Desymmetrisation of *meso* difuryl alcohols, diols and their derivatives: complementary directed and undirected asymmetric dihydroxylation reactions

Robert Hodgson,[a] Tahir Majid[b] and Adam Nelson*[a]

[a] *School of Chemistry, University of Leeds, Leeds, UK LS2 9JT*
[b] *Aventis Pharma US, Route 202-206, Bridgewater, New Jersey 08807, USA*

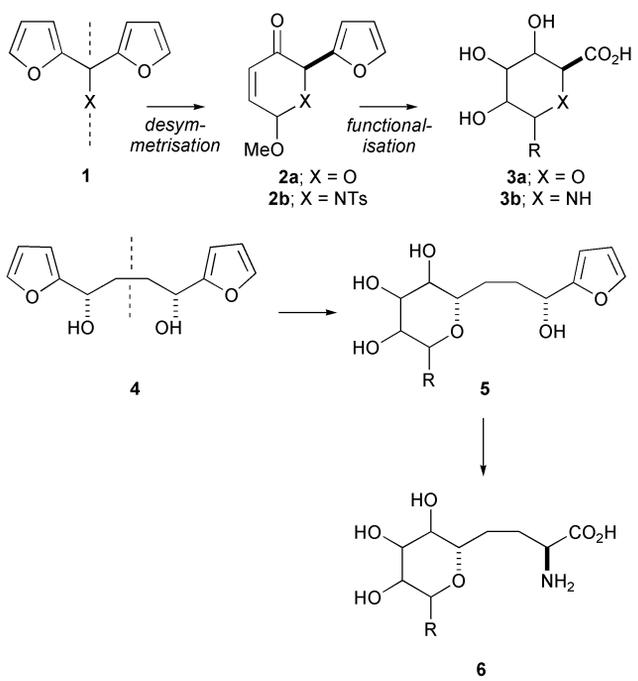
Received (in Cambridge, UK) 22nd May 2002, Accepted 31st May 2002
First published as an Advance Article on the web 27th June 2002

Asymmetric reactions (for example, asymmetric epoxidation and asymmetric dihydroxylation) were examined for the desymmetrisation of the *meso* substrates 1,1-difuran-2-ylmethanol, *N*-(1,1-difuran-2-ylmethyl)-4-methylbenzenesulfonamide, (*R*,*S*)-1,4-difuran-2-ylbutane-1,4-diol and the derivatives of these compounds. The complex OsO_4·(*S*,*S*)-S)-1,2-diphenyl-*N*,*N*′-bis(2,4,6-trimethylbenzyl)ethane-1,2-diamine was found to be an effective reagent for the desymmetrisation of *meso*-1,2-bis(3,6-dihydro-3-hydroxy-2*H*-pyran-2-yl)ethanes and the corresponding di-*p*-methoxybenzoates by asymmetric dihydroxylation. The stereochemical outcome of this process depends critically on the relative stereochemistry and substitution of the substrate, and can occur *anti* to, or be directed by, an allylic alcohol or *p*-methoxybenzoyloxy functional group.

Introduction

The enantioselective desymmetrisation of *meso* compounds is one of the most powerful strategies for asymmetric synthesis.[1] This strategy uses a chiral reagent to differentiate between enantiotopic functional groups in the starting material: provided that the discrimination between these groups is sufficiently effective, the products of the reaction may be obtained in excellent yield and with high enantiomeric excess.†

In this paper, we describe some methods for the desymmetrisation of *meso* difurans (for example **1** and **4**) and closely related derivatives of these compounds (Scheme 1). At the start of our investigation, we planned to differentiate between the enantiotopic rings of the difurans **1** using a chiral oxidising agent; we envisaged that the enantiomerically enriched products of the reaction, for example **2b**, might be of value in the synthesis of pipecolinic acid derivatives **3b**. Polyhydroxylated pipecolinic acid derivatives such as **3b** have value as potent and specific inhibitors of glycosidases.[3] Alternatively, desymmetrisation of the diol **4**, or one of its *meso* derivatives, was expected, after functionalisation, to give enantiomerically enriched functionalised tetrahydropyrans (THPs) **5**; these compounds might be intermediates in the synthesis of *C*-linked glycosyl amino acids[4] of general structure **6**.



Scheme 1

Results and discussion

Synthesis of *meso* starting materials

The difuryl alcohol[5] **8** and the difuryl sulfonamide **10** were synthesised by addition of 2-lithiofuran (**11**), prepared by lithiation of furan, to furfural (**7**) and its *N*-tosylimine[6] (**9**) respectively (Scheme 2).

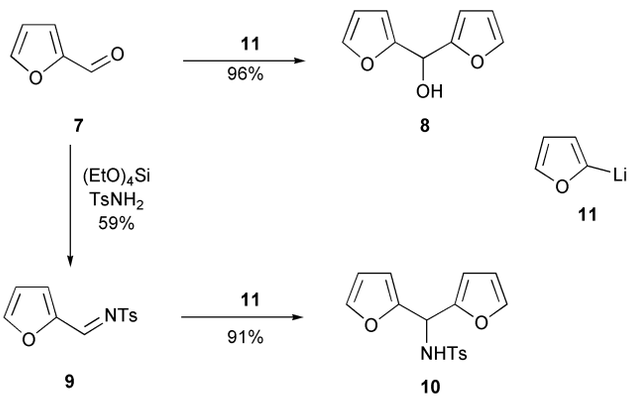
Treatment of a solution of the *meso* diol[7] **4** in dichloromethane with a 5.0 M solution of *tert*-butyl hydroperoxide in decane and catalytic vanadyl acetylacetonoate resulted in a double oxidative ring expansion[8] to give the insoluble dipyranone **14**. The dipyranone **14** was isolated by filtration of the reaction mixture and was obtained as a 75 : 25 mixture of *meso* and unsymmetrical isomers. We investigated the protection of the bis-hemiacetal **14** under two different reaction conditions. Treatment of **14** with trimethyl orthoformate and 20 mol% boron trifluoride in methanol gave the tricycle **15** as a mixture of diastereoisomers; in contrast, the same reaction in dichloromethane gave the required diacetals **12** as a 75 : 25 mixture of anomers in >98% yield, from which the required *meso* diastereoisomer could be crystallised in 52% yield (Scheme 3).

Luche reduction[9] of the dipyranone **12** (75 : 25 mixture of anomers) gave the diol **13** from which the required isomer

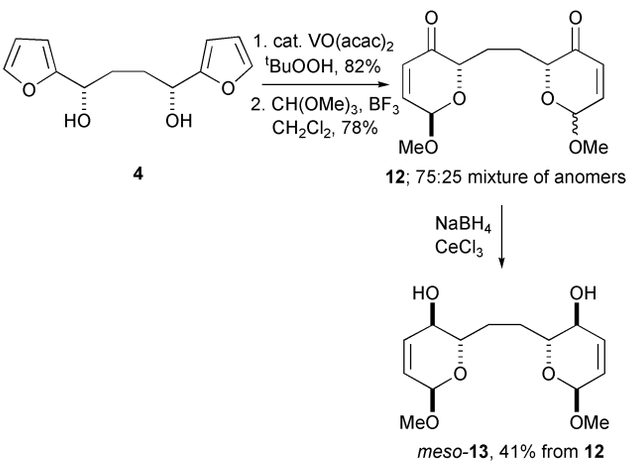
† In contrast, a classical resolution or kinetic resolution can only give up to a 50% yield of enantiomerically pure product. The efficiency of a *dynamic* kinetic resolution[2] can, however, approach that of a perfect enantioselective desymmetrisation reaction.

DOI: 10.1039/b204904j

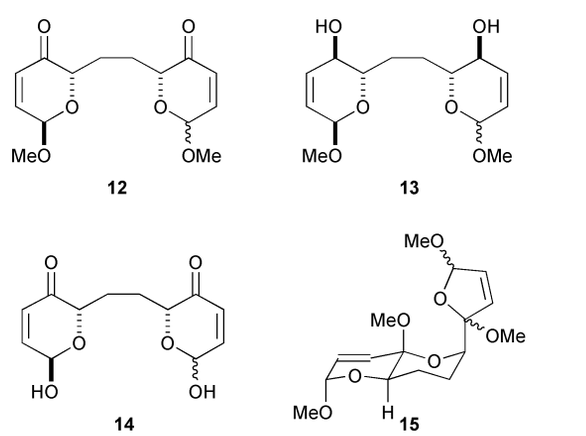
This journal is © The Royal Society of Chemistry 2002



Scheme 2

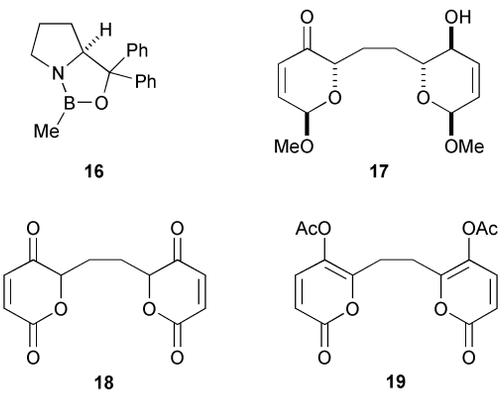


Scheme 3

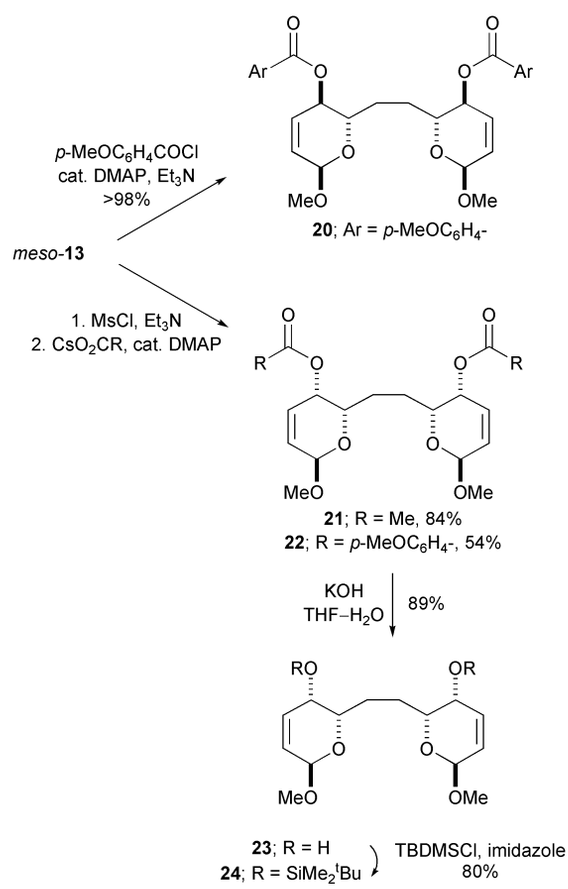


meso-**13** was obtained in 41% yield by crystallisation. In a separate experiment, Luche reduction of the dipyranone *meso*-**12** gave the diol *meso*-**13** in >98% yield. In the context of two-directional stereoselective functionalisation,[10] the isolation of *meso*-**13** in >98% yield as a >99 : 1 mixture of diastereoisomers must reflect a >99.5 : 0.5 diastereo- and regioselectivity for the reduction of each of the enones.

In an attempt to reverse the sense of diastereoselectivity of the reduction **12** ⟶ **13**, we screened a range of reducing agents in the reduction of *meso*-**12**; for example, CBS reduction (BH_3, 10 mol% **16**), conditions known to favour 1,2-reduction of enones,[11] gave the same *meso* diol **13** in 94% yield as well as the unsymmetrical hydroxyketone **17** (4% yield). Clearly the stereochemical control exerted by the substrate **12** overpowers the reagent control offered by the chiral catalyst. The enantiomeric excess of **17** was not determined. The Luche reduction of ketoesters similar to **18** is known to proceed with complementary (*syn*) stereoselectivity to the reductions of enones such as **12**.[12] Unfortunately, the dipyrandione **18**, synthesised by Jones' oxidation of **14**,[12] was extremely insoluble in most organic solvents, and attempted Luche reduction followed by *in situ* acetylation (Ac_2O, pyridine) gave mainly the dienol diacetate **19** (94% yield). In any case, **18** existed as a mixture of keto and enol tautomers, indicating that the valuable 1,4-*syn* stereochemical relationship present in **14** had not been preserved.



The diol *meso*-**13** was converted into other *meso* substrates for the desymmetrisation studies (Scheme 4). Most simply,



Scheme 4

meso-**13** was protected as its *p*-methoxybenzoyl diester **20**. In the other diastereomeric series, the diesters **21** and **22** were prepared by reaction of the corresponding dimesylate with caesium acetate (⟶ **21**) and caesium *p*-methoxybenzoate (⟶ **22**).[13] Hydrolysis of the diacetate **21** gave the diol **23** which was silylated to give the *tert*-butyldimethylsilyl ether **24**. The diol **23** was also prepared from *meso*-**13** in 36% yield by treatment of its dimesylate with potassium superoxide and 18-crown-6 in DMSO.[14]

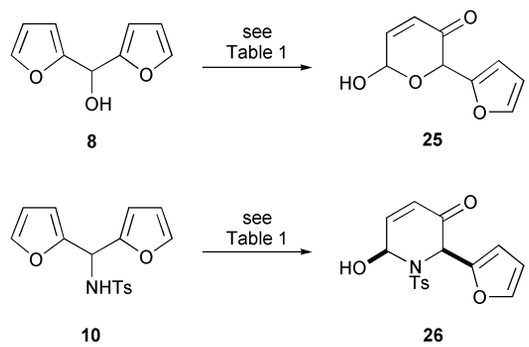
Table 1 Desymmetrisation of the difurans **8** and **10**

Entry	Starting material	Reaction conditions	Product	Yield (%)
1a	**8**	*m*-CPBA, CH_2Cl_2, 0 °C	**25**[a]	48
1b	**8**	NBS, NaOAc, THF–H_2O	**25**[a]	44
1c	**8**	Oxone, $NaHCO_3$, acetone–H_2O	–[b]	[c]
1d	**8**	(+)-DET[f], 3 Å molecular sieves, CH_2Cl_2, $Ti(O^iPr)_4$, ^{t}BuOOH	–[d]	–
2a	**10**	*m*-CPBA, CH_2Cl_2, 0 °C	**26**[e]	29
2b	**10**	NBS, NaOAc, THF–H_2O	**27**	50
2c	**10**	(+)-DET, 3 Å molecular sieves, CH_2Cl_2, $Ti(O^iPr)_4$, ^{t}BuOOH	–[d]	[c]

[a] Isolated as a 75 : 25 mixture of anomers. [b] Analysis of the crude reaction mixture by 300 MHz ^{1}H NMR showed that only starting material was present. [c] A quantitative yield of starting material was recovered. [d] Analysis of the crude reaction mixture by 300 MHz ^{1}H NMR showed that only the starting material and diethyl tartrate were present. [e] Analysis of the crude reaction mixture by 300 MHz ^{1}H NMR showed it consisted of a 47 : 53 mixture of the pyranone **26** and the pyridine **27**. [f] DET = diethyl tartrate.

