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Aspects of stereocontrol in the L-Selectride reduction of 4-acyl-1,3-dioxolane derivatives

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ABSTRACT

The application of L-Selectride, either alone or in combination with $ZnCl_2$, to aryl ketones **1**, **8** and **11** resulted in highly *anti*-stereoselective reduction. In contrast, lactols **22** and **23** gave a moderate *syn*-preference using L-Selectride alone and a high *syn*-preference in the presence of $ZnCl_2$. Uniquely, high *anti*- stereoselectivity was observed in the reduction of *o*-anisyl lactol **37** with L-Selectride alone, which was switched to a high *syn*-preference when $ZnCl_2$ was present.

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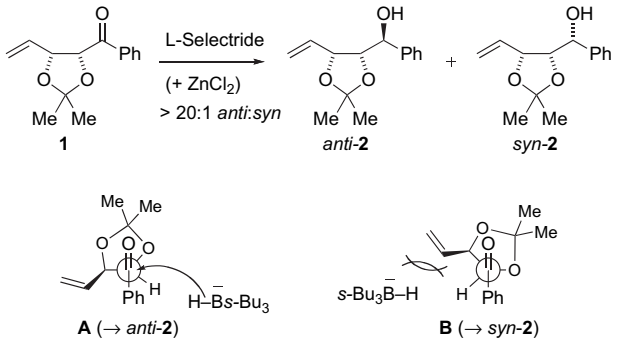
1. Introduction

Enantiospecific synthesis from the chiral pool is a favourite strategy for chemists familiar with the idiosyncracies of what may be polar, multifunctionalised starting materials.[1] Synthesis from carbohydrates must take account of the interplay of many potentially reactive sites, subtle selectivity differences between stereoisomers, misunderstandings that arise as a result of parallel nomenclature systems, and confusing or contradictory literature results. In this context, we describe our results concerning the L-Selectride reduction of ketones such as **1** (Scheme 1), in the presence or absence of $ZnCl_2$, as part of a natural product synthesis.

2. Results and discussion

L-Selectride reduction of ketone **1** gave alcohol **2** predominantly as the *anti*-isomer regardless of whether or not $ZnCl_2$ was added. This outcome runs counter to the commonly-reported trend that such reductions of 1,3-dioxolan-4-yl ketones give moderate to high *syn*-selectivity[2] and our explanation is as follows: in the reduction of **1**, addition via 'steric' Felkin–Anh model (**A**) dominates, with α-chelation by Li^+ or $ZnCl_2$ having no qualitative bearing on the outcome (α-chelation also favours *anti*-**2**). The (σ*–π*)-dominated Felkin–Anh model **B**, which is equivalent to a β-chelation model, is disfavoured in



Scheme 1. *anti*-Selective reduction of ketone **1** using L-Selectride with or without added $ZnCl_2$.

substrate **1** because the *cis*-oriented vinyl group impedes hydride delivery. Reported L-Selectride reductions of 1,3-dioxolan-4-yl ketones concern substrates lacking a *cis*-disposed substituent at the 5-position and reduction can proceed through model **B**.

This explanation does not accommodate Hanessian's results concerning γ-lactol reductions that proceed through analogous ketones generated in situ (Scheme 2).[3] Thus, lactol **3** was reported to give alcohol *anti*-**4** using L-Selectride alone (>20:1 dr) with alcohol *syn*-**4** resulting as a single isomer when $ZnCl_2$ was included. The authors explained that the *anti*-isomer resulted from reduction through model **C**, the *syn*-isomer from Cram α-chelate model **D**. Unfortunately, both Newman projections for **C** and **D** were mis-

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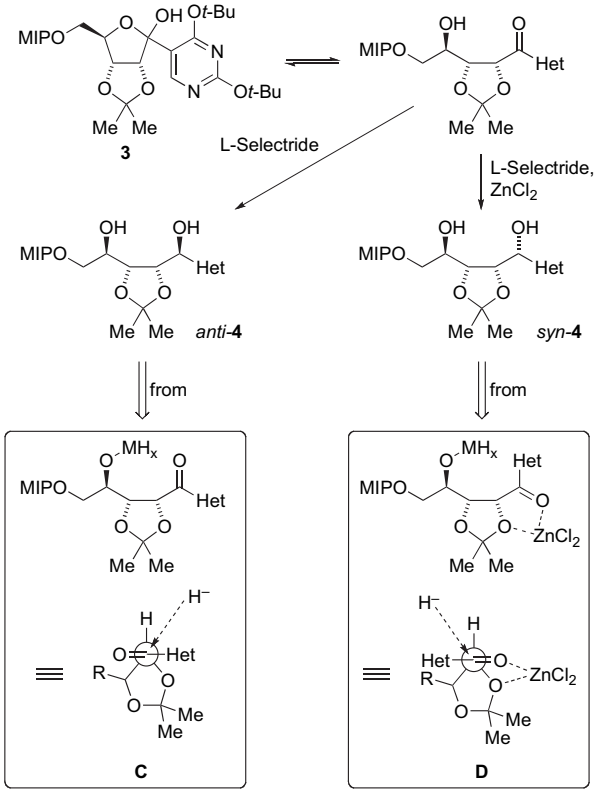
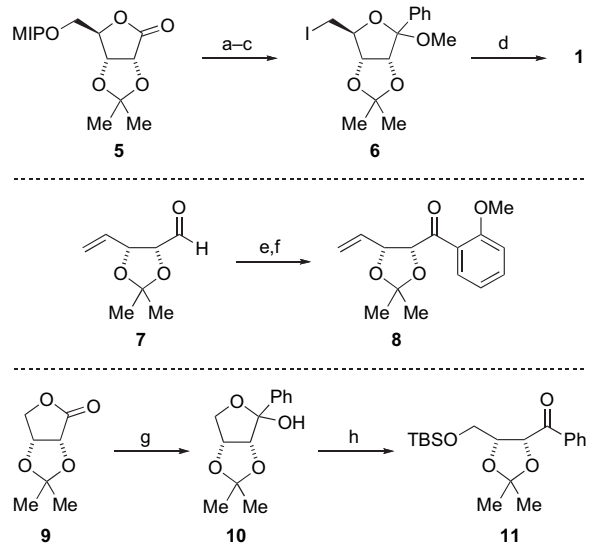
drawn (they are the wrong enantiomers), which means that their correct application predicts stereochemical outcomes opposite to those observed. Whilst the γ-alkoxide is implicit in these depictions, its possible involvement is not mentioned by the authors. Although the explanations are not valid the authors applied these results in successful total syntheses[4] therefore the outcomes appear reliable.



Scheme 2. Hanessian's results and reported stereochemical models for the selective production of 4 diastereomers. [MIP=2-methoxy-2-propyl].

We prepared two further substrates, **8** and **11**, by standard methods (Scheme 3) so as to explore whether the presence of an *ortho*-alkoxy group could influence the outcome (substrate **8**, cf. **3**)



Scheme 3. Synthesis of aryl ketone reduction substrates **1**, **8** and **11**. Reagents: (a) PhLi, THF (91%); (b) concd H_2SO_4, MeOH (95%); (c) PPh_3, I_2, imidazole, toluene (59%); (d) Zn, aq THF,))) (78%); (e) 2-anisyllithium, $ZnCl_2$, THF (10%); (f) Dess–Martin periodinane, CH_2Cl_2 (72%); (g) PhLi, THF (75%); (h) TBSCl, imidazole, DMF (88%).

and whether the vinyl substituent was particularly unusual in conferring insensitivity towards additives during the reduction (substrate **11**). Under the reduction conditions shown (with or without $ZnCl_2$, Table 1) the *anti*-isomers **12** and **13** (Fig. 1) were produced in a high dr, which only fell off slightly as the temperature of the reaction was raised (entry 8). The relative unimportance of solvent choice was established in one case (entry 3).

