethylene)-δ-valerolactone 23

A mixture of ethyl formate (20.0 cm^3, 0.248 mmol) and δ-valerolactone (18.5 cm^3, 0.199 mol) was added in drops over a period of 2 h to a stirred slurry of sodium methoxide [prepared by the addition of Na (4.75 g, 0.206 mol) in small pieces to ice-cold, dry MeOH (100 cm^3) followed, after the reaction was complete, by evaporation] in dry diethyl ether (75 cm^3). After 2.5 days, the solid was collected by filtration to give the salt **28** (23.0 g, 77%); δ_H(300 MHz; D_2O) 1.59–1.67 (2 H, m, γ-H_2), 2.09 (2 H, t, *J* 6.5, β-H_2), 4.02 (2 H, t, *J* 5, δ-H_2), 4.65 (HOD) and 8.58 (1 H, s, C=CH).

A solution of the salt **28** (22.9 g, 153 mmol) in water (75 cm^3) was added to a stirred solution of acetobromoglucose **21** (31.5 g, 76.6 mmol) in acetone (150 cm^3). After 18 h, the mixture was partially concentrated (to remove Me_2CO), and partitioned between dichloromethane and water. Evaporation of the dried ($MgSO_4$) organic phase and crystallisation of the residue from dichloromethane–diethyl ether gave the *title compound* **23** (15.5 g, 44%); mp 122–123 °C; $[\alpha]_D$ −2.5 (*c* 0.88, CH_2Cl_2) (Found: C, 52.6; H, 5.9. $C_{20}H_{26}O_{12}$ requires C, 52.4; H, 5.7%); λ_{max}(EtOH)/nm 239 (ε 11 600); ν_{max}(KBr)/cm^{-1} 1760 and 1730 (ester C=O), 1710 (δ-lactone C=O) and 1630 (C=C); δ_H(300 MHz; $CDCl_3$) 1.81–1.93 (2 H, m, γ-H_2), 2.02, 2.03, 2.05 and 2.09 (each 3 H, s, 4 × $MeCO_2$), 2.33–2.57 (2 H, m, β-H_2), 3.80 (1 H, ddd, *J* 10.5, 5 and 2, 5-H), 4.11 (1 H, dd, *J* 12.5 and 2, 6-H), 4.26–4.32 (3 H, m, 6-H and δ-H_2), 4.90 (1 H, d, *J* 7.5, 1-H), 5.08–5.28 (3 H, m, 2-, 3- and 4-H) and 7.60 (1 H, br t, separation 2, C=CH) (in an NOED spectroscopic experiment, irradiation at δ 7.60 enhanced the d at δ 4.90 by 17%; irradiation at δ 2.40 caused no enhancement); δ_C(75 MHz; $CDCl_3$) 20.53 and 20.69 (4 × CH_3CO), 20.74 and 21.70 (β- and γ-CH_2), 61.49 (6-CH_2), 68.83 (δ-CH_2), 67.71, 70.64, 72.16 and 72.67 (2-, 3-, 4- and 5-CH), 101.0 (1-CH), 108.1 (α-C), 154.7 (C=CH) and 166.6, 169.1, 169.3, 170.0 and 170.6 (4 × CH_3CO and δ-lactone CO); *m/z* (FAB) 459 (MH^+, 13%), 331 ($C_{14}H_{19}O_9^+$, 100) and 169 (95).

Hydrogenation of the methylenevalerolactone 23

Hydrogen was bubbled into a stirred solution of compound **23** (11.0 g, 24 mmol) in a 1:1 mixture of ethyl acetate and ethanol (300 cm^3) in the presence of 3% palladium–carbon (1.10 g, 0.1 mass equiv.). When the reaction was complete (TLC monitoring; *ca.* 10 h), the mixture was filtered through a pad of Celite and the filtrate was concentrated to leave a 75:25 mixture of the dihydro derivatives **32** and **36** [the ratio was calculated from the integrals of the ds (*J* 8) at δ 4.56 and 4.50, attributed to the 1-H atoms of compounds **32** and **36**]. Two crystallisations