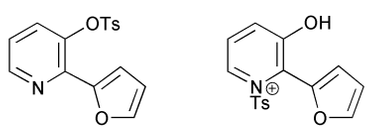
Investigations into desymmetrisations by Sharpless asymmetric oxidation

At the outset of our synthetic studies, we investigated the desymmetrisation of the difurans **8** and **10** (Scheme 5); our



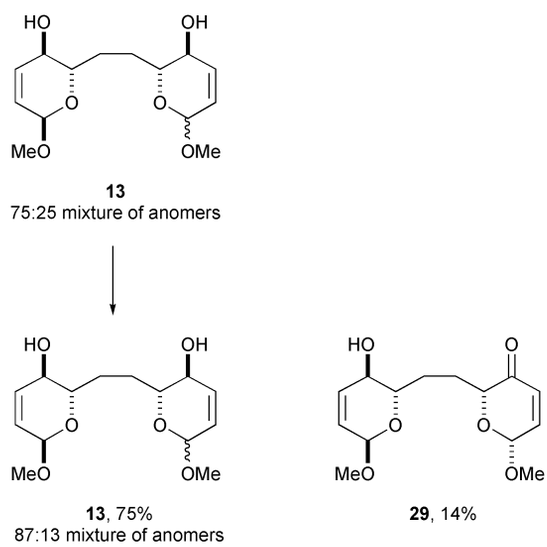
Scheme 5

results are summarised in Table 1. In the first instance, the difuryl alcohol **8** and the difuryl sulfonamide **10** were reacted with achiral oxidants (entries 1a–c and 2a–b, Table 1). Treatment of **8** and **10** with *m*-CPBA gave the expected products **25** and **26**, albeit in poor yield. The sensitivity of the piperidinone product **26** to the reaction conditions was revealed by the observation of the unexpected byproduct **27** (entries 1a and 2a, Table 1). In an attempt to optimise the yield of the reaction, **8** and **10** were reacted under alternative reaction conditions using *N*-bromosuccinimide as the oxidant: this modification did not improve the yield of the pyranone **25** and, in fact, the yield of the unexpected byproduct **27** was increased. We account for the formation of the pyridine **27** by aromatisation of the piperidinone **26** to give the pyridinium derivative **28**, a compound which is analogous to the acylated DMAP complexes[15] which are intermediates in many acylation reactions; intermolecular $N \longrightarrow O$ transfer of the tolylsulfonyl group would give the aryl tosylate **27**. Recently, a related ring expansion has been reported in which 2-acylfurans are converted into the corresponding 3-hydroxypyridines.[5]



An important extension of the Sharpless asymmetric epoxidation has been its exploitation in the kinetic resolution of α-(2-furyl) alcohols[16] and α-(2-furyl) *N*-tosylsulfonamides[17] by oxidative ring expansion. However, attempted desymmetrisation of the difurans **8** and **10** under conditions which have previously been used for similar oxidative ring expansions was not successful; some representative experiments are shown in Table 1 (entries 1d and 2c).

An alternative strategy was to delay the key desymmetrisation step to a later stage, again using the Sharpless asymmetric epoxidation reaction to induce asymmetry (Scheme 6). This



Scheme 6

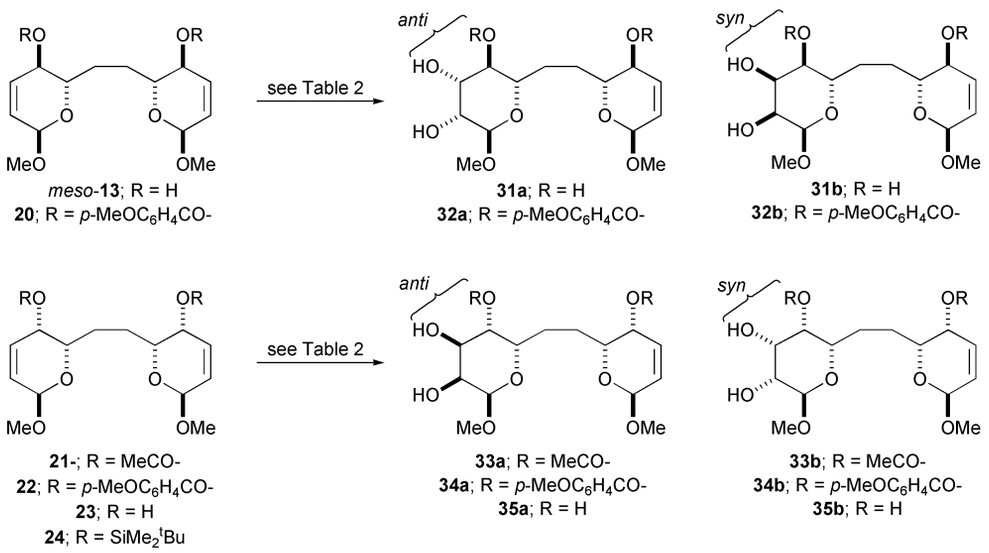
approach has previously been exploited in the desymmetrisation of complex *meso* bis-allylic alcohols.[18] Accordingly, a 75 : 25 mixture of *meso* and unsymmetrical diols **13** was reacted under standard Sharpless asymmetric epoxidation conditions (Scheme 6).[19] After 9 days reaction, a 14% yield of the enone **29** was isolated as a single anomer together with 75% recovered starting material (87 : 13 mixture of anomers). The hydroxy ketone **29** was, however, shown to have >90% ee by conversion into the corresponding (*R*)-Mosher's ester **30**. The sluggish nature of the oxidation reaction was not surprising in view of earlier studies involving cyclohexenols,‡ particularly since **13**'s hydroxy groups are conformationally locked in *pseudo* equatorial positions and are unable to direct the epoxidation reagent. The enantio- and diastereoselectivity of the process **13** $\longrightarrow$ **29** are, however, remarkable. The relative configurations of the anomeric centres completely control which ring is oxidised: *meso*-**13** was essentially inert to the reaction conditions and the ring of the unsymmetrical diastereoisomer with the same relative stereochemistry as *meso*-**13** did not react either. This reaction is a kinetic resolution of the unsymmetrical diastereoisomer **13** and, in fact, the reaction must be highly enantioselective: one of the enantiomers is much more reactive, and is

‡ Previous studies have shown substituted cyclohexen-2-ols to be only poor or moderate substrates in Sharpless kinetic resolution reactions.[20]

Table 2 Desymmetrisation of the dienes *meso*-**13** and **20**–**24** by asymmetric dihydroxylation

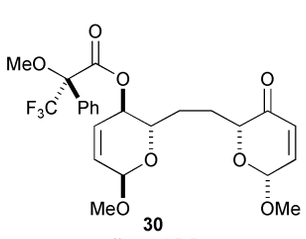
Entry	Starting material	Conditions[a]	Reaction time/days	Product(s)	Diastereomer ratio[b] *anti* : *syn*	Yield (%)	Ee (%)
1	**20**	AD-mix β, ^{t}BuOH–H_2O, $MeSO_2NH_2$	6	**32a**–**b**	60 : 40	12[c] (31[d])	[f]
2a	**20**	$K_3Fe(CN)_6$, 1.0 mol% $OsCl_3$, 2.0 mol% **36**, $MeSO_2NH_2$, ^{t}BuOH–H_2O	7	**32a**,[e] **32b**[f]	85 : 15	17[c] (40[d])	38[g]
2b	**22**	$K_3Fe(CN)_6$, 1.0 mol% $OsCl_3$, 2.0 mol% **36**, $MeSO_2NH_2$, ^{t}BuOH–H_2O	6	**34a**–**b**[f]	75 : 25	16[c] (57[d])	[f]
3a	**20**	OsO_4, **37**, CH_2Cl_2	4	***ent*-32a**[e]	>95 : 5	75[h]	50[g]
3b	**20**	OsO_4, **37**, CH_2Cl_2, −20 ⟶ 25 °C	2	***ent*-32a**[e]	>95 : 5	84[h]	60[g,i]
3c	**22**	OsO_4, **37**, CH_2Cl_2, −20 ⟶ 25 °C	6	**34b**	<5 : 95	34 (71[d])	40[i]
4	**21**	OsO_4, **37**, CH_2Cl_2, −20 ⟶ 25 °C	6	**23**	–	60	[j]
5	**24**	OsO_4, **37**, CH_2Cl_2, −20 ⟶ 25 °C	6	*k*	–	–	–
6a	*meso*-**13**	1. OsO_4, **37**, CH_2Cl_2, −20 ⟶ 25 °C; 2. Ac_2O, pyridine	4	**39**	–	40[h,l] (73[m])	[j]
6b	**23**	1. OsO_4, **37**, CH_2Cl_2, −20 ⟶ 25 °C; 2. Ac_2O, pyridine	6	**40**	<5 : 95	39 (87[d])	93[i]

[a] Reactions conducted at room temperature unless otherwise indicated. [b] Crude ratio determined by 300 MHz ^{1}H NMR spectroscopy. [c] Combined yield of mixture of diastereoisomers. [d] Yield based on recovered starting material. [e] The absolute configuration of **32a** was deduced by comparing the 500 MHz ^{1}H NMR spectra of its (*R*)- and (*S*)-Mosher diesters with those of the optically active diol **41**. [f] Absolute configuration and enantiomeric excess not determined. [g] Determined by conversion into the corresponding (*R*)-Mosher's esters. [h] Yield of single compound. [i] Determined by analytical chiral HPLC. [j] Product(s) not chiral. [k] No reaction. [l] **38** was isolated in 45% yield. [m] Yield based on isolated acetylated starting material **38**.



Scheme 7

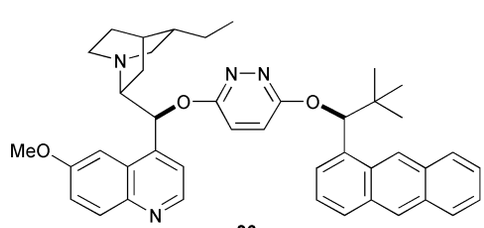
almost completely consumed in its conversion into the hydroxy ketone **29** (which had >90% ee). Similar oxidations have been observed in other conformationally locked systems,[21] though the enantioselectivity of this process has not been previously studied.



30
dias. >95:5

Desymmetrisation by asymmetric dihydroxylation

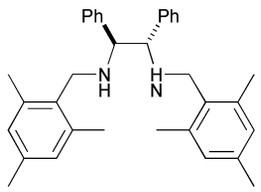
Initial investigations focussed on the desymmetrisation of the *meso* diester **20** by Sharpless asymmetric dihydroxylation (Scheme 7). Protected cyclohexanols, whose kinetic resolutions raise similar issues of diastereo- and enantioselectivity, have proved to be challenging substrates for AD catalysts.[22] Asymmetric dihydroxylation of **20** using AD-mix β was extremely sluggish, and gave a poor yield of the corresponding diols **32** as a 60 : 40 mixture of diastereoisomers (entry 1, Table 2). Results obtained using the ligand **36**, which was designed by Corey specifically for the asymmetric dihydroxylation of allylic *p*-methoxybenzoates,[23] were barely more promising (entries 2a–b): although the dihydroxylations of **20** and **22** were reasonably *anti* diastereoselective, the yield and enantioselectivity of these processes were poor. In each case, dihydroxylation occurred predominantly *anti* to the *p*-methoxybenzoyloxy group, regardless of whether it adopted a *pseudo*-equatorial (as in **20**) or a *psuedo*-axial orientation (as in **22**).



36

The most promising ligand for the dihydroxylation of the *meso*-bis(allylic-*p*-methoxybenzoate) **20** was the C_2-symmetric diamine[24] (*S*,*S*)**-37** which was also introduced by Corey (entries 3a–b, Table 2).[25] Hence, treatment of **20** with OsO_4·**37** led to complete consumption of the starting material and gave the desymmetrised diol ***ent*-32a** as a single diastereoisomer in

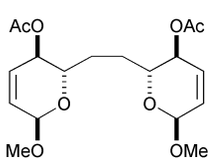
75% yield with 50% ee. The yield and enantioselectivity of the process were improved by performing the reaction at −20 °C; under these reaction conditions, the diol *ent*-**32a** was obtained in 84% yield with 60% ee. The improvement in yield may stem from suppression of competitive aminolysis of the ester (see the reaction of the diacetate **21**, entry 4, Table 2).



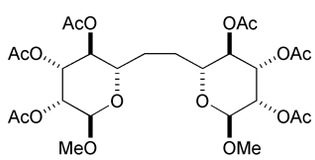
37

The desymmetrisation of the diastereomeric compound **22**, with its *pseudo*-axial *p*-methoxybenzoates, was also studied (entry 3c, Table 2). Treatment of **22** with OsO_4·**37** was *syn* selective (**34b** : **34a** >95 : 5), and gave the diol **34b** in 71% yield based on recovered starting material. The relative stereochemistry of **34b** was determined by comparison of its ^{1}H NMR spectrum with similar model compounds of known configuration.[26] Other Lewis basic groups have been shown to direct osmylations by delivery of osmium tetraoxide.[27] Remarkably, **34b** was isolated with 40% ee. The non-innocent role of the *p*-methoxybenzoyloxy group in the dihydroxylation of **22** is underlined by the unreactive nature of the corresponding *tert*-butyldimethylsilyl ether **24** (entry 5).

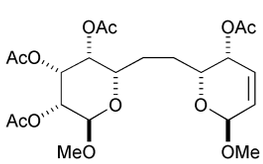
In an attempt to improve the enantioselectivity of the reaction, the desymmetrisations of the diols *meso*-**13** and **23** were investigated (entries 6a and b, Table 2). The dihydroxylation of similar compounds which, like **23**, have *pseudo*-axial allylic hydroxy groups can be controlled by delivery[28] of OsO_4·TMEDA to the double bond.[7] Similarly, the dihydroxylation of **23** with OsO_4·**37** was highly *syn* selective, and gave, after peracetylation, the tetraacetate **40** with 93% ee (87% yield based on recovered starting material). Reaction of the diol *meso*-**13** with one equivalent of OsO_4·**37** gave, after acetylation, the doubly dihydroxylated *meso* product **39** (40% yield) and the acetylated starting material **38** (45% yield). In view of the reactions of similar allylic alcohols with OsO_4·TMEDA complex,[7] it is not surprising that this dihydroxylation was not directed by the *pseudo*equatorial hydroxy group; the fact the second of the dihydroxylations leading to **39** was faster than the first – reflected in the isolation of similar yields of **38** and **39**, but none of the desymmetrised product – is, however, remarkable.



