The effects of different ester and ketal protecting groups on the reactivity and selectivity of tartrate-derived silylketene acetals

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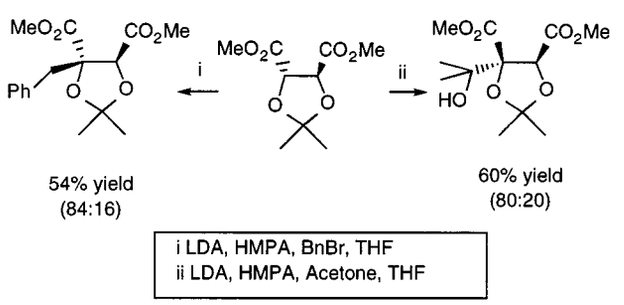
The reaction of tartrate-derived silylketene acetals and benzaldehyde has been investigated and the yields and diastereoselectivities have been found to be dependent upon the nature of the tartrate ester. Utilising the di-*tert*-butyl tartrate derivatives, high yields were achieved using a variety of aldehyde substrates. The reactions all proceeded with excellent levels of stereoselectivity (≥ 82:18); the sense of induction being dependent upon the choice of Lewis acid. $BF_3{\cdot}OEt_2$ and $TiCl_3(O^iPr)$ furnished complementary products in several cases and a model has been proposed to account for this observation.

Introduction

Tartaric acid is a useful and readily available building block in organic synthesis and has widespread use as a chiral ligand in catalytic asymmetric processes, most notably the Sharpless epoxidation reaction.[1] Anion reactions of tartaric acid derivatives were first studied by Seebach who found that in the presence of HMPA or DMPU the lithium enolates of dimethyl isopropylidenetartrate could undergo alkylation and aldol reactions giving adducts in good yields (Scheme 1).[2]



Scheme 1

This approach was utilised within our group in the first published synthesis of the bicyclic core of the squalestatins,[3] a family of naturally occurring compounds found to be effective inhibitors of squalene synthase, an enzyme in the cholesterol biosynthetic pathway.[4]

As part of our continuing work towards the synthesis of the squalestatins[5] we wished to investigate the effects of different ester and ketal protecting groups on the reactivity and selectivity of various tartrate-derived silylketene acetals. We report here our results for the $BF_3{\cdot}OEt_2$-mediated Mukaiyama[6] aldol reaction in which benzaldehyde is utilised as a model.[7] We have also examined the scope of this reaction and found that aldol reactions with unactivated ketones and α,β-unsaturated carbonyl compounds proceed in good to excellent yield and with high levels of selectivity. During the course of this work Evans reported a similar study and his results are discussed alongside our own.[8]

Mukaiyama aldol reactions

In order to probe the effects of different protecting groups, a number of tartrate derivatives (**1a**–**e**) (Fig. 1) were prepared

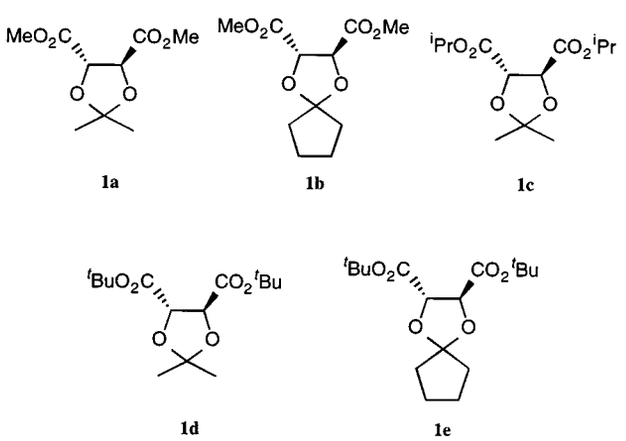


Fig. 1

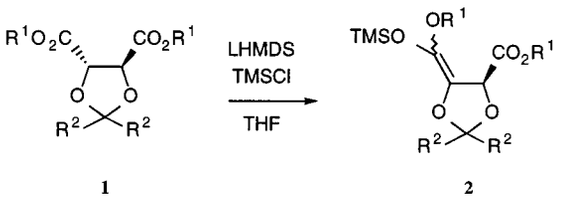
using modifications of known procedures.[8,9] A range of esters (Me, ^{i}Pr, ^{t}Bu) were investigated, as well as both isopropylidene and cyclopentylidene protecting groups.

The silylketene acetals **2** were prepared by *in situ* silylation of the lithium enolates and were isolated as an approximately 2:1 mixture of isomers. Subsequent reaction with benzaldehyde, in the presence of a stoichiometric amount of $BF_3{\cdot}OEt_2$, afforded the aldol adducts **3** and **4** as a mixture of C^3 diastereomers (Scheme 2, Table 1). None of the corresponding C^2 isomers, arising from addition of benzaldehyde to the same face as the ester, was observed.

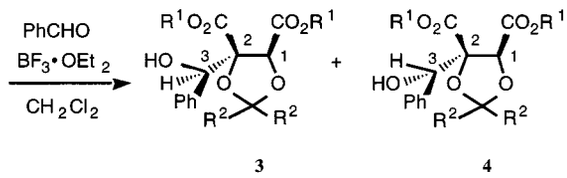
The nature of the tartrate ester significantly affected both the yield and diastereoselectivity of the Mukaiyama reaction. The methyl ester derivatives appeared to be unstable giving low yields of the aldol product and only moderate diastereoselectivity at C^3 (entries 1, 2). In contrast, the isopropyl and *tert*-butyl tartrates (entries 3–5) furnished high yields of the aldol adducts as essentially a single diastereomer (≥ 97:3 selectivity at C^3). Evans has reported similar reactions using $TiCl_3(O^iPr)$ as the Lewis acid[8] (entry 6) but higher yields and diastereoselectivities were observed with $BF_3{\cdot}OEt_2$ (entry 5). The relative stereochemistry of these products was determined unambiguously by X-ray crystallography of **3a**–**d** and by comparison with ^{1}H and ^{13}C NMR data for the *tert*-butyl derivative **3e**.[8] The X-ray structures for **3b** and **3d** are shown below as representative examples (Fig. 2).

The scope of this reaction was examined with α-alkoxy and

α,β-unsaturated aldehydes. Both benzyloxyacetaldehyde and (*E*)-cinnamaldehyde furnished the aldol products in good yield and with high levels of selectivity at the two, newly created chiral centres (≥ 82:18) (Table 2). Interestingly, the reaction with benzyloxyacetaldehyde furnished the opposite diastereomer when $BF_3{\cdot}OEt_2$ was employed, compared to $TiCl_3(O^iPr)$[8] (entries 3, 4).



1 **2**



3 **4**

Scheme 2

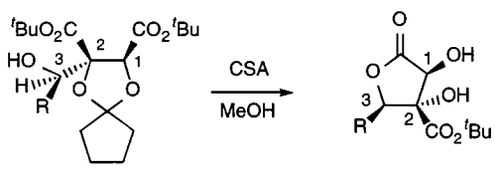
Table 1

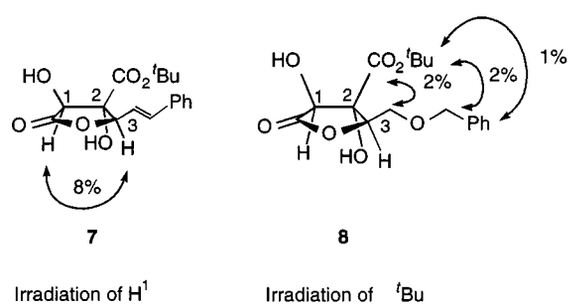
Entry	Tartate	R^1	R^2	Yield (**3** + **4**) (%)	Ratio (**3**:**4**)[a]
1	**1a**	Me	Me	28	86:14
2	**1b**	Me	$(CH_2)_4$	21	86:14
3	**1c**	^{i}Pr	Me	65	>97:3
4	**1d**	^{t}Bu	Me	74	97:3
5	**1e**	^{t}Bu	$(CH_2)_4$	73	97:3
6	**1e**	^{t}Bu	$(CH_2)_4$	67	88:12[b]

[a] Ratios determined by ^{1}H NMR analysis of the unpurified product. [b] Evans' results obtained using $TiCl_3(O^iPr)$.[8]

The relative configuration of these compounds was determined by NOE studies on the cyclised derivatives **7** and **8** (Fig. 3). Treatment of the aldol products **5** and **6** with camphorsulfonic acid (CSA) in methanol led to deprotection of the ketal and lactonisation to give **7** and **8**. NOE enhancements either between H^1 and H^3 (compound **7**) or the *tert*-butyl group and the benzylic protons (compound **8**)[10] established the stereochemistry at C^3 and confirmed that the same sense of induction was observed with all three aldehydes.

