Towards complete stereochemical control: complementary methods for the synthesis of six diastereoisomeric monosaccharide mimetics

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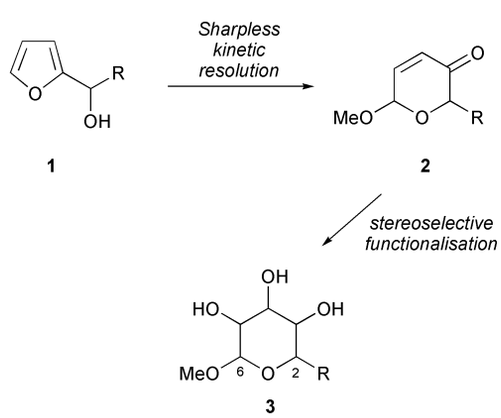
Complementary methods for the synthesis of diastereomeric monosaccharide mimetics are described which rely on the functionalisation of derivatives of 2-butyl-6-methoxy-2,6-dihydropyran-3-one. The stereochemical outcome of dihydroxylation of these derivatives under Upjohn's and Donohoe's (directed) reaction conditions are described. The hydrolyses of diastereomeric 2-butyl-4,5-epoxy-3-hydroxy-6-methoxytetrahydropyrans, generated either by epoxidation with perbenzimidic acid or by cyclisation of the corresponding hydroxy iodides, are described in detail. These methods have enabled stereoselective syntheses of six of a possible eight (ignoring anomers) diastereoisomers of 3,4,5-triacetoxy-2-butyl-6-methoxytetrahydropyran. The power of the general approach lies in the ability to choose at a late stage in the synthesis which diastereoisomer is prepared.

Introduction

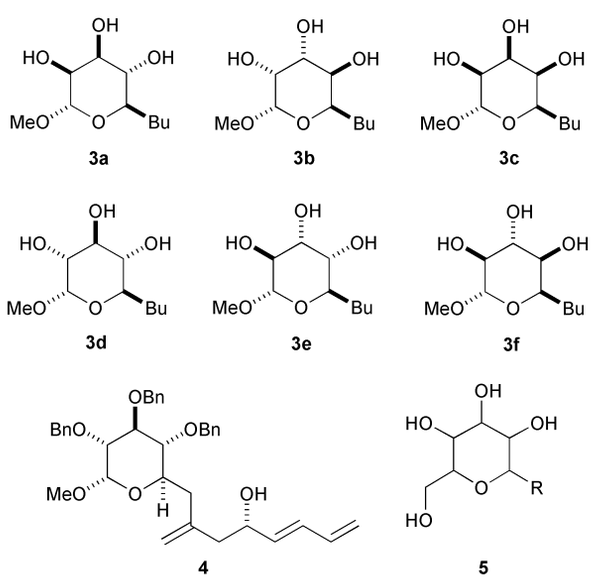
The complete control of stereochemistry, that is the ability to synthesise any stereoisomer at will, is a challenging goal for the synthetic chemist. Flexible methods for the synthesis of libraries of stereoisomeric aldoses[1] and polyketides[2] have been developed.[3] The stereochemical diversity of these libraries stems, in part, from the control of stereochemistry using complementary chiral reagents. In contrast, all six conduritol diastereoisomers have been prepared from common building blocks using only substrate-controlled diastereoselective reactions.[4] An alternative approach, which has been used to synthesise all 16 stereoisomers of a dipeptide mimetic,[5] involved coupling pairs of enantiomerically pure allylic alcohols using ring-closing metathesis reactions.[6] An appreciation of how the relative stereochemistry of substituents in stereotriads, -tetrads and -pentads, *etc.*, influences the conformation of molecules is an essential step towards an understanding of their biological activity.[7]

In this paper, we describe methods for the synthesis of protected versions of the trihydroxylated tetrahydropyrans (THPs) **3** (R = Bu) (Scheme 1).[8] The triols **3** are carbohydrate mimetics



Scheme 1

in which C-6 of a monosaccharide has been further substituted. This substitution pattern is found in the glucose derivative[9] **4** which is active against six human cancer cell lines. Alternatively,



the THPs **3** can be considered to be analogues of *C*-pyranosides **5** in which C-6 has been replaced by a methoxy group.

We envisaged that Sharpless kinetic resolution of the furyl alcohols **1**,[10] and protection, would give the optically active pyranones **2** (Scheme 1). The pyranones **2** are heavily functionalised and might be functionalised stereoselectively, for example by reduction and dihydroxylation, to give the triols **3**. The aim of the project was to develop methods which would be sufficiently flexible to allow the synthesis of any stereoisomer **3** by minor variation of a common reaction scheme.

Synthesis of the starting materials

Sharpless kinetic resolution of the furyl alcohol[10] **6**, followed by acetalisation, gave the pyranone (2*R*)-**7** as a 70 : 30 mixture of anomers with 93% enantiomeric excess (Scheme 2).[11] In one experiment, the diastereomeric pyranones **7** were separated to give *trans*-**7** and *cis*-**7** in 67% and 23% yield, respectively, from the intermediate hemiacetal. Luche reduction[12] ($NaBH_4$, $CeCl_3$) of the pyranone *trans*-**7** gave the alcohol *trans*-**8** as a single diastereoisomer, which was acylated to give the optically active *p*-methoxybenzoate **9**.

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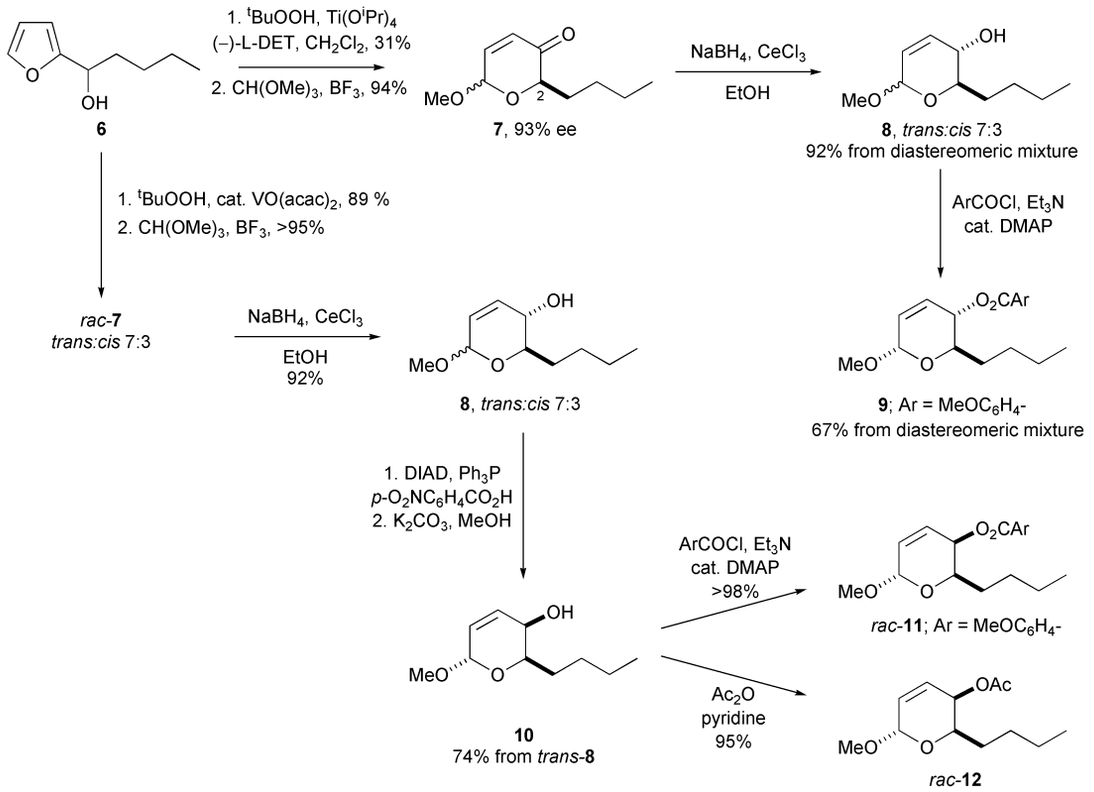


Scheme 2

A racemic sample of the pyranone **7** (7 : 3 mixture of anomers) was synthesised in 89% yield by oxidation of **6** with *tert*-butyl hydroperoxide, catalysed by $VO(acac)_2$,[13] and protection; Luche reduction of this diastereomeric mixture gave the separable alcohols **8**. Mitsunobu inversion of the alcohol *trans*-**8** to give the inverted *p*-nitrobenzoate, followed by hydrolysis, gave its diastereoisomer **10**. The alcohols **8** and **10** were converted into the racemic *p*-methoxybenzoate **11** and the racemic acetate **12**.

Control of relative stereochemistry by diastereoselective dihydroxylation

Dihydroxylation of the allylic *p*-methoxybenzoate **9** under Upjohn's reaction conditions[14] (cat. OsO_4, NMO) was highly diastereoselective, leading to the diol† **13a** in 82% yield (crude ratio of diastereoisomeric products >95 : 5) (Scheme 3). This observation concurs with earlier investigations[14] into the dihydroxylation of allylic alcohol derivatives: the osmylation reaction occurred *anti* to the pseudoequatorial *p*-methoxybenzoyloxy group (Fig. 1). It has previously been shown that

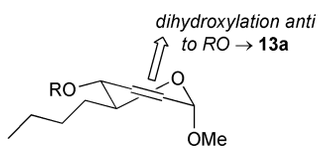


Fig. 1

it is not possible to direct[15] the dihydroxylation of related pseudoequatorial allylic alcohols using Donohoe's reaction conditions (TMEDA, OsO_4, CH_2Cl_2), a process which is probably prevented by the axial methoxy substituent.[16,17] ‡

† In this paper, protected versions of the triols **3** (such as **13a**) are labelled **a–h** according to their relative stereochemistry.

‡ Simple allylic alcohols in which the hydroxy group is conformationally locked in a pseudo-equatorial position are dihydroxylated under these reaction conditions with high *syn* stereoselectivity.[15]

Complementary reactions conditions were available, however, for the diastereoselective dihydroxylation of alkenes such as **10**, **11** and **12** in which the allylic oxygen substituent adopts a pseudo-axial orientation (see Fig. 2). Hence, the dihydroxyl-

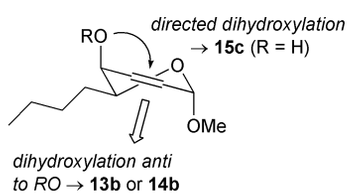
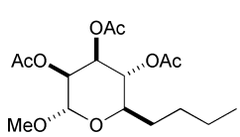


Fig. 2

ations of the allylic *p*-methoxybenzoate **11** and the allylic acetate **12** under Upjohn's reaction conditions were *anti* diastereoselective. The level of diastereoselectivity observed depended significantly on the size of the ester substituent. We[16] and others[17] have previously shown that dihydroxylations of related allylic alcohols under Upjohn's conditions also exhibit moderate levels of *anti* diastereoselectivity. In contrast, the dihydroxylation of the allylic alcohol **10** by OsO_4·TMEDA was directed efficiently by the pseudo-axial hydroxy group (*syn* : *anti* >95 : 5) to give, after acetylation, the all *cis* triacetate **15c** (Fig. 2). The ^1H NMR spectral data of the triacetates **15** are summarised in Table 1.§ The ability to alter the sense of the diastereoselectivity of a functionalisation reaction simply by changing the reagents used is a valuable feature of these dihydroxylation reactions.