38



39



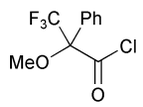
40

Determination and rationalisation of the sense of enantiostereoselectivity of desymmetrisations by asymmetric dihydroxylation

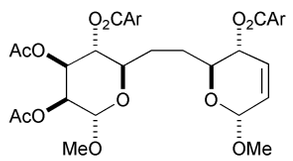
The enantiomeric excess of the diol *ent*-**32a** was determined in two independent ways. The diol *ent*-**32a** was converted into the corresponding (*S*)-Mosher's esters by acylation with (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (*R*)-**46**,[29]

Table 3 Chemical shifts of protons in the Mosher's diesters **42**–**45**

Compound	δ, 2-H	δ, 3-H	δ, 4-H	δ, 5-H	δ, 6-H
42	3.83	5.38	5.85	5.39	4.65
43	3.88	5.33	5.88	5.48	4.85
44	3.86	5.28	5.89	5.48	4.79
45	3.86	5.37	5.86	5.38	4.60



46

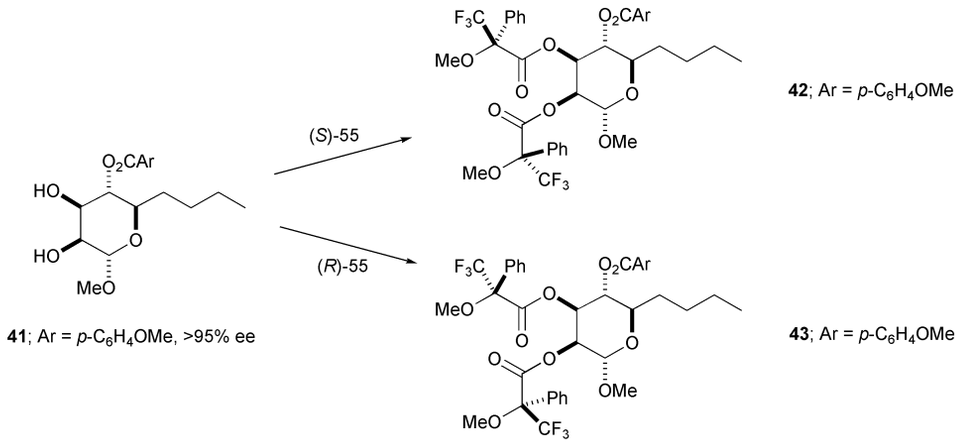


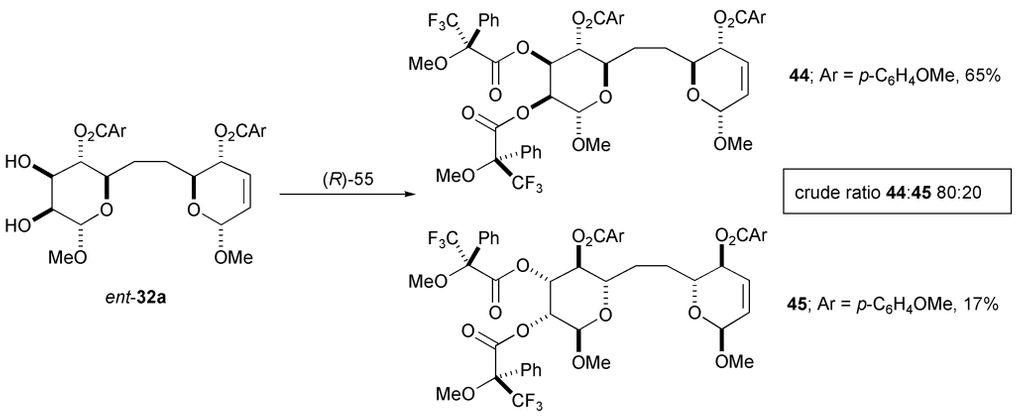
47

and the ratio of the products **44**–**45** was determined by HPLC (Scheme 8). Alternatively, the enantiomeric excess of the diacetate **47**, synthesised by acetylation of *ent*-**32a** (>98% yield) could be determined directly by chiral analytical HPLC. The absolute configuration of a sample of *ent*-**32a** (which had 60% ee) was determined by comparing the 500 MHz ^{1}H NMR spectra of the Mosher's esters **44** and **45** with the (*R*)- and (*S*)-Mosher's esters (**42** and **43** respectively) prepared from the known diol[26] **41**. Careful comparison of the chemical shifts of the protons in the acylated rings of these compounds revealed the pairs of Mosher's esters which had the same relative stereochemistry: **42** and **45** had the same relative stereochemistry as each other, as did the esters **43** and **44** (see Table 3).

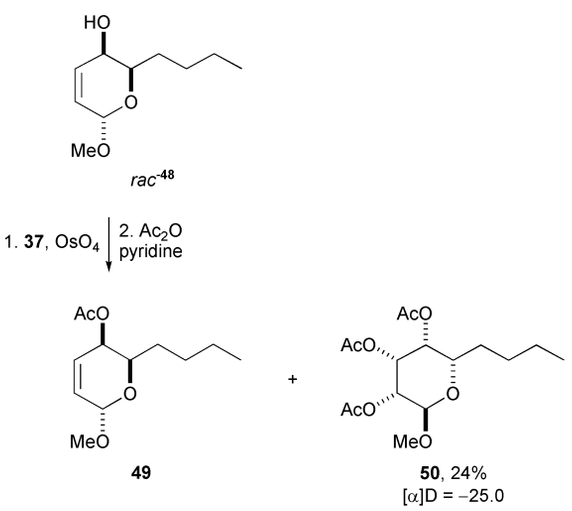
The enantiomeric excess of the tetraacetate **40** was also determined by chiral HPLC, but its absolute stereochemistry was harder to deduce. The kinetic resolution (Scheme 9) of the alcohol **48** was expected to probe similar issues of stereoselectivity to those raised in the desymmetrisation of **23** (entry 6b, Table 2): the absolute and relative stereochemistry of each of the enantiomers of **48** are the same as those found in each of the rings of the *meso* diol **23**. In practise, the reaction of the racemic alcohol **48** with the complex OsO_4·**37** was, like the desymmetrisation of **23**, a rather sluggish reaction. Furthermore, the enantiomers of **48** were, like the enantiotopic rings of **23**, efficiently differentiated by the chiral reagent and the relative stereochemistry of the products was the same: the kinetic resolution was highly enantioselective giving, after acetylation, the triacetate **50** {$[a]_D^{20}$ −25.0 (*c* 0.12 in $CHCl_3$)} in which the reagent had been delivered to same face of the reacting alkene as the allylic hydroxy group (Scheme 9). The triacetate **50** was the enantiomer of a sample of known absolute configuration {which had $[a]_D^{20}$ +30.0 (*c* 0.44 in $CHCl_3$), >95% ee}.[26] We propose, therefore, that the sense of the asymmetry induced in the desymmetrisation **23** ⟶ **35b** is the same (as drawn) as that observed in the kinetic resolution of **48**.

The diastereoselectivity of the desymmetrisation of **20** (⟶ *ent*-**32a**; entry 3b, Table 2) by the complex OsO_4·**37** concurs with previous investigations into the stereoselectivity of osmoylation of allylic alcohol derivatives,[30] and this natural selectivity may be reinforced by the presence of an axial methoxy group. Houk[31] and Corey[32] have proposed models to explain the enantioselectivity of dihydroxylation reactions involving chiral amine–osmium tetraoxide complexes. The enantioselectivity of the dihydroxylation **20** ⟶ *ent*-**32a** may be explained in terms of Houk's model in which the equatorial oxygens attack the alkene, and the two mesityl groups (Ar′ = mesityl) relay chiral information to the substrate (Fig. 1). The desymmetrisation of **23** (⟶ **35b**; entry 6b, Table 2), like the reactions of similar compounds with OsO_4·TMEDA,[7,26] is *syn* selective, and it is probable that the complex OsO_4·**37** is delivered to the reacting alkene by hydrogen bonding to the neighbouring hydroxy group (Fig. 2). This effect may further define the transition state for the asymmetric dihydroxylation





Scheme 8



Scheme 9

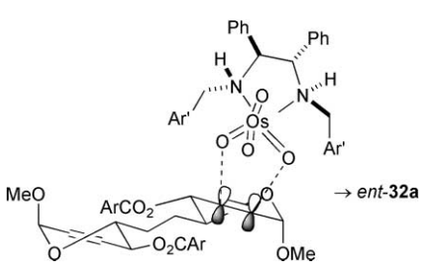


Fig. 1

reaction, thereby enhancing the transfer of stereochemical information between the reactants. We believe that this reaction is the first example of a directed asymmetric dihydroxylation.

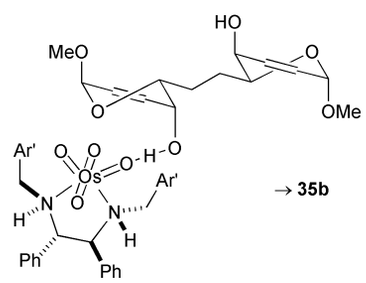


Fig. 2

Conclusions

The complex OsO_4·**37** was found to be an effective reagent for the enantioselective desymmetrisation of *meso* highly functionalised di-DHPs, and the stereochemical outcome of the dihydroxylation process depended critically on the stereochemistry and substitution of the starting material. For example, the di-DHP **20**, with its *pseudo* equatorial *p*-methoxybenzoyloxy groups was converted into the diol *ent*-**32a** (60% ee) in which dihydroxylation had occurred *anti* to the ester groups. In contrast, the asymmetric dihydroxylation of the *meso* diol **23** was directed by one of the enantiotopic *pseudo* axial hydroxy groups to give, after peracetylation, the tetraacetate **40** in 93% ee.

Experimental

General methods have been described previously.[26] Preparative and analytical HPLC were conducted on a Gynkotek HPLC system with diode array detection; unless otherwise stated, the column oven was set at 24 °C. Econosil columns (silica particle size: 10 μm) were used for preparative (22 × 250 mm) and analytical (4.6 × 250 mm) work, and Chiracel OD column

(4.6 × 250 mm) was used for chiral analytical HPLC. Microanalyses were carried out by staff of the Department of Chemistry using a Carlo Erba 1106 automatic analyser.

1,1-Difuran-2-ylmethanol 8

Furan (2.61 ml, 36.6 mmol) and THF (60 ml) were stirred at 0 °C under N_2 and *n*-butyllithium (22.9 ml of a 1.6 mol solution in hexanes, 36.6 mmol) was slowly added over 10 min, and the reaction was stirred for 1 h at 0 °C, added slowly by cannulation to a stirred solution of furfural (2.52 ml, 30.5 mmol) in THF (50 ml) at −78 °C, under N_2. The reaction was stirred for an additional 1 h before warming to room temperature. The reaction mixture was quenched with saturated aqueous ammonium chloride solution (100 ml), the layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 75 ml). The combined organic extracts were washed with brine (50 ml), dried ($MgSO_4$) and evaporated under reduced pressure to give the alcohol[5] **8** (4.82 g, 96%) as a pale yellow oil, R_f 0.20 (20 : 80 EtOAc–petrol) (Found: C, 66.0; H, 4.75; $C_9H_8O_3$ requires C, 65.9; H, 4.90%); ν_{max}/cm^{-1} (film) 3421 (O–H), 1644, 1144 and 1010; δ_H (300 MHz; $CDCl_3$) 7.42 (2H, dd, *J* 1.6 and $^4J_{HH}$ 0.7, furyl 5-H), 6.37 (2H, dd, *J* 3.3 and 1.6, furyl 4-H), 6.32 (2H, dd, *J* 3.3 and $^4J_{HH}$ 0.7, furyl 3-H), 5.83 (1H, d, *J* 5.5, 1-H) and 2.63 (1H, d, *J* 5.5, OH); δ_C (75 MHz; $CDCl_3$) 153.6 (furyl 2-C), 143.0 (furyl 3-C), 110.8 (furyl), 108.1(furyl) and 64.5 (1-C); *m*/*z* (EI) 164 (14%, M^+), 147 (100, M − OH) and 91(19).

N-Furan-2-ylmethylene-4-methylbenzenesulfonamide 9

Furfural (6.03 ml, 72.9 mmol), tetraethyl orthosilicate (17.22 ml, 77.0 mmol) and toluene-*p*-sulfonamide (12.46 g, 72.9 mmol) were heated under N_2 for 30 min at 170 °C, and then ethanol was removed by distillation. After 6 h the reaction mixture was allowed to cool to room temperature, dissolved in warm ethyl acetate (210 ml), petrol (700 ml) added, the solution was left for 24 h and the solid residue was recrystallized from EtOAc–hexane to give the *sulfonamide* **9** (10.77 g, 59%) as light yellow needles, mp 100.7–102.8 °C (from EtOAc–hexane); R_f 0.51 (1 : 1 EtOAc–petrol) (Found: C, 57.8; H, 4.40; N, 5.4 and S, 12.8; $C_{12}H_{11}NO_3S$ requires C, 57.8; H, 5.60 and S, 12.9%); ν_{max}/cm^{-1} ($CHCl_3$ solution) 1651, 1609 (C=C, C=N), 1541, 1315, 1290, 1155 and 1146; δ_H (300 MHz; $CDCl_3$) 8.82 (1H, s, N=CH), 7.88 (2H, d, *J* 8.0, 2-H and 6-H), 7.75 (1H, dd, *J* 1.7 and $^4J_{HH}$ 0.9, furyl 5-H), 7.34 (2H, d, *J* 8.0, 3-H and 5-H), 7.33 (1H, dd, *J* 4.0 and $^4J_{HH}$ 0.9, furyl 3-H), 6.65 (1H, dd, *J* 4.0 and 1.7, furyl 4-H), 2.43 (3H, s, Me); δ_C (75 MHz; $CDCl_3$) 156.0, 150.1, 145.0, 130.2, 128.5, 114.1 (furyl 4-C) and 22.1; *m*/*z* (EI) 249 (6%, M^+), 155 (23, $SO_2C_6H_4CH_3^+$), 91 (100, $C_7H_7^+$) and 39 (47, $C_3H_3^+$).