Ketones were also employed in these reactions. Addition to *trans*-chalcone led to a complex mixture of 1,2 and 1,4 products but pleasingly, reaction with the unactivated ketone, cyclohexanone, proceeded in a modest yield of 32% with the generation of two new quaternary centres (Table 3, entry 1). Methyl pyruvate was also examined and the aldol adduct was obtained in moderate yield, but with good selectivity. As with benzyl-

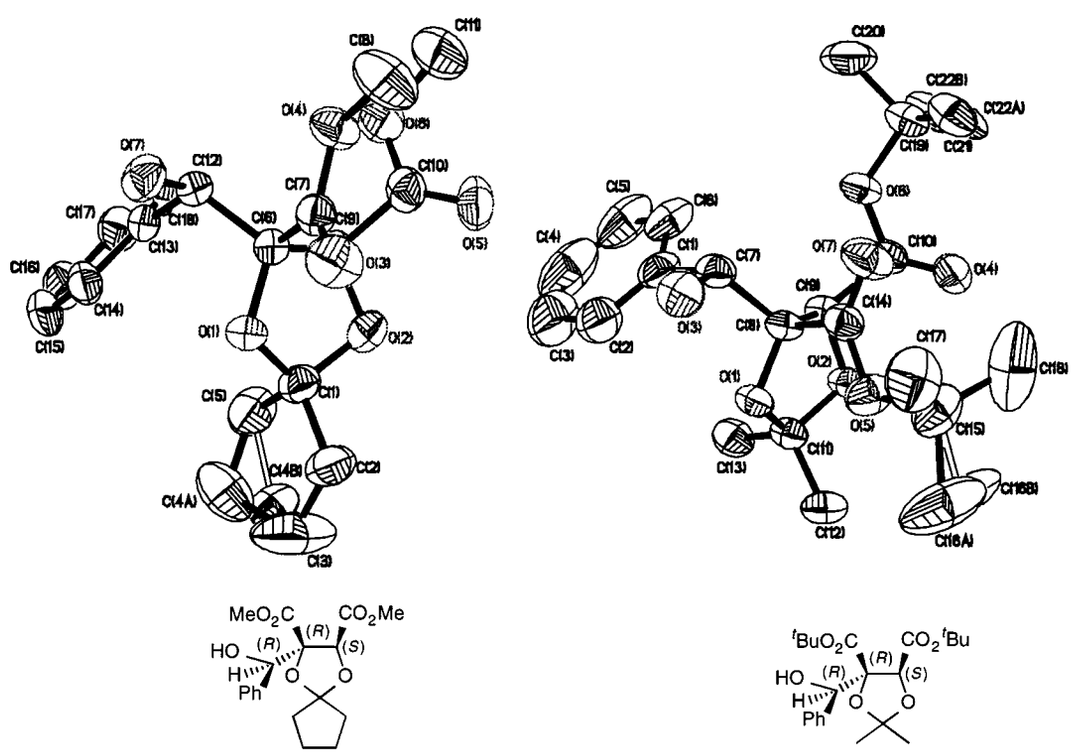




7 **8**

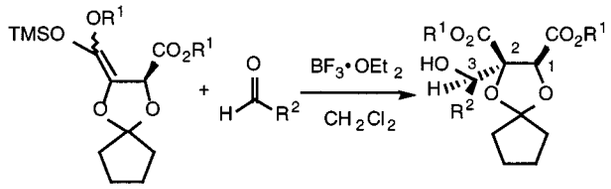
Irradiation of H^1 Irradiation of ^{t}Bu

Fig. 3



3b **3d**

Fig. 2

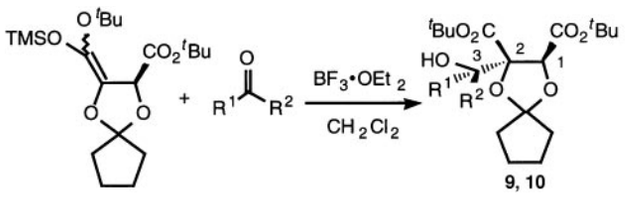


1 5, 6

Table 2

Entry	Tartate	Aldehyde	Product	Yield (%)	C^3 Selectivity
1	**1c**	Cinnamaldehyde	**5c**	59	>97:3
2	**1e**	Cinnamaldehyde	**5e**	75	95:5
3	**1e**	Benzyloxyacetaldehyde	**6e**	63	82:18
4	**1e**	Benzyloxyacetaldehyde	**6e**	64	9:91[a]

[a] Evans' results obtained using $TiCl_3(O^iPr)$.[8]



9, 10

Table 3

Entry	Ketone	Product	Yield (%)	C^3 Selectivity
1	Cyclohexanone	**9**	32	—
2	Methyl pyruvate (R^1 = Me, R^2 = CO_2Me)	**10**	29[a]	85:15[b]
3	Methyl pyruvate (R^1 = Me, R^2 = CO_2Me)	**10**	66	>5:95[c]

[a] Unoptimised yield. [b] Major isomer indicated. [c] Evans' result obtained using $TiCl_3(O^iPr)$.[8]

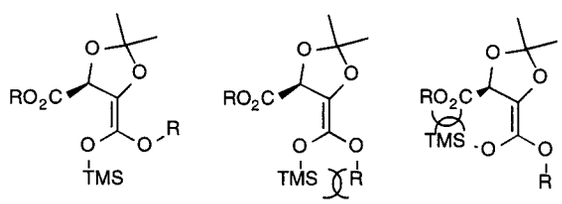
oxyacetaldehyde, the opposite diastereoisomer was obtained with $BF_3{\cdot}OEt_2$, compared to Evans' conditions using $TiCl_3(O^iPr)$[8] (entries 2, 3).

Rationalisation of stereochemistry

Mukaiyama aldol reactions are generally recognised as proceeding *via* an 'open' transition state in which the Lewis acid serves to activate the carbonyl to nucleophilic attack.[11,12] In our system, the silylketene acetal adopts a single conformation **I** in order to minimise steric interactions between the trimethylsilyloxy and the alkoxy groups **II**, and to minimise 1,4 interactions about the olefin **III** (Fig. 4). The aldehyde then approaches from the lower face of the silylketene acetal due to the steric bulk of the ester group. This determines the stereochemistry at C^2.

A number of synclinal and antiperiplanar transition states can then be envisaged in the reaction of silylketene acetal **I** with an aldehyde (Fig. 5).[12] Transition states **A**–**C** lead to the major diastereomer and **D**–**F** to the minor diastereomer. The synclinal transition states (**A**, **C**, **D** and **F**) can be ruled out immediately as in each case the carbon–oxygen bond of the aldehyde lies parallel to one of the carbon–oxygen bonds of the silylketene acetal leading to unfavourable dipole–dipole interactions. The antiperiplanar transition state **E** can also be discounted due to steric hindrance between the aldehyde substituent R^2 and the ester substituent R^1. The observed product is therefore thought to arise from transition state **B**.