of the material from dichloromethane–diethyl ether gave (αS)-α-(2,3,4,6-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxymethyl*)-γ-*valerolactone* **32** (5.36 g, 49%); mp 114 °C; $[\alpha]_D$ −29 (*c* 0.84, CH_2Cl_2) (Found: C, 51.9; H, 6.1. $C_{20}H_{28}O_{12}$ requires C, 52.15; H, 6.15%); λ_{max}(EtOH)/nm 218 (ε 130); ν_{max}(KBr)/cm^{-1} 1750 (ester C=O) and 1725 (δ-lactone C=O); δ_H(300 MHz; $CDCl_3$) 1.73–1.97 (4 H, m, β- and γ-H_2), 2.00, 2.02, 2.05 and 2.09 (each 3 H, s, 4 × $MeCO_2$), 2.61–2.71 (1 H, m, α-H), 3.66 (1 H, ddd, *J* 10, 4 and 2.5, 5-H), 3.90 and 4.11 [each 1 H, dd, (*J* 10.5 and 5) and dd (*J* 10.5 and 5.5), α-CH_2O], 4.15 (1 H, dd, *J* 12.5 and 2, 6-H), 4.25–4.36 (3 H, m, 6-H and δ-H_2), 4.56 (1 H, d, *J* 8, 1-H), 4.99 (1 H, dd, *J* 9.5 and 8, 2-H), 5.08 (1 H, t, *J* 9.5, 4-H) and 5.19 (1 H, t, *J* 9.5, 3-H); δ_C(75 MHz; $CDCl_3$) 20.44, 20.54 and 20.59 (4 × CH_3CO), 21.91 and 22.00 (β- and γ-CH_2), 40.80 (α-CH), 61.43 (6-CH_2), 68.00, 71.02, 71.58 and 72.64 (2-, 3-, 4- and 5-CH), 68.84 and 70.01 (α-CH_2O and δ-CH_2), 101.3 (1-CH), 169.3, 170.0 and 170.5 (4 × CH_3CO) and 171.9 (δ-lactone CO); *m*/*z* (FAB) 483 (MNa^+, 4%), 461 (MH^+, 15) and 331 ($C_{14}H_{19}O_9^+$, 100).

(*E*)-3-Methyl-4-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)but-3-en-2-one 43

(With L. Q. Kong.) A solution of the salt **44** (73 g, 0.598 mol) in water (240 cm^3) was added to a stirred solution of acetobromoglucose **21** (123 g, 0.299 mol) in acetone (450 cm^3). When compound **21** could be no longer detected (TLC monitoring; *ca.* 24 h), the mixture was partially concentrated (to remove Me_2CO), and partitioned between dichloromethane and water. Evaporation of the dried ($MgSO_4$) organic phase and addition of diethyl ether (250 cm^3) to the residue induced the crystallisation of the title compound **43** (60.9 g, 47%); mp 138–140 °C (lit.,[5] 142–144 °C); $[\alpha]_D$ −23 (*c* 1.2, CH_2Cl_2) [lit.,[5] −19 (*c* 0.7, $CHCl_3$)]. The 300 MHz ^{1}H NMR spectrum of the sample matched that previously reported.[5]

Hydrogenation of the butenone 43

(a) A solution of the butenone **43** (2.16 g, 5.02 mmol) in ethyl acetate (100 cm^3) was stirred under hydrogen in the presence of 10% palladium–carbon (0.588 g, 0.27 mass equiv.) for 1 h. The mixture was then filtered through a pad of Celite and the filtrate was concentrated to give a residue which comprised mainly a 3:1:1 mixture of compounds **16**, **19** and **45** by ^{1}H NMR spectroscopy [the proportions were estimated from the integrals of the ds (*J* 7) at δ 1.03 (attributed to the 3-Me group of **16**), 1.12 (attributed to the 3-Me group of **19**), and 0.87/0.88 (attributed to the 3-Me groups of the two diastereomers of **45**)]. Subjection of the product to column chromatography (light petroleum–Et_2O; gradient elution) led to the isolation of seven fractions.

The first fraction (0.029 g, 1%), isolated as a solid, was identified as a 4:1 mixture of compounds **46** and **47** by ^{1}H NMR spectroscopy [the ratio was estimated from the integrals of the dds (*J* 9.5 and 6.5) at δ 3.29 and 3.21 (attributed to a 1-H atom of products **46** and **47**)] (see later for the full ^{1}H NMR spectral properties of compound **47**).

The second fraction (0.094 g, 5%), isolated as a solid, was recrystallised from methanol and identified as 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose **48** by its ^{1}H NMR spectrum {δ(300 MHz; $CDCl_3$) 2.01, 2.03, 2.09 and 2.11 (3, 6, 3 and 3 H, each s, 5 × $MeCO_2$), 3.84 (1 H, ddd, *J* 10, 4.5 and 2, 5-H), 4.11 and 4.29 [each 1 H, dd (*J* 12.5 and 2) and dd (*J* 12.5 and 4.5), 6-H_2], 5.13 (1 H, t, *J* 9.5, 4-H), 5.14 (1 H, dd, *J* 9.5 and 8, 2-H), 5.25 (1 H, t, *J* 9.5, 3-H) and 5.71 (1 H, d, *J* 8, 1-H)} which matched that of an authentic sample.