N-(1,1-Difuran-2-ylmethyl)-4-methylbenzenesulfonamide 10

n-Butyllithium (20.5 ml of a 1.6 mol solution in hexanes, 32.8 mmol) was slowly added to a stirred solution of furan (2.20 ml, 30.3 mmol) in THF (50 ml) at −5 °C over 10 min. This reaction mixture was stirred for 1 h at −5 °C, and then added slowly by cannulation to a stirred solution of sulfonamide **9** (6.28 g, 25.3 mmol) in THF (60 ml) at −78 °C. The reaction mixture was stirred for 1 h, warmed slowly to room temperature, and quenched with saturated aqueous ammonium chloride solution (100 ml), the layers separated and the aqueous layer was extracted with ethyl acetate (4 × 100 ml). The combined organic extracts were washed with brine (50 ml), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which was purified by recrystallization from EtOAc–hexane to give the *difurylsulfonamide* **10** (7.27 g, 91%) as light brown fine needles, mp 175.4–176.9 (from EtOAc–hexane); R_f 0.72 (1 : 1 EtOAc–petrol) (Found: C, 60.4; H, 4.80; N 4.45 and S, 10.1; $C_{16}H_{15}NO_4S$ requires C, 60.5; H, 4.75; N, 4.4 and S, 10.1%); ν_{max}/cm^{-1} ($CHCl_3$ solution) 3401 (N–H), 1656, 1651, 1634, 1328, 1150 and 1074; δ_H (300 MHz; $CDCl_3$) 7.61 (2H, dd, *J* 8.4 and $^4J_{HH}$ 0.5, 2-H and 6-H), 7.25 (2H, dd, *J* 1.9 and $^4J_{HH}$ 1.2, furyl 5-H), 7.19 (2H, dd, *J* 8.4 and $^4J_{HH}$ 0.5, 3-H and 5-H), 6.23 (2H, dd, *J* 3.3 and 1.9, furyl 4-H), 6.11 (2H, dd, *J* 3.3 and $^4J_{HH}$ 1.2, furyl 3-H), 5.72 (1H, d, *J* 8.3, CHN), 5.21 (1H, d, *J* 8.3, NH) and 2.39 (3H, s, Me); δ_C (75 MHz; $CDCl_3$) 150.5 (furyl 2-C), 143.1 (furyl 5-C), 129.8 (2-C and 6-C), 127.4 (3-C and 5-C), 110.8 (furyl), 108.7 (furyl), 77.6, 50.0 (CHN) and 21.9 (Me); *m*/*z* (EI) 317 (8%, M^+), 250 (34), 178 (47), 162 (100), 147 (67) and 91(56).

(2*R*)-2-{2-[(2*S*)-6-Hydroxy-3-oxo-3,6-dihydro-2*H*-pyran-2-yl]-ethyl}-6-hydroxy-3,6-dihydro-2*H*-pyran-3-one 14

tert-Butyl hydroperoxide (6.45 mmol, 1.29 ml as a 5 M solution in decane) was added slowly to a stirred solution of the diol[7,25] **4** (570 mg, 2.57 mmol) and vanadyl acetylacetonate (10 mg, 37.74 μmol) in dichloromethane (10 ml) at room temperature. The reaction mixture was stirred for 7 h, and the heavy suspension filtered and washed with chloroform (5 ml) and dried under reduced pressure to give the *dipyranone* **14** (581 mg, 89%; 75 : 25 mixture of diastereoisomers) as a colourless powder, mp > 260 °C (from dichloromethane); R_f 0.35 (72 : 28 EtOAc–petrol) (Found: C, 56.5; H, 5.60; $C_{12}H_{14}O_6$ requires C, 56.7; H, 5.55%); ν_{max}/cm^{-1} ($CHCl_3$ solution) 3360 (O–H), 2977, 2892, 1674, 1455, 1194 and 1072; δ_H (300 MHz; DMSO-d_6) 7.28 (2H, d, *J* 7.3, OH^{min}), 7.05 (2H, dd, *J* 10.3 and 3.5, 5-H^{maj}), 7.05 (2H, dd, *J* 10.2 and 1.5, 5-H^{min}), 6.96 (2H, d, *J* 6.6, OH^{maj}), 6.06 (2H, dd, *J* 10.2 and $^4J_{HH}$ 1.4, 4-H^{min}), 6.00 (2H, d, *J* 10.3, 4-H^{maj}), 5.56 (2H, dd, *J* 7.3 and 1.5, 6-H^{min}), 5.48 (2H, dd, *J* 6.6 and 3.5, 6-H^{maj}), 4.44 (2H, dd, *J* 7.7and 2.8, 2-H^{maj}), 4.15 (2H, m, broad, 2-H^{min}), 1.99–1.91 (2H, m, CH_aH_b) and 1.65–1.59 (2H, m, CH_aH_b); δ_C(75 MHz; DMSO-d_6) 197.2 (3-C^{maj}), 197.9 (3-C^{min}), 151.8 (5-C^{min}), 148.2 (5-C^{maj}), 127.8 (4-C^{min}), 126.0 (4-C^{maj}), 90.9 (6-C^{min}), 87.0 (6-C^{maj}), 77.9 (2-C^{min}), 73.3 (2-C^{maj}), 26.2 (CH_2^{min}) and 25.6 (CH_2^{maj}); *m*/*z* (EI) 236 (7%, M^+ − CO), 151 (30), 123 (30), 110 (26), 95 (80), 85 (86), 84 (63), 55 (100) and 44 (63).

(2*R*,6*S*)-2-{2-[(2*S*,6*R*)-6-Methoxy-3-oxo-3,6-dihydro-2*H*-pyran-2-yl]ethyl}-6-methoxy-3,6-dihydro-2*H*-pyran-3-one 12

Boron trifluoride–diethyl ether (3 μl, 10 mol%, 0.022 mmol) was added to a stirred solution of the dipyranone **14** (57 mg, 0.224 mmol) and trimethyl orthoformate (61 μl, 0.56 mmol) in dichloromethane (2 ml) at room temperature. The reaction mixture was stirred until TLC indicated the reaction to be complete, quenched with saturated aqueous sodium bicarbonate (2 ml) and stirred for a further 10 min. The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 2 ml), the combined organic was extracted, dried ($MgSO_4$) and evaporated under reduced pressure to give the *diacetal* **12** which was purified by flash chromatography, eluting with 3 : 7 EtOAc–petrol to give the product (62.4 mg, >98%; 75 : 25 mixture of diastereoisomers) as fine colourless needles, mp 152.6–154.2 °C (from EtOAc–petrol); R_f 0.32 (3 : 7 EtOAc–petrol) (Found: 305.0993; $C_{14}H_{18}O_6$ requires [*M* + Na], 305.1001); ν_{max}/cm^{-1} ($CHCl_3$ solution) 2936, 1694m (C=O), 1456, 1393, 1254, 1192, 1049; δ_H (300 MHz; $CDCl_3$) 6.83 (2H, dd, *J* 10.2 and 0.9, 5-H^{min}), 6.84 (2H, dd, *J* 10.2 and 3.4, 5-H^{maj}), 6.14 (2H, dd, *J* 10.3 and 1.6, 4-H^{min}), 6.09 (2H, d, *J* 10.2, 4-H^{maj}), 5.25 (2H, d, *J* 0.9, 6-H^{min}), 5.12 (2H, d, *J* 3.4, 6-H^{maj}), 4.46 (2H, dd, *J* 8.3 and 2.7, 2-H^{maj}), 4.10 (2H, dd, *J* 9.0 and 2.6, 2-H^{min}), 3.59 (3H, s, $-OCH_3^{min}$), 3.58 (3H, s, $-OCH_3^{min}$), 3.53 (3H, s, $-OCH_3^{maj}$), 3.52 (3H, s, $-OCH_3^{maj}$), 2.30–2.18 (2H, m, CH_aH_b) and 1.91–1.74 (2H, m, CH_aH_b); δ_C (75 MHz; $CDCl_3$) 196.6 (3-C^{maj}), 196.4 (3-C^{min}), 147.0 (5-C^{min}), 143.7 (5-C^{maj}), 129.0 (4-C^{min}), 128.0 (4-C^{maj}), 97.2 (6-C^{min}), 94.4 (6-C^{maj}), 79.3 (C^{maj}), 79.2 (C^{min}), 74.2 (C^{maj}), 74.2 (C^{min}), 57.0 (OCH_3^{maj}), 56.9, 57.0 (OCH_3^{min}), 27.6 (CH_2^{min}) and 27.4 (CH_2^{maj}); *m*/*z* 251 (3%), 219 (5), 98 (100) and 83 (25); *m*/*z* 305 (ES) (100%, MNa^+).

2-(2,5-Dimethoxy-2,5-dihydrofuran-2-yl)-6,8a-dimethoxy-2,3,4,4a,6,8a-hexahydropyrano[3,2-*b*]pyran 15

Boron trifluoride–diethyl ether (20 μl, 0.162 mmol) was added to a stirred solution of the dipyranone **14** (206 mg, 0.811 mmol), trimethyl orthoformate (355 μl, 3.244 mmol) and 3 Å molecular seives (0.2 g) in methanol (2 ml) at room temperature. The solution was stirred for 72 h and then quenched with saturated aqueous sodium bicarbonate (2 ml). Excess methanol was removed under reduced pressure and the slurry diluted with water (4 ml) and extracted with chloroform (4 × 5 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which was purified by flash chromatography, eluting with 3 : 7 EtOAc–petrol to give the *pyrano[3,2-b]pyran* **15** (263 mg, >98%; 50 : 50 mixture of diastereoisomers) as a colourless oil, R_f 0.35 (3 : 7 EtOAc–petrol); ν_{max}/cm^{-1} ($CHCl_3$ solution) 2937, 1455, 1104, 1060 and 1019; δ_H (300 MHz; $CDCl_3$) 6.07 (1H, d, *J* 10.4, 3-H), 6.02 (1H, dd, *J* 10.4 and $^4J_{HH}$ 1.4, 3-H), 6.00 (1H, unresolved, 4-H furan), 6.00 (1H, dd, *J* 7.0 and $^4J_{HH}$ 1.2, 3-H furan), 5.84 (1H, dd, *J* 5.9 and $^4J_{HH}$ 1.2, 3-H furan), 5.72 (1H, dd, *J* 10.4 and 2.9, 2-H), 5.34 (1H, dd, *J* 2.3 and $^4J_{HH}$ 1.2, 5-H furan), 5.41 (1H, m, unresolved, 5-H furan), 4.84 (1H, dd, *J* 2.9 and $^4J_{HH}$ 1.5, 1-H), 3.85 (1H, dd, *J* 12.0 and 2.8, 8_a-H), 3.70 (1H, dd, *J* 12.3 and 4.3, 8_a-H), 3.75 (1H, dd, *J* 12.0 and 4.3, 5-H), 3.64 (1H, dd, *J* 14.2 and 2.4, 5-H), 3.44 (3H, s, OCH_3), 3.43 (3H, s, OCH_3), 3.35 (3H, s, OCH_3), 3.35 (3H, s, OCH_3), 3.20 (3H, s, OCH_3), 3.16 (3H, s, OCH_3), 3.15 (3H, s, OCH_3), 3.15 (3H, s, OCH_3), 1.96–1.87 (2H, m, CH_aH_b), 1.85–1.80 (2H, m, CH_aH_b), 1.71–1.62 (2H, m, CH_aH_b) and 1.45–1.37 (2H, m, CH_aH_b); δ_C(75 MHz; $CDCl_3$) 131.9 (furan 3-C), 131.8 (furan 3-C), 131.3 (furan 4-C), 131.1 (furan 4-C), 131.1 (3-C), 130.9 (3-C), 129.2 (2-C), 129.1 (2-C), 113.8 (furan 2-C), 113.2 (furan 2-C), 107.4 (furan 5-C), 107.2 (furan 5-C), 95.9 (1-C), 95.9 (1-C), 91.8 (4_a-C), 91.6 (4_a-C), 74.4 (5-C), 72.9 (8_a-H), 70.5 (5-C), 70.5 (8_a-H), 24.7 (6-C), 24.6 (6-C), 22.7 (7-C) and 22.5 (7-C); *m*/*z* (ES) 351.2 (100%, MNa^+).

(2*R*,3*S*,6*S*)-2-{2-[(2*S*,3*R*,6*R*)-3-Hydroxy-6-methoxy-3,6-dihydro-2*H*-pyran-2-yl]ethyl}-6-methoxy-3,6-dihydro-2*H*-pyran-3-ol *meso*-13

Sodium borohydride (44 mg, 1.17 mmol) was added portionwise to a stirred solution of the diketone **12** (165 mg, 0.585 mmol) and cerium chloride heptahydrate (480 mg, 1.287 mmol) in ethanol (10 ml) at −40 °C. The reaction mixture was stirred for 26 h, quenched with water (1 ml) and evaporated under reduced pressure. The residue was extracted with chloroform (5 × 5 ml), the combined extracts dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which was purified by flash chromatography, eluting with 1 : 1 EtOAc–petrol to give the *diol* (161 mg, 96%; 71 : 29 mixture of anomers) as a viscous colourless oil. On standing in chloroform for 4 days, the diol *meso*-**13** (66 mg, 41%, >98 : 2 mixture of anomers) was obtained as colourless prisms, mp > 270 °C (decomp. 165 °C); R_f 0.35 (60 : 40 EtOAc–petrol) (Found: 309.1328; $C_{14}H_{22}O_6$ requires [*M* + Na], 309.1314); ν_{max}/cm^{-1} ($CHCl_3$ solution) 3418 (OH), 2928, 1447, 1398, 1127, 1044; δ_H (500 MHz; $CDCl_3$) 5.93 (2H, ddd, *J* 10.1, 2.7 and $^4J_{HH}$ 1.3, 4-H), 5.77 (2H, ddd, *J* 10.1, 2.7 and $^4J_{HH}$ 2.1, 5-H), 4.85 (2H, dd, *J* 2.7 and $^4J_{HH}$ 1.3, 6-H), 3.94 (2H, m, 3-H), 3.61 (2H, ddd, *J* 8.2, 4.2 and 2.1, 2-H), 3.45 (6H, s, OCH_3), 2.22 (2H, m, CH_aH_b), 1.59 (2H, m, CH_aH_b) and 1.55 (2H, broad, OH); δ_C (500 MHz; $CDCl_3$) 133.5 (4-C), 126.6 (5-C), 95.3 (6-C), 72.0 (2-C), 68.3 (3-C), 55.9 (OCH_3) and 28.2 (CH_2); *m*/*z* (ES) 309 (100%).

1,2-Di[pyran-2,5-dion-6-yl]ethane 18

Jones's reagent was prepared by slow addition of concentrated sulfuric acid (2.2 ml, 98%) to chromium trioxide (2.67 g) on ice, and the slurry was diluted to 20 ml by addition of water, added slowly and dropwise to a stirred suspension of dipyranone **14** (163 mg) in acetone (5 ml) at room temperature until the yellow colour persisted for a 2 min period. The solution was diluted with water (20 ml) and filtered, the residue was washed with distilled water (50 ml), ethanol (4 ml) and diethyl ether (4 ml) to give the *dione* **18** (158 mg, >98%; 70 : 30 mixture of keto and enol tautomers) as a fine colourless powder, mp > 300 °C (Found: 273.0368; $C_{12}H_{10}O_6$ requires [*M* + Na], 273.0375); ν_{max}/cm^{-1} (Nujol mull) 1716 (C=O), 1684 (C=O), 1448, 1282, 1231, 1120, 1080 and 1013; δ_H (75 MHz; DMSO-d_6) 8.88 (2H, br, s, enol), 7.37 (2H, d, *J* 9.8, enol), 7.03 (2H, d, *J* 10.2, keto), 6.93 (2H, d, *J* 10.2, keto), 6.12 (2H, d, *J* 9.8, enol), 5.20 (2H, dd, *J* 3.3 and 1.6, keto), 2.75 (4H, m, enol) and 2.00 (4H, br m, taut); δ_C (75 MHz; DMSO-d_6) 161.2, 147.2, 142.1, 136.0, 113.7 and 25.6 (keto resonances only indicated); *m*/*z* (ES) 273 (100%).