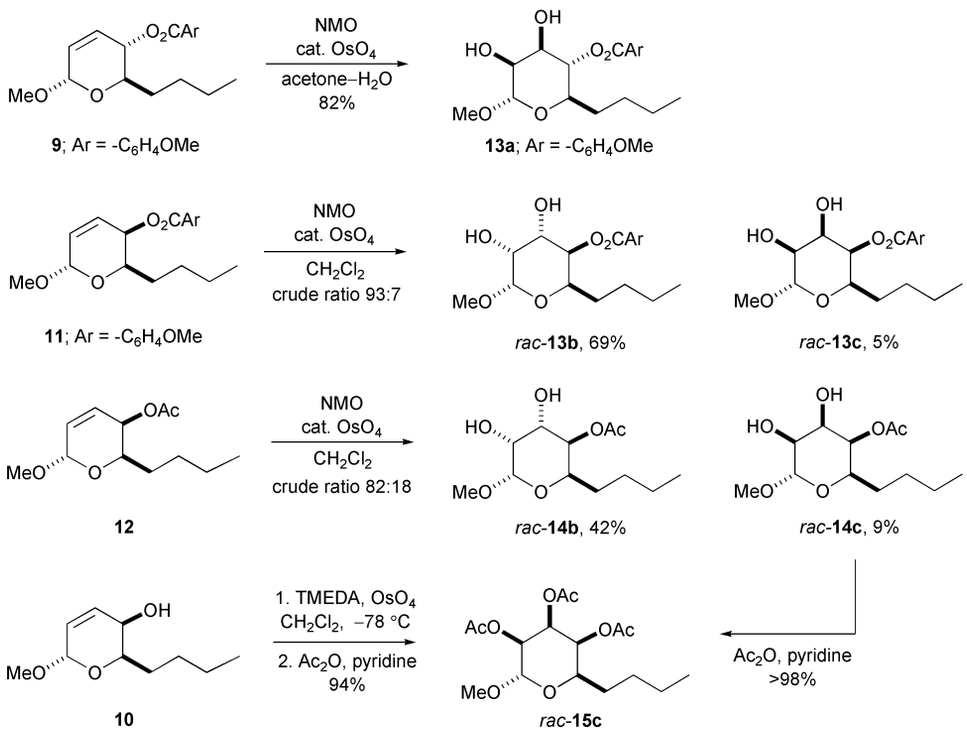


15a

§ The atoms in the triacetates **15** are labelled as tetrahydropyrans (*i.e. not* sugar numbering).

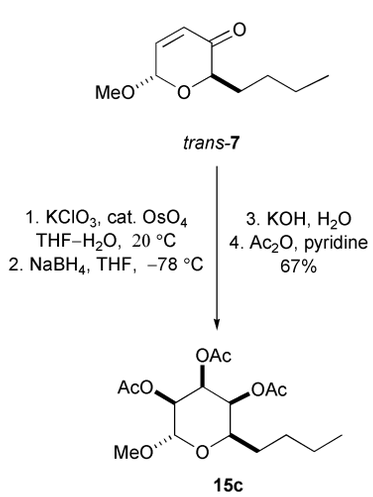
Table 1 Coupling constants and chemical shifts of the triacetates **15**

Compound	$J(H^2H^{1'})$/ Hz	$J(H^2H^3)$/ Hz	$J(H^3H^4)$/ Hz	$J(H^4H^5)$/ Hz	$J(H^5H^6)$/ Hz	^4J/Hz	δ (H^2) (ppm)	δ (H^3) (ppm)	δ (H^4) (ppm)	δ (H^5) (ppm)	δ (H^6) (ppm)
15a	1.9, 9.8	9.8	9.8	3.5	1.7	—	3.71	5.09	5.28	5.23	4.63
15b	4.1, 8.8	2.1	4.1	4.1	4.1	0.7 (H^4H^6)	4.11	4.92	5.20	5.16	4.81
15c	3.8, 9.3	0	3.8	3.8	1.2	1.2 (H^3H^5)	3.91	5.22	5.26	5.10	4.76
15d	2.2, 9.6	9.6	9.6	10.1	3.7	—	3.76	4.84	5.43	4.83	4.89
15e	3.2, 8.8	8.8	4.0	4.0	2.0	—	3.95	4.93	5.13	4.89	4.51
15f	3.6, 9.5	2.3	3.8	3.8	1.8	—	4.10	4.85	4.97	4.82	4.68



Scheme 3

An alternative approach to the triacetate **15c** involved reversing the order of the dihydroxylation and reduction steps. Hence, dihydroxylation of the enone *trans*-**7** was followed by reduction of the ketone with sodium borohydride and acetylation (Scheme 4); the triacetate **15c** was obtained in 67% yield

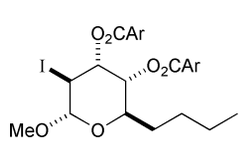


Scheme 4

from the enone *trans*-**7**. Dihydroxylations of compounds similar to the epimeric enone *cis*-**7** have been shown to proceed with complementary stereoselectivity, that is with dihydroxylation occurring *anti* to the C-2 side chain.[18]

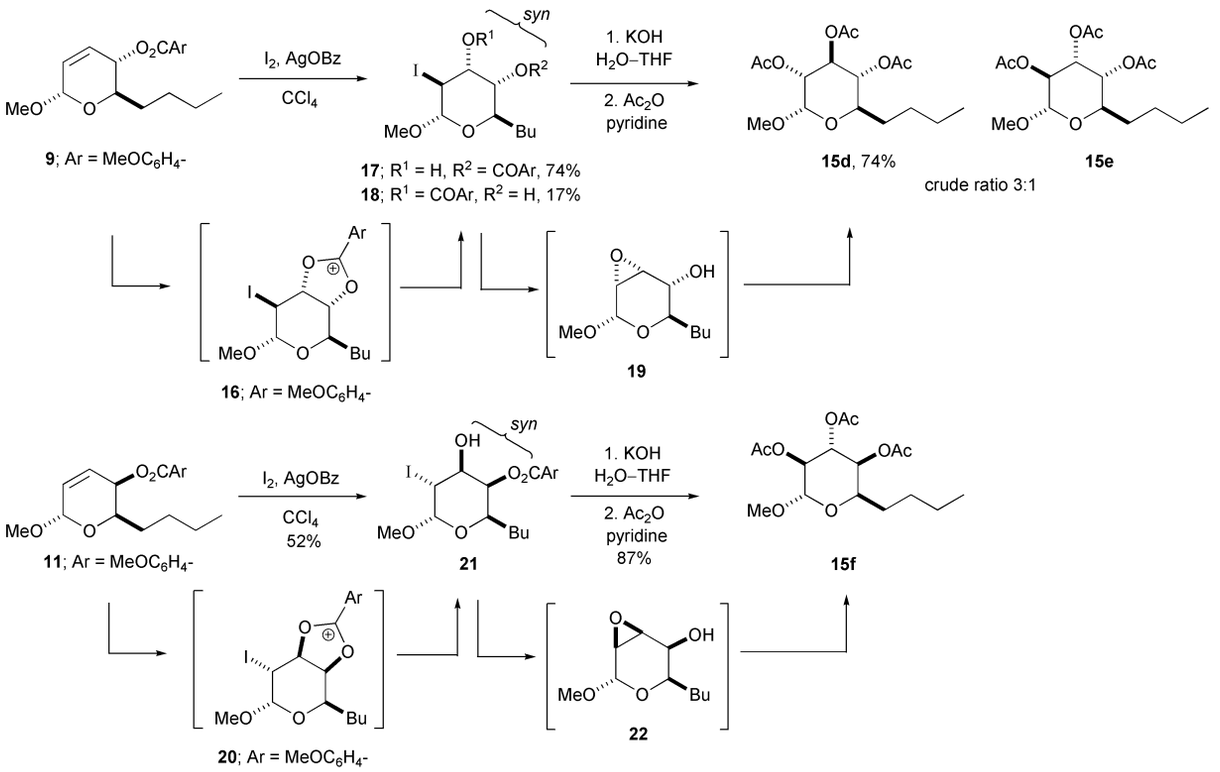
Control of relative stereochemistry under Prévost's reaction conditions

We have investigated the functionalisation of the diastereomeric allylic *p*-methoxybenzoates **9** and **11** using iodine and silver benzoate in carbon tetrachloride (Scheme 5).[19] In view of the rigorously dry reaction conditions of these reactions, the *syn* stereospecificity of this process (**9** ⟶ **17/18**; **11** ⟶ **21**) and the absence of benzoate from the products are remarkable.[20] Presumably, participation[21] of *p*-methoxybenzoyloxy group of **9** and **11** gave the dioxonium ions **16** and **20** which were stable to the reaction conditions;¶ subsequent hydrolysis of these intermediates, presumably on aqueous work-up, gave the observed *cis* hydroxy *p*-methoxybenzoates. The hydroxy esters **17** and **18** were shown to have the same relative stereochemistry by conversion into the same diester **23**.



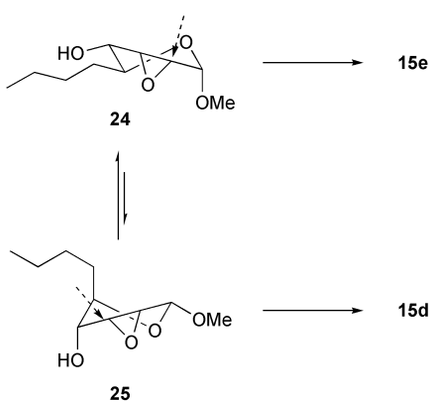
The iodides **17/18** (4 : 1 mixture of regioisomers) and **21** were treated with potassium hydroxide in water–THF, and the products of the reaction were converted into the corresponding peracetates. Hydrolysis of the *p*-methoxybenzoate ester is

¶ An alternative explanation is that benzoate traps the dioxonium ions **16** and **20** as the corresponding anomeric benzoates.



Scheme 5

believed to have been followed by epoxide formation (⟶ **19** or **22**) and hydrolysis to give the corresponding triols.[22] The regioselectivity of this ring-opening process deserves further comment. In the major conformer of **19** (conformer **24**, Scheme 6),

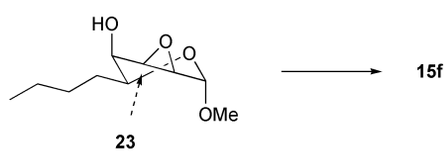


Scheme 6

the stereoelectronic preference[23] for *trans*-diaxial opening (⟶ **15e**) requires that **24** be opened at the site which is β to the two oxygens of the acetal; consequently, reaction *via* the conformer **25** (⟶ **15d**)—that is, away from the two β oxygens[24]—is competitive with, and in fact dominates over, this process. After peracetylation, a 3 : 1 mixture of the triacetates **15d** and **15e** was obtained. The diastereomeric epoxy alcohol **22** was, however, opened with much higher regioselectivity to give, after acetylation, the triacetate **15f** in 87% yield; in this case, the major conformer (**26**, Scheme 7) can be opened *trans*-diaxially at the carbon which is further from the anomeric centre (Scheme 7). The conversion of the epoxy ester **29** into the same triacetate **15f** (Scheme 8) reinforces the proposal that **22** is an intermediate in the reaction sequence **21** ⟶ **15f** (Scheme 5).