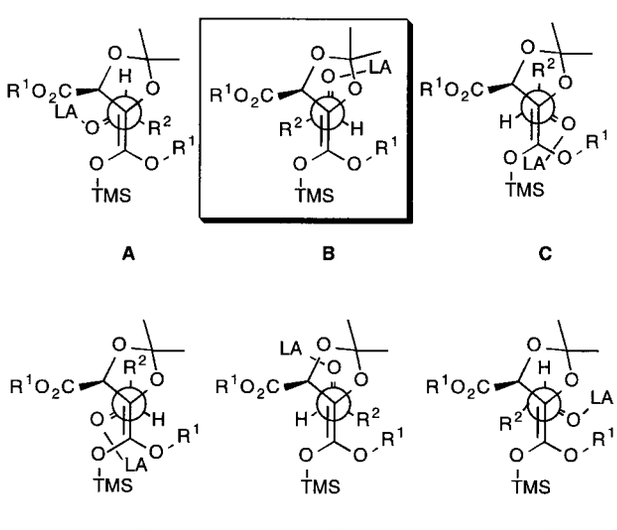
Reduction in the size of the ester (R^1) would be expected to reduce the selectivity of this reaction and indeed this was found to be true (Table 1). For R^1 = ^{t}Bu the aldol adducts were isolated as a 97:3 mixture of isomers (entries 4, 5). By comparison, the methyl esters yielded the products in a reduced



I II III

R = Me, ^{i}Pr, ^{t}Bu

Fig. 4



A B C

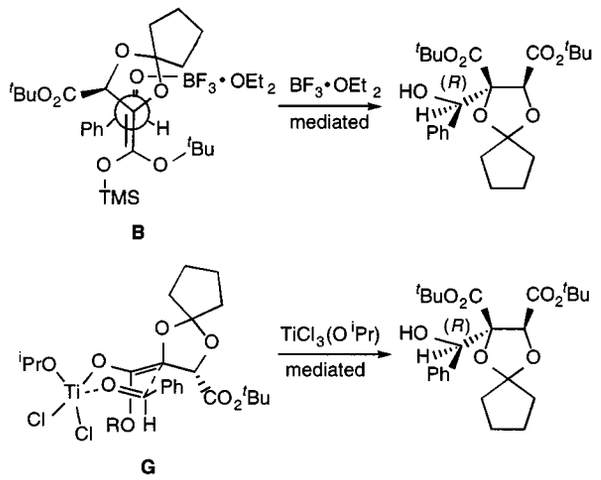
D E F

Fig. 5

ratio of 86:14 (entries 1, 2). The model also predicts that both *E* and *Z* enolate geometries will react *via* conformation **I** to yield the same major product.

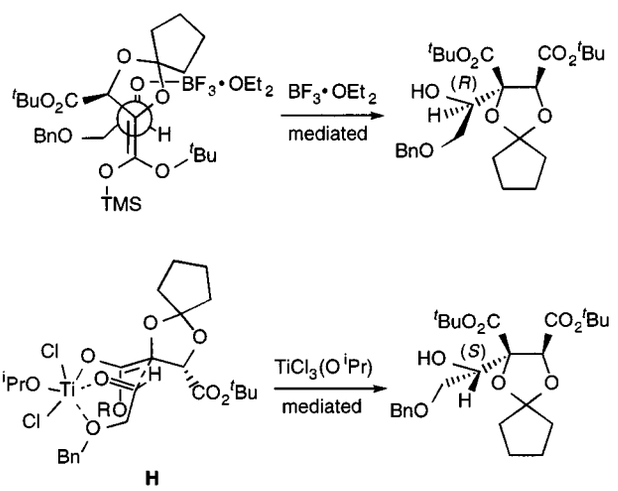
By contrast, Evans proposes a chair transition state for the $TiCl_3(O^iPr)$-mediated reaction of silylketene acetal **2e** with aldehydes.[8] It is suggested that transmetallation occurs initially to give a titanium enolate, which then reacts with the aldehyde *via* a Zimmerman–Traxler[13] transition state **G** (Scheme 3). For simple aldehydes the major product of the reaction is the *R* isomer which, coincidentally, is the same major isomer obtained using $BF_3{\cdot}OEt_2$ *via* the open transition state **B**.

In contrast, the diastereoselectivity of the reactions with benzyloxyacetaldehyde and methyl pyruvate are clearly affected by the choice of Lewis acid. In reactions with benzyloxyacetaldehyde $BF_3{\cdot}OEt_2$ furnishes the *R* isomer as the major product. Evans however, isolates the opposite C^3 diastereomer. This reversal in selectivity is due to the multidentate nature of



Scheme 3

$TiCl_3(O^iPr)$ which binds not only the carbonyl but also the ether of benzyloxyacetaldehyde. Such binding can only be achieved *via* a pseudo axial orientation of the benzyl ether (transition state **H**, Scheme 4) and this results in the formation



Scheme 4

of the opposite diastereomer.[8] Methyl pyruvate can similarly coordinate to the titanium thus affording different products according to the choice of Lewis acid.

Conclusion

In summary, we have shown that the $BF_3{\cdot}OEt_2$-mediated Mukaiyama reactions of tartrate-derived silylketene acetals with aldehydes is an efficient method for the preparation of highly oxygenated, functionalised aldol adducts. The yield and diastereoselectivity of the reaction are significantly affected by the nature of the tartrate ester; the best results being obtained with either isopropyl or *tert*-butyl tartrates which furnish a single diastereomer in high yield. The sense of induction can be easily predicted from transition state models. We have proposed the open transition state model to account for the observed selectivities in reactions with $BF_3{\cdot}OEt_2$, whilst a closed chair transition state is used to explain Evans' observations with $TiCl_3(O^iPr)$.[8] Careful choice of Lewis acid allows both isomers to be accessed with high diastereoselectivity.

Experimental

Melting points were recorded on a Kofler Hot Stage Micro Melting Point Apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 141 or an AA-10 polarimeter. Values are given in 10^{-1} deg cm^2 g^{-1}. Elemental analyses were performed using a Perkin-Elmer 2400 CHN elemental analyser. Infrared spectra were recorded on a Perkin-Elmer 157G spectrophotometer. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AC-250 FT spectrophotometer supported by an Aspect 4000 data system and a Bruker WH-400 spectrophotometer supported by an Aspect 2000 data system. The chemical shifts were recorded on the δ scale and were measured relative to the residual proton signal of the deuterated solvent. J values are given in Hz. Mass spectra were obtained using either a Kratos MS 25 or MS 80 spectrometer supported by a DS 55 data system. High resolution mass spectra were obtained using a Kratos MS 80 spectrometer supported by a DS 90 data system. Chemical ionisation used ammonia as the reagent. Thin layer chromatography (TLC) was performed on Merck 5554 60F silica gel coated plates and BDH silica (mesh 40–63) was used for column chromatograpy. Petrol refers to light petroleum (bp 40–65 °C) and ether refers to diethyl ether. All reactions were conducted in oven-dried glassware under nitrogen and where necessary solvents and reagents were dried and distilled before use. THF was refluxed over potassium benzophenone ketyl under a nitrogen atmosphere until anhydrous. 1,1,1,3,3,3-Hexamethyldisilazane, dichloromethane, chlorotrimethylsilane and pentane were all distilled from calcium hydride. (*S*,*S*)-Di-*tert*-butyl tartrate and the silylketene acetals **2** were prepared as described.[8]

Dimethyl (4*S*,5*S*)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate 1a[9]

A suspension of (*S*,*S*)-tartaric acid (10.3 g, 69 mmol) and toluene-*p*-sulfonic acid (69 mg, 0.4 mmol) in 2,2-dimethoxypropane (29.5 mL, 240 mmol) and methanol (4.6 mL) was heated under reflux for 1.5 hours. 2,2-Dimethoxypropane (9.6 mL, 78 mmol) and cyclohexane (50 mL) were added to the deep red solution and during 20 hours 20 mL of distillate was separated using a Dean–Stark apparatus. More 2,2-dimethoxypropane (9.6 mL, 78 mmol), methanol (4.6 mL) and cyclohexane (70 mL) were added and over 22 hours a further 27 mL of distillate were separated.

Sodium carbonate (330 mg) was added to the mixture and stirred for 5 minutes before being removed by filtration. The solvents were removed *in vacuo* and distillation gave the methyl ester **1a** as a colourless liquid (11.79 g, 79%), bp 102 °C/0.6 mmHg (lit.,[14] 80 °C/0.1 mmHg); $[\alpha]_D^{20}$ +44.0 (neat) [lit.,[14] +53.0 (neat)]; δ_H(250 MHz; $CDCl_3$) 1.50 (6 H, s, CMe_2), 3.82 (6 H, s, OMe), 4.80 (2 H, s, CH).