1,2-Bis[3-Acetoxy-6-oxo-6*H*-pyran-2-yl]ethane 19

The dione **18** (20 mg, 0.08 mmol) was dissolved in a mixture of acetic anhydride (2 ml) and pyridine (1 ml) and stirred at room temperature under N_2 for 24 h and the solvent was removed under reduced pressure. The residue was preabsorbed onto silica gel and purified by flash chromatography, eluting with 1 : 1 EtOAc–petrol, to give **19** (26.4 mg, >98%) as a semi-crystalline solid, R_f 0.19 (1 : 1 EtOAc–petrol); ν_{max}/cm^{-1} (thin film) 1771, 1727, 1652, 1428, 1370, 1102; δ_H (300 MHz; $CDCl_3$) 7.12 (2H, d, *J* 9.9), 6.19 (2H, d, *J* 9.9), 2.29 (6H, s, OAc), 2.15 (2H, dd, *J* 12.5 and 3.4, CH_aH_b) and 2.07 (2H, dd, *J* 12.5 and 3.4, CH_aH_b); δ_C (75 MHz; $CDCl_3$) 169.5 (C=O), 161.1 (C=O), 154.0, 142.0 (4-C), 132.0, 114.6 (5-C), 25.7 (CH_3) and 20.8 (CH_2).

(2*R*,6*R*)-2-{2-[(2*S*,3*R*,6*R*)-3-Hydroxy-6-methoxy-3,6-dihydro-2*H*-pyran-2-yl]ethyl}-6-methoxy-6*H*-pyran-3-one 29

(+)-Diethyl tartrate (117 μl, 0.684 mmol) and titanium tetraisopropoxide (170 μl, 0.570 mmol) were stirred under nitrogen at −40 °C in dichloromethane (2 ml) with 3 Å molecular sieves (0.5 g). This solution was stirred for 40 min and the *diol* **13** (163 mg, 0.570 mmol; 75 : 25 mixture of diastereoisomers) was added dropwise as a solution in dichloromethane (1 ml). The solution was stirred for a further 30 min and *tert*-butyl hydroperoxide (285 μl of a 5 M solution in decane, 1.42 mmol) was added. After 48 hours at −40 °C, the reaction mixture was quenched with water (2 ml) and filtered though Celite, eluting with dichloromethane. The aqueous layer was extracted with dichloromethane (4 × 5 ml) and the combined organic extracts dried ($MgSO_4$), evaporated under reduced pressure, preabsorbed on silica gel and purified by flash chromatography (gradient elution: 1 : 1 ⟶ 7 : 3 ethyl acetate–petrol) to give the *enone* **29** (23 mg, 14%; >98 : 2 mixture of diastereoisomers) as colourless prisms, $[\alpha]_D$ = +28.4 (*c* = 0.38, $CHCl_3$); R_f 0.22 (1 : 1 EtOAc–petrol); ν_{max}/cm^{-1} ($CHCl_3$ solution) 1699, 1456, 1099, 1049; δ_H (300 MHz; $CDCl_3$) 6.85 (1H, dd, *J* 10.2 and 3.5, 5-H), 6.09 (1H, d, *J* 10.2, 4-H), 5.94 (1H, d, *J* 10.1, 4-H′), 5.76 (1H, dd, *J* 10.1 and 4.6, 3-H′), 5.58 (1H, m, 1-H′), 5.12 (1H, d, *J* 3.5, 6-H), 4.85 (1H, broad, 5-H′), 4.47 (1H, dd, *J* 8.3 and 3.6, 2-H′), 4.22 (1H, dd, *J* 5.6 and 3.7, 2-H), 3.54 (1H, s, OCH_3), 3.45 (1H, s, OCH_3), 3.19 (1H, broad, OH) and 1.80–1.50 (4H, m, CH_2); δ_C (75 MHz; $CDCl_3$) 196.8 (3-C), 143.7 (5-C), 133.9 (4-C), 128.1 (4-C′), 127.0 (3-C′), 95.6 (5-C′), 94.5 (6-C), 74.4, 72.3, 68.6, 57.0 (OCH_3), 56.4 (OCH_3), 28.0 (CH_2) and 26.3 (CH_2); *m*/*z* (EI) 284 (3%), 267 (14), 253 (32), 237 (27), 100 (100), 98 (52), 85 (28), 71 (35) and 55 (31); *m*/*z* (ES) 307 (100%, MNa^+). The alcohol **38** was shown to have >95% ee by conversion into the corresponding (*R*)-Mosher's ester.

Also obtained was **22** (122 mg, 75%; 87 : 13 mixture of diastereoisomers) which was recrystallised from chloroform to give the diol **22** (94 mg, 67%; >98 : 2 mixture of diastereomers)

as colourless prisms, spectroscopically identical to that obtained previously.

4-Methoxybenzoic acid (2*R*,3*S*,6*S*)-2-{2-[(2*S*,3*R*,6*R*)-6-methoxy-3-(4-methoxybenzoyloxy)-3,6-dihydro-2*H*-pyran-2-yl]-ethyl}-6-methoxy-3,6-dihydro-2*H*-pyran-3-yl ester 20

p-Anisoyl chloride (211 μl, 1.553 mmol) was added to a stirred solution of the diol *meso*-**13** (202 mg, 0.706 mmol) and triethylamine (354 μl, 2.542 mmol) at room temperature in dichloromethane (2.4 ml). The reaction mixture was treated with 4-(*N,N*-dimethylamino)pyridine (35 mg, 0.035 mmol) and stirred for 3 hours, quenched with saturated aqueous sodium bicarbonate (3 ml) and diluted with chloroform (10 ml). The organic layer was separated and washed with saturated aqueous sodium bicarbonate (2 × 4 ml), brine (2 × 4 ml), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which was pre-absorbed onto silica gel and purified by flash chromatography (gradient elution: 2 : 8 ⟶ 3 : 7 EtOAc–petrol) to give the *diester* **20** (386 mg, >98%) as colourless plates, mp 169.2–170.6 °C; R_f 0.28 (3 : 7 EtOAc–petrol) (Found: 577.2053; $C_{30}H_{34}O_{10}$ requires [*M* + Na], 577.2050); ν_{max}/cm^{-1} ($CHCl_3$ solution) 2931, 1713, 1699, 1511, 1463, 1256 and 1168; δ_H (300 MHz; $CDCl_3$) 7.97 (4H, dd, *J* 6.9 and $^5J_{HH}$ 2.1, Ar), 6.91 (4H, dd, *J* 6.9 and $^5J_{HH}$ 2.1, Ar), 5.95 (2H, ddd, *J* 10.2, 1.7, $^4J_{HH}$ 1.1, 4-H), 5.82 (2H, ddd, *J* 10.2 and 2.6, $^4J_{HH}$ 2.0, 5-H), 5.34 (2H, ddd, *J* 9.3, 5.5, and 1.7, 4-H), 4.87 (2H, dd, *J* 2.2 and $^4J_{HH}$1.1, 6-H), 3.99 (2H, m, 2-H), 3.87 (6H, s, OCH_3), 3.37 (6H, s, OCH_3), 2.07–2.04 (2H, m, CH_aH_b), 1.59 (2H, m, CH_aH_b); δ_C (75 MHz; $CDCl_3$) 166.1, 164.0, 132.2, 130.5, 128.0, 122.6, 114.0, 95.7 (6-C), 70.0, 69.4, 56.3 (Ar OCH_3), 55.8 (pyranone OCH_3) and 28.5 (CH_2); *m*/*z* (ES) 577 (100%, MNa^+).

Methanesulfonic acid (2*R*,3*S*,6*S*)-2-{2-[(2*S*,3*R*,6*R*)-6-methoxy-3-methylsulfonyloxy-3,6-dihydro-2*H*-pyran-2-yl]ethyl}-6-methoxy-3,6-dihydro-2*H*-pyran-3-yl ester

Methanesulfonyl chloride (78 μl, 1.008 mmol) was added to a stirred solution of the diol *meso*-**13** (71 mg, 0.252 mmol) and triethylamine (142 μl, 1.021 mmol) in dichloromethane (2 ml) at room temperature. The reaction mixture was stirred for 17 h, diluted with dichloromethane (15 ml), and the organic layer was washed with saturated aqueous sodium bicarbonate solution (2 × 5 ml), dried ($MgSO_4$) and evaporated under reduced pressure to give the *dimesylate* (108 mg, 98%) as an amorphous pale yellow solid; mp 112.2–114.3 °C; ν_{max}/cm^{-1} ($CHCl_3$ solution) 2976, 1639, 1457, 1401, 1367, 1351, 1181, 1130, 1097 and 1045; δ_H (300 MHz; $CDCl_3$) 6.02 (2H, d, *J* 10.2, 5-H), 5.89 (2H, ddd, *J* 10.2, 2.5 and $^4J_{HH}$ 1.4, 4-H), 4.95 (2H, dd, *J* 8.8 and 2.5, 3-H), 4.89 (2H, s, 6-H), 3.89 (2H, td, *J* 8.8 and 2.1, 2-H), 3.46 (6H, s, OCH_3), 3.07 (6H, s, SO_2CH_3), 2.19 (2H, m, CH_aH_b) and 1.57 (2H, m, CH_aH_b).

(2*R*,3*R*,6*S*)-2-{2-[(2*S*,3*S*,6*R*)-3-Hydroxy-6-methoxy-3,6-dihydro-2*H*-pyran-2-yl]ethyl}-6-methoxy-3,6-dihydro-2*H*-pyran-3-ol 23

Potassium superoxide (96 mg, 1.36 mmol) and 18-crown-6 (3.6 mg, 13.6 μmol) was added to a stirred solution of methanesulfonic acid (2*R*,3*S*,6*S*)-2-{2-[(2*S*,3*R*,6*R*)-6-methoxy-3-methylsulfonyloxy-3,6-dihydro-2*H*-pyran-2-yl]ethyl}-6-methoxy-3,6-dihydro-2*H*-pyran-3-yl ester (60 mg, 0.136 mmol) in dry DMSO at room temperature. The reaction mixture was stirred for 4 days, quenched by slow addition of water (0.5 ml), diluted with water (10 ml) and extracted with chloroform (4 × 10 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which pre-absorbed on to silica gel and was purified by flash chromatography, eluting with 8 : 2 EtOAc–petrol to give the *diol* **23** (13.8 mg, 36%) as colourless prisms, mp 178.7–180.4 °C; R_f 0.19 (7 : 3 EtOAc–petrol) (Found: 309.1309; $C_{14}H_{22}O_6$ requires [*M* + Na], 309.1314); ν_{max}/cm^{-1} (thin film) 3431 (O–H), 2899, 1446, 1404, 1183, 1112, 1080, 1022; δ_H (300 MHz; $CDCl_3$) 6.19 (2H, dd, *J* 10.0 and 5.6, 4-H), 5.90 (2H, dd, *J* 10.0 and 3.0, 5-H), 4.89 (2H, d, *J* 3.0, 6-H), 3.98 (2H, m, broad, 3-H), 3.70 (2H, m, br, 2-H), 3.45 (6H, s, OCH_3), 2.26 (2H, m, CH_aH_b) and 1.91–1.83 (2H, m, CH_aH_b); δ_C (75 MHz; $CDCl_3$) 130.6 (4-C), 128.6 (5-C), 95.7 (6-C), 77.4, 71.0, 63.4 (OCH_3) and 27.0 (CH_2); *m*/*z* (ES) 309 (M + Na).

Acetic acid (2*R*,3*R*,6*S*)-2-{2-[(2*S*,3*S*,6*R*)-3-acetoxy-6-methoxy-3,6-dihydro-2*H*-pyran-2-yl]ethyl}-6-methoxy-3,6-dihydro-2*H*-pyran-3-yl ester 21

Anhydrous caesium acetate (147 mg, 0.77 mmol) and 4-(*N,N*-dimethylamino)pyridine (4.7 mg, 38.5 μmol) were added to a stirred solution of methanesulfonic acid (2*R*,3*S*,6*S*)-2-{2-[(2*S*,3*R*,6*R*)-6-methoxy-3-methylsulfonyloxy-3,6-dihydro-2*H*-pyran-2-yl]ethyl}-6-methoxy-3,6-dihydro-2*H*-pyran-3-yl ester (33.9 mg, 77 μmol) in dry toluene (3.5 ml). The reaction mixture was refluxed for 3 days, cooled to room temperature and filtered. The residue was extracted with toluene (2 × 10 ml) and the combined organic extracts were washed with water (5 ml), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which was pre-absorbed on to silica gel and purified by flash chromatography, eluting with 3 : 7 EtOAc–petrol to give the *diacetate* **21** (23.8 mg, 84%) as colourless plates, mp 189.1–190.2 °C (from EtOAc–petrol); R_f 0.22 (7 : 3 EtOAc–petrol); (Found MNa^+ 393.1525. $C_{18}H_{26}NaO_8$ requires *MNa*, 393.1534); ν_{max}/cm^{-1} (thin film) 2922, 1727, 1372, 1249, 1182, 1071, 1045 and 1020; δ_H (300 MHz; $CDCl_3$) 6.09 (2H, dd, *J* 10.1 and 5.2, 4-H), 6.02 (2H, dd, *J* 10.1 and 2.8, 5-H), 4.96 (2H, d, *J* 2.8, 6-H), 4.94 (2H, dd, *J* 5.2 and 2.6, 3-H), 4.09 (2H, m, 2-H), 3.43 (6H, s, OCH_3), 2.10 (6H, s, OAc) and 1.83–1.65 (4H, m, CH_2); δ_C (75 MHz; $CDCl_3$) 171.0 (C=O), 130.8 (4-C), 126.3 (5-C), 95.6 (6-C), 69.1, 64.8, 56.0, 27.1 and 21.3; *m*/*z* 339 (28%), 279 (46), 219 (33), 142 (63) and 137 (49); *m*/*z* (ES) 393 (100%, MNa^+).