Control of relative stereochemistry by epoxidation and hydrolysis

An alternative approach for controlling the relative stereochemistry of the triacetates **15** would involve epoxidation of the



Scheme 7

allylic *p*-methoxybenzoates **9** and **11**, followed by hydrolysis and acetetylation. The epoxidations of **9** and **11** with perbenzimidic acid,[25] generated *in situ* from hydrogen peroxide and benzonitrile, were *anti* selective (Scheme 8). It is surprising that the epoxidation of **11** (*anti* : *syn* 70 : 30) was markedly less stereoselective than that of **9** (*anti* : *syn* >95 : 5) given that the *p*-methoxybenzoyloxy group of **11** can shield the *syn* face of the alkene more effectively. Perhaps, the *p*-methoxybenzoyloxy group can direct the epoxidation by perbenzimidic acid to some extent (Fig. 3).[26]

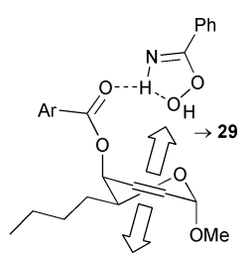
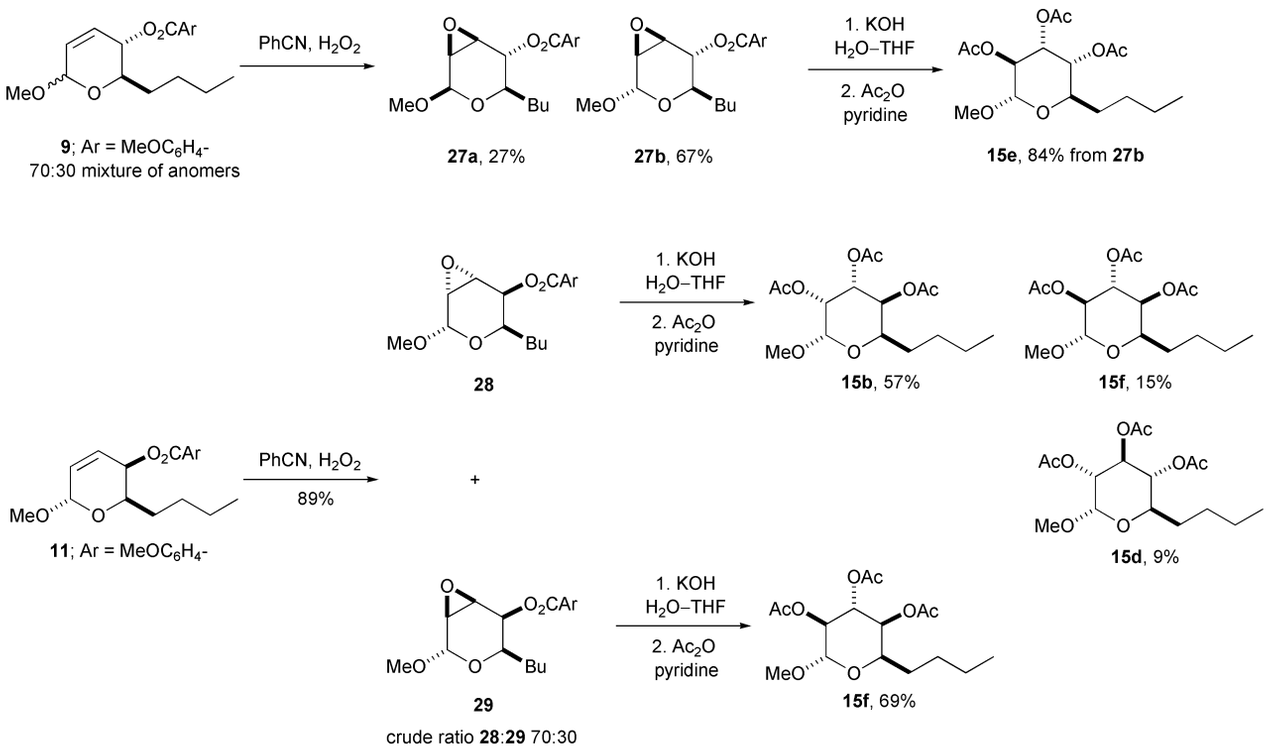
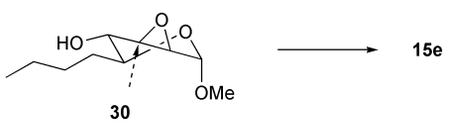


Fig. 3

The hydrolyses of the epoxy esters **27b** and **28** (Scheme 8) complement those of the epoxides **19** and **22** (Scheme 5). Hence, *trans*-diaxial opening of **27b**, that is away from the anomeric centre (conformer **30**, Scheme 9), followed by acetylation, gave the triacetate **15e**, the minor diastereoisomer obtained from the hydrolysis of **17**/**18**. The hydrolysis of **28** was, however, much more complicated since not only were the preferences for *trans*-diaxial opening and substitution away from the anomeric centre opposed, but the epoxy alcohol **34** was also



Scheme 8



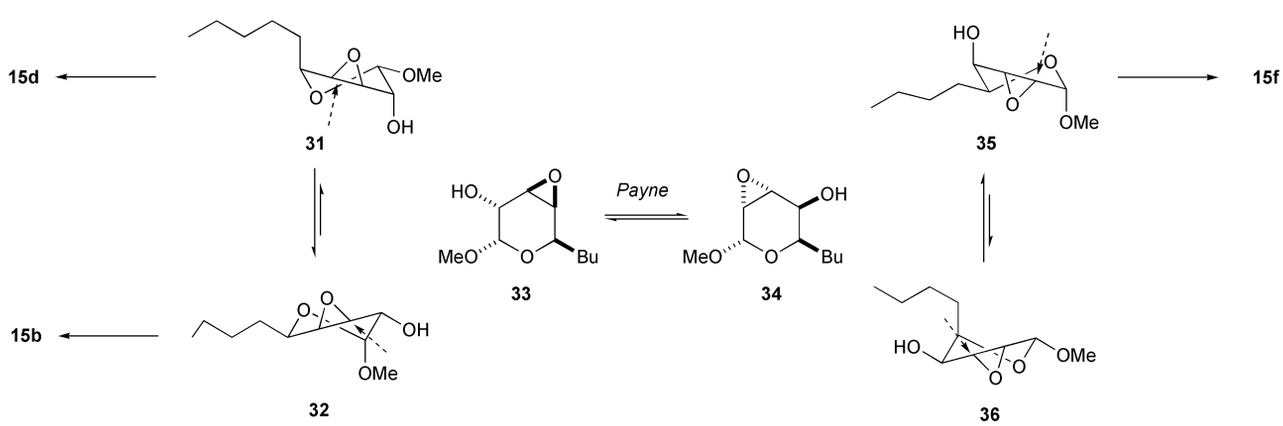
Scheme 9

prone to Payne rearrangement[27] (Scheme 10). In this case, after acetylation, the triacetates **15b**, **15f** and **15d** were obtained in 57%, 15% and 9% yield, respectively. Presumably, **15b** and **15d** were derived from hydrolysis of the Payne-rearranged epoxy alcohol **33**; **15f**, on the other hand, was obtained from *trans*-diaxial opening of conformer **35** of the epoxy alcohol **34** (Scheme 10). The relative stereochemistry of major product (**15b**) was determined by hydrolysis and peracetylation of the diol **13b** of known stereochemistry.

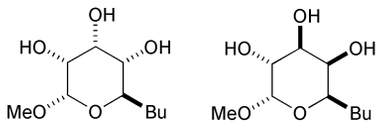
Conclusions

In this paper, we have described methods for the synthesis of six diastereoisomers (of a possible eight, ignoring anomers) of the protected monosaccharide mimetics **15**. The methods exploited involved diastereoselective functionalisation of dihydropyrans such as **9** and **11**, by dihydroxylation, Prévost reaction or epoxidation. We have shown that asymmetry may be introduced into the divergent reaction sequence: the common intermediate **7** was synthesised with 93% ee by kinetic resolution of the furyl alcohol **6**.

Complementary dihydroxylation reactions enabled the synthesis of protected versions of the mimetics **15a**–**c**: it was possible to direct the dihydroxylation of **10** using OsO_4–TMEDA as an alternative to the usual *anti* stereoselectivity for this process (see Figs. 1 and 2). We were, however, unable to direct the dihydroxylation of the pseudo-equatorial alcohol *trans*-**8**, which would have been required for the synthesis of the triol **3g**. Regioselective ring-openings of diastereomeric hydroxy epoxides enabled the synthesis of protected versions of the mimetics **15d**–**f**; unfortunately, the hydroxy epoxide **34** was susceptible to Payne rearrangement, preventing the synthesis of the triol **3h** using this methodology. On the whole, the synthetic methods developed were highly diastereoselective and complemented each other effectively. The divergent nature of the approach meant that the six diastereomeric mimetics could be made from a common intermediate by making minor variations at a relatively late stage in each synthesis.



Scheme 10



3g 3h

Experimental

All solvents were distilled before use. THF and Et_2O were freshly distilled from lithium aluminium hydride whilst CH_2Cl_2 and toluene were freshly distilled from calcium hydride. Benzophenone was used as indicator for THF. Ether refers to diethyl ether and petrol refers to petroleum spirit (bp 40–60 °C) unless otherwise stated. Solvents were removed under reduced pressure using a Büchi rotary evaporator and a Laboport diaphragm pump. *n*-Butyllithium was titrated against diphenylacetic acid before use. All non-aqueous reactions were carried out under argon using oven-dried glassware.

Flash column chromatography was carried out using silica (35–70 μm particles) according to the method of Still, Kahn and Mitra.[28] Thin layer chromatography was carried out on commercially available pre-coated plates (Merck silica Kieselgel $60F_{254}$). Preparative HPLC was conducted on a Gynkotek HPLC system with diode array detection using an Econosil column (silica particle size: 10 μm; 22 × 250 mm). Proton and carbon NMR spectra were recorded on a Bruker WM 250, DPX 300 or DRX 500 Fourier transform spectrometers using an internal deuterium lock. Chemical shifts are quoted in parts per million downfield of tetramethylsilane and values of coupling constants (J) are given in Hz. The symbol * after the proton NMR chemical shift indicates that the signal disappears after a D_2O "shake". Carbon NMR spectra were recorded with broad band proton decoupling and the DEPT pulse sequence was routinely used to aid the assignment of spectra.

Melting points were determined on a Reichert hot stage apparatus and are uncorrected. Infrared spectra were recorded on a Nicolet Avatar 360 FT-IR ESP infrared spectrophotometer and signals were referenced to the polystyrene 1601 cm^{-1} absorption. Mass spectra were recorded either on a VG autospec mass spectrometer, operating at 70 eV, using both the electron impact and fast atom bombardment methods of ionisation, or using a Micromass LCT-KA111 electrospray mass spectrometer. Accurate molecular weights were generally obtained using electrospray mass spectrometry using reserpine as the lock mass and sodium iodide as the standard. The method used is indicated in each case: electron impact (EI), fast atom bombardment (FAB) or electrospray (ES). Optical rotations were recorded for all optically active compounds on a Perkin Elmer 241 polarimeter (using the sodium D line; 589 nm) and $[\alpha]_D^{20}$ are given in units of 10^{-1} deg cm^2 g^{-1}.