Table 1
Stereoselective L-Selectride reductions[a] of ketones **1**, **8** and **11**

Entry	Substrate	$ZnCl_2$?	Yield[b] (%)	dr[c] (*anti*:*syn*)
1	**1**	✓	67	>20:1
2	**1**	—	69	>20:1
3[a]	**1**	—	71	>20:1
4	**8**	✓	75	>20:1
5	**8**	—	72	>20:1
6	**11**	✓	83	>20:1
7	**11**	—	84	>20:1
8[a]	**11**	—	89	~10:1

[a] Reactions were run in dichloromethane at −78 °C except in entries 3 (THF) and 8 (20 °C).
[b] Yields refer to isolated yields after chromatography.
[c] Estimated by inspection of the ^{1}H NMR spectra of crude products.[5]

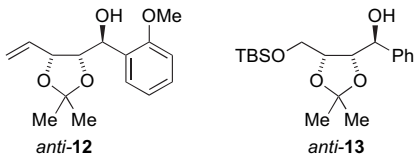
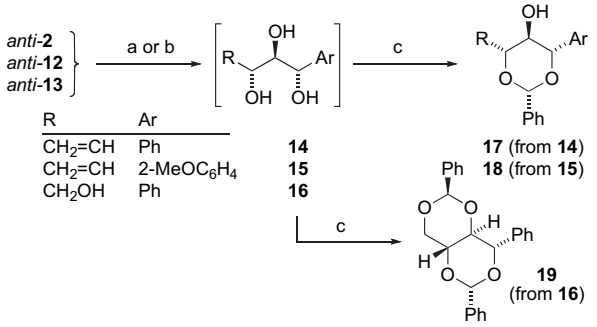


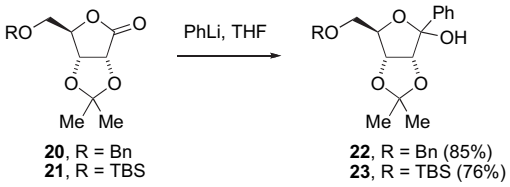
Figure 1. Ketone reduction products.

The stereochemistry of the major *anti*-isomers **2**, **12**, and **13** was established by acetonide hydrolysis and benzylidene acetal formation to afford dioxanes **17** and **18**, and bisacetal **19** (Scheme 4). In all cases, the assignments were supported by large diaxial couplings in the ^{1}H NMR spectra (see Experimental section).

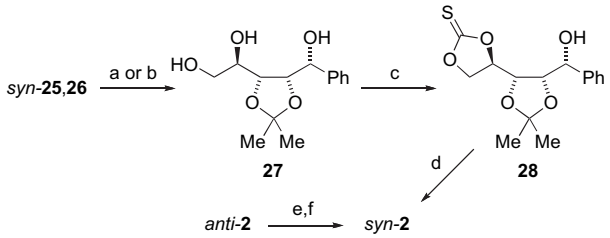


Scheme 4. Synthesis of benzylidene acetals **17**–**19** used to establish *anti*-stereoselective reductions. Reagents: (a) (for **2**, **12**) concd HCl, MeOH; (b) (for **13**) aq AcOH; (c) $PhCH(OMe)_2$, *p*-TsOH, CH_2Cl_2 (54% from **2**, 75% from **12**).

These results gave us confidence that the *anti*-selective L-Selectride reduction of substrate **1** was not an isolated case, that Hanessian's lactol reduction in the absence of $ZnCl_2$ could also be accommodated by model **A**, and therefore that Hanessian's result in the presence of $ZnCl_2$ depended on the presence of a free γ-alkoxide. The last conclusion was easily tested by surveying the reductions of substrate **10** (Scheme 3) and ribonolactone derivatives **22** and **23** (Scheme 5). The results of this survey are summarised in Table 2.



Scheme 5. Preparation of lactol reduction precursors.



Scheme 6. (a) H_2, Pd/C, MeOH (quant. from **25**); (b) TBAF, THF, (57% from **26**); (c) thiocarbonyl diimidazole, THF (58%); (d) $P(OMe)_3$, heat (quant. crude); (e) PPh_3, DIAD, p-$NO_2C_6H_4CO_2H$, C_6H_6; (f) NaOH, aq MeOH.

Table 2
Stereoselective L-Selectride reductions[a] of lactols **10**, **22** and **23**

Entry	Substrate	$ZnCl_2$?	Yield[b] (%)	dr[c] (*anti*:*syn*)
1	**10**	✓	59	1:3
2	**10**	—	87	~15:1
3	**22**	✓	63	~1:15
4	**22**	—	57	1:2
5	**23**	✓	64	~1:15
6	**23**	—	73	1:1.5
7[a]	**23**	—	78	1:2

[a] All reactions were run in dichloromethane at −78 °C with slow warming to 20 °C except in entry 7 (THF).
[b] Yields refer to yields of the combined diastereomers after chromatography.
[c] Estimated by inspection of the ^1H NMR spectra of the product mixtures after chromatography.[5]

With one exception (entry 2), the reductions afforded the *syn*-alcohol diastereomers **24**–**26** (Fig. 2) as major products, with essentially complete stereoselectivity resulting in the reductions with added $ZnCl_2$. Omission of $ZnCl_2$ did not result in high *anti*-selectivity (cf. Hanessian's examples), merely a relaxation of the *syn*-preference.

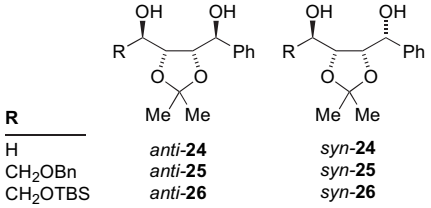


Figure 2. Lactol reduction products.

Stereochemical assignments for the reduction products were made as follows. First, *syn*-**24** was assigned by comparison of spectroscopic data with literature data (see Experimental section); *anti*-**24** was then assigned by default, supported by oxidation experiments with MnO_2, which returned lactol **10** from both **24** isomers. This, and similar MnO_2 oxidations of *syn*-**25** and *syn*-**26** (→**22** and **23**, respectively) also ruled out epimerisation α- to the intermediate ketone. Finally, *syn*-**25** and *syn*-**26** were correlated with *anti*-**2** by alcohol deprotection and Corey–Winter elimination to give *syn*-**2**, identical to the product of Mitsunobu inversion of *anti*-**2** (Scheme 6). The esterification step of the Mitsunobu reaction gave a ca. 1:1 ratio of *syn*- and *anti*- benzoate esters; accordingly, the hydrolysis afforded a mixture of *syn*- and *anti*-**2** but this did not complicate comparison with *syn*-**2** generated from intermediate **28**.

The tendency for *syn*-stereoselective reduction revealed by the data in Table 2 is opposite to that seen with the ketone substrates **1**, **8** and **11**. This supports the involvement of the (metallated) γ-hydroxy group in the reductions of lactols **10**, **22** and **23**. Reduction from the *exo*-face of a chelated intermediate (**E**, Fig. 3) or internal delivery (**F**), as suggested by others,[6,2a] would appear to operate. In the absence of added $ZnCl_2$, with a less-strongly co-ordinating counterion (Li^+), chelation-control would be more closely balanced with reduction occurring through an arrangement similar to **A** (Scheme 1). The outlier in these reactions, entry 2, could be explained by γ-chelation strengthened by chelation with the α-oxygen of the acetonide (**G**, Fig. 3), and hydride delivery to the more exposed face of the carbonyl, the *endo*-face being shielded by the axial proton, H^*. In substrates **22** and **23** such an arrangement would be disfavoured because the CH_2OBn/TBS substituent would be placed in the axial site occupied by H^* in **G**.[7]

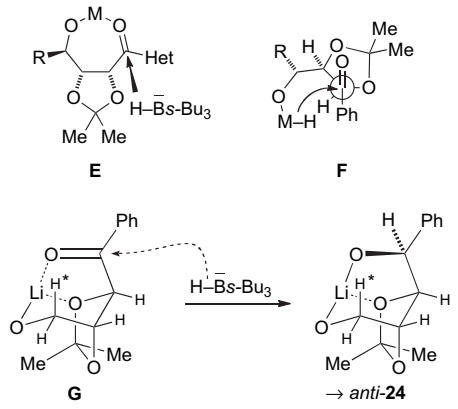


Figure 3. Models for *syn*-selective reductions of lactols **10**, **22** and **23**, and *anti*-selective reduction of lactol **10** in the absence of $ZnCl_2$.

It remains to address the question of why Hanessian's substrates afford cleanly the *anti*-isomers in the absence of $ZnCl_2$ whereas ours do not. Assuming that the 1°-hydroxy protecting group does not influence the outcome then the acyl substituent is implicated. Literature examples of L-Selectride reductions of lactols in this series are restricted to heteroaryl-derivatives; within these, there are clear trends. L-Selectride reduction of thiazole derivatives **29**–**31** (Fig. 4) shows a clear *anti*-preference[8,2f] and the L-Selectride/$ZnCl_2$ combination returns the *syn*-reduction products from **32** and **33**, in full agreement with Hanessian's results.[9,4] However, it was reported recently that the 5-bromothiophen-2-yl derivative **34** affords the *syn*- alcohol using L-Selectride alone and the *anti*- alcohol in the presence of $ZnCl_2$, both in opposition to the trend seen elsewhere.[10] In the same report it was noted that the 3-bromothiophen-2-yl derivatives **35** and **36** failed to react with L-Selectride alone (as also reported for a related thiazolyl derivative)[2f] but the usual trend was followed in the presence of $ZnCl_2$ where the *syn*-reduction products were obtained.