4-Methoxybenzoic acid (2*R*,3*R*,6*S*)-2-{2-[(2*S*,3*S*,6*R*)-6-methoxy-3-(4-methoxybenzoyloxy)-3,6-dihydro-2*H*-pyran-2-yl]ethyl}-6-methoxy-3,6-dihydro-2*H*-pyran-3-yl ester 22

By the same general method, methanesulfonic acid (2*R*,3*S*,6*S*)-2-{2-[(2*S*,3*R*,6*R*)-6-methoxy-3-methylsulfonyloxy-3,6-dihydro-2*H*-pyran-2-yl]ethyl}-6-methoxy-3,6-dihydro-2*H*-pyran-3-yl ester (67 mg, 152 μmol), anhydrous caesium *p*-methoxybenzoate (400 mg, 1.52 mmol) and 4-(*N,N*-dimethylamino)-pyridine (8.5 mg, 76 μmol) gave a crude product which was pre-absorbed onto silica gel and purified by flash chromatography, eluting with 3 : 7 EtOAc–petrol to give the *diester* **22** (45.2 mg, 54%) as colourless needles; mp 142.9–143.7 °C; R_f 0.27 (3 : 7 EtOAc–petrol) (Found: 577.2070; $C_{30}H_{34}O_{10}$ requires [*M* + Na], 577.2050); ν_{max}/cm^{-1} (CH_3Cl solution) 2934, 1713, 1693, 1465 and 1256; δ_H (300 MHz; $CDCl_3$) 8.00 (4H, d, *J* 8.8, Ar), 6.91 (4H, d, *J* 8.8, Ar), 6.19 (2H, dd, *J* 10.0 and 5.4, 4-H), 6.01 (2H, dd, *J* 10.0 and 3.0, 5-H), 5.13 (2H, dd, *J* 5.3 and 2.1, 3-H), 4.92 (2H, d, *J* 3.0, 6-H), 4.12 (2H, dt, *J* 7.3 and 2.1, 2-H), 3.87 (6H, s, OCH_3), 3.32 (6H, s, OCH_3) and 1.97–1.73 (4H, m, CH_2); δ_C (75 MHz; $CDCl_3$) 166.3 (Ar), 163.9 (Ar), 132.2 (Ar), 130.8 (Ar), 126.6, 122.6, 114.0, 95.6 (6-C), 69.5, 65.1, 55.9 and 27.4 (CH_2); *m*/*z* (ES) 577 (M + Na).

(2*R*,3*R*,6*S*)-2-{2-[(2*S*,3*S*,6*R*)-3-Hydroxy-6-methoxy-3,6-dihydro-2*H*-pyran-2-yl]ethyl}-6-methoxy-3,6-dihydro-2*H*-pyran-3-ol 23

Anhydrous potassium carbonate (50 mg, 362 μmol) was added to a stirred solution of the diacetate **21** (24 mg, 64.9 μmol) in methanol (2 ml) at room temperature. The reaction mixture was stirred for 6 h, evaporated under reduced pressure and the residue dissolved in chloroform (4 × 5 ml). The organic

fractions were combined, washed with brine (5 ml), dried ($MgSO_4$) and evaporated under reduced pressure to give the diol **23** (16.1 mg, 89%), spectroscopically identical to that obtained previously.

(2*R*,3*R*,6*S*)-2-{2-[(2*S*,3*S*,6*R*)-6-Methoxy-3-*tert*-butyldimethylsilyloxy-3,6-dihydro-2*H*-pyran-2-yl]ethyl}-6-methoxy-3,6-dihydro-2*H*-pyran-3-yl *tert*-butyldimethylsilyl ether 24

Imidazole (31 mg, 454 μmol) and *tert*-butyldimethylsilyl chloride (51 mg, 340 μmol) were added to a stirred solution of the diol **23** (16 mg, 56.7 μmol) in dry dimethylformamide (0.5 ml). The reaction mixture was stirred for 27 h at room temperature, diluted with chloroform (10 ml), washed with saturated aqueous sodium bicarbonate solution (4 ml) and water (5 × 5 ml), and the organic layer was dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product, which was pre-absorbed onto silica gel and purified by flash chromatography, eluting with 15 : 85 EtOAc–petrol to give the *disilyl ether* **24** (23.1 mg, 80%) as a colourless flocculent amorphous solid; mp 105.7–106.1 °C; R_f 0.52 (15 : 85 EtOAc–petrol); δ_H (300 MHz; $CDCl_3$) 5.95 (2H, dd, *J* 10.0 and 5.1, 4-H), 5.78 (2H, dd, *J* 10.0 and 2.9, 5-H), 4.84 (2H, d, *J* 2.9, 6-H), 3.82, (2H, m, broad, 2-H), 3.67 (2H, dd, *J* 5.1 and 2.8, 3-H), 3.34 (6H, s, OCH_3), 1.75 (4H, m, CH_2), 0.81 (18H, s, *t*-butyl) and 0.00 (12H, s, $SiMe_2$).

2-(Furan-2-yl)-6-hydroxy-6*H*-pyran-3-one 25

m-Chloroperbenzoic acid (900 mg, 57–86%) was added slowly in small portions to a stirred solution of alcohol **8** (521 mg, 3.18 mmol) in dichloromethane (20 ml) at 0 °C. The reaction mixture was stirred for 5 h, quenched with saturated aqueous sodium thiosulfate solution (10 ml) and the layers separated. The aqueous layer was extracted with dichloromethane (3 × 20 ml) and the combined organic layers were washed with aqueous sodium bicarbonate (10 ml). This aqueous layer was extracted with dichloromethane (3 × 20 ml) and the combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which was purified by flash chromatography, eluting with 3 : 7 EtOAc–petrol to give the *pyranone* **25** (272 mg, 48%; 75 : 25 mixture of anomers) as brown prisms, mp 48.1–50.8 °C (from EtOAc–petrol); R_f 0.28 (3 : 7 EtOAc–petrol); ν_{max}/cm^{-1} ($CHCl_3$ solution) 3401 (O–H), 1699 (C=O), 1152, 1027 and 1017; δ_H (500 MHz; $CDCl_3$) 7.45 (1H, dd, *J* 1.8 and $^4J_{HH}$ 0.7, furyl 5-H^{maj}), 7.44 (1H, dd, *J* 1.9 and $^4J_{HH}$ 0.7, furyl 5-H^{min}), 7.03 (1H, dd, *J* 10.4 and 2.3, 5-H^{min}), 6.99 (1H, dd, *J* 11.9 and 3.0, 5-H^{maj}), 6.45 (1H, dd, *J* 3.3 and $^4J_{HH}$ 0.7, furyl 3-H^{min}), 6.44 (1H, dd, *J* 3.3 and $^4J_{HH}$ 0.7, furyl 3-H^{maj}), 6.39 (1H, dd, *J* 3.3 and 1.8, 4-H $furyl^{maj}$), 6.38 (1H, dd, *J* 3.3 and 1.9, 4-H $furyl^{min}$), 6.31 (1H, dd, *J* 10.4 and $^4J_{HH}$ 1.4, 4-H^{min}), 6.25 (1H, dd, *J* 11.9 and $^4J_{HH}$ 0.9, 4-H^{maj}), 5.74 (1H, dd, *J* 2.8 and $^4J_{HH}$ 1.1, 6-H), 5.65 (1H, s, 2-H) and 3.3 (1H, s, OH); δ_C (500 MHz; $CDCl_3$) 191.8 (3-C^{maj}), 191.3 (3-C^{min}), 149.2 (furyl 2-C^{min}), 148.2 (furyl 2-C^{maj}), 147.1 (5-C^{min}), 145.4 (5-C^{maj}), 143.6 (furyl 5-C^{maj}), 143.4 (furyl 5-C^{min}), 128.3 (4-C^{min}), 128.0 (4-C^{maj}), 110.8 (furyl 3-C^{maj}), 110.8 (3-C^{min}), 110.7 (furyl 4-C^{min}), 110.5 (furyl 4-C^{maj}), 89.8 (6-C^{min}), 88.3 (6-C^{maj}) and 71.3 (2-C); *m*/*z* (EI) 180 (8%, M^+), 149 (40), 95 (47), 81 (59), 69 (61) and 55 (100).

Toluene-4-sulfonic acid 2-furan-2-ylpyridin-3-yl ester 27

By the same general method, *m*-chloroperbenzoic acid (988 mg, 57–86%) and the sulfonamide **10** (521 mg, 2.00 mmol) gave a crude product after 6 h. Analysis of the crude reaction mixture by 500 MHz ^{1}H NMR revealed a 47 : 53 mixture of the pyridine **27** and the piperidine **26**. The crude mixture was purified by flash chromatography, eluting with 3 : 7 EtOAc–petrol to give the *pyridine* **27** (144 mg, 29%) as light brown prisms, mp 71.2–73.4 °C; R_f 0.31 (3 : 7 EtOAc–petrol) (Found: 316.0642; $C_{16}H_{13}NO_4S$ requires [*M* + *H*], 316.0643); ν_{max}/cm^{-1} ($CHCl_3$ solution) 1435, 1377, 1195, 1174 and 1093; δ_H (500 MHz; $CDCl_3$) 8.52 (1H, dd, *J* 4.6 and $^4J_{HH}$ 1.4, pyr 6-H), 7.71 (1H, dd, *J* 8.3 and $^4J_{HH}$ 1.4, pyr 4-H), 7.59 (2H, d, *J* 8.4, 2-H and 6-H), 7.47 (1H, dd, *J* 1.7 and $^4J_{HH}$ 0.6, furyl 5-H), 7.19 (1H, dd, *J* 8.3 and 4.6, pyr 5-H), 7.18 (2H, d, *J* 8.4, 3-H and 5-H), 7.04 (1H, dd, *J* 3.4 and $^4J_{HH}$ 0.6, furyl 3-H), 6.45 (1H, dd, *J* 3.4 and 1.7, furyl 4-H) and 2.37 (3H, s, Me); δ_C (500 MHz; $CDCl_3$) 148.6 (furyl 2-C), 147.7 (pyr 6-C), 145.9 (pyr, 2-C), 143.8 (furyl 5-C), 131.9, 130.7 (pyr, 4-C), 129.5 (3-C and 5-C), 128.5 (2-C and 6-C), 127.9 (pyr, 3-C), 126.4 (4-C), 122.3 (pyr, 5-C), 113.8 (furyl 3-C), 111.8 (furyl, 4-C), and 21.6 (Me); *m*/*z* (EI) 315 (28%, M^+), 160 (61), 132 (100) and 39 (62).

2-(Furan-2-yl)-6-hydroxy-6*H*-pyran-3-one 25

N-Bromosuccinimide (727 mg, 4.08 mmol) was added slowly in small portions over 2 hours to a mixture of the alcohol **8** (515 mg, 3.14 mmol) in THF (10 ml) and sodium acetate trihydrate (512 mg, 3.77 mmol) in water (2.5 ml) at 0 °C. The reaction mixture was stirred for 3 h, poured into dichloromethane (30 ml), the layers separated and the organic layer was washed with 10% aqueous potassium iodide solution (10 ml), 15% aqueous sodium thiosulfate solution (10 ml) and 10% aqueous sodium bicarbonate solution (10 ml). The combined aqueous washings were evaporated under reduced pressure and the solid residue was extracted with dichloromethane (3 × 10 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which was purified by flash chromatography, eluting with 3 : 7 EtOAc–petrol to give the pyranone **25** (243 mg, 43%; 73 : 27 mixture of anomers) as a brown crystalline solid, spectroscopically identical to that obtained previously.

2-Furan-2-yl-6-hydroxy-1-(4-tolylsulfonyl)-1,6-dihydro-2*H*-pyridin-3-one 26

By the same general method, *N*-bromosuccinimide (1.424 g, 4.00 mmol), the sulfonamide **10** (1.268 g, 4.00 mmol) and sodium acetate trihydrate (652.8 mg, 4.80 mmol) gave the *piperidine* **26** (659 mg, 50%) as a brown oil, R_f 0.25 (3 : 7 EtOAc–petrol) (Found: 316.0641; $C_{16}H_{14}NO_4S$ requires [*M* − OH], 316.0644); ν_{max}/cm^{-1} ($CHCl_3$ solution) 1597, 1492, 1439 and 1378; δ_H (500 MHz; $CDCl_3$) 7.64 (2H, dd, *J* 8.5 and $^5J_{HH}$ 0.6, aryl, 2-H and 6-H), 7.28 (2H, dd, *J* 8.5 and $^5J_{HH}$ 0.6, aryl, 3-H and 5-H), 7.18 (1H, dd, *J* 1.7 and $^4J_{HH}$ 0.6, furyl 5-H), 7.02 (1H, dd, *J* 10.4 and 4.6, pip, 5-H), 6.32 (1H, dd, *J* 3.3 and $^4J_{HH}$ 0.6, furyl 3-H), 6.22 (1H, dd, *J* 3.3 and 1.7, furyl 4-H), 6.19 (1H, dd, *J* 10.4 and $^4J_{HH}$ 1.2, 4-H), 6.07 (1H, dd, *J* 4.6 and $^4J_{HH}$ 1.2, 6-H), 5.61 (1H, s, 2-H) and 2.36 (3H, s, Me); *m*/*z* (EI) 333 (8%, M^+), 331 (51), 91 (100).

4-Methoxybenzoic acid (2*R*,3*S*,4*R*,5*S*,6*S*)-2-{2′-[(2*S*′,6*R*′)-3′-(4-methoxylbenzoyloxy)-6′-methoxy-3′,6′-dihydro-2*H*-pyran-2′-yl]ethyl}-4,5-dihydroxy-6-methoxytetrahydropyran-3-yl ester *ent*-32a

A solution of the diamine **37** (74 mg, 0.155 mmol) in dry dichloromethane (0.5 ml) was added to a stirred solution of osmium tetroxide (40 mg, 0.155 mmol) in dichloromethane (1.5 ml). The yellow solution was cooled to −20 °C, the diester **20** (86 mg, 0.155 mmol) added in one portion and the reaction mixture was stirred for 5 h, warmed to room temperature, stirred for 2 days and evaporated under reduced pressure. The residue was dissolved in 1 : 1 saturated aqueous sodium sulfite solution-tetrahydrofuran (2 ml), refluxed for 2 h and evaporated under reduced pressure to give a crude product, which was pre-absorbed on to silica gel and purification by flash chromatography, eluting with 55 : 45 EtOAc : petrol, gave the *diol ent*-**32a** (76.9 mg, 84%) as a viscous colourless oil, $[\alpha]_D^{20}$ = −27.6 (*c* = 0.48, $CHCl_3$); R_f 0.23 (6 : 4 EtOAc–petrol); (Found

MNa^+ 611.2104. $C_{30}H_{36}O_{12}$ requires *MNa*, 611.2114); ν_{max}/cm^{-1} 3415 (O–H), 2932, 1713, 1606, 1512, 1454, 1258, 1168, 1102 and 1045; δ_H (300 MHz; $CDCl_3$) 7.92 (2H, d, *J* 8.9, Ar), 7.89 (2H, d, *J* 8.9, Ar), 6.85 (2H, d, *J* 8.9, Ar), 6.84 (2H, d, *J* 8.9, Ar), 5.87 (1H, d, *J* 10.2, 5-H′), 5.73 (1H, ddd, *J* 10.2, 4.6 and $^4J_{HH}$ 2.4, 4-H′), 5.23 (1H, dd, *J* 9.4 and 1.4, 3-H′), 4.95 (1H, t, *J* 9.5, 3-H), 4.75 (1H, d, *J* 2.1, 6-H′), 4.67 (1H, s, 6-H), 3.91 (2H, td, *J* 9.6 and 3.0, 2-H and 2-H′), 3.84 (1H, dd, *J* 9.5 and 3.3, 4-H), 3.81 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 3.78 (1H, d, *J* 3.3, 5-H), 3.38 (1H, br, OH), 3.27 (3H, s, OCH_3), 3.20 (3H, s, OCH_3), 2.75 (1H, br, OH) and 1.90–1.30 (4H, m, CH_2); δ_C (75 MHz; $CDCl_3$) 167.9 (Ar), 166.2 (Ar), 164.2 (Ar), 164.0 (Ar), 132.4 (Ar), 132.2 (Ar), 130.5 (4-C′), 127.9 (5-C′), 122.5 (Ar), 122.0 (Ar), 114.1 (Ar), 114.1 (Ar), 100.5 (6-C), 95.7 (6-C′), 75.4 (3-C), 71.0 (2-C), 70.9 (2-C′), 69.8, (4-C), 69.7 (5-C), 69.3 (3-C′), 56.3 (OCH_3), 55.9 (OCH_3), 55.9 (OCH_3), 55.5 (OCH_3), 28.4 (CH_2) and 28.0 (CH_2); *m*/*z* (ES) 611 (100%, MNa^+).