Dimethyl (2*S*,3*S*)-1,4-dioxaspiro[4.4]nonane-2,3-dicarboxylate 1b

Cyclopentanone (5 mL, 56 mmol), trimethyl orthoformate (0.46 mL, 4.2 mmol) and toluene-*p*-sulfonic acid (2.7 mg, 14 μmol) were stirred in a stoppered flask at room temperature for 2.5 hours. (*S*,*S*)-Dimethyl tartrate (500 mg, 2.8 mmol) was added and the flask warmed to 62 °C. The reaction was stirred for 3 days before methanolic sodium methoxide was added to basify the reaction (pH 8). The solvents were removed *in vacuo* and the resulting residue was preabsorbed on silica. Purification by column chromatography (10–15% ethyl acetate–petrol) yielded *tartrate* **1b** as a colourless liquid (328 mg, 63%), $[\alpha]_D^{22}$ +35.5 (*c* 2.2 in CH_2Cl_2) [lit.,[15] $[\alpha]_D^{25}$ −29.1 for (2*R*,3*R*) enantiomer (*c* 1 in $CHCl_3$); R_f 0.29 (20% EtOAc–petrol); ν_{max} (thin film)/cm^{-1} 1763 (ester); δ_H(250 MHz; $CDCl_3$) 1.70 (4 H, m, $C(CH_2CH_2)_2$), 1.91 (4 H, m, $C(CH_2CH_2)_2$), 3.81 (6 H, s, OMe), 4.77 (2 H, s, CH); δ_C(63 MHz; $CDCl_3$) 23.5 (t), 36.5 (t), 52.8 (q), 76.8 (d), 123.4 (s), 170.0 (s); *m*/*z* (EI) 244 (M^+, 42%), 215 (100), 185 (30), 55 (45) (Found: M^+, 244.0940. $C_{11}H_{16}O_6$ requires 244.0947).

Diisopropyl (4*S*,5*S*)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate 1c

A solution of (*S*,*S*)-diisopropyl tartrate (1 g, 4.3 mmol) and toluene-*p*-sulfonic acid (0.8 mg, 4.3 μmol) in 2,2-dimethoxypropane (580 μL, 4.7 mmol) and toluene (5 mL) was heated at reflux for 24 hours. The reaction was then cooled and potassium carbonate (10 mg, 72 μmol) added. The mixture was stirred for 1 hour before excess potassium carbonate was removed by filtration. Removal of the solvents *in vacuo* and column chromatography (10% ethyl acetate–petrol) yielded the tartrate **1c** as a white solid (1.08 g, 93%), mp 41.5–42.5 °C (from $^{i}Pr_2O$) (lit.,[16] 41.5–42.5 °C); $[\alpha]_D^{22}$ +43.8 (*c* 3.8 in $CHCl_3$) [lit.,[16] +42 (*c* 4.0 in $CHCl_3$)]; δ_H(250 MHz; $CDCl_3$) 1.27 (12 H, d, *J* 6.3, CH*Me*$_2$), 1.47 (6 H, s, CMe_2), 4.66 (2 H, s, C*H*($CO_2^{i}Pr$)), 5.10 (2 H, qq, *J* 6.3, 6.3, C*H*Me_2).

Di-*tert*-butyl (4*S*,5*S*)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate 1d

A solution of (*S*,*S*)-di-*tert*-butyl tartrate[8] (4 g, 19 mmol) and toluene-*p*-sulfonic acid (14.4 mg, 76 μmol) in 2,2-dimethoxypropane (14 mL, 114 mmol) and toluene (20 mL) was stirred at 60 °C for 5 days. Potassium carbonate (50 mg, 0.2 mmol) was added and the mixture stirred for 1 hour before excess potassium carbonate was removed by filtration. Removal of the solvents *in vacuo* and column chromatography (10–25% ethyl acetate–petrol) yielded the *tartrate* **1d** as a white solid (3.94 g, 68%) together with unreacted starting material (934 mg, 19%), mp 76–78 °C; $[\alpha]_D^{22}$ +42.8 (*c* 0.8 in CH_2Cl_2); R_f 0.43 (10% EtOAc–petrol) (Found: C, 59.7; H, 8.7. $C_{15}H_{26}O_6$ requires C, 59.6; H, 8.7%); ν_{max} (CH_2Cl_2 soln.)/cm^{-1} 1736 (ester); δ_H(250 MHz; $CDCl_3$) 1.48 (6 H, s, CMe_2), 1.48 (18 H, s, ^{t}Bu), 4.52 (2 H, s, CH); δ_C(63 MHz; $CDCl_3$) 26.5 (q), 27.9 (q), 77.9 (d), 82.5 (s), 113.5 (s), 168.8 (s); *m*/*z* (CI) 320 (M^+NH_4, 16%), 303 (M^+H, 7), 264 (100) (Found: M^+H, 303.1797. $C_{15}H_{27}O_6$ requires 303.1808).

Di-*tert*-butyl (2*S*,3*S*)-1,4-dioxaspiro[4.4]nonane-2,3-dicarboxylate 1e[4]

Cyclopentanone (8.5 mL, 95 mmol), trimethyl orthoformate (0.78 mL, 7.2 mmol) and toluene-*p*-sulfonic acid (4.5 mg, 24 μmol) were stirred in a stoppered flask at room temperature for 2.5 hours. (*S*,*S*)-Di-*tert*-butyl tartrate[8] (1.25 g, 4.8 mmol) was added and the flask warmed to 68 °C. The reaction was stirred for 3 days before quenching with methanolic sodium methoxide. The solvents were removed *in vacuo* and the resulting residue was preabsorbed on silica. Purification by column chromatography (2% ethyl acetate–petrol) yielded tartrate **1e** (1.00 g, 64%) as a white crystalline solid together with unreacted starting material (258 mg, 20%), mp 64–65 °C (lit.,[8] 64–65 °C); $[\alpha]_D^{22}$ +38.6 (*c* 1.4 in CH_2Cl_2) [lit.,[8] +36 (*c* 1.39 in CH_2Cl_2)]; δ_H(250 MHz; $CDCl_3$) 1.49 (18 H, s, ^{t}Bu), 1.70 (4 H, m, C(CH_2CH_2)$_2$), 1.85 (2 H, m, C(CH_2CH_2)$_2$), 1.95 (2 H, m, C(CH_2CH_2)$_2$), 4.50 (2 H, s, CH).

General procedure for aldol reactions with aldehydes

Silylketene acetal **2**[8] (1 mmol) was dissolved in dichloromethane (4 mL) and added to a −78 °C solution of the aldehyde (1.2 mmol) and dichloromethane (4 mL). Boron trifluoride–diethyl ether (150 μL, 1.2 mmol) was added and the reaction stirred for 2 hours at −78 °C, then warmed to −40 °C over 2.5 hours. The reaction was quenched by addition of saturated aqueous sodium hydrogen carbonate (10 mL), then allowed to warm to room temperature. The organic phase was separated and the aqueous extracted with more dichloromethane (2 × 5 mL). The combined organic layers were then washed with brine, dried (Na_2SO_4), filtered and concentrated yielding an oil, which was purified by column chromatography.

Dimethyl (4*R*,5*S*)-4-(1-hydroxy-1-phenylmethyl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate 3a and 4a. Column chromatography (20% ethyl acetate–petrol) yielded the minor *alcohol* **4a** (13 mg, 4%), $[\alpha]_D^{22}$ −8.0 (*c* 1.0 in CH_2Cl_2); R_f 0.31 (40% EtOAc–petrol); ν_{max} ($CHCl_3$ soln.)/cm^{-1} 1762 (ester), 1750 (ester); δ_H(250 MHz; $CDCl_3$) 1.25 (3 H, s, CMe_2), 1.60 (3 H, s, CMe_2), 3.55 (1 H, d, *J* 10.1, OH), 3.63 (3 H, s, OMe), 3.90 (3 H, s, OMe), 4.74 (1 H, s, C*H*(CO_2Me)), 5.17 (1 H, d, *J* 10.1, C*H*(OH)), 7.33 (3 H, m, Ph), 7.42 (2 H, m, Ph); δ_C(63 MHz; $CDCl_3$) 26.1 (q), 26.9 (q), 52.6 (q), 52.9 (q), 72.9 (d), 77.4 (d), 88.3 (s), 112.4 (s), 127.6 (d), 128.3 (d), 128.4 (d), 138.4 (s), 169.3 (s), 170.5 (s); *m*/*z* (CI) 325 (M^+, 39%), 267 (100), 249 (90) (Found: M^+, 325.1286. $C_{16}H_{20}O_7$ requires 325.1287).