The third fraction (0.189 g, 9%), isolated as prisms after crystallisation from diethyl ether–light petroleum, was (3S)-3-*methyl*-4-(2′,3′,4′,6′-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)*butan*-2-*one* **16**; mp 100–101 °C; $[\alpha]_D$ −18 (*c* 0.6, CH_2Cl_2) (Found: C, 52.7; H, 6.8. $C_{19}H_{28}O_{11}$ requires C, 52.8; H, 6.55%); λ_{max}(EtOH)/nm 208 (ε 210) and 279 (35); ν_{max}(KBr)/cm^{-1} 1760, 1750 and 1730 (ester C=O), and 1715 (ketone C=O); δ_H(300 MHz; $CDCl_3$) 1.03 (3 H, d, *J* 7, 3-Me), 1.99, 2.017, 2.022 and 2.09 (each 3 H, s, 4 × $MeCO_2$), 2.15 (3 H, s, 1-H_3), 2.82–2.96 (1 H, m, 3-H), 3.63 and 3.87 [each 1 H, t (*J* 9) and dd (*J* 9 and 4.5), 4-H_2], 3.68 (1 H, ddd, *J* 10, 4.5 and 2.5, 5′-H), 4.13 and 4.26 [each 1 H, dd (*J* 12.5 and 2.5) and dd (*J* 12.5 and 4.5), 6′-H_2], 4.45 (1 H, d, *J* 8, 1′-H), 4.94 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.06 (1 H, t, *J* 9.5, 4′-H) and 5.18 (1 H, t, *J* 9.5, 3′-H); δ_C(75 MHz; $CDCl_3$) 12.90 (3-CH_3), 20.39, 20.42 and 20.56 (4 × CH_3CO), 29.69 (1-CH_3), 46.05 (3-CH), 61.66 (6′-CH_2), 68.17, 70.84, 71.60 and 72.41 (2′-, 3′-, 4′- and 5′-CH), 71.82 (4-CH_2), 101.0 (1′-CH), 169.2, 170.0 and 170.5 (4 × CH_3CO) and 210.6 (2-CO); *m*/*z* (FAB) 433 (MH^+, 3%), 331 ($C_{14}H_{19}O_9^+$, 100) and 169 (90).

The fourth (0.515 g, 24%), fifth (0.514 g, 24%) and sixth fractions (0.127 g, 6%), isolated as solids, were identified as 6:1, 2:1 and 1:1 mixtures of the dihydro derivatives **16** and **19** by ^{1}H NMR spectroscopy.

The seventh fraction (0.426 g, 20%), was crystallised from chloroform–diethyl ether–light petroleum to give mainly a 2:1 mixture of the diastereomers of 3-*methyl*-4-(2′,3′,4′,6′-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)*butan*-2-*ol* **45**; mp 69–71 °C; $[\alpha]_D$ −18 (*c* 0.37, CH_2Cl_2) (Found: C, 52.6; H, 7.2. $C_{19}H_{30}O_{11}$ requires C, 52.55; H, 6.95%); λ_{max}(EtOH)/nm 207 (ε 220); ν_{max}(KBr)/cm^{-1} 3560 (OH) and 1755br (ester C=O); δ_H(300 MHz; $CDCl_3$) 0.87 and 0.88 (1 and 2 H, each d, *J* 7, 3-Me), 1.14 and 1.16 (1 and 2 H, each d, *J* 6, 1-H_3), 1.67–1.77 and 1.78–1.90 (0.67 and 0.33 H, each m, 3-H), 2.00, 2.02, 2.05, 2.06 and 2.09 (3, 3, 2, 1 and 3 H, each s, 4 × $MeCO_2$), 2.3 (0.67 H, br s, OH), 3.46, 3.92 and 4.01 [1, 0.33 and 0.67 H, dd (*J* 9.5 and 6), dd (*J* 9.5 and 5) and dd (*J* 9.5 and 4.5), 4-H_2], 3.64–3.73 and ~3.85–3.95 (1.33 and 0.67 H, each m, 2- and 5′-H), 4.11–4.31 (2 H, m, 6′-H_2), 4.48 and 4.50 (0.33 and 0.67 H, each d, *J* 8, 1′-H), 4.96–5.03 (1 H, m, 2′-H), 5.077 and 5.083 (0.67 and 0.33 H, each t, *J* 9.5, 4′-H) and 5.21 and 5.22 (0.67 and 0.33 H, each t, *J* 9.5, 3′-H) (addition of D_2O caused the signal at δ 2.3 to disappear); *m*/*z* (FAB) 435 (MH^+, 3%), 331 ($C_{14}H_{19}O_9^+$, 20), 169 (100) and 109 (55).