(2*R*)-2-Butyl-2,6-dihydro-6-hydroxypyran-3-one

(−)-L-DIPT (15 mole %, 827 μl, 3.90 mmol) and titanium(IV) isopropoxide (772 μl, 2.60 mmol) were stirred in dry dichloromethane (120 ml) at −40 °C over 3 Å molecular sieves (1.2 g) for 30 min after which a solution of racemic furyl alcohol **6** (4.00 g, 26.0 mmol) in dichloromethane (10 ml) was added. After a further 10 min of stirring, *tert*-butyl hydroperoxide (18.2 mmol, 3.03 ml, 5.0 M solution in decane) was added and the solution stirred for a further 4 h. This solution was quenched by slow addition with stirring of a large excess of saturated aqueous tartaric acid–ferrous sulfate solution. The organic layer was separated and washed with brine (2 × 50 ml). The organic layer was dried ($MgSO_4$), after which the solvent was removed under vacuum and the residue pre-absorbed directly onto silica gel. Analysis of a portion of the crude product by 300 MHz ^1H NMR spectroscopy indicated that the reaction had reached 34% completion. Purification by flash chromatography, eluting with 2 : 8 EtOAc–petrol gave the pyranone[10] (1.48 g, 31%, 69 : 31 mixture of anomers), as a colourless viscous oil, $[\alpha]_D^{20}$ +34.7 (*c* 0.78, $CHCl_3$; 93% ee); R_f 0.22 (2 : 8 EtOAc–petrol); ν_{max}/cm^{-1} (thin film) 3431 (O–H), 2958, 2862, 1682 (C=O), 1468, 1379, 1158, 1088, 1027; δ_H (300 MHz; $CDCl_3$) 6.92 (1H, dd, *J* 10.3 and 1.5, 5-H^{min}), 6.90 (1H, dd, *J* 10.2 and 3.4, 5-H^{maj}), 6.14 (1H, dd, *J* 10.3 and $^4J_{HH}$ 1.6, 4-H^{min}), 6.10 (1H, dd, *J* 10.2 and $^4J_{HH}$ 0.6, 4-H^{maj}), 5.65 (1H, m, 6-$H^{maj\ +\ min}$), 4.56 (1H, dd, *J* 8.0 and 3.9, 2-H^{maj}), 4.08 (1H, dd, *J* 8.0 and 3.9, 2-H^{min}) 2.0–1.2 (6H, m, butyl), 0.91 (3H, t, *J* 7.1, CH_3); ν_C (75 MHz; $CDCl_3$) 197.4 (3-C^{maj}), 196.9 (3-C^{min}), 148.4 (5-C^{min}), 145.0 (5-C^{maj}), 127.9 (4-C^{maj}), 129.1 (4-C^{min}), 91.3 (6-C^{min}), 87.9 (6-C^{maj}), 79.3 (2-C^{min}), 74.6 (2-C^{maj}), 29.7 (maj), 30.6 (min), 27.7 (min), 27.5 (maj), 26.9 (maj) and 14.4 ($CH_3^{maj\ +\ min}$).

2-Butyl-2,6-dihydro-6-hydroxypyran-3-one

The furyl alcohol **6** (8.78 g, 57 mmol) and vanadyl acetylacetonate (50 mg, 0.144 mmol) were stirred in dry dichloromethane (150 ml) at room temperature and *tert*-butyl hydroperoxide (62.7 mmol, 14.41 ml as a 4.35 M solution in toluene) was added. The reaction mixture was stirred for 5 h and quenched by slow addition of a large excess of saturated aqueous ferrous sulfate solution. The organic layer was separated, washed with brine (2 × 50 ml), dried ($MgSO_4$) and the solvent removed under reduced pressure. The residue was pre-absorbed directly onto silica gel, and purified by flash chromatography, eluting with 2 : 8 EtOAc–petrol to give the racemic pyranone[10] (9.33 g, 89%; 69 : 31 mixture of anomers) as a colourless viscous oil, spectroscopically identical to that obtained previously.

(2*R*,6*S*)- and (2*R*,6*R*)-2-Butyl-6-methoxy-2,6-dihydropyran-3-one: *trans*- and *cis*-7

(2*R*)-2-Butyl-6-hydroxy-2,6-dihydropyran-3-one (9.00 g, 52.9 mmol) and trimethyl orthoformate (6.97 ml, 63.5 mmol) were stirred in dry dichloromethane (150 ml) at room temperature and boron trifluoride–diethyl ether complex (2.6 mmol, 336 μl) added. The solution was stirred for 2 h and then quenched with saturated aqueous sodium bicarbonate solution (2 × 50 ml). The organic layer was washed with brine (50 ml) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue pre-absorbed directly onto silica gel. Purification by flash chromatography, eluting with 6 : 94 EtOAc–petrol gave the *pyranone trans*-**7** (6.53 g, 67%) as a colourless oil, $[\alpha]_D^{20}$ +84.2 (*c* 0.32, $CHCl_3$; 93% ee); R_f 0.34 (6 : 94 EtOAc–petrol); ν_{max}/cm^{-1} (thin film) 2957, 2862, 1695, 1468, 1396, 1101, 1049, 965; δ_H (300 MHz; $CDCl_3$) 6.85 (1H, dd, *J* 10.2 and 3.5, 5-H), 6.08 (1H, dd, *J* 10.2 and $^4J_{HH}$ 0.4, 4-H), 5.11 (1H, d, *J* 3.5, 6-H), 4.38 (1H, dd, *J* 8.5 and 3.5, 2-H), 3.52 (3H, s, OCH_3), 2.0–1.3 (6H, m, butyl), 0.92 (3H, t, *J* 7.1, CH_3); δ_C (75 MHz; $CDCl_3$) 197.1 (3-C), 143.5 (5-C), 128.1 (4-C), 94.5 (6-C), 74.3 (2-C), 56.8 (OCH_3), 29.5, 27.6, 22.9 and 14.4 (CH_3).

Also obtained was the *pyranone cis*-**7** (2.63 g, 27%) as a colourless oil, R_f 0.29 (6 : 94 EtOAc–petrol); δ_H (300 MHz; $CDCl_3$) 6.88 (1H, dd, *J* 10.3 and 1.9, 5-H), 6.13 (1H, dd, *J* 10.3 and $^4J_{HH}$ 1.6, 4-H), 5.23 (1H, dd, *J* 1.9 and $^4J_{HH}$ 1.6, 6-H), 4.05 (1H, dd, *J* 8.7 and 4.1, 2-H), 3.57 (3H, s, OCH_3), 2.0–1.3 (6H, m, butyl), 0.92 (3H, t, *J* 7.1, CH_3); δ_C (75 MHz; $CDCl_3$) 197.1 (3-C), 146.7 (5-C), 129.0 (4-C), 97.1 (6-C), 79.4 (2-C), 56.7 (OCH_3), 31.4, 28.0, 22.8 and 14.4 (CH_3).

(2*R*,3*S*)-2-Butyl-6-methoxy-3,6-dihydro-2*H*-pyran-3-ol 8

The pyranone **7** (2.82 g, 15.34 mmol, *trans* : *cis* 70 : 30) and cerium trichloride heptahydrate (6.87 g, 18.4 mmol) were stirred in absolute ethanol (60 ml) at −40 °C, and sodium borohydride (583 mg, 15.3 mmol) added slowly and in small portions. The mixture was stirred for 4 h and allowed to warm to room temperature before being cautiously quenched with water (5 ml). After a further 10 min of stirring, the ethanol

was removed under vacuum and the residue diluted with water (40 ml). The residue was extracted with chloroform (4 × 60 ml) and the combined organic extracts dried ($MgSO_4$) and the solvent removed under reduced pressure to give the *alcohol* **8** (2.62 g, 92%, 70 : 30 mixture of anomers) as a colourless viscous oil, $[\alpha]_D^{20}$ +98.7 (*c* 0.21, $CHCl_3$; 93% ee); R_f 0.32 (15 : 85 EtOAc–petrol); ν_{max}/cm^{-1} (thin film) 2453, 2956, 2873, 1651, 1467, 1399, 1043, 1001 and 955; δ_H (300 MHz; $CDCl_3$) 6.14 (1H, ddd, *J* 10.2, 5.3 and $^4J_{HH}$ 1.6, 4-H^{min}), 5.94 (1H, ddd, *J* 10.0, 2.6 and $^4J_{HH}$ 1.3, 5-H^{maj}), 5.82 (1H, d, *J* 10.0, 4-H^{maj}), 5.75 (1H, ddd, *J* 10.2, 2.8 and $^4J_{HH}$ 2.1, 5-H^{min}), 4.95 (1H, dd, *J* 2.8 and $^4J_{HH}$ 1.6, 6-H^{min}), 4.84 (1H, d, *J* 1.3, 6-H^{maj}), 3.88 (1H, td, *J* 8.9 and $^4J_{HH}$ 1.3, 3-H^{maj}), 3.72 (1H, m, 3-H^{min}), 3.48 (1H, m, 2-H$^{maj\ +\ min}$), 1.75 (1H, d, *J* 11.1, OH^{min}), 1.64 (1H, d, *J* 8.9, OH^{maj}), 2.0–1.25 (6H, m, butyl) and 0.92 (3H, t, *J* 7.2, CH_3); *m*/*z* 186 (32%), 155 (29), 114 (41), 100 (100), 55(90) and 41 (99).

(2*R*,3*S*,6*S*)-2-Butyl-6-methoxy-3,6-dihydro-2*H*-pyran-3-yl 4-methoxybenzoate 9

The alcohol **8** (2.172 g, 11.7 mmol, *trans : cis* 70 : 30) and triethylamine (2.604 ml, 18.72 mmol) were stirred in dry dichloromethane (50 ml) at room temperature and *p*-anisoyl chloride (1.75 ml, 12.87 mmol) was added *via* syringe. The resulting solution was treated with DMAP (71 mg, 0.585 mmol) and stirred for 8 h. The solution was quenched with saturated aqueous sodium bicarbonate solution (20 ml) and diluted with dichloromethane (100 ml). The organic layer was separated and washed with a further portion of saturated sodium bicarbonate solution (2 × 30 ml) followed by a washing with brine (50 ml). The organic layer was dried ($MgSO_4$) and the solvent removed under reduced pressure. The crude residue was pre-absorbed onto silica gel and purified by flash chromatography, eluting with 1 : 9 EtOAc–petrol to give the *ester* **9** (2.50 g, 67%) as a colourless viscous oil, $[\alpha]_D^{20}$ +147.0 (*c* 0.68, $CHCl_3$); R_f 0.32 (7 : 93 EtOAc–petrol); (Found MNa^+ 343.1521. $C_{18}H_{24}O_6$ requires *M*Na, 343.1520); ν_{max}/cm^{-1} 2956, 2954, 2872, 1716 (C=O), 1606, 1512, 1257, 1168, 1101, 1048, 964, 847; δ_H (300 MHz; $CDCl_3$) 7.98 (2H, d, *J* 9.0, Aryl), 6.92 (2H, d, *J* 9.0, aryl), 5.97 (1H, d, *J* 10.2, 5-H), 5.84 (1H, ddd, *J* 10.2, 4.6 and $^4J_{HH}$ 2.0, 4-H), 5.34 (1H, ddd, *J* 8.5, 4.6 and $^4J_{HH}$ 1.5, 3-H), 4.92 (1H, s, 6-H), 3.94 (1H, td, *J* 8.5 and 2.4, 2-H), 3.86 (3H, s, OCH_3), 3.48 (3H, s, OCH_3), 1.8–1.2 (6H, m, butyl) and 0.87 (3H, t, *J* 7.1, CH_3); δ_C (75 MHz; $CDCl_3$) 166.2 (C=O), 164.0 (aryl), 132.4 (aryl), 130.7 (4-C), 128.0 (5-C), 122.6 (aryl), 114.1 (aryl), 95.8 (6-C), 70.0 (3-C), 68.9 (2-C), 56.3 (OCH_3), 55.9 (OCH_3), 30.0, 27.9, 22.9 and 14.4 (CH_3); *m*/*z* (ES) 343 (100%, MNa^+).

Also obtained was the *ester* 4-methoxybenzoic acid (2*R*,3*S*,6*R*)-2-butyl-6-methoxy-3,6-dihydro-2*H*-pyran-3-yl ester (1.08 g, 29%) as a colourless viscous oil, $[\alpha]_D^{20}$ −65.1 (*c* 0.36, $CHCl_3$); R_f 0.26 (7 : 93 EtOAc–petrol); δ_H (300 MHz; $CDCl_3$) 8.03 (2H, d, *J* 8.9, Aryl), 6.90 (2H, d, *J* 8.9, aryl), 6.19 (1H, dd, *J* 10.2 and 5.2, 4-H), 5.84 (1H, dd, *J* 10.2 and 1.3, 5-H), 5.24 (1H, m, 3-H), 5.05 (1H, s, 6-H), 3.75 (1H, m, 2-H), 3.86 (3H, s, OCH_3), 3.55 (3H, s, OCH_3), 1.8–1.2 (6H, m, butyl) and 0.87 (3H, t, *J* 7.1, CH_3); *m*/*z* (ES) 343 (100%, MNa^+).