Further elution afforded the major *alcohol* **3a** as a white solid (79 mg, 24%), mp 141.5–142.5 °C; $[\alpha]_D^{22}$ −10.0 (*c* 0.5 in CH_2Cl_2); R_f 0.23 (40% EtOAc–petrol) (Found: C, 59.3; H, 6.25. $C_{16}H_{20}O_7$ requires C, 59.25; H, 6.2%); ν_{max} (CH_2Cl_2 soln.)/cm^{-1} 1765 (ester), 1736 (ester); δ_H(250 MHz; $CDCl_3$) 0.86 (3 H, s, CMe_2), 1.61 (3 H, s, CMe_2), 2.76 (1 H, d, *J* 6.3, OH), 3.80 (3 H, s, OMe), 3.87 (3 H, s, OMe), 4.30 (1 H, s, C*H*(CO_2Me)), 5.26 (1 H, d, *J* 6.3, C*H*(OH)), 7.37 (3 H, m, Ph), 7.52 (2 H, m, Ph); δ_C(63 MHz; $CDCl_3$) 26.0 (q), 26.6 (q), 52.7 (q), 52.9 (q), 75.6 (d), 78.9 (d), 88.8 (s), 112.8 (s), 128.1 (d), 128.7 (d), 128.8 (d), 137.7 (s), 167.7 (s), 171.2 (s); *m*/*z* (CI) 325 (M^+, 10%), 267 (80), 249 (100) (Found: M^+, 325.1286. $C_{16}H_{20}O_7$ requires 325.1287).

Dimethyl (2*R*,3*S*)-2-(1-hydroxy-1-phenylmethyl)-1,4-dioxaspiro[4.4]nonane-2,3-dicarboxylate 3b and 4b. Column chromatography (10–20% ethyl acetate–petrol) yielded the minor *alcohol* **4b** (11 mg, 3%), $[\alpha]_D^{22}$ +3.3 (*c* 0.6 in CH_2Cl_2); R_f 0.42 (40% EtOAc–petrol); ν_{max} (CH_2Cl_2 soln.)/cm^{-1} 1764 (ester), 1737 (ester); δ_H(250 MHz; $CDCl_3$) 1.60–1.80 (6 H, m, CH_2), 1.90–2.13 (2 H, m, CH_2), 3.45 (1 H, d, *J* 9.4, OH), 3.60 (3 H, s, OMe), 3.87 (3 H, s, OMe), 4.69 (1 H, s, C*H*(CO_2Me)), 5.16 (1 H, d, *J* 9.4, C*H*(OH)), 7.57 (5 H, m, Ph); δ_C(63 MHz; $CDCl_3$) 23.1 (t), 23.4 (t), 36.5 (t), 37.3 (t), 52.6 (q), 52.9 (q), 72.9 (d), 77.7 (d), 87.9 (s), 122.2 (s), 127.7 (d), 128.3 (d), 128.4 (d), 138.4 (s), 169.1 (s), 170.5 (s); *m*/*z* (EI) 350 (M^+, 3%), 244 (M^+ − PhCHO, 85), 160 (84), 107 (35), 101 (100) (Found: M^+, 350.1358. $C_{18}H_{22}O_7$ requires 350.1366).

Further elution afforded the major *alcohol* **3b** as a cream solid (67 mg, 18%), mp 138–141 °C; $[\alpha]_D^{22}$ +4.2 (*c* 2.4 in CH_2Cl_2); R_f 0.29 (40% EtOAc–petrol) (Found: C, 61.6; H, 6.3. $C_{18}H_{22}O_7$ requires C, 61.7; H, 6.3%); ν_{max} (CH_2Cl_2 soln.)/cm^{-1} 1765 (ester), 1734 (ester); δ_H(250 MHz; $CDCl_3$) 0.78–1.70 (6 H, m, CH_2), 1.97 (1 H, m, CH_2), 2.20 (1 H, m, CH_2), 2.95 (1 H, br s, OH), 3.74 (3 H, s, OMe), 3.82 (3 H, s, OMe), 4.14 (1 H, s, C*H*(CO_2Me)), 5.50 (1 H, s, C*H*(OH)), 7.35 (3 H, m, Ph), 7.49 (2 H, m, Ph); δ_C(63 MHz; $CDCl_3$) 22.9 (t), 23.3 (t), 36.0 (t), 36.9 (t), 52.7 (q), 52.9 (q), 75.2 (d), 79.1 (d), 88.5 (s), 122.2 (s), 128.0 (d), 128.6 (d), 128.7 (d), 137.9 (s), 167.6 (s), 171.2 (s); *m*/*z* (EI) 350 (M^+, 3%), 244 (M^+ − PhCHO, 95), 160 (80), 107 (85), 101 (100) (Found: M^+, 350.1367. $C_{18}H_{22}O_7$ requires 350.1366).

Diisopropyl (4*R*,5*S*)-4-[(*R*)-1-hydroxy-1-phenylmethyl]-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate 3c. The crude mixture (>97 : 3 mixture of diastereomers by ^{1}H NMR) was purified by column chromatography (10–15% ethyl acetate–petrol) to afford the major *alcohol* **3d** as a white solid (199 mg, 65%), mp 66–67 °C; $[\alpha]_D^{22}$ −2.31 (*c* 3.77 in CH_2Cl_2); R_f 0.20 (15% EtOAc–petrol) (Found: C, 63.1; H, 7.6. $C_{20}H_{28}O_7$ requires C, 63.1; H, 7.4%); ν_{max} (CH_2Cl_2 soln.)/cm^{-1} 3055 (OH), 2987 (CH), 1756 (C=O); δ_H(300 MHz; $CDCl_3$) 0.94 (3 H, s, CMe_2), 1.25 (3 H, d, *J* 6.2, CH*Me*$_2$), 1.30 (3 H, d, *J* 6.2, CH*Me*$_2$), 1.35 (3 H, d, *J* 6.2, CH*Me*$_2$), 1.40 (3 H, d, *J* 6.2, CH*Me*$_2$), 1.63 (3 H, s, CMe_2), 2.86 (1 H, d, *J* 6.6, CH(O*H*)), 4.27 (1 H, s, C*H*($CO_2^{i}Pr$)), 5.11 (1 H, qq, *J* 6.2, 6.2, C*H*Me_2), 5.16 (1 H, qq, *J* 6.2, 6.2, C*H*Me_2), 5.25 (1 H, d, *J* 6.6, C*H*(OH)), 7.36 (3 H, m, Ph), 7.52 (2 H, m, Ph); δ_C(63 MHz; $CDCl_3$) 21.6 (q), 21.7 (2 × q), 21.9 (q), 26.2 (q), 26.6 (q), 69.7 (d), 70.3 (d), 75.9 (d), 79.1 (d), 88.4 (s), 112.4 (s),

128.0 (d), 128.6 (d), 128.7 (d), 138.1 (s), 166.0 (s), 170.5 (s); *m*/*z* (CI) 398 (M^+NH_4, 6%), 381 (M^+H, 2), 340 (34), 323 (100) (Found: M^+H, 381.1897. $C_{20}H_{29}O_7$ requires 381.1913).