(b) A solution of the butenone **43** (2.58 g, 6.0 mmol) in propan-2-ol (120 cm^3) was stirred under hydrogen in the presence of 3% palladium–carbon (0.72 g, 0.28 mass equiv.) for 2.5 h. The mixture was then filtered through a pad of Celite and the filtrate was concentrated to leave a residue which comprised mainly an 83:17 mixture of the dihydro derivatives **16** and **19** by ^{1}H NMR spectroscopy. Crystallisation of the material from diethyl ether–light petroleum gave a product (1.94 g, 75%) containing a similar ratio of the dihydro derivatives. A portion (1.60 g) of this mixture was fractionated by HPLC [hexanes–EtOAc (3:2) as eluent] to afford two fractions.

The first fraction was crystallised from diethyl ether–light petroleum to give the (3*S*)-dihydro derivative **16** (0.832 g, 52%), identified by its 300 MHz ^{1}H NMR spectrum.

The second fraction was resubjected to HPLC fractionation and the product was crystallised from diethyl ether–light petroleum to give (3R)-3-*methyl*-4-(2′,3′,4′,6′-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)*butan*-2-*one* **19** (0.176 g, 11%); mp 95–96 °C; $[\alpha]_D$ −21 (*c* 0.1, CH_2Cl_2) (Found: C, 53.1; H, 6.6. $C_{19}H_{28}O_{11}$ requires C, 52.8; H, 6.55%); λ_{max}(EtOH)/nm 214 (ε 110) and 280 (20); ν_{max}(KBr)/cm^{-1} 1755 (ester C=O) and 1710 (ketone C=O); δ_H(300 MHz; $CDCl_3$) 1.12 (3 H, d, *J* 6.5, 3-Me), 2.00, 2.02, 2.04 and 2.09 (each 3 H, s, 4 × $MeCO_2$), 2.16 (3 H, s, 1-H_3), 2.79 (1 H, br sextet, separation 6.5, 3-H), 3.53 and 4.04 (each 1 H, dd, *J* 10 and 6.5, 4-H_2), 3.67 (1 H, ddd, *J* 10, 4.5 and 2.5, 5′-H), 4.12 and 4.26 [each 1 H, dd (*J* 12.5 and 2.5) and dd (*J* 12.5 and 4.5), 6′-H_2], 4.49 (1 H, d, *J* 8, 1′-H), 4.98 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.07 (1 H, t, *J* 9.5, 4′-H) and 5.19 (1 H, t, *J* 9.5, 3′-H); *m*/*z* (FAB) 433 (MH^+, 4%) and 331 ($C_{14}H_{19}O_9^+$, 100) and 169 (75).

Reaction of the butanone 19 with ethane-1,2-dithiol

Titanium(IV) chloride (0.040 cm^3, 0.36 mmol) was added to a

stirred, ice-cooled solution of the butanone **19** (0.164 g, 0.38 mmol) and ethane-1,2-dithiol (0.040 cm^3, 0.48 mmol) in dry dichloromethane (5 cm^3). After 2 h, saturated aq. ammonium chloride was added to the mixture, which was extracted (3 ×) with dichloromethane. Evaporation of the dried ($MgSO_4$) organic extracts left an oil, which was purified by column chromatography (CH_2Cl_2–EtOAc; gradient elution). The product was then subjected to preparative HPLC [hexanes–EtOAc (3:2) as eluent] to give two fractions.