(2*R**,3*R**,6*S**)-2-Butyl-6-methoxy-3,6-dihydro-2*H*-pyran-3-yl 4-nitrobenzoate

A solution of diisopropyl azodicarboxylate (1.629 g, 8.065 mmol) in THF was added dropwise to a solution of alcohol *trans*-**8** (750 mg, 4.03 mmol), triphenylphosphine (2.112 g, 8.065 mmol) and *p*-nitrobenzoic acid (1.347 g, 8.065 mmol) which was stirred under nitrogen at 0 °C. After 14 h of stirring the solvent was removed under vacuum and the residue pre-absorbed onto silica gel. Purification by flash chromatography (gradient elution: 5 : 95 ⟶ 15 : 85 EtOAc–petrol) gave the *ester* (1.036g, 74%) as colourless prisms, m.p. 74–75 °C, R_f 0.31 (7 : 93 EtOAc–petrol); (Found MNa^+ 358.1271. $C_{17}H_{21}NO_6$ requires *M*Na, 358.1267); ν_{max}/cm^{-1} 2951, 2870, 1717, 1530, 1347, 1274, 1111, 1064; δ_H (300 MHz; $CDCl_3$) 8.30 (2H, d, *J* 9.1, Ar), 8.24 (2H, d, *J* 9.1, Ar), 6.22 (1H, ddd, *J* 10.0, 5.5 and $^4J_{HH}$ 0.9, 4-H), 6.09 (1H, dd, *J* 10.0 and 3.0, 5-H), 5.18 (1H, dd, *J* 5.5 and 2.3, 3-H), 5.00 (1H, dd, *J* 3.0 and $^4J_{HH}$ 0.5, 6-H), 4.16 (1H, ddd, *J* 8.8, 3.9 and 2.3, 2-H), 3.49 (3H, s, OCH_3), 1.8–1.5 (3H, m, butyl), 1.45–1.30 (3H, m, butyl) and 0.90 (3H, t, *J* 6.9, CH_3); δ_C (75 MHz; $CDCl_3$) 164.7, 151.1, 135.7, 131.6, 131.3, 125.8, 123.9, 95.6, 69.0, 67.4, 66.6, 56.0, 30.6, 28.2, 22.9 and 14.4.

(2*R**,3*R**,6*S**)-2-Butyl-6-methoxy-3,6-dihydro-2*H*-pyran-3-ol 10

(2*R**, 3*R**, 6*S**)-2-Butyl-6-methoxy-3,6-dihydro-2*H*-pyran-3-yl 4-nitrobenzoate (749 mg, 2.16 mmol) and potassium carbonate (294 mg, 2.16 mmol) were stirred under nitrogen at room temperature in methanol (20 ml) for 2 days. The solvent was removed under vacuum and the residue dissolved in chloroform (30 ml)–water (20 ml). The organic layer was separated and washed with a further portion of water (2 × 20 ml). The organic layer was dried ($MgSO_4$) and the solvent removed under reduced pressure to give the *alcohol* **10** (399 mg, >98%) as a viscous colourless oil, R_f 0.35 (15 : 85 EtOAc–petrol); (Found: MNa 187.1336. $C_{10}H_{18}O_3$ requires *M*Na, 187.1334); ν_{max}/cm^{-1} 3422 (O–H), 2956, 2932, 1651, 1467, 1398, 1187, 1034; δ_H (300 MHz; $CDCl_3$) 6.17 (1H, ddd, *J* 10.0, 5.6 and $^4J_{HH}$ 0.8, 4-H), 5.89 (1H, dd, *J* 10.0 and 3.1, 5-H), 4.86 (1H, d, *J* 3.1, 6-H), 3.91 [1H, ddd, *J* 7.9 (OH), 5.2 and 2.1 3-H], 3.63 (1H, br, 2-H), 3.43 (3H, s, OCH_3), 1.85–1.30 (6H, m, butyl), 0.93 (3H, t, *J* 7.2, CH_3); δ_C (75 MHz; $CDCl_3$) 130.9 (4-H), 128.5 (5-H), 95.8 (6-H), 70.9, 63.6, 55.9, 30.6, 28.2, 23.1 and 14.5.

(2*R**,3*R**,6*S**)-2-Butyl-6-methoxy-3,6-dihydro-2*H*-pyran-3-yl 4-methoxybenzoate 11

p-Anisoyl chloride (1.145 g, 910 µl, 6.70 mmol) was added *via* syringe to a stirred solution of alcohol **10** (1.133 g, 6.09 mmol), triethylamine (1.44 ml, 10.35 mmol) and DMAP (37 mg, 0.305 mmol) in dichloromethane (15 ml) under nitrogen at room temperature. After being stirred for a further 24 h, the solution was diluted with chloroform (40 ml) and the organic layer washed sequentially with saturated sodium bicarbonate (2 × 20 ml), brine (10 ml) and water (10 ml). The organic layer was dried ($MgSO_4$) and the solvent removed under reduced pressure. Purification by flash chromatography (gradient elution: 5 : 95 ⟶ 15 : 85 EtOAc–petrol) gave the *ester* **11** (1.84 g, 95%) as colourless prisms; R_f 0.36 (7 : 93 EtOAc–petrol); (Found: MNa 343.1528. $C_{18}H_{24}O_5$ requires *M*Na, 343.1521); ν_{max}/cm^{-1} 2955, 1710 (C=O), 1606, 1511, 1257, 1168, 1110, 1044; δ_H (300 MHz; $CDCl_3$) 8.02 (2H, d, *J* 9.0, Ar), 6.91 (2H, d, *J* 9.0, Ar), 6.21 (1H, ddd, *J* 10.0, 5.5 and $^4J_{HH}$ 0.9, 4-H), 6.04 (1H, dd, *J* 10.0 and 3.0, 5-H), 5.13 (1H, dd, *J* 5.5 and 2.3, 3-H), 4.99 (1H, d, *J* 3.0, 6-H), 4.11 (1H, dt, 7.2 and 2.3, 2-H), 3.87 (3H, s, OCH_3), 3.47 (3H, s, OCH_3), 1.80–1.30 (6H, m, butyl) and 0.88 (3H, t, *J* 7.3, CH_3); δ_C (75 MHz; $CDCl_3$) 166.3, 163.9, 132.3, 130.7, 126.8, 122.7, 114.0, 95.7, 69.3, 65.1, 56.0, 55.9, 30.6, 28.2, 22.9 and 14.4; *m*/*z* (ES) 343 (100%, MNa^+).

(2*R**,3*R**,6*S**)-2-Butyl-6-methoxy-3,6-dihydro-2*H*-pyran-3-yl acetate 12

The alcohol **10** (612 mg, 3.29 mmol) was stirred for 4 h at room temperature in a solvent mixture of acetic anhydride (6 ml) and pyridine (3 ml). The solvent was removed under high vacuum and the residue pre-absorbed onto silica gel. Purification by flash chromatography, eluting with 15 : 85 EtOAc–petrol gave the *acetate* **12** (745 mg, >98%) as a colourless oil, R_f 0.29 (7 : 93 EtOAc–petrol); (Found: MNa 251.1260. $C_{12}H_{20}O_4$ requires *M*Na, 251.1259); ν_{max}/cm^{-1} 2955, 1733 (C=O), 1372, 1237, 1187, 1111, 1046, 1023, 960; δ_H (300 MHz; $CDCl_3$) 6.10 (1H, ddd, *J* 10.0, 5.4 and $^4J_{HH}$ 0.9, 4-H), 6.00 (1H, dd, *J* 10.0 and 2.9, 5-H), 4.93 (1H, d, *J* 2.9, 6-H), 4.92 (1H, dd, *J* 5.4 and 2.3, 3-H),

4.03 (1H, dt, 7.2 and 2.3, 2-H), 3.44 (3H, s, OCH_3), 2.10 (3H, s, OAc), 1.75–1.30 (6H, m, butyl) and 0.93 (3H, t, *J* 7.3, CH_3); δ_C (75 MHz; $CDCl_3$) 171.1 (C=O), 130.7 (4-C), 126.5 (5-C), 95.6 (6-C), 68.9, 65.0, 56.0, 30.3, 28.1, 22.9, 21.3 and 14.4; *m*/*z* (ES) 251 (100%, MNa^+).

(2*R*,3*S*,4*R*,5*S*,6*S*)-2-Butyl-4,5-dihydroxy-6-methoxytetrahydropyran-3-yl 4-methoxybenzoate 13a

The ester **9** (110 mg, 0.344 mmol, >95% ee) and NMO (81 mg, 0.688 mmol) were stirred at room temperature in an 8 : 1 acetone–water mixture (2.4 ml) and osmium tetraoxide (5 mg, 0.02 mmol) was added. After 24 h, the mixture was quenched with a saturated aqueous sodium sulfite solution (0.5 ml) and stirred for a further 10 min. The solvent was removed under reduced pressure and the residue pre-absorbed onto silica gel before purification by flash chromatography, eluting with 4 : 6 EtOAc–petrol to give the *diol* **13a** (99.6 mg, 82%) as a colourless viscous syrup; $[\alpha]_D^{20}$ +75.0 (*c* = 0.43, $CHCl_3$); R_f 0.22 (4 : 6 EtOAc–petrol); (Found: MNa 377.1576. $C_{18}H_{26}O_7$ requires *M*Na, 377.1576); ν_{max}/cm^{-1} 3403 (O–H), 2936, 1716, 1606, 1512, 1463, 1259, 1168, 1105, 1071; δ_H (300 MHz; $CDCl_3$) 7.97 (2H, d, *J* 8.9, aryl), 6.90 (2H, d, *J* 8.9, aryl), 5.00 (1H, t, *J* 9.5, 3-H), 4.77 (1H, s, 6-H), 3.97 (2H, m, br, 4-H and 5-H), 3.86 (3H, s, OCH_3), 3.78 (1H, td, *J* 9.0 and 1.4, 2-H), 3.59 (1H, d, J_{OH} 3.6), 3.38 (3H, s, OCH_3), 2.97 (1H, br, OH), 1.64–1.46 (3H, m, CH_2), 1.44–1.20 (3H, m, CH_2) and 0.91 (3H, t, *J* 7.1, CH_3); *m*/*z* (ES) 377 (100%, MNa^+).

The diol **13a** was shown to have 93% ee by analysis, by 500 MHz ^{1}H NMR spectroscopy, of the mixtures obtained by derivatisation[11] as the corresponding (*R*)- and (*S*)-Mosher's diesters.

(2*R**,3*R**,4*S**,5*R**,6*S**)-2-Butyl-4,5-dihydroxy-6-methoxytetrahydropyran-3-yl 4-methoxybenzoate 13b

NMO (310 mg, 2.644 mmol) was added to a stirred solution of the ester **11** (423 mg, 1.322 mmol) and osmium tetraoxide (20 mg, 78.7 μmol) in dichloromethane at room temperature under nitrogen. The solution was stirred for 24 h and the solvent removed under reduced pressure. The residue was stirred at room temperature in a mixture of THF (2 ml) and saturated aqueous sodium sulfite solution (2 ml) for 1 h and the solvent removed under reduced pressure. Analysis of the crude reaction mixture by 300 MHz ^{1}H NMR spectroscopy showed a 93 : 7 mixture of the diols **13b** and **13c**. The residue was pre-absorbed onto silica gel and purified by flash chromatography (gradient elution: 4 : 6 ⟶ 1 : 1 EtOAc–petrol) to give the *diol* **13b** (320 mg, 69%) as a colourless viscous oil, R_f 0.32 (4 : 6 EtOAc–petrol); (Found: MNa 377.1578. $C_{18}H_{26}O_7$ requires *M*Na, 377.1576); δ_H (300 MHz; $CDCl_3$) 7.93 (2H, d, *J* 8.9, Ar), 6.86 (2H, d, *J* 8.9, Ar), 5.15 (1H, dd, *J* 3.1 and 1.8, 3-H), 4.81 (1H, d, *J* 3.6, 6-H), 4.03 (1H, ddd, *J* 8.4, 4.6 and 1.8, 2-H), 3.96 (1H, br, 4-H), 3.86 (1H, br, 5-H), 3.79 (3H, s, OCH_3), 3.43 (3H, s, OCH_3), 2.82 (1H, br, OH), 1.60–1.24 (6H, m, butyl) and 0.91 (3H, t, *J* 7.3, CH_3); δ_C (75 MHz; $CDCl_3$) 165.6, 164.1, 132.3, 122.2, 114.2, 101.5, 73.4, 70.2, 69.9, 66.1, 56.5, 55.9, 30.2, 28.4, 23.0 and 14.4; *m*/*z* (ES) 377 (100%, MNa^+).