Di-*tert*-butyl (4*R*,5*S*)-4-[(*R*)-1-hydroxy-1-phenylmethyl]-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate 3d. The crude mixture (97 : 3 mixture of diastereomers by ^{1}H NMR) was purified by column chromatography (5–10% ethyl acetate–petrol) to afford the major *alcohol* **3d** as a white solid (99 mg, 72%), mp 129–131 °C; $[\alpha]_D^{22}$ −2.20 (*c* 3.45 in CH_2Cl_2); R_f 0.38 (15% EtOAc–petrol) (Found: C, 64.3; H, 7.95. $C_{22}H_{32}O_7$ requires C, 64.7; H, 7.9%); ν_{max} (CH_2Cl_2 soln.)/cm^{-1} 3055 (OH), 2986 (CH), 1753 (C=O), 1725 (C=O); δ_H(250 MHz; $CDCl_3$) 0.88 (3 H, s, CMe_2), 1.49 (9 H, s, ^{t}Bu), 1.57 (9 H, s, ^{t}Bu), 1.63 (3 H, s, CMe_2), 2.95 (1 H, d, *J* 6.5, OH), 4.23 (1 H, s, C*H*($CO_2{}^t$Bu)), 5.27 (1 H, d, *J* 6.5, C*H*(OH)), 7.34 (3 H, m, Ph), 7.51 (2 H, m, Ph); δ_C(63 MHz; $CDCl_3$) 26.3 (q), 26.6 (q), 28.0 (q), 28.1 (q), 76.1 (d), 79.5 (d), 83.0 (s), 83.6 (s), 88.2 (s), 112.2 (s), 127.9 (d), 128.4 (d), 128.7 (d), 138.4 (s), 165.9 (s), 170.6 (s); *m*/*z* (CI) 426 (M^+NH_4, 10%), 409 (M^+H, 4), 370 (100), 314 (31) (Found: M^+H, 409.2228. $C_{22}H_{33}O_7$ requires 409.2226).

Di-*tert*-butyl (2*R*,3*S*)-2-(1-hydroxy-1-phenylmethyl)-1,4-dioxaspiro[4.4]nonane-2,3-dicarboxylate 3e and 4e.[8] Reaction on a 0.2 mmol scale afforded a mixture of diastereomers (97 : 3 by ^{1}H NMR). Purification by column chromatography (15–20% ethyl acetate–hexane) yielded the minor *alcohol* **4e** (2 mg, 3%), R_f 0.36 (15% EtOAc–petrol); ν_{max} (CH_2Cl_2 soln.)/cm^{-1} 3502 (OH), 1750 (C=O), 1724 (C=O); δ_H(250 MHz; $CDCl_3$) 1.26 (9 H, s, ^{t}Bu), 1.54 (9 H, s, ^{t}Bu), 1.56–1.80 (6 H, m, CH_2), 2.05–2.22 (2 H, m, CH_2), 3.10 (1 H, d, *J* 9.5, OH), 4.63 (1 H, s, C*H*($CO_2{}^t$Bu)), 5.08 (1 H, d, *J* 9.5, C*H*(OH)), 7.25–7.35 (3 H, m, Ph), 7.40–7.47 (2 H, m, Ph); δ_C(63 MHz; $CDCl_3$) 23.3 (t), 23.5 (t), 27.7 (q), 28.1 (q), 36.7 (t), 37.6 (t), 73.3 (d), 78.4 (d), 82.8 (s), 83.0 (s), 87.3 (s), 121.7 (s), 128.1 (d), 128.2 (d), 128.3 (d), 139.2 (s), 166.7 (s), 169.5 (s); *m*/*z* (EI) 434 (M^+, 2%), 216 (76), 85 (100) (Found: M^+: 434.2309. $C_{24}H_{34}O_7$ requires 434.2304).

Further elution afforded the major alcohol **3e** as a white solid (58 mg, 70%), mp 95 °C; $[\alpha]_D^{22}$ +13.8 (*c* 3.62 in CH_2Cl_2) [lit.,[8] +11 (*c* 3.51 in CH_2Cl_2)]; δ_H(250 MHz; $CDCl_3$) 1.00–1.35 (2 H, m, CH_2), 1.50 (9 H, s, ^{t}Bu), 1.52–1.72 (4 H, m, CH_2), 1.56 (9 H, s, ^{t}Bu), 2.05 (1 H, m, CH_2), 2.20 (1 H, m, CH_2), 2.89 (1 H, d, *J* 6.3, OH), 4.04 (1 H, s, C*H*($CO_2{}^t$Bu)), 5.30 (1 H, d, *J* 6.3, C*H*(OH)), 7.30–7.40 (3 H, m, Ph), 7.48–7.55 (2 H, m, Ph).

Diisopropyl (4*R*,5*S*)-4-[(1*R*,2*E*)-1-hydroxy-3-phenylprop-2-enyl]-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate 5c. The crude mixture (>97 : 3 mixture of diastereomers by ^{1}H NMR) was purified by column chromatography (10–20% ethyl acetate–petrol) to afford the major *alcohol* **5c** as a hard gum (179 mg, 59%), $[\alpha]_D^{22}$ +45.3 (*c* 1.8 in CH_2Cl_2); R_f 0.22 (15% EtOAc–petrol); ν_{max} (CH_2Cl_2 soln.)/cm^{-1} 3054 (OH), 2986 (CH), 1754 (C=O); δ_H(300 MHz; $CDCl_3$) 1.26 (3 H, d, *J* 6.2, CH*Me*$_2$), 1.29 (3 H, d, *J* 6.2, CH*Me*$_2$), 1.29 (3 H, d, *J* 6.2, CH*Me*$_2$), 1.32 (3 H, d, *J* 6.2, CH*Me*$_2$), 1.46 (3 H, s, CMe_2), 1.66 (3 H, s, CMe_2), 2.77 (1 H, d, *J* 7.3, CH(O*H*)), 4.64 (1 H, s, C*H*($CO_2{}^i$Pr)), 4.69 (1 H, dd, *J* 7.3, 6.6, C*H*(OH)), 5.08 (1 H, qq, *J* 6.2, 6.2, C*H*Me$_2$), 5.11 (1 H, qq, *J* 6.2, 6.2, C*H*Me$_2$), 6.36 (1 H, dd, *J* 16.1 and 6.6, PhCH=C*H*), 6.74 (1 H, d, *J* 16.1, PhC*H*=CH), 7.24–7.43 (5 H, m, Ph); δ_C(63 MHz; $CDCl_3$) 21.7 (2 × q), 21.8 (2 × q), 26.7 (q), 26.8 (q), 69.6 (d), 70.1 (d), 75.2 (d), 79.4 (d), 88.1 (s), 112.8 (s), 125.7 (d), 126.7 (d), 128.2 (d), 128.7 (d), 134.2 (d), 136.2 (s), 169.1 (s), 169.9 (s); *m*/*z* (CI) 424 (M^+NH_4, 36%), 406 (M^+, 28), 389 (M^+ − OH, 100), 274 (M^+ − PhCH=CHCHO, 20) (Found: M^+NH_4, 424.2320. $C_{22}H_{34}NO_7$ requires 424.2335).

Di-*tert*-butyl (2*R*,3*S*)-2-[(1*R*,2*E*)-1-hydroxy-3-phenylprop-2-enyl]-1,4-dioxaspiro[4.4]nonane-2,3-dicarboxylate 5e. The crude mixture (95 : 5 mixture of diastereomers by ^{1}H NMR) was purified by column chromatography (5–30% ethyl acetate–hexane) to afford the major *alcohol* **5e** as a hard gum (268 mg, 72%), $[\alpha]_D^{22}$ +38.8 (*c* 2.43 in CH_2Cl_2); R_f 0.53 (35% EtOAc–hexane) (Found: C, 66.6; H, 8.0. $C_{26}H_{36}O_7$ + 0.5 mol EtOAc requires C, 66.6; H, 8.0%); ν_{max} (thin film)/cm^{-1} 3494 (OH), 2978, 1728 (C=O); δ_H(300 MHz; $CDCl_3$) 1.48 (9 H, s, ^{t}Bu), 1.52 (9 H, s, ^{t}Bu), 1.78 (6 H, m, CH_2), 2.19 (2H, m, CH_2), 2.82 (1 H, d, *J* 7.0, CH(O*H*)), 4.46 (1 H, s, C*H*($CO_2{}^t$Bu)), 4.69 (1 H, dd, *J* 7.0, 7.0, C*H*(OH)), 6.34 (1 H, dd, *J* 16.0, 7.0, PhCH=C*H*), 6.72 (1 H, d, *J* 16.0, PhC*H*=CH), 7.32 (5 H, m, Ph); δ_C(63 MHz; $CDCl_3$) 23.3 (t), 23.5 (t), 28.0 (2 × q), 36.7 (t), 37.9 (t), 75.1 (d), 79.9 (d), 82.7 (s), 83.3 (s), 87.5 (s), 122.2 (s), 126.1 (d), 126.6 (d), 128.0 (d), 128.6 (d), 133.7 (d), 136.4 (s), 166.4 (s), 169.9 (s); *m*/*z* (CI) 460 (M^+, 3%), 347 (83), 331 (90), 261 (95), 123 (100) (Found: M^+, 460.2463. $C_{26}H_{36}O_7$ requires 460.2461).