(2*R*,3*S*,4*S*,5*S*,6*S*)-2-{2′-[(2*S*′,3*S*′,6*R*′)-3′-Acetoxy-6′-methoxy-3′,6′-dihydro-2*H*-pyran-2′-yl]ethyl}-6-methoxytetrahydropyran-3,4,5-triyl triacetate 40

By the same general method, the diamine **37** (33.9 mg, 0.071 mmol), and the diol **32**(20 mg, 0.071 mmol) gave a crude product which was dissolved in a mixture of acetic anhydride (2 ml) and pyridine (1ml), stirred for 5 h at room temperature, and evaporated under reduced pressure to give a crude product which was pre-absorbed onto silica gel and purified by flash chromatography, eluting with 3 : 7 EtOAc–petrol, to give the *tetraacetate* **40** (13.2 mg, 39%) as a viscous colourless oil, $[\alpha]_D^{20}$ = +90.9 (*c* = 0.033, $CHCl_3$); R_f 0.31 (3 : 7 EtOAc–petrol); (Found: 511.1768; $C_{22}H_{32}O_{12}$ requires [*M* + *Na*], 511.1791); ν_{max}/cm^{-1} (thin film) 2960, 2924, 2853, 1742 (C=O), 1678, 1455, 1373, 1259, 1083; δ_H (500 MHz; $CDCl_3$) 6.08 (1H, ddd, *J* 10.0, 5.5 and $^4J_{HH}$ 1.0, 4-H′), 6.00 (1H, ddd, *J* 10.0, 3.0 and $^4J_{HH}$ 0.4, 5-H′), 5.27 (1H, t, *J* 3.8, 4-H), 5.21 (1H, dd, *J* 3.8 and 1.2, 3-H), 5.10 (1H, dt, *J* 3.8 and 1.2, 5-H), 4.91 (1H, d, *J* 3.0, 6-H′), 4.76 (1H, d, *J* 1.2, 6-H), 4.02 (1H, td, *J* 9.3 and 2.6, 2-H′), 3.97 (1H, ddd, *J* 9.3, 3.8 and $^4J_{HH}$ 1.0, 2-H), 3.41 (3H, s, OCH_3), 3.39 (3H, s, OCH_3), 2.14 (3H, s, OAc), 2.14 (3H, s, OAc), 2.08 (3H, s, OAc), 1.99 (3H, s, OAc) and 1.77–1.68 (4H, m, CH_2); δ_C (125 MHz; $CDCl_3$) 170.6 (C=O), 170.4 (C=O), 170.1 (C=O), 169.6 (C=O), 130.4 (5-C′), 125.9 (4-C′), 99.4 (6-C), 95.2 (6-C′), 64.5 (3-C′), 68.8 (2-C′), 68.8 (2-C), 68.3 (3-C), 67.5 (5-C), 66.0 (4-C), 55.7 (OCH_3), 55.2 (OCH_3), 27.1 (CH_2), 26.4 (CH_2), 21.0 (OAc), 20.8 (OAc), 20.7 (OAc) and 20.6 (OAc); *m*/*z* (ES) 511 (M + Na).

(2*S*,3*S*,4*S*,5*R*,6*R*)-2-Methoxy-6-{2-[(2*R*,3*R*,4*S*,5*S*,6*S*)-3,4,5-triacetoxy-6-methox-tetrahydropyran-2-yl]ethyl}tetrahydropyran-3,4,5-triyl triacetate 39

By the same general method, the diamine **37** (57 mg, 0.119 mmol), osmium tetraoxide (31 mg, 0.119 mmol), the diol *meso*-**13** (34 mg, 0.119 mmol), acetic anhydride (2 ml) and pyridine (1 ml) gave a crude product which was pre-absorbed onto silica gel and purified by flash chromatography, eluting with 3 : 7 EtOAc–petrol, to give the *hexaacetate* **39** (28.8 mg, 40%) as colourless prisms, R_f 0.23 (3 : 7 EtOAc–petrol); (Found: 629.2075; $C_{26}H_{38}O_{16}$ requires [*M* + *Na*], 629.2065); ν_{max}/cm^{-1} 2925, 1750 (C=O), 1679, 1447, 1370, 1247, 1224, 1134, 1084, 1050; δ_H (300 MHz; $CDCl_3$) 5.28 (2H, dd, *J* 10.0 and 3.5, 4-H and 4-H′), 5.23 (2H, dd, *J* 3.5, and 1.7, 3-H and 5-H′), 5.10, (2H, t, *J* 10.0, 5-H and 3-H′), 4.64 (2H, d, *J* 0.5, 2-H and 6-H′), 3.72 (2H, t, *J* 8.9, 6-H and 2-H′), 3.37 (6H, s, OCH_3), 2.14 (6H, s, OAc), 2.04 (6H, s, OAc), 1.98 (6H, s, OAc), 1.86 (2H, m, CH_2) and 1.50 (2H, m, CH_2); δ_C (75 MHz; $CDCl_3$) 98.4 (2-C and 6-C′), 69.9 (6-C and 2-C′), 69.8 (3-C and 5-C′), 69.6 (5-C and 3-C′), 69.2 (4-C and 4-C′), 55.1 (OCH_3), 27.1 (CH_2), 20.9 (OAc), 20.8 (OAc) and 20.7 (OAc); *m*/*z* (ES) 629 (M + Na).

Also obtained was the diacetate **38** (19.8 mg, 45%).

Kinetic resolution of the allylic alcohol 48

By the same general methods, the diamine **37** (244 mg, 0.513 mmol), osmium tetraoxide (130 mg, 0.513 mmol), the allylic alcohol[26] **48** (136.3 mg, 0.733 mmol), acetic anhydride (2 ml) and pyridine (1ml) gave a crude product which was purified by flash chromatography, eluting with 15 : 85 EtOAc : petrol, to give the triacetate[26] **50** (24%) as a colourless oil, $[\alpha]_D$ = −25.0 [*c* = 0.12, $CHCl_3$].

4-Methoxybenzoic acid (2*R*,3*R*,4*R*,5*S*,6*S*)-4,5-diacetoxy-2-{2-[(2*S*′,6*R*′)-3′-(4-methoxybenzoyl)-6′-methoxy-3′,6′-dihydro-2*H*-pyran-2′-yl]ethyl}-6-methoxytetrahydropyran-3-yl ester 47

The diol *ent*-**32a** (57 mg, 0.097 mmol) was dissolved in a mixture of acetic anhydride (2 ml) and pyridine (1 ml) and stirred at room temperature for 5 h. The reaction mixture was evaporated under reduced pressure to give a crude product which was pre-absorbed onto silica gel and purified by flash chromatography, eluting with 3 : 7 EtOAc–petrol, to give the *diacetate* **47** (64.4 mg, >98%) as a colourless oil, $[\alpha]_D^{20}$ = −25.9 (*c* = 0.54, $CHCl_3$); R_f 0.35 (3 : 7 EtOAc–petrol); ν_{max}/cm^{-1} 2924, 2853, 2360, 2342, 1753 (C=O), 1721 (C=O), 1606, 1512 and 1259; δ_H (300 MHz; $CDCl_3$) 7.95 (2H, d, *J* 8.9, Ar), 7.92 (2H, d, *J* 8.9, Ar), 6.92 (2H, d, *J* 8.9, Ar), 6.90 (2H, d, *J* 8.9, Ar), 5.93 (1H, d, *J* 10.2, 5-H′), 5.80 (1H, dt, *J* 10.2 and 2.5, 4-H′), 5.48, (1H, dd, *J* 10.1 and 3.5, 4-H), 5.33 (1H, t, *J* 10.1, 3-H), 5.27 (1H, dd, *J* 9.4 and 2.5, 3-H′), 5.27 (1H, dd, *J* 3.5 and 1.5, 5-H′), 4.81 (1H, s, 6-H′), 4.65 (1H, d, *J* 1.5, 6-C), 3.88 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 3.36 (1H, d, *J* 3.3, 5-H), 3.28 (3H, s, OCH_3), 2.88 (3H, s, OAc), 2.15 (3H, s, OAc) and 1.75–1.40 (4H, m, CH_2); δ_C (75 MHz; $CDCl_3$) 132.2 (Ar), 130.5 (4-C′), 127.9 (5-C′), 114.2 (Ar), 114.1 (Ar), 98.8 (6-C), 95.7 (6-C′), 70.9 (2-C′), 70.5 (2-C), 70.4 (4-C), 70.0 (3-C), 69.5 (5-C), 69.3 (3-C′), 56.2, 55.9, 55.2, 28.4 and 28.0.

The diacetate was found to have 60% ee by analytical chiral HPLC (Chiracel OD column; column oven 24 °C; monitoring at λ_{max} 204 nm; gradient elution: 98 : 2 ⟶ 70 : 30 hexane : isopropanol over 30 min), retention times 24.3 min (minor enantiomer) and 25.8 min (major enantiomer).

4-Methoxybenzoic acid (2*R*,3*R*,4*S*,5*R*,6*S*)-4,5-dihydroxy-2-{2-[(2*S*,3*S*,6*R*)-3-(4-methoxybenzoyl)-6-methoxy-3,6-dihydro-2*H*-pyran-2-yl]ethyl}-6-methoxytetrahydropyran-3-yl ester 32a

Potassium ferricyanide (25.0 mg, 76 μmol), potassium carbonate (10.5 mg, 76 μmol), methanesulfonamide (3.6 mg, 38 μmol) and potassium osmate dihydrate (0.4 mg, 1 μmol) were stirred at room temperature in a 1 : 1 mixture of water–*tert*-butanol (2-methylpropan-2-ol). A solution of the ligand **36** (1.3 mg, 2 μmol) in *tert*-butanol (100 μl) was added, the reaction mixture was stirred for 10 min, cooled to 0 °C and the diester **22** (21 mg, 38 μmol) added. The reaction mixture was stirred for 5 days, quenched with sodium sulfite (200 mg), stirred for 30 min at room temperature and evaporated under reduced pressure. The residue was extracted with EtOAc (4 × 5 ml), and the combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give a crude residue which was pre-absorbed onto silica gel, and purified by flash chromatography (gradient elution: 4 : 6 ⟶ 7 : 3 EtOAc–petrol) to give the *diester* **32a** (4 mg, 16%; 75 : 25 **32a** : **32b**), as a colourless viscous syrup, $[\alpha]_D$ = +25.8 (*c* = 0.093, $CHCl_3$); R_f 0.11 (6 : 4 EtOAc–petrol) (Found: 611.2109; $C_{30}H_{36}O_{12}$ requires [*M* + Na], 611.2104); ν_{max}/cm^{-1} (thin film) 3385 (broad), 2925, 1711 (C=O), 1606, 1443, 1259, 1099 and 1044; δ_H (300 MHz; $CDCl_3$) 7.93 (2H, d, *J* 9.0, Ar), 7.89 (2H, d, *J* 9.0, Ar), 6.87 (2H, d, *J* 9.0, Ar), 6.84 (2H, d, *J* 9.0, Ar), 6.09 (1H, ddd, *J* 10.0, 5.5, $^4J_{HH}$ 1.0, 4-H′), 5.93 (1H, dd, *J* 10.0 and 2.8, 5-H′), 5.37 (1H, d, *J* 3.4, 3-H), 5.03 (1H, dd, *J* 5.5 and 2.3, 3-H′), 4.83 (1H, d, *J* 2.8, 6-H′), 4.71 (1H, d, *J* 1.4, 6-H), 3.99 (1H, dt, *J* 9.3 and 2.3, 2-H′), 3.94 (1H, dd, J_{HH} 3.7 and J_{OH} 8.9, 4-H), 3.83 (1H, ddd, *J* 9.4, 3.4 and 2.3, 2-H), 3.81 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 3.68 (1H, ddd,

J_{HH} 3.7, 1.4 and J_{OH} 9.2, 5-H), 3.24 (3H, s, OCH_3), 3.21 (3H, s, OCH_3), 2.57 (1H, d, J_{OH} 8.9, OH), 2.30 (1H, d, J_{OH} 9.2, OH) and 1.85–1.54 (4H, m, CH_2) (data for **32a** only); *m*/*z* (ES) 611 (M + Na).

Also obtained was unreacted starting material (15.3 mg, 72%).