Also obtained was the *diol* **13c** (23 mg, 5 %) as colourless prisms, m.p. 119–121 °C; R_f 0.37 (4 : 6 EtOAc–petrol); (Found: MNa 377.1565. $C_{18}H_{26}O_7$ requires *M*Na, 377.1576); ν_{max}/cm^{-1} 3312 (O–H), 2934, 1708, 1607, 1509, 1277, 1255, 1167, 1119 and 1060; δ_H (300 MHz; $CDCl_3$) 7.91 (2H, d, *J* 8.9, Ar), 6.85 (2H, d, *J* 8.9, Ar), 5.35 (1H, d, *J* 3.7, 3-H), 4.79 (1H, d, *J* 1.3, 6-H), 3.96 (1H, dt, *J* 8.4 and 3.7, 4-H), 3.79 (3H, s, OCH_3), 3.79 (1H, m, 2-H), 3.71 (1H, ddd, *J* 10.2, 3.7 and 1.3, 5-H), 3.33 (3H, s, OCH_3), 2.83 (1H, d, *J* 8.4, OH), 2.49 (1H, d, *J* 10.2, OH), 1.60–1.15 (6H, m, butyl) and 0.79 (3H, t, *J* 7.3, CH_3); δ_C (75 MHz; $CDCl_3$) 166.4, 164.2, 132.2, 121.9, 114.3, 102.0, 73.4, 70.2, 69.1, 66.3, 55.9, 55.6, 30.9, 28.3, 22.9 and 14.4; *m*/*z* (ES) 377 (100%, MNa^+).

(2*R**,3*R**,4*S**,5*R**,6*S**)-2-Butyl-4,5-dihydroxy-6-methoxytetrahydropyran-3-yl acetate 14b

NMO (405 mg, 3.46 mmol) was added to a stirred solution of the acetate **12** (395 mg, 1.73 mmol) and osmium tetraoxide (78.7 μmol, 20 mg) in dichloromethane at room temperature under nitrogen. The solution was stirred for 24 h and the solvent removed under reduced pressure. The residue was stirred at room temperature in a mixture of THF (2 ml) and saturated aqueous sodium sulfite solution (2 ml) for 1 h and the solvent removed under reduced pressure. The residue was pre-absorbed onto silica gel and purified by flash chromatography (gradient elution: 4 : 6 ⟶ 1 : 1 EtOAc–petrol) to give the *diol* **14b** (191 mg, 42%) as a colourless viscous oil, R_f 0.24 (4 : 6 EtOAc–petrol); (Found: MNa 285.1306. $C_{12}H_{22}O_6$ requires *M*Na, 285.1314); δ_H (300 MHz; $CDCl_3$) 5.00 (1H, d, *J* 2.6, 3-H), 4.81 (1H, d, *J* 3.7, 6-H), 4.02 (1H, dd, *J* 8.9 and 3.1, 2-H), 3.89 (1H, m, 4-H), 3.82 (1H, m, 5-H), 3.47 (3H, s, OCH_3), 2.12 (1H, d, *J* 8.4, OH), 2.82 (1H, br, OH), 1.60–1.25 (6H, m, butyl) and 0.91 (3H, t, *J* 7.3, CH_3); δ_C (75 MHz; $CDCl_3$) 170.5, 101.3, 73.2, 70.0, 65.8, 64.5, 56.5, 30.0, 28.3, 22.9, 21.3 and 14.4; *m*/*z* (ES) 285 (100%, MNa^+).

Also obtained was the *diol* **14c** (40 mg, 9 %) as a colourless semi-crystalline solid, R_f 0.33 (4 : 6 EtOAc–petrol); (Found MNa 285.1320. $C_{12}H_{22}O_6$ requires *M*Na, 285.1314); ν_{max}/cm^{-1} 3288 (O–H), 2940, 1737, 1232, 1117, 1069, 995; δ_H (300 MHz; $CDCl_3$) 5.22 (1H, d, *J* 3.7, 3-H), 4.81 (1H, d, *J* 1.1, 6-H), 3.95 (1H, dt, *J* 7.9 and 3.7, 4-H), 3.77 (1H, dd, *J* 8.7 and 3.2, 2-H), 3.72 (1H, ddd, *J* 11.0, 3.7 and 1.1, 5-H), 3.38 (3H, s, OCH_3), 2.87 (1H, d, *J* 8.4, OH), 2.52 (1H, d, *J* 11.0, OH), 2.18 (3H, s, OAc), 1.70–1.25 (6H, m, butyl) and 0.90 (3H, t, *J* 7.3, CH_3); δ_C (75 MHz; $CDCl_3$) 170.8, 102.0, 73.4, 70.2, 68.8, 65.9, 55.6, 30.8, 28.2, 22.9, 21.3 and 14.4; *m*/*z* (ES) 285 (100%, MNa^+).

(2*R**,3*S**,4*S**,5*S**,6*S**)-4,5-Diacetoxy-2-butyl-6-methoxytetrahydropyran-3-yl acetate 15c

A solution of the alcohol **10** (113 mg, 0.609 mmol) and TMEDA (110 μl, 0.731 mmol) in dichloromethane (6 ml) was cooled to −78 °C under nitrogen. A solution of osmium tetraoxide (186 mg, 0.731 mmol) in dichloromethane (0.7 ml) was added and the solution stirred for 8 h at −78 °C. The solution was allowed to warm to room temperature and *N,N,N′,N′*-tetramethylethane-1,2-diamine added (244 μl, 3.655 mmol) added. The solution was stirred for 24 h before being poured into brine and extracted with ethyl acetate (4 × 40 ml). The combined organic extracts were dried (Na_2SO_4) and the solvent removed under reduced pressure. The residue was dissolved in acetic anhydride–pyridine (3 : 1, 3 ml) and stirred at room temperature for 4 h. The solvent was removed under reduced pressure and the crude residue was pre-absorbed onto silica gel and purified by flash chromatography, eluting with 15 : 85 EtOAc–petrol, to give the *triacetate* **15c** (197 mg, 94%) as a colourless oil, R_f 0.32 (15 : 85 EtOAc–petrol); (Found MNa 369.1537. $C_{16}H_{26}O_8$ requires *M*Na, 369.1525); ν_{max}/cm^{-1} 2957, 2873, 1744, 1373, 1256, 1227, 1133, 1080, 1023; δ_H (300 MHz; $CDCl_3$) 5.26 (1H, t, *J* 3.7, 4-H), 5.22 (1H, d, *J* 3.7, 3-H), 5.10 (1H, dt, *J* 3.7 and 1.1, 5-H), 4.76 (1H, d, *J* 1.1, 6-H), 3.91 (1H, dd, *J* 7.6 and 2.7, 2-H), 3.39 (3H, s, OCH_3), 2.16 (3H, s, OAc), 2.09 (3H, s, OAc), 1.99 (3H, s, OAc), 1.80–1.20 (6H, m, butyl) and 0.90 (3H, t, *J* 7.3, CH_3); δ_C (75 MHz; $CDCl_3$) 170.9 (C=O), 170.5 (C=O), 170.1 (C=O), 99.7 (6-C), 70.0, 68.8, 68.0, 66.5, 55.5, 30.6, 28.0, 22.9, 21.4, 21.2, 21.1 and 14.4; *m*/*z* (ES) 369 (100%, MNa^+).

(2*R**,3*S**,4*R**,5*S**,6*S**)-2-Butyl-4-hydroxy-5-iodo-6-methoxytetrahydropyran-3-yl 4-methoxybenzoate 17 and (2*R**,3*R**,4*R**,5*S**,6*S**)-2-butyl-3-hydroxy-5-iodo-6-methoxytetrahydropyran-4-yl 4-methoxybenzoate 18

A mixture of the ester **9** (170 mg, 0.531 mmol) and freshly

prepared silver benzoate (300 mg, 2.125 mmol, 4 mol equiv.) was dried azeotropically using toluene and then dissolved in dry carbon tetrachloride (6 ml). Iodine (270 mg, 1.06 mmol) was added to the stirred suspension under N_2 and the mixture stirred for a further 4 days with protection from light. The suspension was diluted with chloroform (15 ml) and the silver salts removed by centrifugation. The organic fraction was washed with 10% aqueous sodium sulfite solution (2 × 5 ml) and saturated aqueous sodium bicarbonate solution (2 × 5ml), dried ($MgSO_4$) and the solvent removed under reduced pressure. The crude residue was pre-absorbed onto silica gel and purified by flash chromatography, eluting with 15 : 85 EtOAc–petrol, to give the *ester* **17** as a colourless oil (182.6 mg, 74%), R_f 0.34 (15 : 85 EtOAc–petrol); (Found MNa^+ 487.0578. $C_{18}H_{25}IO_6$ requires *M*Na, 487.0594); ν_{max}/cm^{-1} 3484, 2956, 2858, 1716 (C=O), 1606, 1511, 1258, 1169, 1122, 1030, 847, 769; δ_H (300 MHz; $CDCl_3$) 8.00 (2H, d, *J* 8.9, Ar), 6.92 (2H, d, *J* 8.9, Ar), 5.50 (1H, dd, *J* 9.2 and 2.6, 3-H), 5.01 (1H, s, 6-H), 4.31 (1H, d, *J* 1.7, 5-H), 4.30, (1H, ddd, *J* 2.6, 1.7 and J_{OH} 8.9, 4-H), 4.14 (1H, td, *J* 9.2 and 4.7, 2-H), 3.87 (3H, s, OMe), 3.46, (3H, s, OMe), 3.41 (1H, d, *J* 8.9, OH), 1.8–1.2 (6H, m, butyl) and 0.91 (3H, t, *J* 7.1, CH_3); δ_C (75 MHz; $CDCl_3$) 165.8 (C=O), 164.0 (Ar), 132.3 (Ar), 122.4 (Ar), 114.1 (Ar), 102.7 (6-C), 71.6 (4-C), 70.1 (3-C), 67.3 (2-C), 56.2 (OCH_3), 55.9 (OCH_3), 31.2, 27.8, 25.8, 23.0 and 14.5 (CH_3); *m*/*z* (ES) 487 (100%, MNa^+).