Di-*tert*-butyl (2*R*,3*S*)-2-[(1*R*)-2-(benzyloxy)-1-hydroxyethyl]-1,4-dioxaspiro[4.4]nonane-2,3-dicarboxylate 6e. Reaction on a 0.5 mmol scale afforded a mixture of diastereomers (82 : 18 by ^{1}H NMR) which was purified by column chromatography (25% petrol–$CHCl_3$) yielding the major *alcohol* **6e** as a clear oil (121 mg, 56%), $[\alpha]_{546}^{22}$ +23.0 (*c* 0.61 in CH_2Cl_2); R_f 0.54 (15% EtOAc–petrol); ν_{max} (thin film)/cm^{-1} 3496 (OH), 1744 (C=O), 1728 (C=O); δ_H(250 MHz; $CDCl_3$) 1.44 (9 H, s, ^{t}Bu), 1.47 (9 H, s, ^{t}Bu), 1.60–1.80 (6 H, m, $(CH_2)_4$), 2.03–2.20 (2 H, m $(CH_2)_4$), 3.30 (1 H, br s, OH), 3.63 (1 H, dd, *J* 10.2, 6.3, CH_AH$_B$OBn), 3.74 (1 H, dd, *J* 10.2, 3.5, CH$_A$$H_B$OBn), 4.18 (1 H, dd, *J* 6.3, 3.5, C*H*(OH)), 4.51 (1 H, d, *J* 12, CH_AH$_B$Ph), 4.57 (1 H, d, *J* 12, CH$_A$$H_B$Ph), 7.20–7.36 (5 H, m, Ph); δ_C(63 MHz; $CDCl_3$) 23.4 (t), 23.5 (t), 27.9 (q), 28.0 (q), 36.8 (t), 37.8 (t), 70.4 (t), 73.2 (t), 73.3 (d), 79.6 (d), 82.8 (s), 83.3 (s), 85.9 (s), 122.0 (s), 127.6 (d), 127.7 (d), 128.4 (d), 137.9 (s), 166.6 (s), 169.6 (s); *m*/*z* (CI) 479 (M^+H, 14%), 367 (M^+ − $CO_2{}^t$Bu, 100), 283 (45), 91 (44) (Found: M^+H, 479.2635. $C_{26}H_{39}O_8$ requires 479.2645).

***tert*-Butyl (2*R*,3*R*,4*S*)-3,4-dihydroxy-5-oxo-2-[(*E*)-2-phenylethen-1-yl]tetrahydrofuran-3-carboxylate 7**[8]

Camphorsulfonic acid (7.3 mg, 32 μmol) was added to a solution of aldol adduct **5e** (87 mg, 0.19 mmol) in methanol (2 mL). The reaction was stirred for four days at room temperature then heated to 45 °C for six hours. The solution was diluted with ethyl acetate (15 mL), washed with saturated aqueous sodium hydrogen carbonate (10 mL) and brine (10 mL). The organic phase was dried (Na_2SO_4), filtered and concentrated then purified by column chromatography (20–30% ethyl acetate–hexane) to yield *lactone* **7** as a clear oil (19.9 mg, 33%), $[\alpha]_D^{22}$ +38.3 (*c* 0.995 in CH_2Cl_2); R_f 0.26 (40% EtOAc–petrol); ν_{max} (thin film)/cm^{-1} 3424 (OH), 1787 (C=O, lactone), 1748 (C=O, ester); δ_H(300 MHz; $CDCl_3$) 1.46 (9 H, s, ^{t}Bu), 3.14 (1 H, br s, CH(O*H*)), 4.08 (1 H, br s, C(OH)), 4.70 (1 H, br s, C*H*(OH)), 4.95 (1 H, dd, *J* 6.2, 1.1, PhCH=CHC*H*), 6.10 (1 H, dd, *J* 16.1, 6.2, PhCH=C*H*), 6.83 (1 H, dd, *J* 16.1, 1.1, PhC*H*=CH), 7.28–7.38 (5 H, m, Ph); δ_C(63 MHz; $CDCl_3$) 27.9 (q), 75.1 (d), 80.9 (d), 83.3 (s), 86.0 (s), 119.0 (d), 126.7 (d), 128.7 (d), 128.9 (d), 133.5 (d), 135.3 (s), 168.5 (s), 172.7 (s); *m*/*z* (EI) 320 (M^+, 14%), 264 (M^+ − C_4H_8, 44), 133 (100) (Found: M^+, 320.1265. $C_{17}H_{20}O_6$ requires 320.1260).

***tert*-Butyl (2*R*,3*R*,4*S*)-2-benzyloxymethyl-3,4-dihydroxy-5-oxotetrahydrofuran-3-carboxylate 8**[8]

Camphorsulfonic acid (17.7 mg, 76 μmol) was added to a solution of aldol adduct **6e** (104 mg, 0.22 mmol) in methanol (2 mL). The reaction was stirred for six days at room temperature then diluted with ethyl acetate (10 mL), washed with saturated aqueous sodium hydrogen carbonate (10 mL) and brine (10 mL). The organic phase was dried (Na_2SO_4), filtered and concentrated then purified by column chromatography (20–40% ethyl acetate–hexane) to yield *lactone* **8** as a white solid (27 mg, 37%), mp 132 °C; $[\alpha]_D^{22}$ +35.8 (*c* 0.81 in CH_2Cl_2); R_f 0.29 (50% EtOAc–petrol); ν_{max} (KBr disc)/cm^{-1} 3471 (OH), 1795 (C=O,

lactone), 1731 (C=O, ester); δ_H(250 MHz; $CDCl_3$) 1.41 (9 H, s, ^{t}Bu), 3.21 (1 H, br s, CH(O*H*)), 3.61 (1 H, dd, *J* 10.7, 4.0 CH_AH$_B$OBn), 3.71 (1 H, dd, *J* 10.7, 7.3 CH$_A$*H*$_B$OBn), 3.96 (1 H, br s, C(OH)), 4.54 (1H, dd, *J* 7.3, 4.0, C*H*CH$_2$OBn), 4.56 (2 H, s, C*H*$_2$Ph), 4.62 (1 H, s, C*H*(OH)), 7.28–7.40 (5 H, m, Ph); δ_C(100 MHz; $CDCl_3$) 27.8 (q), 66.8 (t), 73.5 (t), 75.1 (d), 79.6 (d), 81.0 (s), 86.1 (s), 127.8 (d), 128.0 (d), 128.5 (d), 137.0 (s), 168.1 (s), 172.9 (s); *m*/*z* (FAB) 339 (M^+H, 9%), 281 ($M^+ - {}^t$Bu, 32) (Found: M^+H, 339.1448. $C_{17}H_{23}O_7$ requires 339.1444).