(*R*)-α-Methoxy-α-(trifluoromethyl)phenylacetic acid (2*S*,3*R*,6*R*)-2-{2-[(2*R*,6*R*)-3-oxo-6-methoxy-3,6-dihydro-2*H*-pyran-2-yl]ethyl}-6-methoxy-6*H*-pyran-3-yl ester 30

(*S*)-(+)-α-Methoxy-α-(trifluoromethyl)phenylacetyl chloride (6.7 μl, 0.036 mmol) was added to a stirred solution of the enone **29** (9 mg, 0.032 mmol) in pyridine (4 drops) and carbon tetrachloride (6 drops). The reaction mixture was stirred at room temperature for 36 hours, diluted with chloroform (3 ml) and washed with saturated aqueous sodium bicarbonate solution (2 × 0.5 ml), 5% aqueous cupric sulfate solution (3 × 1 ml) and brine (1 ml), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which was pre-absorbed on silica gel and purified by flash chromatography, eluting with 3 : 7 EtOAc–petrol, to give the *ester* **30** (15.9 mg, >98%) as colourless needles, R_f 0.35 (3 : 7 EtOAc–petrol); δ_H (500 MHz; $CDCl_3$) 7.50–7.30 (5H, m, Ph), 6.75 (1H, dd, *J* 10.3 and 3.5, 5-H), 5.99 (1H, dd, *J* 10.3 and $^4J_{HH}$ 0.5, 4-H), 5.82 (1H, d, *J* 10.1 and 2.5, 4-H′), 5.85 (1H, m, 3-H′), 5.22 (1H, td, *J* 9.4 and 1.5, 2-H′), 4.99 (1H, d, *J* 3.5, H-6), 4.82 (1H, broad, 5-H′), 4.27 (1H, dd, *J* 8.5 and 3.6, 2-H), 3.85 (1H, td, *J* 9.5 and 2.5, 1-H′), 3.47 (1H, s, OCH_3), 3.37 (1H, s, OCH_3), 3.36 (1H, s, OCH_3) and 1.70–1.40 (4H, m, CH_2); δ_C (75 MHz; $CDCl_3$) 143.6, 130.1, 129.3, 128.9, 128.6, 128.0, 127.6, 95.6, 94.5, 74.3, 72.2, 68.5, 56.7, 56.5, 55.8, 31.3, 27.8 and 25.8.

(2*R*,3*S*,4*S*,5*R*,6*S*)-2-{2′-[(2*S*′,6*R*′)-3′-(4-Methoxybenzoyl)-6′-methoxy-3′,6′-dihydro-2*H*-pyran-2′-yl]ethyl}-3-(4-methoxybenzoyloxy)-6-methoxytetrahydropyran-4,5-diyl bis[(*S*)-α-methoxy-α-(trifluoromethyl)phenylacetate] 44

By the same general method, the diol *ent*-**32a** (16.2 mg, 27.6 μmol) and (*R*)-(−)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (70 μl, 374 μmol) gave a crude product which was pre-absorped onto silica gel and purified by flash chromatography, eluting with 2 : 8 EtOAc–petrol, to give the tetraester **44** (26.4 mg, 96%; 80 : 20 **44** : **45**). Purification by preparative HPLC (gradient elution: 100 : 0 ⟶ 98 : 2 hexane–isopropanol (propan-2–ol) over 40 min) monitoring at λ_{max} 250 nm, gave the *tetraester* **44** (18.4 mg, 65%) as a viscous colourless oil, retention time 33.7 min; $[\alpha]_D^{20} = -91.8$ (*c* = 0.22, $CHCl_3$); R_f 0.28 (2 : 8 EtOAc–petrol); ν_{max}/cm^{-1} 2964, 2926, 2849, 1760 (C=O), 1720 (C=O), 1606, 1260, 1168, 1079, 1451; δ_H (300 MHz; $CDCl_3$) 7.98 (2H, d, *J* 9.0, Ar), 7.87 (2H, d, *J* 9.0, Ar), 7.52 (2H, d, *J* 7.2, Ar), 7.35–7.13 (6H, m, Ar), 7.01 (2H, t, *J* 7.7, Ar), 6.92 (2H, d, *J* 9.0, Ar), 6.92 (2H, d, *J* 9.0, Ar), 5.93 (1H, d, *J* 10.0, 5-H′), 5.90 (1H, dd, *J* 10.2 and 3.0, 4-H), 5.79 (1H, dt, *J* 10.0 and 1.9, 4-H′), 5.48 (1H, dd, *J* 3.0 and 3.0, 5-H), 5.28 (1H, t, *J* 10.2, 3-H), 5.25 (1H, dd, *J* 10.1 and 1.9, 3-H′), 4.79 (1H, d, *J* 1.5, 6-H), 4.78 (1H, s, 6-H′), 3.88 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 3.86 (2H, m, 2-H and 2-H′), 3.43 (3H, s, OCH_3), 3.41 (3H, s, OCH_3), 3.24 (3H, s, OCH_3), 3.19 (3H, s, OCH_3), 2.05–1.80 (2H, m, CH_2) and 1.55–1.35 (2H, m, CH_2).

Also obtained was the *tetraester* **45** (4.8 mg, 17%) as a viscous colourless oil, retention time 30.8 min; $[\alpha]_D^{20} = +31.4$ (*c* = 0.22, $CHCl_3$); R_f 0.28 (2 : 8 EtOAc–petrol); ν_{max}/cm^{-1} 2964, 2926, 2849, 1760 (C=O), 1720 (C=O), 1606, 1260, 1168, 1079, 1451; δ_H (300 MHz; $CDCl_3$) 7.98 (2H, d, *J* 8.7, Ar), 7.92 (2H, d, *J* 9.0, Ar), 7.44–7.12 (10H, m, Ar), 6.93 (2H, d, *J* 8.7, Ar), 6.91 (2H, d, *J* 9.0, Ar), 5.93 (1H, d, *J* 10.2, 5-H′), 5.86 (1H, dd, *J* 10.1, and 2.6, 4-H), 5.78 (1H, dt, *J* 10.2 and 1.6, 4-H′), 5.38 (1H, d, *J* 2.6, 5-H), 5.36 (1H, t, *J* 10.1, 3-H), 5.21 (1H, dd, *J* 9.2 and 1.6, 3-H′), 4.80 (1H, s, 6-H), 4.61 (1H, s, 6-H′), 3.88 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 3.86 (2H, m, 2-H and 2-H′), 3.38 (3H, s, OCH_3), 3.27 (6H, s, OCH_3), 3.23 (3H, s, OCH_3), 2.05–1.80 (2H, m, CH_2) and 1.55–1.35 (2H, m, CH_2).

(2*R*,3*S*,4*S*,5*R*,6*S*)-2-Butyl-6-methoxy-3-(4-methoxybenzoyloxy)-tetrahydropyran-4,5-diyl bis[(*R*)-α-methoxy-α-(trifluoromethyl)-phenylacetate]42

By the same general method, the diol[26] **41** (13.5 mg, 38.1 μmol) and (*S*)-(−)-MPTA acid chloride (50 μl, 267 μmol) gave a crude product which was pre-absorbed onto silica gel and purified by flash chromatography, eluting with 1 : 9 EtOAc–petrol, to give the *triester* **42** (25.2 mg, 84%) as a colourless oil, $[\alpha]_D = +35.2$ (*c* = 0.073, $CHCl_3$); R_f 0.30 (1 : 9 EtOAc–petrol); ν_{max}/cm^{-1} 2957, 2849, 1760, 1726, 1607, 1261, 1168, 1105, 1080, 1027; δ_H (300 MHz; $CDCl_3$) 7.96 (2H, d, *J* 9.0, Ar), 7.45–7.14 (10H, m, Ar), 6.93 (2H, d, *J* 9.0, Ar), 5.85 (1H, dd, *J* 10.1 and 3.0, 4-H), 5.39 (1H, dd, *J* 3.0 and 1.9, 5-H), 5.38 (1H, t, *J* 10.1, 3-H), 4.65 (1H, d, *J* 1.9, 6-H), 3.87 (3H, s, OCH_3), 3.43 (3H, s, OCH_3), 3.33 (3H, s, OCH_3), 3.29 (3H, s, OCH_3), 1.57–1.14 (6H, m, CH_2), and 0.84 (3H, t, *J* 7.1, CH_3); *m*/*z* (ES) 809 (100%, MNa^+); *m*/*z* (EI) 755 (6%), 493 (12), 369 (41), 189 (94), 135 (100).

(2*R*,3*S*,4*S*,5*R*,6*S*)-2-Butyl-6-methoxy-3-(4-methoxybenzoyloxy)tetrahydropyran-4,5-diyl bis[(*S*)-α-methoxy-α-(trifluoromethyl)phenylacetate] 43

By the same general method, the diol[26] **41** (23.8 mg, 67.2 μmol) and (*R*)-(−)-MPTA acid chloride (70 μl, 374 μmol) gave a crude product which was preabsorbed onto silica gel and purified by flash chromatography, eluting with 1 : 9 EtOAc–petrol gave the *triester* **43** (46 mg, 87%) as a colourless oil, $[\alpha]_D = -38.2$ (*c* = 0.545, $CHCl_3$); R_f 0.30 (1 : 9 EtOAc–petrol); ν_{max}/cm^{-1} 2958, 2848, 1760, 1728, 1606, 1260, 1168, 1105 and 1080; δ_H (300 MHz; $CDCl_3$) 7.89 (2H, d, *J* 8.9, Ar), 7.55 (2H, d, *J* 7.4, Ar), 7.43–6.93 (8H, m, Ar), 6.91 (2H, d, *J* 8.9, Ar), 5.88 (1H, dd, *J* 10.0 and 3.1, 4-H), 5.49 (1H, dd, *J* 3.1 and 1.8, 5-H), 5.32 (1H, t, *J* 10.0, 3-H), 4.85 (1H, d, *J* 1.8, 6-H), 3.88 (3H, s, OCH_3), 3.50 (3H, s, OCH_3), 3.47 (3H, s, OCH_3), 3.16 (3H, s, OCH_3), 1.45–1.37 (3H, m, CH_2), 1.35–1.24 (3H, m, CH_2) and 0.85 (3H, t, *J* 7.1, CH_3); *m*/*z* (ES) 809 (100%, MNa^+); *m*/*z* (EI) 755 (5%), 493 (10), 369 (37), 189 (97), 135 (100).

Acknowledgements

We thank EPSRC and Aventis for funds provided under the CASE award scheme for new appointees, the Royal Society for a research grant, and Pfizer and AstraZeneca for strategic research funding.

References

1 M. C. Willis, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1765.
2 (*a*) R. Noyori, M. Tokunaga and M. Kitamura, *Bull. Chem. Soc. Jpn.*, 1995, **68**, 36; (*b*) R. S. Ward, *Tetrahedron: Asymmetry*, 1995, **6**, 1475.
3 For example, see: (*a*) I. Bruce, G. W. J. Fleet, I. C. di Bello and B. Winchester, *Tetrahedron*, 1992, **48**, 10191; (*b*) M. K. Tong, E. M. Blumenthal and B. Ganem, *Tetrahedron Lett.*, 1990, **31**, 1683; (*c*) B. P. Bashyal, H.-F. Chow and G. W. J. Fleet, *Tetrahedron Lett.*, 1986, **27**, 3205.
4 (*a*) A. D. Campbell, D. E. Paterson, R. J. K. Taylor and T. M. Raynham, *Chem. Commun.*, 1999, 1599; (*b*) B. J. Dorgan and R. F. W. Jackson, *Synlett*, 1996, 859.
5 R. W. J. Chubb, M. R. Bryce and B. Tarbit, *J. Chem. Soc., Perkin Trans. 1*, 2001, 1853.
6 B. E. Love, P. S. Raje and T. C. Williams II, *Synlett*, 1994, 493.
7 M. Harding and A. Nelson, *Chem. Commun.*, 2001, 695.
8 S. F. Martin and P. W. Zinke, *J. Am. Chem. Soc.*, 1989, **111**, 2311.
9 J.-L. Luche, *J. Am. Chem. Soc.*, 1978, **100**, 2226.
10 C. Poss and S. L. Schreiber, *Acc. Chem. Res.*, 1994, **27**, 9.
11 For example, see: M. Loegers, L. E. Overman and G. S. Welmaker, *J. Am. Chem. Soc.*, 1995, **117**, 9139.
12 J. A. Harris and G. A. O'Doherty, *Org. Lett.*, 2000, **2**, 2983.
13 J. W. Huffman and R. C. Desai, *Synth. Commun.*, 1983, **13**, 553.

14 J. San Filippo Jnr., C. I. Chern and J. S. Valentine, *J. Org. Chem.*, 1975, **40**, 1678.
15 G. Höfle, W. Steglich and H. Vorbrüggen, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 569.
16 T. Kametani, M. Tsubuki, Y. Tatsuzaki and T. Honda, *J. Chem. Soc., Perkin Trans. 1*, 1990, 639.
17 W.-S. Zhou, Z.-H. Lu and Z.-M. Wang, *Tetrahedron*, 1993, **49**, 2641.
18 S. L. Schreiber, M. T. Goulet and G. Schulte, *J. Am. Chem. Soc.*, 1987, **109**, 4718.
19 See T. Katsuki and V. S. Martin, *Organic Reactions*, ed. L. A. Paquette, Wiley, New York, 1996, vol. 48, pp. 1–299.
20 (*a*) V. S. Martin, S. S. Woodard, T. Katsuki, Y. Yamada, M. Ikeda and K. B. Sharpless, *J. Am. Chem. Soc.*, 1981, **103**, 6237; (*b*) S. M. Brown, S. G. Davies and J. A. A. de Sousa, *Tetrahedron: Asymmetry*, 1991, **2**, 511; (*c*) K. Mori and P. Puapoomchareon, *Justus Liebigs Ann. Chem.*, 1991, 1053.
21 J. A. Marshall and K. E. Flynn, *J. Am. Chem. Soc.*, 1982, **104**, 7430.
22 H. C. Kolb, M. S. VanNieuwenhze and K. B. Sharpless, *Chem. Rev.*, 1994, **94**, 2483.
23 E. J. Corey, M. C. Noe and A. Guzman-Perez, *J. Am. Chem. Soc.*, 1995, **117**, 10817.
24 E. J. Corey, P. D. Jardine, S. Virgil, P.-W. Yuen and R. D. Connell, *J. Am. Chem. Soc.*, 1989, **111**, 9243.
25 Preliminary communication: R. Hodgson, T. Mahid and A. Nelson, *Chem. Commun.*, 2001, 2076.
26 R. Hodgson, T. Mahid and A. Nelson, *J. Chem. Soc., Perkin Trans. 1*, 2002 in the press, DOI: 10.1039/b202890e.
27 (*a*) F. M. Hauser, S. R. Ellenberger, J. C. Clardy and L. S. Bass, *J. Am. Chem. Soc.*, 1984, **106**, 2458; (*b*) S. B. King and B. Ganem, *J. Am. Chem. Soc.*, 1991, **113**, 5089.
28 T. J. Donohoe, P. R. Moore, M. J. Waring and N. J. Newcombe, *Tetrahedron Lett.*, 1997, **38**, 5027.
29 J. A. Dale, D. L. Dull and H. S. Mosher, *J. Org. Chem.*, 1969, **34**, 2543.
30 J. K. Cha, W. J. Christ and Y. Kishi, *Tetrahedron*, 1984, **40**, 2247.
31 Y.-D. Wu, Y. Wang and K. N. Houk, *J. Org. Chem.*, 1992, **57**, 1362.
32 G. I. Lotto and E. J. Corey, *Tetrahedron Lett.*, 1990, **31**, 2665.