The first fraction (0.043 g, 22%), isolated as an oil, was identified as (3R)-3-*methyl*-4-(2′,3′,4′,6′-*tetra*-O-*acetyl*-α-D-*glucopyranosyloxy*)*butan*-2-*one ethylene dithioketal* **51**; $[\alpha]_D$ −9 (*c* 0.27, CH_2Cl_2) (Found: C, 49.7; H, 6.5; S, 12.6. $C_{21}H_{32}O_{10}S_2$ requires C, 49.6; H, 6.35; S, 12.6%); λ_{max}(EtOH)/nm 206 (ε 2800); ν_{max}(film)/cm^{-1} 1750br (ester C=O); δ_H(300 MHz; $CDCl_3$) 1.22 (3 H, d, *J* 6.5, 3-Me), 1.75 (3 H, s, 1-H_3), 2.01, 2.04, 2.07 and 2.10 (each 3 H, s, 4 × $MeCO_2$), 2.23–2.29 (1 H, m, 3-H), 3.22–3.36 (4 H, m, SCH_2CH_2S), 3.65 and 3.72 [each 1 H, dd (*J* 9.5 and 8) and dd (*J* 9.5 and 4), 4-H_2], 4.02 (1 H, ddd, *J* 10.5, 5 and 2.5, 5′-H), 4.12 and 4.25 [each 1 H, dd (*J* 12.5 and 2.5) and dd (*J* 12.5 and 5), 6′-H_2], 4.87 (1 H, dd, *J* 10 and 3.5, 2′-H), 5.05 (1 H, t, *J* 10, 4′-H), 5.06 (1 H, d, *J* 3.5, 1′-H) and 5.47 (1 H, t, *J* 10, 3′-H); *m*/*z* (FAB) 509 (MH^+, 10%), 508 (M^+, 6), 331 ($C_{14}H_{19}O_9^+$, 40) and 137 (100).

The second fraction (0.064 g, 33%), isolated as an oil which solidified on storage, was identified as (3R)-3-*methyl*-4-(2′,3′,4′,6′-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)*butan*-2-*one ethylene dithioketal* **49**; $[\alpha]_D$ +72 (*c* 0.37, CH_2Cl_2) (Found: C, 49.3; H, 6.6; S, 12.6%); λ_{max}(EtOH)/nm 203 (ε 3000) and 234 (410); ν_{max}(KBr)/cm^{-1} 1755 (ester C=O); δ_H(300 MHz; $CDCl_3$) 1.15 (3 H, d, *J* 6.5, 3-Me), 1.71 (3 H, s, 1-H_3), 2.00, 2.02, 2.04 and 2.09 (each 3 H, s, 4 × $MeCO_2$), 2.20–2.28 (1 H, m, 3-H), 3.19–3.37 (4 H, m, SCH_2CH_2S), 3.37 (1 H, t, *J* 9, 4-H), 3.69 (1 H, ddd, *J* 10, 5 and 2.5, 5′-H), 4.13 (1 H, dd, *J* 12.5 and 2.5, 6′-H), 4.23–4.32 (2 H, m, 4- and 6′-H), 4.49 (1 H, d, *J* 8, 1′-H), 5.01 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.09 (1 H, t, *J* 9.5, 4′-H) and 5.20 (1 H, t, *J* 9.5, 3′-H); *m*/*z* (FAB) 509 (MH^+, 8%), 508 (M^+, 7), 331 ($C_{14}H_{19}O_9^+$, 35) and 119 (100).

(2*S*)-2-Methyl-1-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)butane 47

(a) A solution of the dithioketal **49** (0.044 g, 0.086 mmol) in ethanol (5 cm^3) was stirred with a slurry of Raney nickel (~10 mass equiv.) in ethanol under hydrogen for 2 days. The mixture was filtered through a pad of Celite and the filtrate was concentrated to leave the title compound **47** (0.028 g, 77%) as an oil which solidifed on storage; $[\alpha]_D$ −14 (*c* 0.39, CH_2Cl_2); λ_{max}(EtOH)/nm no significant absorption; ν_{max}(KBr)/cm^{-1} 1760 and 1745 (ester C=O); δ_H(300 MHz; $CDCl_3$) 0.87 (3 H, t, *J* 7.5, 4-H_3), 0.88 (3 H, d, *J* 6.5, 2-Me), 1.06–1.20 and 1.29–1.44 (each 1 H, m, 3-H_2), 1.52–1.74 (1 H, m, 2-H), 2.01, 2.02, 2.03 and 2.09 (each 3 H, s, 4 × $MeCO_2$), 3.20 and 3.79 [each 1 H, dd (*J* 9.5 and 7) and dd (*J* 9.5 and 5.5), 1-H_2], 3.68 (1 H, ddd, *J* 10, 4.5 and 2.5, 5′-H), 4.13 and 4.27 [each 1 H, dd (*J* 12.5 and 2.5) and dd (*J* 12.5 and 4.5), 6′-H_2], 4.47 (1 H, d, *J* 8, 1′-H), 5.00 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.09 (1 H, t, *J* 9.5, 4′-H) and 5.21 (1 H, t, *J* 9.5, 3′-H); *m*/*z* (FAB) 551 (MCs^+, 15), 441 (MNa^+, 13), 331 ($C_{14}H_{19}O_9^+$, 100) and 169 (80).