In view of this background we prepared a final substrate (**37**, Scheme 7) differing from lactol **22** merely by the presence of an *ortho*-methoxy substituent. Reduction of this compound in the presence of $ZnCl_2$ gave the expected high *syn*- selectivity but, in contrast to the reactions of substrates **22** and **23**, reduction with

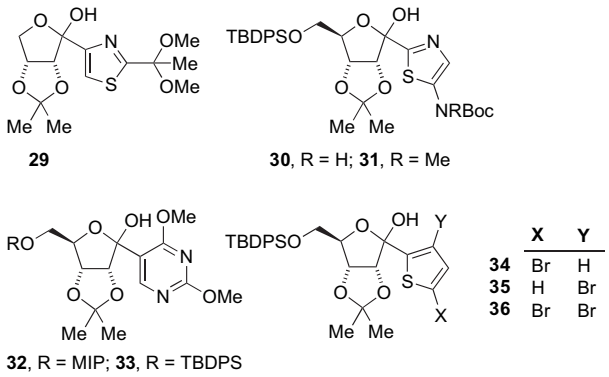
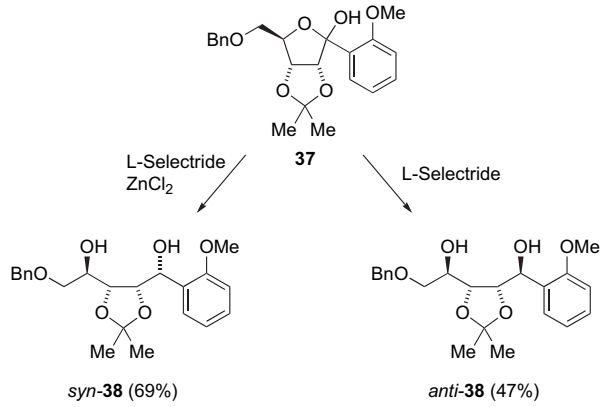


Figure 4. Reported lactol substrates for L-Selectride reduction.

L-Selectride alone was highly *anti*-selective, in agreement with Hanessian's results.[11,12]



Scheme 7. Stereochemical outcomes in the reduction of *o*-anisyl lactol **37**.

In conclusion, the L-Selectride reduction of 4-aroyl-1,3-dioxolanes and related lactols provides complementary routes to *anti*- and *syn*- benzylic alcohols, respectively. The observed sense of diastereoselection can be accommodated by a number of models (**A** and **E**–**G**) but their predictive relevance, particularly in the lactol reductions, has to be tempered by the possible influence of the acyl or hemiacetal substituent.

3. Experimental section

Starting materials **5**,[4b] **7**,[13] **9**,[14] **10**,[15] **20**[16] and **21**[17] were prepared following literature procedures.

3.1. (3a*R*,6*R*,6a*R*)-6-(2-Methoxypropan-2-yloxy)methyl-2,2-dimethyl-4-phenyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-ol

To a stirred solution of bromobenzene (0.89 mL, 8.46 mmol) in THF (80 mL) at −78 °C was added *tert*-butyllithium (10.4 mL, 1.7 M solution in hexanes, 17.7 mmol). After stirring for 30 min, a solution of lactone **5** (2.0 g, 7.69 mmol) in THF (40 mL), cooled to −78 °C, was added dropwise via cannula. The mixture was stirred for 90 min at −78 °C, quenched with brine (40 mL), then allowed to warm to rt, extracted with ethyl acetate (3×80 mL) and dried over $MgSO_4$. Concentration in vacuo and purification by column chromatography (petrol/ethyl acetate, 10:1→4:1→0.5:1) afforded the *title compound* as a mixture of anomers (A:B, 8:1) as a white solid (2.37 g, 91%). A trace quantity of the product of double phenyl addition was also obtained (data not shown). R_f 0.62 (petrol/ethyl acetate, 2:1); mp 74–76 °C; $[\alpha]_D^{20}$ −26.0 (*c* 1.0, CH_2Cl_2); ν_{max} (thin film)/cm^{-1} 3384br, 1450w, 1381m, 1212s, 1160w, 1079s, 872w, 734w, 701w; δ_H (400 MHz, $CDCl_3$) anomer A: 1.27, 1.41, 1.44 and 1.45 (4×3H, 4×s, 4×CH_3), 3.26 (3H, s, OCH_3), 3.68–3.70 (2H, m, OCH_2), 4.56–4.58 (1H, m, CH_2CH), 4.66 (1H, d, *J* 5.6) and 4.94 (1H, dd, *J* 5.6, 1.5, 2×CH), 5.14 (1H, s, OH), 7.36–7.40 (3H, m) and 7.55–7.65 (2H, m, Ph); δ_C (100 MHz, $CDCl_3$) anomer A: 24.1 (CH_3), 24.3 (CH_3), 24.9 (CH_3), 26.5 (CH_3), 49.2 (OCH_3), 62.2 (CH_2), 82.4 (CH), 85.0 (CH), 88.5 (CH), 101.1 (C), 107.2 (C), 112.8 (C), 126.9 (CH), 127.6 (CH), 128.2 (CH), 139.0 (C); anomer B: 24.4 (CH_3), 24.4 (CH_3), 25.1 (CH_3), 26.6 (CH_3), 48.7 (OCH_3), 60.6 (CH_2), 81.0 (CH), 81.4 (CH), 86.2 (CH), 100.2 (C), 102.1 (C), 116.1 (C), 125.7 (CH), 126.9 (CH), 128.1 (CH), 142.3 (C); *m*/*z* (ESI^+) 361 (MNa^+, 100%), 321 (70), 249 (60); HRMS (ESI^+) found 361.1618, $C_{18}H_{26}NaO_6$ (MNa^+) requires 361.1622.

3.2. (3a*R*,6*R*,6a*R*)-6-Hydroxymethyl-4-methoxy-2,2-dimethyl-4-phenyltetrahydrofuro[3,4-*d*][1,3]dioxole

To a solution of (3a*R*,6*R*,6a*R*)-6-(2-*methoxypropan*-2-*yloxy*)*methyl*-2,2-*dimethyl*-4-*phenyltetrahydrofuro*[3,4-*d*][1,3]*dioxol*-4-*ol* (722 mg, 2.14 mmol) in methanol (100 mL) was added concentrated sulfuric acid (58 μL, 1.07 mmol). After stirring for 5 min, the reaction was quenched by the addition of triethylamine (1.49 mL, 10.7 mmol) and the mixture was concentrated in vacuo. The residue was dissolved in ethyl acetate (5.0 mL), loaded onto a short plug of silica, and flushed through with more ethyl acetate (50 mL) to afford the *title compound* as a colourless viscous oil with an anomeric ratio >20:1 (569 mg, 95%). R_f 0.35 (petrol/ethyl acetate, 2:1); $[\alpha]_D^{20}$ −36.7 (*c* 0.7, CH_2Cl_2); ν_{max} (thin film)/cm^{-1} 3443br, 1450w, 1373w, 1261m, 1212m, 1096s, 1027s, 872w, 762w; δ_H (500 MHz, $CDCl_3$) 1.21 and 1.24 (2×3H, 2×s, 2×CH_3), 3.11 (3H, s, OCH_3), 3.21 (1H, dd, *J* 9.0, 3.2, OH), 3.79 (1H, ddd, *J* 12.2, 9.0, 4.7) and 3.85 (1H, app dt, *J* 12.2, 3.2, CH_2), 4.56–4.60 (1H, m, CH_2CH), 4.76 (1H, d, *J* 5.7, *CH*CHO), 4.96 (1H, d, *J* 5.7, *CH*CPh), 7.32 (3H, m) and 7.49 (2H, d, *J* 7.1, Ph); δ_C (125 MHz, $CDCl_3$) 24.8 (CH_3), 26.0 (CH_3), 49.8 (OCH_3), 64.3 (CH_2), 81.8 (CH), 87.0 (CH), 88.1 (CH), 112.2 (C), 112.4 (C), 127.5 (CH), 128.0 (CH), 128.4 (CH), 136.1 (C); *m*/*z* (ESI^+) 583 (M_2Na^+, 20%), 303 (MNa^+, 100), 249 (100); HRMS (ESI^+) found 303.1206, $C_{15}H_{20}NaO_5$ (MNa^+) requires 303.1203.

3.3. (3a*R*,6*S*,6a*S*)-6-Iodomethyl-4-methoxy-2,2-dimethyl-4-phenyltetrahydrofuro[3,4-*d*][1,3]dioxole (6)

[Note: this compound is unstable when stored neat at rt and was either used immediately or stored in benzene at −18 °C].