Also obtained was the *ester* **18** as a colourless oil (42 mg, 17%), R_f 0.34 (15 : 85 EtOAc–petrol); (Found MNa^+ 487.0594. $C_{18}H_{25}IO_6$ requires *M*Na, 487.0594); ν_{max}/cm^{-1} 3459 (O–H), 2955, 1714 (C=O), 1606, 1512, 1257, 1169, 1101 and 1030; δ_H (300 MHz; $CDCl_3$) 8.00 (2H, d, *J* 8.9, Ar), 6.93 (2H, d, *J* 8.9, Ar), 5.40 (1H, t, *J* 3.9, 4-H), 4.96 (1H, d, *J* 2.3, 6-H), 4.42 (1H, dd, *J* 3.9 and 2.3, 5-H), 4.20, (1H, td, *J* 9.2 and 3.9, 3-H), 3.98 (1H, td, *J* 9.2 and 2.9, 2-H), 3.87 (3H, s, OMe), 3.40, (3H, s, OMe), 2.31 (1H, d, *J* 9.2, OH), 1.8–1.3 (6H, m, butyl) and 0.92 (3H, t, *J* 7.1, CH_3); δ_C (75 MHz; $CDCl_3$) 166.1 (C=O), 164.2 (Ar), 132.4 (Ar), 122.2 (Ar), 114.2 (Ar), 102.2 (6-C), 74.4 (4-C), 70.8 (2-C), 67.6 (3-C), 56.0 (OCH_3), 55.9 (OCH_3), 31.2, 28.0, 24.8, 23.1 and 14.5 (CH_3); *m*/*z* (ES) 487 (100%, MNa^+).

(2*R**,3*R**,4*S**,5*R**,6*S**)-2-Butyl-5-iodo-6-methoxy-4-hydroxytetrahydropyran-3-yl 4-methoxybenzoate 21

By the same general method, the ester **11** (115 mg, 0.359 mmol) gave a crude product which was pre-absorbed onto silica gel and purified by flash chromatography (gradient elution: 8 : 92 ⟶ 15 : 85 EtOAc–petrol) to give the *iodo alcohol* **21** (87 mg, 52 %) as a colourless oil, R_f 0.35 (15 : 85 EtOAc–petrol); (Found MNa^+ 487.0594. $C_{18}H_{25}IO_6$ requires *M*Na, 487.0594); ν_{max}/cm^{-1} 3473 (O–H), 2955, 2871, 2838, 1713, 1606, 1511, 1463, 1258, 1169, 1122, 1029; δ_H (300 MHz; $CDCl_3$) 7.97 (2H, d, *J* 8.9, Ar), 6.85 (2H, d, *J* 8.9, Ar), 5.34 (1H, d, *J* 3.0, 3-H), 4.85 (1H, d, *J* 3.0, 6-H), 4.25 (1H, dd, *J* 11.2 and 3.0, 5-H), 4.18 (1H, dt, *J* 11.2 and 3.0, 4-H), 3.93 (1H, dd, 8.5 and 3.2, 2-H), 3.80 (3H, s, OCH_3), 3.37 (3H, s, OCH_3), 2.50 (1H, d, *J* 3.0, OH), 1.60–1.20 (6H, m, butyl) and 0.79 (3H, t, *J* 7.2, CH_3); δ_C (75 MHz; $CDCl_3$) 166.9 (C=O), 164.2 (Ar), 132.5 (Ar), 122.1 (Ar), 114.1 (Ar), 101.1 (6-C), 73.1 (3-C), 70.4 (4-C), 69.8 (2-C), 56.4 (OCH_3), 55.9 (OCH_3), 32.8 (5-C), 30.7, 28.2, 22.9 and 14.6); *m*/*z* (ES) 487 (100%, MNa^+).

(2*R**,3*R**,4*S**,5*R**,6*S**)-3,5-Diacetoxy-2-butyl-6-methoxytetrahydropyran-4-yl acetate 15d

The iodo alcohols **17** and **18** (15 mg, 32.3 μmol, **17** : **18** 81 : 19) were refluxed for 3 days under N_2 in aqueous potassium hydroxide solution (3 ml of a 0.3 M solution). The solvent was removed under reduced pressure and the crude product was dissolved in acetic anhydride–pyridine (3 : 1, 3 ml) and stirred at room temperature for 4 h. The solvent was again removed under reduced pressure. Analysis of the crude reaction mixture by 300 MHz ^1H NMR spectroscopy revealed a 75 : 25 mixture of **15d** and **15e**. The crude residue was pre-absorbed onto silica gel and purified by flash chromatography, eluting with 15 : 85 EtOAc–petrol, to give the *triacetate* **15d** (8.3 mg, 74%) as a colourless viscous oil, R_f 0.21 (15 : 85 EtOAc–petrol); (Found MNa^+ 369.1529. $C_{16}H_{26}O_8$ requires *M*Na, 369.1525); δ_H (300 MHz; $CDCl_3$) 5.43 (1H, t, *J* 9.5, 4-H), 4.88 (1H, d, *J* 9.5, 5-H), 4.88 (1H, s, 6-H), 4.85 (1H, t, *J* 9.5, 3-H), 3.73 (1H, td, 9.5 and 3.2, 2-H), 3.39 (3H, s, OCH_3), 2.08 (3H, s, OAc), 2.05 (3H, s, OAc), 2.01 (3H, s, OAc), 1.65–1.2 (6H, m, butyl) and 0.90 (3H, t, *J* 7.1, CH_3); *m*/*z* (ES) 369 (100%, MNa^+).

Also obtained was the triacetate **15e** (1.2 mg, 11%), spectroscopically identical to that obtained from **27b**, see below.

(2*R**,3*S**,4*R**,5*S**,6*S**)-4,5-Diacetoxy-2-butyl-6-methoxytetrahydropyran-3-yl acetate 15f

By the same general method, the iodo alcohol **21** (50.2 mg, 108 μmol) gave a crude product residue which was was pre-absorbed onto silica gel and purified by flash chromatography, eluting with 15 : 85 EtOAc–petrol, to give *triacetate* **15f** (33 mg, 87%) as a colourless viscous oil, R_f 0.23 (15 : 85 EtOAc–petrol); (Found MNa^+ 369.1533. $C_{16}H_{26}O_8$ requires *M*Na, 369.1525); ν_{max}/cm^{-1} 2957, 1746, 1605, 1372, 1224, 1113, 1048; δ_H (300 MHz; $CDCl_3$) 4.97 (1H, t, *J* 3.8, 4-H), 4.85 (1H, dd, *J* 3.8 and 2.3, 3-H), 4.82 (1H, dd, *J* 3.8 and 1.8, 5-H), 4.68 (1H, d, *J* 1.8, 6-H), 4.10 (1H, ddd, *J* 9.5, 3.6 and 2.3, 2-H), 2.13 (3H, s, OAc), 2.10 (3H, s, OAc), 2.09 (3H, s, OAc), 1.72–1.20 (6H, m, butyl) and 0.91 (3H, t, *J* 7.3, CH_3); δ_C (75 MHz; $CDCl_3$) 170.5 (C=O), 169.8 (C=O), 99.4 (6-C), 69.7, 68.7, 68.1, 66.8, 55.9, 29.9, 28.1, 22.9, 21.3, 21.2 and 14.4; *m*/*z* (ES) 369 (100%, MNa^+).

(2*R**,3*R**,4*S**,5*S**,6*S**)-4,5-Diacetoxy-2-butyl-6-methoxytetrahydropyran-3-yl acetate 15a

By the same general method, the ester **13a** (20 mg, 108 μmol) gave a crude product residue which was was pre-absorbed onto silica gel and purified by flash chromatography, eluting with 15 : 85 EtOAc–petrol, to give *triacetate* **15a** (12 mg, 60%) as a colourless viscous oil, R_f 0.23 (15 : 85 EtOAc–petrol); (Found MNa^+ 369.1535. $C_{16}H_{26}O_8$ requires *M*Na, 369.1525); ν_{max}/cm^{-1} 2957, 1746, 1605, 1372, 1224, 1113, 1048; δ_H (300 MHz; $CDCl_3$) 5.28 (1H, dd, *J* 9.8 and 3.5, 4-H), 5.23 (1H, dd, *J* 3.5 and 1.7, 5-H), 5.09 (1H, t, *J* 9.8, 3-H), 4.63 (1H, d, *J* 1.7, 6-H), 3.71 (td, *J* 9.8 and 1.9, 2-H), 2.14 (3H, s, OAc), 2.10 (6H, s, OAc), 2.08 (3H, s, OAc), 1.72–1.20 (6H, m, butyl) and 0.91 (3H, t, *J* 7.3, CH_3); *m*/*z* (ES) 369 (100%, MNa^+).

(2*R**,3*S**,4*R**,5*S**,6*S**)-2-Butyl-4,5-epoxy-6-methoxytetrahydropyran-3-yl 4-methoxybenzoate 27b and (2*R**,3*S**,4*R**,5*S**,6*R**)-2-butyl-4,5-epoxy-6-methoxytetrahydropyran-3-yl 4-methoxybenzoate 27a

Hydrogen peroxide (500 μl, 30% aqueous solution) was added dropwise to a stirred suspension of the ester **9** (200 mg, 0.625 mmol, 70 : 30 mixture of anomers), benzonitrile (420 μl) and sodium bicarbonate (170 mg) in methanol (1.5 ml) at 0 °C. The suspension was allowed to warm to room temperature and stirred for a further 3 days before dilution with brine (5 ml) and extraction with ethyl acetate (4 × 5 ml). The combined organic extracts were dried ($MgSO_4$) and the solvent evaporated under reduced pressure. The crude residue was pre-absorbed onto silica gel and purified by flash column chromatography, eluting with 15 : 85 EtOAc–petrol to give the *epoxide* **27b** (141 mg, 67%) as a colourless crystalline solid, m.p. 112–113 °C, R_f 0.25 (15 : 85 EtOAc–petrol); (Found MNa^+ 359.1488. $C_{18}H_{24}O_6$ requires *M*Na, 359.1471); ν_{max}/cm^{-1} 2954, 2859, 1716 (C=O), 1608, 1255, 1167, 1098, 769; δ_H (300 MHz; $CDCl_3$) 8.10 (2H, d, *J* 9.0, Ar), 6.92 (2H, d, *J* 9.0, Ar), 5.10 (1H, dd, *J* 3.5 and 4.8, 5-H), 4.74 (1H, s, 2-H), 3.87 (3H, s, OCH_3), 3.73 (1H, dd, *J* 4.8 and 3.9, 6-H), 3.61 (3H, s, OCH_3), 3.54 (1H, m, 4-H), 3.28 (1H, d, *J* 3.9, 1-H), 2.0–1.2 (6H, m, butyl) and 0.87 (3H, t, *J* 7.1,

CH_3); δ_C (75 MHz; $CDCl_3$) 166.6 (Ar), 164.0 (Ar), 132.6 (Ar), 114.0 (Ar), 99.6 (2-C), 76.2 (4-C), 66.3 (5-C), 57.3 (OCH_3), 55.9 (OCH_3), 52.0 (6-C), 51.4 (1-C), 29.2, 28.2, 22.8 and 14.4 (CH_3); *m*/*z* (ES) 359 (100% MNa^+).

Also obtained was the *epoxide* **27a** (56.9 mg, 27%) as a colourless oil, R_f 0.52 (15 : 85 EtOAc–petrol); (Found MNa^+ 359.1488. $C_{18}H_{24}O_6$ requires *M*Na, 359.1471); ν_{max}/cm^{-1} 2955, 2872, 1717 (C=O), 1606, 1512, 1258, 1168, 1082, 1024; δ_H (300 MHz; $CDCl_3$) 8.02 (2H, d, *J* 9.0, Ar), 6.95 (2H, d, *J* 9.0, Ar), 4.93 (1H, s, 2-H), 4.89 (1H, d, *J* 9.1, 5-H), 3.88 (3H, s, OCH_3), 3.76 (1H, td, *J* 9.1 and 2.4, 4-H), 3.51 (3H, s, OCH_3), 3.31 (1H, d, *J* 3.5, 6-H), 3.11 (1H, d, *J* 3.5, 1-H), 2.0–1.2 (6H, m, butyl) and 0.88 (3H, t, *J* 7.3, CH_3); δ_C (75 MHz; $CDCl_3$) 165.5 (aryl), 164.1 (aryl), 132.3 (aryl), 114.2 (aryl), 96.5 (2-C), 67.6 (5-C), 66.6 (4-C), 56.2 (OCH_3), 55.9 (OCH_3), 54.2 (6-C), 49.8 (1-C), 32.4, 27.8, 22.9 and 14.4 (CH_3); *m*/*z* (ES) 359 (100% M + Na^+).