(b) A mixture of acetobromoglucose **21** (0.411 g, 1.0 mmol), (*S*)-2-methylbutan-1-ol **50** (1.0 cm^3, 9.2 mmol) and silver(I) carbonate (0.414 g, 1.5 mmol) was stirred together for 15 h. The mixture was then diluted with dichloromethane and filtered through a pad of Celite. Evaporation of the filtrate left a residue, which was crystallised from diethyl ether–light petroleum to give the *title compound* **47** (0.210 g, 50%) [the 300 MHz ^1H NMR spectrum of the material matched that of the product obtained in **(a)**]; mp 93–95 °C; $[\alpha]_D$ −10.5 (*c* 0.44, CH_2Cl_2) (Found: C, 54.2; H, 7.5. $C_{19}H_{30}O_{10}$ requires C, 54.55; H, 7.25%).

(*E*)-2-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glucopyranosyloxymethylene)cyclopentanone 24

A mixture of ethyl formate (50.0 cm^3, 0.619 mol) and cyclopentanone (53.0 cm^3, 0.599 mol) was added slowly to an ice-cooled, stirred slurry of sodium methoxide [prepared by addition of Na (11.5 g, 0.50 mol) in small pieces to dry MeOH (200 cm^3) followed, after the reaction was complete, by evaporation, addition of dry PhMe to the residue and re-evaporation] in dry diethyl ether (300 cm^3). After the addition was complete, the mixture was allowed to warm to room temperature and was stirred for 15 h. The mixture was then filtered and the residue was washed well with diethyl ether to give a solid (50.3 g) which comprised mainly a 4:1 mixture of the salt **29** and sodium formate; δ_H(300 MHz; D_2O) (for **29**) 1.74 (2 H, apparent quintet, separation 7.5, 4-H_2), 2.21 and 2.36 [each 2 H, t (*J* 8) and t (*J* 7.5), 3- and 5-H_2], 4.80 (HOD) and 8.68 (1 H, s, C=CH).

A solution of the impure salt **29** (13.5 g) in water (100 cm^3) was added to a stirred solution of acetobromoglucose **21** (33.2 g, 0.081 mol) in acetone (200 cm^3). When the reaction was complete (TLC monitoring; *ca.* 24 h), the mixture was partially concentrated (to remove Me_2CO) and extracted (3 ×) with dichloromethane. Evaporation of the dried ($MgSO_4$) extracts and crystallisation of the residue from diethyl ether gave the *title compound* **24** (10.5 g, 30%); mp 139–140 °C; $[\alpha]_D$ −12 (*c* 1.0, CH_2Cl_2) (Found: C, 54.1; H, 6.0. $C_{20}H_{26}O_{11}$ requires C, 54.3; H, 5.9%); λ_{max}(EtOH)/nm 259 (ε 15 700); ν_{max}(KBr)/cm^{-1} 1760, 1740 and 1735 (ester C=O), 1715 (vinylogous ester C=O) and 1640 (C=C); δ_H(300 MHz; $CDCl_3$) 1.86–1.97 (2 H, m, 4-H_2), 2.02, 2.04, 2.05 and 2.09 (each 3 H, s, 4 × $MeCO_2$), 2.31 (2 H, t, *J* 8, 5-H_2), 2.48–2.70 (2 H, m, 3-H_2), 3.80 (1 H, ddd, *J* 9.5, 5 and 2, 5′-H), 4.12 and 4.28 [each 1 H, dd (*J* 12.5 and 2) and dd (*J* 12.5 and 5), 6′-H_2], 4.87 (1 H, d, *J* 7.5, 1′-H), 5.09–5.19 (2 H, m, 2′-and 4′-H), 5.25 (1 H, t, *J* 9, 3′-H) and 7.29 (1 H, t, *J* 2.5, C=CH) (in an NOED spectroscopic experiment, irradiation at δ 7.29 enhanced the d at δ 4.87 by 12%); *m*/*z* (FAB) 884 (M_2^+, 2%), 773 [$M(C_{14}H_{19}O_9)^+$, 2], 443 (MH^+, 2), 331 ($C_{14}H_{19}O_9^+$, 75) and 169 (100).