Procedure A. To a solution of (3a*R*,6*R*,6a*R*)-6-*hydroxymethyl*-4-*methoxy*-2,2-*dimethyl*-4-*phenyltetrahydrofuro*[3,4-*d*][1,3]*dioxole* (350 mg, 1.25 mmol) in toluene (15 mL) was added sequentially: triphenylphosphine (493 mg, 1.87 mmol), imidazole (128 mg, 1.87 mmol) and iodine (477 mg, 1.87 mmol), and the mixture was stirred at rt for 2 h. The reaction mixture was then washed with aq $Na_2S_2O_3$ solution (20 mL, 10%) and the washings extracted with ethyl acetate (3×20 mL). The combined organic solutions were dried over $MgSO_4$, concentrated in vacuo, and the residue purified by column chromatography (petrol/ethyl acetate, 20:1) to afford the *title compound* as a white solid with an anomeric ratio >20:1 (286 mg, 59%). R_f 0.61 (petrol/ethyl acetate, 10:1); mp 62 °C; $[\alpha]_D^{23}$ −59.3 (*c* 0.3, $CDCl_3$); ν_{max} (thin film)/cm^{-1} 1450w, 1373m, 1262m, 1211w, 1097s, 1021s, 872m, 760w, 700w; δ_H (500 MHz, $CDCl_3$) 1.26 and 1.33 (2×3H, 2×s, 2×CH_3), 3.06 (3H, s, OCH_3), 3.37 (1H, app t, *J* 10.0) and 3.45 (1H, dd, *J* 10.0, 5.7, CH_2), 4.61 (1H, dd, *J* 10.0, 5.7, CH_2CH), 4.76 (1H, d, *J* 5.7, *CH*CHO), 4.91 (1H, d, *J* 5.7, *CH*CPh), 7.32–7.42 (3H, m) and 7.45–7.50 (2H, m, Ph); δ_C (125 MHz, $CDCl_3$) 6.9 (CH_2), 25.2 (CH_3), 26.5 (CH_3), 49.6 (OCH_3), 84.1 (CH), 87.1 (CH),

87.8 (CH), 112.3 (C), 113.0 (C), 127.4 (CH), 128.0 (CH), 128.4 (CH), 136.1 (C); *m*/*z* (ESI^+) 563 (100%), 413 (MNa^+, 30), 295 (40); HRMS (ESI^+) found 413.0229, $C_{15}H_{19}INaO_4$ (MNa^+) requires 413.0220.

Procedure B. To a solution of (3a*R*,6*R*,6a*R*)-4-*methoxy*-2,2-*dimethyl*-4-*phenyl*-6-(*p*-*toluenesulfonyloxy*)*methyltetrahydrofuro*[3,4-*d*][1,3]*dioxole* (see below) (1.43 g, 3.30 mmol) in acetonitrile (10 mL) was added NaI (977 mg, 6.52 mmol). The reaction mixture was heated to reflux and stirred for 18 h. After cooling to rt the solids were removed by filtration, and the solution was concentrated in vacuo. The residue was dissolved in ether (50 mL) and washed sequentially with aq $Na_2S_2O_3$ solution (20 mL, 10%), water (20 mL) and brine (20 mL), then dried over $MgSO_4$. Concentration in vacuo and purification by column chromatography (petrol/ethyl acetate, 20:1) afforded the *title compound* (692 mg, 54%). Data as above.

3.4. (3a*R*,6*R*,6a*R*)-4-Methoxy-2,2-dimethyl-4-phenyl-6-(*p*-toluenesulfonyloxy)methyltetrahydrofuro[3,4-*d*][1,3]dioxole

To a stirred solution of (3a*R*,6*R*,6a*R*)-6-(*hydroxymethyl*)-4-*methoxy*-2,2-*dimethyl*-4-*phenyltetrahydrofuro*[3,4-*d*][1,3]*dioxole* (1.71 g, 6.11 mmol) in pyridine (3.05 mL) at 0 °C was slowly added *p*-toluenesulfonyl chloride (1.28 g. 6.72 mmol) and then DMAP (75 mg, 0.615 mmol). The reaction mixture was allowed to warm to rt, stirred for 1 h, and then concentrated in vacuo. The crude product was then dissolved in dichloromethane (50 mL), washed successively with hydrochloric acid (20 mL, 1 M), aq $NaHCO_3$ solution (20 mL, saturated) and brine (20 mL), then dried over $MgSO_4$ and concentrated in vacuo. Purification by column chromatography (petrol/ethyl acetate, 7:1) afforded the *title compound* as a white solid (1.57 g, 59%). R_f 0.28 (petrol/ethyl acetate, 5:1); mp 76 °C; $[\alpha]_D^{23}$ −59.3 (*c* 0.3, $CDCl_3$); ν_{max} (thin film)/cm^{-1} 2991w, 1451w, 1361s, 1179m, 1098s, 1047w, 969s, 836m, 815m, 764w, 704m, 666m; δ_H (400 MHz, $CDCl_3$) 1.21 and 1.28 (2×3H, 2×s, 2×CH_3), 2.47 (3H, s, ArCH_3), 2.90 (3H, s, OCH_3), 4.16 and 4.21 (2×1H, 2×dd, *J* 9.9, 7.2, CH_2), 4.48 (1H, td, *J* 7.2, 1.3, *CH*CH_2), 4.66 (1H, dd, *J* 5.8, 1.3, C*H*CHO), 4.72 (1H, d, *J* 5.8, C*H*CPh), 7.31–7.45 (7H, m, Ph and two of Ts), 7.85 (2H, d, *J* 8.2, two of Ts); δ_C (100 MHz, $CDCl_3$) 21.7 (CH_3), 25.1 (CH_3), 26.4 (CH_3), 49.4 (CH_3), 69.5 (CH_2), 82.0 (CH), 83.2 (CH), 87.1 (CH), 112.2 (C), 113.1 (C), 127.4 (CH), 128.0 (CH), 128.1 (CH), 128.4 (CH), 130.0 (CH), 132.6 (C), 136.1 (C), 145.2 (C); *m*/*z* (ESI^+) 457 (MNa^+, 60%), 403 (MH^+−MeOH, 100); HRMS (ESI^+) found 457.1298, $C_{22}H_{26}NaO_7S$ (MNa^+) requires 457.1291.

3.5. (4*R*,5*R*)-4-Benzoyl-2,2-dimethyl-5-vinyl-1,3-dioxolane (1)

Zinc dust (SigmaAldrich, particle size <10 μm) was activated and dried immediately prior to use as follows. A suspension of zinc dust (5.0 g) in hydrochloric acid (50 mL, 1 M) was stirred at rt for 15 min. The zinc was then removed by filtration, washed sequentially with water (2×50 mL) and ether (2×50 mL), and dried under high vacuum with moderate heating (heat gun). Upon cooling, a sample of this activated zinc (123 mg, 1.88 mmol) was added to a solution of iodide **6** (75 mg, 0.192 mmol) in THF (1.5 mL) and water (0.4 mL). The reaction flask was then placed in an ultrasonic bath for 1 h at 40 °C and the mixture was then filtered through Celite®, rinsing through with dichloromethane (50 mL). The filtrate was washed with aq $NaHCO_3$ solution (50 mL, saturated), dried over $MgSO_4$, concentrated in vacuo, and purified by column chromatography (petrol/ethyl acetate, 10:1) to afford the *title compound* (**1**) as a colourless viscous oil (35 mg, 79%). R_f 0.28 (petrol/ethyl acetate, 10:1); $[\alpha]_D^{23}$ +23.7 (*c* 0.6, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 1697s, 1598w, 1449w, 1381m, 1216s, 1163w, 1100m, 1047m, 875w, 693m; δ_H (400MHz, $CDCl_3$) 1.49 and 1.70 (2×3H, 2×s, 2×CH_3), 4.98 (1H, app t, *J* 7.7, *CH*CH=), 5.02 (1H, d, *J* 10.1) and 5.20 (1H, d, *J* 17.1, =CH_2), 5.57 (1H, ddd, *J* 17.1, 10.1, 7.7, *CH*=CH_2), 5.60 (1H, d, *J* 7.7, *CH*C=O), 7.45 (2H, app t, *J* 7.6), 7.57 (1H, t, *J* 7.6) and 7.88 (2H, d, *J* 7.6, Ph); δ_C (125 MHz, $CDCl_3$) 27.4 (CH_3), 27.2 (CH_3), 79.5 (CH), 80.5 (CH), 110.6 (C), 119.7 (CH_2), 128.5 (CH), 128.6 (CH), 133.1 (CH), 133.5 (CH), 135.9 (C), 195.1 (C); *m*/*z* (ESI^+) 487 (M_2Na^+, 70%), 269 (100), 255 (MNa^+, 90); HRMS (ESI^+) found 255.0992, $C_{14}H_{16}NaO_3$ (MNa^+) requires 255.0992.