(2*R**,3*R**,4*S**,5*R**,6*S**)-2-Butyl-4,5-epoxy-6-methoxytetrahydropyran-3-yl 4-methoxybenzoate 28 and (2*R**,3*R**,4*R**,5*S**,6*S**)-2-butyl-4,5-epoxy-6-methoxytetrahydropyran-3-yl 4-methoxybenzoate 29

By the same general method, the ester **11** (116 mg, 0.363 mmol,) gave a crude product which was pre-absorbed onto silica gel and purified by flash column chromatography, eluting with 15 : 85 EtOAc–petrol to give a mixture of the epoxides **28** and **29** (108 mg, 89 %, **28** : **29** 70 : 30) Separation by preparative HPLC (gradient elution: 100 : 0 ⟶ 94 : 6 hexane–isopropyl alcohol over 30 min) gave the *epoxide* **28** (71 mg, 59%) as a colourless oil, R_f 0.32 (15 : 85 EtOAc–petrol); retention time 25.1 min; (Found MNa^+ 359.1479. $C_{18}H_{24}O_6$ requires *M*Na, 359.1471); ν_{max}/cm^{-1} 2956, 1713, 1606, 1511, 1259, 1168, 1101, 1072; δ_H (300 MHz; $CDCl_3$) 8.06 (2H, d, *J* 8.9, Ar), 6.94 (2H, d, *J* 8.9, Ar), 5.32 (1H, t, *J* 1.7, 3-H), 5.05 (1H, d, *J* 3.2, 6-H), 3.98 (1H, ddd, *J* 9.1, 2.3 and 1.7, 2-H), 3.88 (3H, s, OCH_3), 3.51 (3H, s, OCH_3), 3.49 (1H, dd, *J* 3.8 and 1.7, 4-H), 3.44 (1H, dd, *J* 3.8 and 3.2, 5-H), 1.70–1.20 (6H, m, butyl) and 0.86 (3H, t, *J* 7.3, CH_3); δ_C (75 MHz; $CDCl_3$) 164.2 (Ar), 132.4 (Ar), 114.2 (Ar), 95.3 (6-C), 67.8 (3-C), 66.7 (2-C), 56.0 (OCH_3), 55.9 (OCH_3), 51.7 (4-C), 50.9 (5-H), 30.4, 28.2, 22.8 and 14.4; *m*/*z* (ES) 359 (100% M + Na^+).

Also obtained was the *epoxide* **29** (30 mg, 25%) as a colourless oil, R_f 0.32 (15 : 85 EtOAc–petrol); retention time 23.3 min; (Found MNa^+ 359.1472. $C_{18}H_{24}O_6$ requires *M*Na, 359.1471); ν_{max}/cm^{-1} 2956, 1713, 1606, 1511, 1259, 1168, 1101, 1072; δ_H (300 MHz; $CDCl_3$) 8.07 (2H, d, *J* 9.0, Ar), 6.93 (2H, d, *J* 9.0, Ar), 5.08 (1H, dd, *J* 5.3 and 3.2, 3-H), 4.98 (1H, d, *J* 0.4, 6-H), 3.91 (1H, dt, *J* 8.6 and 3.2, 2-H), 3.87 (3H, s, OCH_3), 3.75 (1H, dd, *J* 3.6 and 3.2, 4-H), 3.49 (3H, s, OCH_3) 3.15 (1H, dd, *J* 3.6 and 0.4, 5-H), 1.80–1.20 (6H, m, butyl) and 0.88 (3H, t, *J* 7.3, CH_3); δ_C (75 MHz; $CDCl_3$) 166.5 (C=O), 164.0 (Ar), 132.4 (Ar), 122.4 (Ar), 114.1 (Ar), 96.6 (6-C), 67.3 (3-C), 66.7 (2-C), 56.4 (OCH_3), 55.9 (OCH_3), 50.7 (4-C), 50.7 (5-C), 29.6, 28.3, 22.9 and 14.4; *m*/*z* (ES) 359 (100% M + Na^+).

(2*R**,3*R**,4*R**,5*S**,6*S**)-4,5-Diacetoxy-2-butyl-6-methoxytetrahydropyran-3-yl acetate 15e

The epoxide **27b** (12.4 mg, 36.9 μmol) was refluxed for 3 days under N_2 in aqueous KOH (20 mg in 3 ml of water). The solvent was removed under reduced pressure and the crude product was dissolved in acetic anhydride–pyridine (3 : 1, 3 ml) and stirred at room temperature for 4 h. The solvent was again removed under reduced pressure and the crude residue pre-absorbed onto silica gel and purified by flash chromatography, eluting with 15 : 85 EtOAc–petrol to give the *triacetate* **15e** (10.7 mg, 84%) as a colourless viscous syrup, R_f 0.23 (15 : 85 EtOAc–petrol); (Found MNa^+ 369.1529. $C_{16}H_{26}O_8$ requires *M*Na, 369.1529); ν_{max}/cm^{-1} 2956, 2924, 2856, 1748, 1263, 1371, 1249, 1223, 1050; δ_H (500 MHz; $CDCl_3$) 5.13 (1H, t, *J* 4.0, 4-H), 4.93 (1H, dd, *J* 8.8 and 4.0, 3-H), 4.89 (1H, dd, *J* 4.0 and 2.0, 5-H), 4.51 (1H, d, *J* 2.0, 6-H), 3.95 (1H, td, *J* 8.8 and 3.2, 2-H), 3.33 (3H, s, OCH_3), 2.05 (3H, s, OAc), 2.03 (3H, s, OAc), 1.98 (3H, s, OAc), 1.6–1.1 (6H, m, butyl) and 0.84 (3H, t, *J* 7.1, CH_3); δ_C (125 MHz; $CDCl_3$) 98.8 (6-C), 70.1, 69.3, 67.9, 67.2, 56.0 (OCH_3), 31.0 (OAc), 21.3 (OAc), 21.3 (OAc), 30.1, 27.8, 23.0 and 14.4 (CH_3); *m*/*z* (ES) 369 (100%, MNa^+).

Hydrolysis of the epoxide 28

The epoxide **28** (18.7 mg, 55.6 μmol) was refluxed for 3 days under N_2 in aqueous potassium hydroxide solution (2 ml of a 0.3 M solution). The solvent was removed under reduced pressure and the crude product was dissolved in acetic anhydride–pyridine mixture (3 : 1, 3 ml) and stirred at room temperature for 4 h. The solvent was again removed under reduced pressure and the crude residue was pre-absorbed onto silica gel and purified by flash chromatography, eluting with 15 : 85 EtOAc–petrol to give the *triacetate* **15b** (11.0 mg, 57%), as a colourless oil, R_f 0.26 (15 : 85 EtOAc–petrol); (Found : MNa 369.1517. $C_{16}H_{26}O_8$ requires *M*Na, 369.1525); ν_{max}/cm^{-1} 2957, 1750, 1372, 1250, 1224, 1045; δ_H (500 MHz; $CDCl_3$) 5.20 (1H, td, *J* 4.1 and $^4J_{HH}$ 0.7, 4-H), 5.16 (1H, t, *J* 4.1, 5-H), 4.92 (1H, dd, *J* 4.1 and 2.1, 3-H), 4.81 (1H, d, *J* 4.1, 6-H), 4.11 (1H, ddd, *J* 8.8, 4.1 and 2.1, 2-H), 2.15 (3H, s, OAc), 2.14 (3H, s, OAc), 2.08 (3H, s, OAc), 1.55–1.25 (6H, m, butyl) and 0.91 (3H, t, *J* 7.3, CH_3); δ_C (125 MHz; $CDCl_3$) 170.2 (C=O), 169.9 (C=O), 169.8 (C=O), 97.1 (6-C), 70.5, 67.0, 66.4, 65.4, 55.8, 29.6, 27.9, 22.6, 21.0, 20.9, 20.8 and 14.0; *m*/*z* (ES) 369 (100%, MNa^+).

Also obtained were the *triacetates* **15f** (2.9 mg, 15%) and **15d** (1.7 mg, 9%), spectroscopically identical to those obtained previously.

(2*R**,3*S**,4*R**,5*S**,6*S**)-4,5-Diacetoxy-2-butyl-6-methoxytetrahydropyran-3-yl acetate 15f

By the same general method, the epoxide **29** (12.7 mg, 37.8 μmol) gave a crude product which was pre-absorbed onto silica gel and purified by flash chromatography, eluting with 15 : 85 EtOAc–petrol to give the *triacetate* **15f** (9.0 mg, 69%), spectroscopically identical to that obtained previously.

(2*R**,3*R**,4*R**,5*S**,6*S**)-2-Butyl-5-iodo-6-methoxytetrahydropyran-3,4-diyl di(4-methoxybenzoate) 23

The diol **17** (31 mg, 66.8 μmol) and triethylamine (17 μl, 0.120 mmol, 1.8 equiv.) were stirred under N_2 in dichloromethane (1.1 ml) at room temperature and *p*-anisoyl chloride (11 μl, 80 μmol, 1.2 mol equiv.) was added *via* syringe. The resulting solution was treated with 4-(dimethylamino)pyridine (2 mg, 16 μmol) and stirred for 6 h. The solution was quenched with saturated aqueous sodium bicarbonate solution (5 ml) and diluted with dichloromethane (20 ml). The organic layer was separated and washed with a further portion of saturated sodium bicarbonate solution (2 × 5 ml) followed by a washing with brine (5 ml). The organic layer was dried ($MgSO_4$) and the solvent removed under reduced pressure. The crude residue was pre-absorbed onto silica gel and purified by flash chromatography, eluting with 1 : 9 EtOAc–petrol to give *diester* **23** (36.8 mg, 92%) as a colourless oil, R_f 0.42 (15 : 85 EtOAc–petrol); (Found MNa^+ 621.0961. $C_{16}H_{26}O_8$ requires *M*Na, 621.0946); ν_{max}/cm^{-1} 2961, 2871, 2840, 1720 (C=O), 1606, 1512, 1260, 1169, 1095, 1031; δ_H (300 MHz; $CDCl_3$) 7.97 (2H, d, *J* 8.9, Ar), 7.89 (2H, d, *J* 8.9, Ar), 6.91 (2H, d, *J* 8.9, Ar), 6.86 (2H, d, *J* 8.9, Ar), 5.64 (1H, dd, *J* 5.9 and 3.3, 4-H), 5.60 (1H, dd, *J* 7.1 and 3.3, 3-H), 5.02 (1H, d, *J* 3.6, 6-H), 4.42 (1H, dd, *J* 5.9 and 3.6, 5-H), 3.86 (3H, s, OCH_3), 3.84 (3H,s, OCH_3), 3.49 (3H, s, OCH_3), 4.30 (1H, td, *J* 7.1 and 2.1, 2-H), 1.8–1.2 (6H, m, butyl) and 0.91 (3H, t, *J* 7.1, CH_3); δ_C (75 MHz; $CDCl_3$) 165.5 (C=O), 165.4 (C=O), 164.0 (Ar), 132.4 (Ar), 132.0 (Ar), 122.4 (Ar), 122.3 (Ar), 114.1 (Ar), 114.0 (Ar), 102.2 (6-C), 72.0 (3-C), 70.1

(4-C), 69.4 (2-C), 56.5 (OCH_3), 55.9 (OCH_3), 30.8 (5-C), 27.9, 25.3, 23.0 and 14.5; *m/z* (ES) 621 (100%, MNa^+).

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