Hydrogenation of the methylenecyclopentanone 24

A solution of compound **24** (3.65 g, 8.25 mmol) in ethyl acetate (150 cm^3) was stirred under hydrogen in the presence of 3% palladium–carbon (1.12 g, 0.31 mass equiv.) for 2 h. The mixture was then filtered through a pad of Celite and the filtrate was concentrated to leave an 80:20 mixture of the dihydro derivatives **33** and **37** by NMR spectroscopy [the ratio was estimated from the integrals of the ds (*J* 8) at δ 4.48 and 4.45, attributed to the 1′-H atoms of products **33** and **37**]. Crystallisation of the material from ethyl acetate–light petroleum gave (2S)-2-(2′,3′,4′,6′-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxymethyl*)*cyclopentanone* **33** (1.84 g, 50%); mp 98–100 °C; $[\alpha]_D$ −49 (*c* 0.5, CH_2Cl_2) (Found: C, 54.1; H, 6.1. $C_{20}H_{28}O_{11}$ requires C, 54.05; H, 6.35%); λ_{max}(EtOH)/nm 206 (ε 210); ν_{max}(KBr)/cm^{-1} 1760 and 1740 (ester and cyclopentanone C=O); δ_H(300 MHz; $CDCl_3$) 1.71–1.87 (2 H, m, 3-H_2), 2.00, 2.02, 2.05 and 2.09 (each 3 H, s, 4 × $MeCO_2$), ~2.07–2.37 (5 H, m, 2-H and 4- and 5-H_2), 3.66 (1 H, ddd, *J* 10, 4.5 and 2.5, 5′-H), 3.73 and 3.97 [each 1 H, dd (*J* 10 and 4) and dd (*J* 10 and 6), 2-CH_2O], 4.12 and 4.24 [each 1 H, dd (*J* 12.5 and 2.5) and dd (*J* 12.5 and 4.5), 6′-H_2], 4.48 (1 H, d, *J* 8, 1′-H), 4.97 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.06 (1 H, t, *J* 9.5, 4′-H) and 5.18 (1 H, t, *J* 9.5, 3′-H); δ_C(75 MHz; $CDCl_3$) 20.62, 20.67 and 20.77 (4 × CH_3CO), 20.84 and 26.89 (3- and 4-CH_2), 38.42 (5-CH_2), 49.15 (2-CH), 61.87 (6′-CH_2), 68.37, 71.21, 71.81 and 72.80 (2′-, 3′-, 4′- and 5′-CH), 69.03 (2-CH_2O), 101.0 (1′-CH), 169.3, 169.4, 170.2 and 170.7 (4 × CH_3CO), and 218.5 (1-CO); *m*/*z* (FAB) 467 (MNa^+, 2%), 462 (4), 445 (MH^+, 3), 331 ($C_{14}H_{19}O_9^+$, 100) and 169 (95).

(*E*)-2-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glucopyranosyloxymethylene)cyclohexanone 25

(With L. Q. Kong.) A mixture of ethyl formate (10.0 cm^3, 0.124

mol) and cyclohexanone (11.5 cm^3, 0.111 mol) was added slowly to an ice-cooled, stirred slurry of sodium methoxide [prepared by addition of Na (2.3 g, 0.10 mol) in small pieces to dry MeOH (20 cm^3) followed (after the reaction was complete) by evaporation, addition of dry PhMe and re-evaporation] in dry diethyl ether (80 cm^3). When the addition was complete, the mixture was allowed to warm to room temperature and stirred for 15 h. Filtration of the mixture gave a solid, which was washed well with diethyl ether and dried to give mainly a 3:1 mixture of the salt **30** and sodium formate (16.6 g); δ_H(300 MHz; D_2O) (for **30**) 1.47–1.66 (4 H, m, 4- and 5-H_2), 2.10–2.16 (2 H, m, 3- and 6-H_2), 4.80 (HOD) and 9.00 (1 H, s, C=CH).