3.6. (4*S*,5*R*)-4-[1-(2-Methoxyphenyl)]hydroxymethyl-2,2-dimethyl-5-vinyl-1,3-dioxolane

To a solution of (4*R*,5*R*)-2,2-*dimethyl*-5-*vinyl*-1,3-*dioxolane*-4-*carbaldehyde* (**7**) (240 mg, 1.54 mmol) in THF (10 mL) at −78 °C was added a solution of $ZnCl_2$ (2.0 mL, 1 M in ether, 2.0 mmol) dropwise and the mixture was stirred for 30 min. Meanwhile, to a solution of 2-bromoanisole (0.191 mL, 1.54 mmol) in THF (10 mL) at −78 °C was added *tert*-butyllithium (1.99 mL, 1.7 M solution in hexanes, 3.38 mmol) and the mixture was stirred for 30 min. The resulting organolithium solution was then transferred into the aldehyde solution at −78 °C dropwise via cannula, and stirring was continued at this temperature for 30 min. The cold bath was then removed and stirring continued for a further 30 min at rt. The reaction was quenched by the addition of aq NH_4Cl solution (5 mL, saturated). The mixture was extracted with ethyl acetate (3×10 mL), the extracts dried over $MgSO_4$ and concentrated in vacuo, and the residue purified by column chromatography (petrol/ethyl acetate, 7:1) to afford the *title compound* as a mixture of diastereomers (A:B, 5:2) and as a pale yellow oil (42 mg, 10%). R_f 0.28 (petrol/ethyl acetate, 3:1); ν_{max} (thin film)/cm^{-1} 3745br, 1492m, 1464w, 1379w, 1242s, 1164w, 1097w, 1029s, 928w, 888w, 755m; δ_H (500 MHz, $CDCl_3$) 1.35 (3H, s, CH_3, B), 1.40 (3H, s, CH_3, A), 1.46 (3H, s, CH_3, B), 1.61 (3H, s, CH_3, A), 2.81 (1H, d, *J* 6.7, OH, A), 2.94 (1H, d, *J* 7.0, OH, B), 3.83 (3H, s, OCH_3, A), 3.88 (3H, s, OCH_3, B), 4.50 (1H, dd, *J* 6.9, 3.9, C*H*CHOH, A), 4.53 (1H, dd, *J* 9.0, 6.2, C*H*CHOH, B), 4.61–4.66 (1H, m, C*H*CH=, A), 4.75–4.78 (1H, m, C*H*CH=, B), 4.85 (1H, dd, *J* 9.0, 7.0, C*H*OH, B), 5.03 (1H, dd, *J* 6.7, 3.9, C*H*OH, A), 5.27 (1H, app dt, *J* 10.2, 1.4,=C*H*H′, A), 5.31–5.36 (2H, m, =C*H*H′, B and =CH*H*′, A), 5.48 (1H, app dt, *J* 17.2, 1.4, =CH*H*′, B), 6.10 (1H, ddd, *J* 17.7, 10.2, 7.6, C*H*=CH_2, A), 6.21 (1H, ddd, *J* 17.2, 10.4, 6.9, C*H*=CH_2, B), 6.86 (1H, d, *J* 8.2, Ar-A), 6.91 (1H, d, *J* 8.2, Ar-B), 6.95–7.00 (2H, m, Ar-A and Ar-B), 7.24–7.33 (3H, m, Ar-A and 2×Ar-B), 7.41 (1H, dd, *J* 7.5, 1.5, Ar-A); δ_C (125 MHz, $CDCl_3$) isomer A: 24.9 (CH_3), 27.2 (CH_3), 55.3 (OCH_3), 66.8 (CH), 79.3 (CH), 80.1 (CH), 108.7 (C), 110.2 (CH), 119.2 (CH_2), 120.6 (CH), 127.6 (CH), 128.7 (CH), 129.2 (CH), 133.1 (CH), 156.1 (C); isomer B: 25.5 (CH_3), 27.8 (CH_3), 55.3 (OCH_3), 70.1 (CH), 79.1 (CH), 79.2 (CH), 108.7 (C), 110.7 (CH), 117.7 (CH_2), 120.8 (CH), 128.7 (C), 128.9 (CH), 129.2 (CH), 134.1 (CH), 157.1 (C); *m*/*z* (ESI^+) 287 (MNa^+, 100%); HRMS (ESI^+) found 287.1249, $C_{15}H_{20}NaO_4$ (MNa^+) requires 287.1254.

3.7. (4*R*,5*R*)-4-(2-Methoxybenzoyl)-2,2-dimethyl-5-vinyl-1,3-dioxolane (8)

To a solution of (4*S*,5*R*)-4-[1-(2-*methoxyphenyl*)]*hydroxymethyl*-2,2-*dimethyl*-5-*vinyl*-1,3-*dioxolane* (42 mg, 0.159 mmol) in dichloromethane (4.0 mL) at 0 °C was added Dess–Martin periodinane (101 mg, 0.239 mmol) and the mixture was stirred for 1 h. After this time the reaction mixture was allowed to warm to rt and stirred for a further 4 h, concentrated in vacuo, and purified by column chromatography (petrol/ethyl acetate, 6:1), to afford the *title compound* (**8**) as a colourless oil (30 mg, 72%). R_f 0.51 (petrol/ethyl acetate, 2:1); $[\alpha]_D^{23}$ +46 (*c* 0.3, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 2986w, 1683s, 1598m, 1485m, 1467w, 1438w, 1379w, 1286m, 1245s, 1208m, 1090m, 1019m, 878w; δ_H (500 MHz, $CDCl_3$) 1.47 and 1.68 (2×3H, 2×s, 2×CH_3), 3.92 (3H, s, OCH_3), 4.95 (1H, app t, *J* 7.5, C*H*CH=), 5.00 (1H, d, *J* 10.3) and 5.21 (1H, d, *J* 16.9, =CH_2), 5.61 (1H, ddd, *J* 16.9, 10.3,

7.5, C*H*=CH_2), 5.71 (1H, d, *J* 7.5, C*H*C=O), 6.94 (1H, d, *J* 8.4), 7.02 (1H, t, *J* 7.9), 7.49 (1H, ddd, *J* 8.4, 7.9, 1.8) and 7.84 (1H, dd, *J* 7.9, 1.8, Ar); δ_C (125 MHz, $CDCl_3$) 25.5 (CH_3), 27.1 (CH_3), 55.4 (OCH_3), 79.1 (CH), 83.2 (CH), 110.1 (C), 111.4 (CH), 118.6 (CH_2), 121.0 (CH), 126.1 (C), 131.2 (CH), 133.8 (CH), 134.5 (CH), 158.5 (C), 195.9 (C); *m*/*z* (ESI^+) 547 (M_2Na^+, 10%), 326 (80), 285 (MNa^+, 20); HRMS (ESI^+) found 285.1084, $C_{15}H_{18}NaO_4$ (MNa^+) requires 285.1097.

3.8. (4*R*,5*R*)-4-Benzoyl-5-(*tert*-butyldimethylsilyloxy)methyl-2,2-dimethyl-1,3-dioxolane (11)

To a solution of lactol **10** (196 mg, 0.831 mmol) in DMF (1.0 mL) at 0 °C were added imidazole (283 mg, 4.16 mmol) and *tert*-butyldimethylsilyl chloride (313 mg, 2.08 mmol). The reaction mixture was warmed to rt and stirred for 18 h. Water (5.0 mL) was added, the mixture extracted with ether (3×5.0 mL), and the combined organic portions dried over $MgSO_4$. The residue was purified by column chromatography (petrol/ether, 10:1) to afford the title compound (**11**) as a colourless oil (257 mg, 88%). R_f 0.27 (petrol/ether, 5:1); $[\alpha]_D^{23}$ +9.1 (*c* 0.9, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 2930m, 1699s, 1471w, 1381w, 1254m, 1104s, 837s, 780m; δ_H (400 MHz, $CDCl_3$) −0.25 and −0.21 (2×3H, 2×s, $SiMe_2$), 0.65 (9H, s, *t*-Bu), 1.45 and 1.62 (2×3H, 2×s, 2×CH_3), 3.55 (1H, dd, *J* 10.4, 4.4) and 3.62 (1H, dd, *J* 10.4, 7.4, CH_2), 4.63 (1H, ddd, *J* 7.4, 6.8, 4.4, C*H*CH_2), 5.53 (1H, d, *J* 6.8, CHC=O), 7.43–7.47 (2H, m), 7.53–7.57 (1H, m) and 7.95–7.98 (2H, m, Ph); δ_C (125 MHz, $CDCl_3$) −5.9 (CH_3), −5.9 (CH_3), 18.2 (C), 25.5 (CH_3), 25.6 (CH_3), 27.5 (CH_3), 61.8 (CH_2), 78.7 (CH), 78.9 (CH), 109.7 (C), 128.3 (CH), 128.4 (CH), 133.1 (CH), 136.3 (C), 193.8 (C); *m*/*z* (ESI^+) 723 (M_2Na^+, 30%), 718 ($M_2NH_4^+$, 40), 373 (MNa^+, 60), 351 (MNH_4^+, 100), 219 (50); HRMS (ESI^+) found 373.1799, $C_{19}H_{30}NaO_4Si$ (MNa^+) requires 373.1806.