Di-*tert*-butyl (2*S*,3*S*)-2-(1-hydroxycyclohexyl)-1,4-dioxaspiro-[4.4]nonane-2,3-dicarboxylate 9

Silylketene acetal **2e** (0.5 mmol) was dissolved in dichloromethane (1.5 mL) and added to a −78 °C solution of cyclohexanone (62 μL, 0.6 mmol) and dichloromethane (1.5 mL). Boron trifluoride–diethyl ether (75 μL, 0.6 mmol) was added and the reaction stirred for 6 hours warming to −30 °C. The reaction was quenched by addition of saturated aqueous sodium hydrogen carbonate (5 mL), then allowed to reach room temperature. The organic phase was separated and the aqueous extracted with more dichloromethane (2 × 5 mL). The combined organic layers were then washed with brine, dried (Na_2SO_4), filtered and concentrated yielding an oil. Purification by column chromatography (5% ethyl acetate–petrol) yielded the *alcohol* **9** as a white solid (58 mg, 32%), mp 118.5–120 °C; $[\alpha]_D^{22}$ +3.8 (*c* 0.78 in CH_2Cl_2); R_f 0.40 (10% EtOAc–petrol); ν_{max} (CH_2Cl_2 soln.)/cm^{-1} 3498 (OH), 1741 (ester); δ_H(250 MHz; $CDCl_3$) 1.46 (9 H, s, ^{t}Bu), 1.48 (9 H, s, ^{t}Bu), 1.65–1.76 (14 H, m, CH_2), 1.80–1.88 (2 H, m, CH_2), 2.04–2.13 (2 H, m, CH_2), 3.05 (1 H, s, OH), 4.49 (1 H, s, CH); δ_C(63 MHz; $CDCl_3$) 21.3 (t), 21.5 (t), 22.8 (t), 23.5 (t), 25.6 (t), 28.0 (2 × q), 31.3 (t), 32.1 (t), 37.0 (t), 37.3 (t), 74.4 (s), 78.9 (d), 82.2 (s), 82.3 (s), 90.7 (s), 123.2 (s), 168.7 (s), 171.6 (s); *m*/*z* (EI) 427 (M^+H, 1%), 216 (58), 99 (53), 85 (100), 57 (55) (Found: M^+, 426.2610. $C_{23}H_{38}O_7$ requires 426.2618).

Di-*tert*-butyl (2*S*,3*S*)-2-(1-hydroxy-2-methoxy-1-methyl-2-oxo-ethyl)-1,4-dioxaspiro[4.4]nonane-2,3-dicarboxylate 10[8]

Silylketene acetal **2e** (0.31 mmol) was dissolved in dichloromethane (2 mL) and added to a −78 °C solution of methyl pyruvate (45 μL, 0.5 mmol) and dichloromethane (2 mL). Boron trifluoride–diethyl ether (65 μL, 0.5 mmol) was added and the reaction stirred for 3 hours at −78 °C then warmed to −40 °C and left overnight. The reaction was quenched by addition of saturated aqueous sodium hydrogen carbonate (5 mL), then allowed to reach room temperature. The organic phase was separated and the aqueous extracted with more dichloromethane (2 × 5 mL). The combined organic layers were then washed with brine, dried (Na_2SO_4), filtered and concentrated yielding an oil. Purification by column chromatography (12% ethyl acetate–petrol) yielded the alcohol **10** as a 85:15 mixture of diastereoisomers (39 mg, 29%). The NMR data for both diastereoisomers was consistent with that reported.[8] δ_H(250 MHz; $CDCl_3$) 1.46 (9 H, s, ^{t}Bu [minor]), 1.48 (18 H, s, ^{t}Bu [major]), 1.49 (9 H, s, ^{t}Bu [minor]), 1.56 (3 H, s, C(OH)*Me* [major + minor]), 1.60–1.84 (6 H, m, CH_2 [major + minor]), 2.05–2.19 (2 H, m, CH_2 [major + minor]), 3.67 (1 H, br s, OH [minor]), 3.76 (3 H, s, OMe [major]), 3.78 (3 H, s, OMe [minor]), 3.95 (1 H, br s, OH [major]), 4.84 (1 H, s, CH [minor]) 4.84 (1 H, s, CH [major]) [lit.,[8] 1.47, 1.48, 1.49, 1.57, 1.62, 1.62–1.70, 1.76, 1.82, 2.01–2.15, 3.67, 3.77, 3.78, 3.95, 4.84, 4.85].

Crystal data for dimethyl (2*R*,3*S*)-2-[(*R*)-1-hydroxy-1-phenyl-methyl]-1,4-dioxaspiro[4.4]nonane-2,3-dicarboxylate 3b

Crystal data for $C_{18}H_{22}O_7$; $M = 350.36$; crystallises from ethyl acetate–petrol as colourless blocks; crystal dimensions 0.60 × 0.50 × 0.40 mm. Orthorhombic, $a = 9.2450(18)$, $b = 11.518(2)$, $c = 16.602(3)$ Å, $U = 1767.8(6)$ Å^3, $Z = 4$, $D_c = 1.316$ Mg m^{-3}, space group $P2_12_12_1$ (D_2^4 No. 19), Mo-Kα radiation ($\bar{\lambda} = 0.71073$ Å), μ(Mo-Kα) = 0.101 mm^{-1}, $F(000) = 744$.

Three-dimensional, room temperature X-ray data were collected in the range $3.5 < 2\theta < 60°$ on a Siemens P4 diffractometer by the omega scan method. Of the 3695 reflections measured, all of which were corrected for Lorentz and polarisation effects (but not for absorption), 2462 independent reflections exceeded the significance level $|F|/\sigma(|F|) > 4.0$. The structure was solved by direct methods and refined by blocked cascade least squares methods. Hydrogen atoms were placed geometrically and refined with a riding model (including torsional freedom for methyl groups) and with U_{iso} constrained to be 1.2 (1.5 for methyl groups) times U_{eq} of the carrier atom. Refinement converged at a final $R = 0.0664$ ($wR_2 = 0.2021$, for all 3488 unique data; 229 parameters, mean and maximum δ/σ 0.000, 0.000), with allowance for the thermal anisotropy of all non-hydrogen atoms (with the exception of C4A and C4b; C4A and C4b were found to be disordered in the order of 0.7 to 0.3). Minimum and maximum final electron density −0.412 and 0.398 e A^{-3}. A weighting scheme $w = 1/[\sigma^2(F_o^2) + (0.0969 *P)^2 + 0.4326*P]$ where $P = (F_o^2 + 2*F_c^2)/3$ was used in the latter stages of refinement. Complex scattering factors were taken from the program package SHELXL93[17] as implemented on the Viglen 486dx computer.†

Crystal data for di-*tert*-butyl (4*R*,5*S*)-4-[(*R*)-1-hydroxy-1-phenylmethyl]-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate 3d

Crystal data for $C_{22}H_{32}O_7$; $M = 408.48$; crystallises from ethyl acetate–petrol as colourless blocks; crystal dimensions 0.6 × 0.4 × 0.2 mm. Monoclinic, $a = 10.217(2)$, $b = 11.655(2)$, $c = 10.936(2)$ Å, $\beta = 117.38°(3)$, $U = 1156.4(4)$ Å^3, $Z = 2$, $D_c = 1.173$ g cm^{-3}, space group $P2_1$ (C_2^2 No. 4), Mo-Kα radiation (O($\bar{\lambda}$) = 0.71073 Å), μ(Mo-Kα) = 0.087 mm^{-1}, $F(000) = 440$. Three-dimensional, room temperature X-ray data were collected in the range $3.5 < 2\theta < 50°$ on a Siemens P4 diffractometer by the omega scan method. Of the 2741 reflections measured, all of which were corrected for Lorentz and polarisation effects (but not for absorption), 2020 independent reflections exceeded the significance level $|F|/\sigma(|F|) > 4.0$. The structure was solved by direct methods and refined by full matrix least squares on F^2. Hydrogen atoms were placed geometrically and refined with a riding model (including torsional freedom for methyl groups) and with U_{iso} constrained to be 1.2 (1.5 for methyl groups) times U_{eq} of the carrier atom. Refinement converged at a final $R = 0.0495$ ($wR_2 = 0.1816$ for all 2325 unique data, 291 parameters, mean and maximum δ/σ 0.000, 0.000), with allowance for the thermal anisotropy of all non-hydrogen atoms (C16A , C16b and C22A , C22B were found to be disordered in the order of 0.72 to 0.28). Minimum and maximum final electron density −0.258 and 0.194 e Å^{-3}. A weighting scheme $w = 1/[\sigma^2(F_o^2) + (0.0717*P)^2 + 0.3857*P]$ where $P = (F_o^2 + 2*F_c^2)/3$ was used in the latter stages of refinement. Complex scattering factors were taken from the program package SHELXL93[17] as implemented on the Viglen 486dx computer.†

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† Full crystallographic details for **3b** and **3d**, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, available *via* the RSC web page (http://www.rsc.org/authors). Any request to the CCDC for this material should quote the full literature citation and the reference number 207/283. See http://www.rsc.org/suppdata/perkin1/1999/155/ for crystallographic files for **3d** in .cif format.

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