The impure salt **30** (7.40 g) followed by water (25 cm^3) were added to a stirred solution of acetobromoglucose **21** (10.3 g, 25 mmol) in acetone (50 cm^3). When the reaction was complete (TLC monitoring; *ca.* 24 h), the mixture was partially concentrated (to remove Me_2CO) and extracted (2×) with dichloromethane. Evaporation of the dried ($MgSO_4$) extracts left a dark oil, which was dissolved in dichloromethane (50 cm^3); the solution was treated with a 1:1 mixture of diethyl ether and light petroleum (100 cm^3) and allowed to crystallise. Filtration gave the *title compound* **25** (3.05 g, 27%); mp 146–148 °C; $[\alpha]_D$ −19 (*c* 0.26, CH_2Cl_2) (Found: C, 55.0; H, 6.2. $C_{21}H_{28}O_{11}$ requires C, 55.25; H, 6.2%); λ_{max}(EtOH)/nm 262 (ε 11 500); ν_{max}(KBr)/cm^{-1} 1760 and 1740 (ester C=O), 1680 (vinylogous carbonate C=O) and 1600 (C=C); δ_H(300 MHz; $CDCl_3$) 1.63–1.72 and 1.75–1.84 (each 2 H, m, 4- and 5-H_2), 2.02, 2.03, 2.05 and 2.09 (each 3 H, s, 4 × $MeCO_2$), 2.30–2.40 and 2.45–2.57 (3 and 1 H, each m, 3- and 6-H_2), 3.79 (1 H, ddd, *J* 10, 5 and 2.5, 5′-H), 4.12 and 4.29 [each 1 H, dd (*J* 12.5 and 2.5) and dd (*J* 12.5 and 5), 6′-H_2], 4.87 (1 H, d, *J* 7.5, 1′-H), 5.12 (1 H, t, *J* 9.5, 4′-H), 5.16 (1 H, dd, *J* 9.5 and 7.5, 2′-H), 5.25 (1 H, t, *J* 9.5, 3′-H) and 7.34 (1 H, t, *J* 2, C=CH) (in an NOED spectroscopic experiment, irradiation at δ 7.34 enhanced the d at δ 4.87 by 15%); *m/z* (FAB) 913 (M_2H^+, 0.5%), 787 [$M(C_{14}H_{19}O_9)^+$, 0.5], 479 (MNa^+, 0.5), 455 ($M^+ - H$, 0.5), 331 ($C_{14}H_{19}O_9^+$, 55) and 169 (100).

Hydrogenation of the methylenecyclohexanone 25

A solution of compound **25** (0.439 g, 0.962 mmol) in ethyl acetate (25 cm^3) was stirred under hydrogen in the presence of 5% palladium–carbon (0.150 g, 0.34 mass equiv.) for 1.5 h. The mixture was then filtered through a pad of Celite and the filtrate was concentrated to leave mainly a 67:33 mixture of the dihydro derivatives **34** and **38** by ^1H NMR spectroscopy {the ratio was estimated from the heights of the signals at δ 4.56 and 4.51 [the outer lines of two ds (*J* 8) centred at δ 4.55 and 4.52 and attributed to the 1′-H atoms of products **34** and **38**]}. After chromatographic purification (light petroleum–Et_2O; gradient elution) and crystallisation from diethyl ether–light petroleum, the sample (0.190 g, 43%) was a 67:33 mixture of (2S)- and (2R)-2-(2′,3′,4′,6′-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxymethyl*)-*cyclohexanone* **34** and **38**; mp 74–76 °C; $[\alpha]_D$ −15 (*c* 0.15, CH_2Cl_2) (Found: C, 55.3; H, 6.6. $C_{21}H_{30}O_{11}$ requires C, 55.0; H, 6.6%); ν_{max}(KBr)/cm^{-1} 1760 and 1730 (ester C=O), and 1705 (cyclohexanone C=O); δ_H(300 MHz; $CDCl_3$) 1.28–1.46, 1.58–1.70, 1.83–1.97, 2.12–2.44 and 2.53–2.67 (~1, 2, 1, 4 and 1 H, each m, 2-H and 3-, 4-, 5- and 6-H_2), 2.01, 2.02, 2.03, 2.04 and 2.09 (3, 3, 1, 2 and 3 H, each s, 4 × $MeCO_2$), 3.56, 3.74, 3.86 and 4.16 [0.33, 0.67, 0.67 and 0.33 H, dd (*J* 9.5 and 7), dd (*J* 9.5 and 6), dd (*J* 9.5 and 6) and dd (*J* 9.5 and 4), 2-CH_2O], 3.68 (1 H, ddd, *J* 10, 4.5 and 2.5, 5′-H), 4.12 and 4.26 [each 1 H, dd (*J* 12.5 and 2.5) and dd (*J* 12.5 and 4.5), 6′-H_2], 4.52 and 4.55 (0.33 and 0.67 H, each d, *J* 8, 1′-H), 4.95 and 4.97 (0.67 and 0.33 H, each dd, *J* 9.5 and 8, 2′-H), 5.07 (1 H, t, *J* 9.5, 4′-H) and 5.21 (1 H, t, *J* 9.5, 3′-H); *m/z* (FAB) 789 [$M(C_{14}H_{19}O_9)^+$, 2%], 481 (MNa^+, 2), 476 (2), 459 (MH^+, 2), 331 ($C_{14}H_{19}O_9^+$, 100) and 169 (90).

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