3.9. (3a*R*,6*R*,6a*R*)-6-Benzyloxymethyl-2,2-dimethyl-4-phenyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-ol (22)

To a stirred solution of phenyllithium (2.47 mL, 1.80 M in dibutyl ether, 4.44 mmol) in THF (50 mL) at −78 °C was added a solution of lactone **20** (1.03 g, 3.70 mmol) in THF (10 mL) dropwise via cannula. The mixture was stirred for 90 min at −78 °C, quenched with brine (25 mL), allowed to warm to rt, then extracted with ethyl acetate (3×50 mL), and dried over $MgSO_4$. The solution was concentrated in vacuo and purified by column chromatography (petrol/ethyl acetate, 8:1) to afford the *lactol* (**22**) as a mixture of anomers (A:B, 5:1) and as a colourless oil (998 mg, 76%). R_f 0.48 (petrol/ethyl acetate, 4:1); $[\alpha]_D^{22}$ −35.0 (*c* 0.6, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3386br, 3032w, 2987w, 2938m, 1452m, 1374s, 1211s, 1077s, 912w, 872m, 735m, 699s; δ_H (400 MHz, $CDCl_3$) isomer A: 1.26 and 1.40 (2×3H, 2×s, 2×CH_3), 3.73 (1H, dd, *J* 10.2, 3.3) and 3.78 (1H, dd, *J* 10.2, 3.1, CH_2CH), 4.54–4.57 (1H, m, CH_2C*H*), 4.62 (1H, d, *J* 11.8, C*H*H′Ph), 4.65 (1H, d, *J* 5.8, C*H*CPh), 4.71 (1H, d, *J* 11.8, CH*H*′Ph), 4.97 (1H, dd, *J* 5.8, 1.5, C*H*CHO), 5.06 (1H, s, OH), 7.30–7.42 (8H, m) and 7.57–7.65 (2H, m, 2×Ph); isomer B (selected data): 1.40 and 1.70 (2×3H, 2×s, 2×CH_3), 4.42–4.45 (1H, m, C*H*CH_2), 4.87 (1H, dd, *J* 7.3, 4.4, C*H*CHO); δ_C (100 MHz, $CDCl_3$) isomer A: 24.8 (CH_3), 26.4 (CH_3), 71.3 (CH_2), 74.0 (CH_2), 82.3 (CH), 84.7 (CH), 88.5 (CH), 107.3 (C), 112.7 (C), 127.0 (CH), 127.6 (CH), 128.1 (CH), 128.2 (CH), 128.4 (CH), 128.7 (CH), 136.4 (C), 139.0 (C); isomer B: 25.0 (CH_3) 25.6 (CH_3), 69.6 (CH_2), 73.6 (CH_2), 81.0 (CH), 81.4 (CH), 86.2 (CH), 102.2 (C), 116.2 (C), 125.7 (CH), 127.5 (CH), 127.7 (CH), 128.2 (CH), 128.3 (CH), 128.4 (CH), 138.0 (C), 142.2 (C); *m*/*z* (ESI^+) 735 (M_2Na^+, 90%), 730 ($M_2NH_4^+$, 100), 379 (MNa^+, 60), 339 (100); HRMS (ESI^+) found 379.1516, $C_{21}H_{24}NaO_5$ (MNa^+) requires 379.1516.

3.10. (3a*R*,6*R*,6a*R*)-6-(*tert*-Butyldimethylsilyloxy)methyl-2,2-dimethyl-4-phenyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-ol (23)[18]

To a stirred solution of phenyllithium (1.01 mL, 1.8 M in dibutyl ether, 1.82 mmol) in THF (20 mL) at −78 °C was added a solution of lactone **21** (458 mg, 1.52 mmol) in THF (5.0 mL) dropwise via cannula. The mixture was stirred for 90 min at −78 °C, quenched with brine (10 mL), allowed to warm to rt, then extracted with ethyl acetate (3×20 mL), and dried over $MgSO_4$. The solution was concentrated in vacuo and purified by column chromatography (petrol/ethyl acetate, 20:1) to afford the lactol (**23**) as a mixture of anomers (A:B, 4:1) and as a colourless oil (490 mg, 85%). R_f 0.40 (petrol/ethyl acetate, 10:1); $[\alpha]_D^{25}$ −37.6 (*c* 1.4, $CHCl_3$), lit.[18a] $[\alpha]_D^{23}$ −20.0 (*c* 1.5, EtOH); ν_{max} (thin film)/cm^{-1} 3387br, 1451w, 1373m, 1257s, 1162w, 1076s, 837s, 779m, 669m, 666w; δ_H (400 MHz, $CDCl_3$) 0.10 and 0.11 (2×3H, 2×s, $SiMe_2$, B), 0.18 and 0.20 (2×3H, 2×s, $SiMe_2$, A), 0.92 (9H, s, *t*-Bu, B), 0.98 (9H, s, *t*-Bu, A), 1.27 (3H, s, CH_3, A), 1.41 (6H, s, CH_3, A and CH_3, B), 1.69 (3H, s, CH_3, B), 3.84–3.95 (4H, m, CH_2, A and B), 4.30–4.33 (1H, m, C*H*CH_2, B), 4.48–4.52 (1H, m, C*H*CH_2, A), 4.60 (1H, d, *J* 7.2, C*H*CPh, B), 4.65 (1H, d, *J* 5.7, C*H*CPh, A), 4.90 (1H, dd, *J* 7.2, 4.2, C*H*CHO, B), 4.92–4.96 (1H, m, C*H*CHO, A), 5.30 (1H, s, OH, B), 5.32 (1H, s, OH, A), 7.30–7.40 (6H, m) and 7.58–7.66 (4H, m, 2×Ph, A and B); δ_C (100 MHz, $CDCl_3$) anomer A: −5.6 ($SiCH_3$), −5.6 ($SiCH_3$), 18.3 (C), 24.9 (CH_3), 25.9 (CH_3), 26.4 (CH_3), 64.9 (CH_2), 81.9 (CH), 86.2 (CH), 88.8 (CH), 106.9 (C), 112.7 (C), 127.0 (CH), 127.5 (CH), 128.1 (CH), 138.9 (C); *m*/*z* (ESI^+) 783 (M_2Na^+, 40%), 778 ($M_2NH_4^+$, 90), 444 (40), 403 (MNa^+, 20), 363 (100); HRMS (ESI^+) found 403.1900, $C_{20}H_{32}NaO_5Si$ (MNa^+) requires 403.1911.

3.11. General procedure for L-Selectride and L-Selectride/$ZnCl_2$ reductions of ketones (1), (8) and (11) and lactols (10), (22) and (23)

A solution of $ZnCl_2$ (0.39 mL, 1.0 M solution in ether, 0.39 mmol) was added dropwise to a solution of ketone **1**, **8** or **11** or lactol **10**, **22** or **23** (0.29 mmol) in dichloromethane (11 mL) at −78 °C. After stirring for 30 min, L-Selectride (1.0 mL, 1 M solution in THF, 1.0 mmol) was then added dropwise and stirring continued at the same temperature for 90 min.[†] For the reduction of ketones **1**, **8** and **11** the reaction was quenched at this point, see below; for the reduction of lactols **10**, **22** and **23** the mixture was allowed to warm slowly to rt and stirred for 18 h prior to quenching. In both cases, the reaction was quenched by the careful sequential addition of methanol (0.25 mL), water (0.125 mL), aq H_2O_2 solution (0.125 mL, 30%) and aq NaOH solution (0.125 mL, 6.0 M). Stirring was continued while the mixture warmed to rt (for the ketones). The mixture was then diluted with water (5.0 mL), extracted with dichloromethane (3×15 mL), and the extracts washed successively with aq $NaHCO_3$ solution (10 mL, saturated), aq Na_2CO_3 solution (10 mL, saturated) and brine (10 mL). The organic solution was dried over $MgSO_4$, concentrated in vacuo and purified by column chromatography to provide pure products (**2**, **12**, **13**, and **24**–**26**).

3.12. (4*S*,5*R*,1′*S*)-2,2-Dimethyl-4-(1-phenyl)hydroxymethyl-5-vinyl-1,3-dioxolane [*anti*-(2)]

Prepared from ketone **1** as a white waxy solid (in the presence of $ZnCl_2$: 111 mg, 67% on a 0.708 mmol scale; no $ZnCl_2$: 41 mg, 69% on a 0.254 mmol scale). R_f 0.35 (petrol/ethyl acetate, 3:1); mp 51 °C;

[†] For the reductions performed in the absence of $ZnCl_2$, the reactions were initiated by the dropwise addition of L-Selectride (1.0 mL, 1 M solution in THF, 1.0 mmol) to a solution of ketone **1**, **8** or **11** or lactol **10**, **22** or **23** (0.29 mmol) in dichloromethane (11 mL) at −78 °C. Otherwise, the reductions followed the above procedure.

$[\alpha]_D^{23}$ −17.0 (*c* 0.2, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3398br, 1381w, 1262m, 1218s, 1165m, 1074w, 1047s, 1024s, 921m, 879m, 804w, 752m, 699s; δ_H (500 MHz, $CDCl_3$) 1.32 and 1.48 (2×3H, 2×s, 2×CH_3), 2.03 (1H, d, *J* 3.2, OH), 4.31 (1H, dd, *J* 8.7, 6.1, C*H*CHOH), 4.69 (1H, dd, *J* 8.7, 3.2, C*H*OH), 4.76 (1H, dd, *J* 7.0, 6.1, C*H*CH═), 5.36 (1H, d, *J* 10.4) and 5.50 (1H, d, *J* 17.3, ═CH_2), 6.16 (1H, ddd, *J* 17.4, 10.4, 7.0, C*H*═CH_2), 7.30–7.42 (5H, m, Ph); δ_C (125 MHz, $CDCl_3$) 25.2 (CH_3), 27.8 (CH_3), 72.4 (CH), 78.9 (CH), 80.8 (CH), 108.9 (C), 118.4 (CH_2), 127.0 (CH), 128.0 (CH), 128.2 (CH), 134.2 (CH), 141.2 (C); *m*/*z* (ESI^+) 257 (MNa^+, 100%); HRMS (ESI^+) found 257.1148, $C_{14}H_{18}NaO_3$ (MNa^+) requires 257.1148.

3.13. (4*S*,5*R*,1′*S*)-2,2-Dimethyl-4-[1-(2-methoxyphenyl)]-hydroxymethyl-5-vinyl-1,3-dioxolane *anti*-(12)

Prepared from ketone **8** as a colourless oil (in the presence of $ZnCl_2$: 9.5 mg, 75% on a 0.048 mmol scale; no $ZnCl_2$: 13 mg, 72% on a 0.068 mmol scale). R_f 0.69 (petrol/ethyl acetate, 1:1); $[\alpha]_D^{25}$ −7.0 (*c* 0.3, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3453br, 2986m, 2937m, 1602w, 1494m, 1464w, 1380w, 1244s, 1166w, 1031s, 927w, 896w, 755m; δ_H (500 MHz, $CDCl_3$) 1.35 and 1.46 (2×3H, 2×s, 2×CH_3), 2.90 (1H, d, *J* 7.0, OH), 3.88 (3H, s, OCH_3), 4.53 (1H, dd, *J* 9.0, 6.2, C*H*CHOH), 4.75–4.78 (1H, m, C*H*CH═), 4.85 (1H, dd, *J* 9.0, 7.0, C*H*OH), 5.34 (1H, app dt, *J* 10.4, 1.4) and 5.48 (1H, app dt, *J* 17.2, 1.4, ═CH_2), 6.21 (1H, ddd, *J* 17.2, 10.4, 6.9, C*H*═CH_2), 6.91 (1H, d, *J* 8.2), 6.98 (1H, app td, *J* 7.6, 0.9) and 7.26–7.32 (2H, m, Ar); δ_C (125 MHz, $CDCl_3$) 25.5 (CH_3), 27.8 (CH_3), 55.3 (CH_3), 70.1 (CH), 79.1 (CH), 79.2 (CH), 108.7 (C), 110.7 (CH), 117.7 (CH_2), 120.8 (CH), 128.7 (C), 128.9 (CH), 129.2 (CH), 134.1 (CH), 157.1 (C); *m*/*z* (ESI^+) 257 (MNa^+, 100%); HRMS (ESI^+) found 287.1250, $C_{15}H_{20}NaO_4$ (MNa^+) requires 287.1254.

3.14. (4*S*,5*R*,1′*S*)-5-(*tert*-Butyldimethylsilyloxy)methyl-2,2-dimethyl-4-(1-phenyl)hydroxymethyl-1,3-dioxolane [*anti*-(13)]

Prepared from ketone **11** as a colourless oil (in the presence of $ZnCl_2$: 61 mg, 83% on a 0.209 mmol scale; no $ZnCl_2$: 73 mg, 84% on a 0.246 mmol scale). R_f 0.24 (petrol/ether, 5:1); $[\alpha]_D^{23}$ −7.8 (*c* 0.9, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3444br, 2932m, 2859w, 1472w, 1380w, 1253m, 1220m, 1076s, 838s, 781w; δ_H (400 MHz, $CDCl_3$) 0.18 and 0.18 (2×3H, 2×s, $SiMe_2$), 0.95 (9H, s, *t*-Bu), 1.26 and 1.39 (2×3H, 2×s, 2×CH_3), 3.72 (1H, dd, *J* 10.3, 3.3) and 3.62 (1H, app t, *J* 10.3 CH_2), 4.32–4.39 (2H, m, C*H*C*H*CH_2), 4.55 (1H, d, *J* 3.1, OH), 4.82 (1H, dd, *J* 9.0, 3.1, C*H*Ph), 7.31 (1H, d, *J* 7.3), 7.38 (2H, t, *J* 7.3) and 7.48 (2H, d, *J* 7.3, Ph); δ_C (125 MHz, $CDCl_3$) −5.6 (CH_3), −5.6 (CH_3), 18.2 (C), 25.2 (CH_3), 25.8 (CH_3), 28.1 (CH_3), 62.0 (CH_2), 71.5 (CH), 77.3 (CH), 81.3 (CH), 108.7 (C), 127.0 (CH), 127.7 (CH), 128.2 (CH), 141.2 (C); *m*/*z* (ESI^+) 727 (M_2Na^+, 90%), 705 (M_2H^+, 40), 375 (MNa^+, 80), 335 (100), 295 (70), 277 (40); HRMS (ESI^+) found 375.1959, $C_{19}H_{32}NaO_4Si$ (MNa^+) requires 375.1962.

3.15. (4*S*,5*R*,1′*R*)-5-Hydroxymethyl-2,2-dimethyl-4-(1-phenyl)hydroxymethyl-1,3-dioxolane [*syn*-(24)][6b]

Prepared from lactol **10** in the presence of $ZnCl_2$, following column chromatography (petrol/ethyl acetate, 4:1→2:1), as a colourless oil (71 mg, 44% on a 0.68 mmol scale) as well as a small amount of the epimer *anti*-**24** (24 mg, 15%). Data for *syn*-**24**: R_f 0.38 (ethyl acetate); $[\alpha]_D^{25}$ −36.5 (*c* 0.4, $CHCl_3$), lit.[6b] $[\alpha]_D$ −43.0 (*c* 1.05, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3418br, 1496w, 1455w, 1381m, 1217s, 1164m, 1042s, 860w, 739w, 702m; δ_H (500 MHz, $CDCl_3$) 1.41 and 1.59 (2×3H, 2×s, 2×CH_3), 2.29 and 3.12 (2×1H, 2×br s, 2×OH), 3.68 (1H, dd, *J* 11.8, 3.8) and 3.76 (1H, dd, *J* 11.8, 5.8, CH_2), 4.19 (1H, ddd, *J* 6.8, 5.8, 3.8, C*H*CH_2), 4.46 (1H, dd, *J* 6.8, 5.2, C*H*CHPh), 4.79 (1H, d, *J* 5.2, C*H*Ph), 7.30–7.44 (5H, m, Ph); δ_C (125 MHz, $CDCl_3$) 25.1 (CH_3), 27.4 (CH_3), 61.1 (CH_2), 71.8 (CH), 77.3 (CH), 80.2 (CH), 108.7 (C), 127.1 (CH), 128.4 (CH), 128.7 (CH), 140.2 (C); *m*/*z* (ESI^+) 499 (M_2Na^+, 100%), 302 (70), 261 (MNa^+, 60), 221 (40); HRMS (ESI^+) found 261.1096, $C_{13}H_{18}NaO_4$ (MNa^+) requires 261.1097. Data for *anti*-**24**: R_f 0.46 (ethyl acetate); $[\alpha]_D^{25}$ −15.8 (*c* 0.4, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3383br, 1455w, 1381m, 1219s, 1166m, 1050s, 864w, 762w, 700w; δ_H (400 MHz, $CDCl_3$) 1.30 and 1.44 (2×3H, 2×s, 2×CH_3), 3.12 (2H, br s, 2×OH), 3.85 (1H, dd, *J* 11.5, 4.0) and 3.96 (1H, dd, *J* 11.5, 7.1, CH_2), 4.32 (2H, m, C*H*C*H*CH_2), 4.82 (1H, d, *J* 8.5, C*H*Ph), 7.30–7.44 (5H, m, Ph); δ_C (100 MHz, $CDCl_3$) 25.2 (CH_3), 27.8 (CH_3), 60.9 (CH_2), 72.4 (CH), 77.5 (CH), 80.0 (CH), 108.5 (C), 126.9 (CH), 128.2 (CH), 128.5 (CH), 141.2 (C); *m*/*z* (ESI^+) 499 (M_2Na^+, 60%), 337 (70), 302 (100), 261 (MNa^+, 50), 235 (40), 221 (40); HRMS (ESI^+) found 261.1097, $C_{13}H_{18}NaO_4$ (MNa^+) requires 261.1097.

3.16. (4*S*,5*R*,1′*S*)-5-Hydroxymethyl-2,2-dimethyl-4-(1-phenyl)hydroxymethyl-1,3-dioxolane [*anti*-(24)]

Prepared from lactol **10** in the absence of $ZnCl_2$, following column chromatography (petrol/ethyl acetate, 4:1→2:1), as a colourless oil (127 mg, 78% on a 0.68 mmol scale); a mixed fraction (18 mg, 11%) was also obtained that contained a small amount of epimer *syn*-**24**. Data as above.

3.17. (4*S*,5*R*,1′*R*,1″*R*)-5-(1-Benzyloxymethyl)hydroxymethyl-2,2-dimethyl-4-(1-phenyl)hydroxymethyl-1,3-dioxolane [*syn*-(25)]

Prepared from lactol **22**, in the presence of $ZnCl_2$, as a colourless oil (130 mg, 63% on a 0.58 mmol scale) following column chromatography (petrol/ethyl acetate, 10:1→6:1→2:1). R_f 0.16 (petrol/ethyl acetate, 4:1); $[\alpha]_D^{22}$ −26.5 (*c* 0.4, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3425br, 2934w, 1454m, 1380m, 1214s, 1064s, 884w, 700 m; δ_H (400 MHz, $CDCl_3$) 1.34 and 1.54 (2×3H, 2×s, 2×CH_3), 2.74 (1H, d, *J* 4.7, CH(O*H*)Ph), 3.00 (1H, d, *J* 7.1, CH(O*H*)CH_2), 3.62 (1H, dd, *J* 9.6, 6.2) and 3.79 (1H, d, *J* 9.6, 2.8, CH_2OBn), 4.19 (1H, dd, *J* 6.3, 2.5, C*H*CH(OH)CH_2), 4.29–4.34 (1H, m, C*H*CH_2), 4.42 (1H, dd, *J* 6.3, 2.2, C*H*CHPh), 5.14–5.17 (1H, m, C*H*Ph), 7.25–7.43 (10H, m, 2×Ph); δ_C (125 MHz, $CDCl_3$) 24.8 (CH_3), 27.0 (CH_3), 68.7 (CH), 70.7 (CH), 71.8 (CH_2), 76.4 (CH_2), 76.9 (CH), 80.3 (CH), 108.6 (C), 126.5 (CH), 127.5 (CH), 127.8 (CH), 127.8 (CH), 128.3 (CH), 128.5 (CH), 137.9 (C), 142.4 (C); *m*/*z* (ESI^+) 739 (M_2Na^+, 100%), 734 ($M_2NH_4^+$, 80), 717 (M_2H^+, 30), 381 (MNa^+, 80), 376 (MNH_4^+, 40), 283 (50), 233 (30); HRMS (ESI^+) found 381.1670, $C_{21}H_{26}NaO_5$ (MNa^+) requires 381.1672.

3.18. (4*S*,5*R*,1′*R*,1″*R*)- and (4*S*,5*R*,1′*R*,1″*S*)-5-(1-Benzyloxymethyl)hydroxymethyl-2,2-dimethyl-4-(1-phenyl)-hydroxymethyl-1,3-dioxolane [*syn*- and *anti*-(25)]

Prepared from lactol **22**, in the absence of $ZnCl_2$, as a colourless oil and as a 2:1 *syn*-: *anti*- mixture (117 mg, 57% on a 0.576 mmol scale) following column chromatography (petrol/ethyl acetate, 6:1→2:1). Selected data for *anti*-**25**: δ_H (400 MHz, $CDCl_3$) 1.24 and 1.36 (2×3H, 2×s, 2×CH_3), 3.64 (1H, dd, *J* 9.8, 6.9) and 3.85 (1H, d, *J* 9.8, 2.7, CH_2OBn), 4.17–4.35 (3H, C*H*C*H*C*H*CH_2, overlapping with resonances from *syn*-**25**), 4.64 (2H, s, C*H*$_2$Ph), 4.82 (1H, d, *J* 9.5, C*H*Ph), 7.25–7.43 (10H, m, 2×Ph); δ_C (125 MHz, $CDCl_3$) 25.3 (CH_3), 28.0 (CH_3), 68.6 (CH), 71.5 (CH), 71.8 (CH_2), 73.5 (CH_2), 77.5 (CH), 81.1 (CH), 108.9 (C), 127.2 (CH), 127.8 (CH), 127.9 (CH), 127.9 (CH), 128.3 (CH), 128.5 (CH), 137.2 (C), 141.2 (C).

3.19. (4*S*,5*R*,1′*R*,1″*R*)-5-(1-*tert*-Butyldimethylsilyloxy)-hydroxymethyl-2,2-dimethyl-4-(1-phenyl)-hydroxymethyl-1,3-dioxolane [*syn*-(26)]

Prepared from lactol **23**, in the presence of $ZnCl_2$, as a colourless oil (135 mg, 64% on a 0.554 mmol scale) following column chromatography (petrol/ethyl acetate, 10:1). R_f 0.16 (petrol/ethyl acetate, 10:1); $[\alpha]_D^{25}$ −33.6 (*c* 0.7, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3454br, 2930m, 1463w, 1381w, 1255s, 1214m, 875s, 837m, 700w; δ_H (400 MHz, $CDCl_3$) 0.11 (6H, s, $SiMe_2$), 0.93 (9H, s, *t*-Bu), 1.34 and 1.56 (2×3H, 2×s, 2×CH_3), 2.75 (1H, d, *J* 4.3) and 3.00 (1H, d, *J* 7.3, 2×OH), 3.74 (1H, dd, *J* 9.7, 4.2) and 3.88 (1H, d, *J* 9.7, 2.5, CH_2), 4.12–4.19 (2H, m, C*H*CH_2 and C*H*CHPh), 4.42–4.45 (1H, m, C*H*CHCH_2), 5.17–5.19 (1H, m, C*H*Ph), 7.25–7.30 (1H, m), 7.34–7.39 (2H, m) and 7.42–7.46 (2H, m, Ph); δ_C (125 MHz, $CDCl_3$) −5.5 (CH_3), −5.4 (CH_3), 18.3 (C), 24.6 (CH_3), 25.9 (CH_3), 27.0 (CH_3), 64.4 (CH_2), 69.4 (CH), 70.4 (CH), 76.4 (CH), 80.4 (CH), 108.6 (C), 126.5 (CH), 127.4 (CH), 128.3 (CH), 142.4 (C); *m*/*z* (ESI^+) 787 (M_2Na^+, 100%), 782 ($M_2NH_4^+$, 80), 765 (M_2H^+, 60), 405 (MNa^+, 30), 325 (80), 243 (50); HRMS (ESI^+) found 405.2064, $C_{20}H_{34}NaO_5Si$ (MNa^+) requires 405.2068.

3.20. (4*S*,5*R*,1′*R*,1″*R*)- and (4*S*,5*R*,1′*R*,1″*S*)-5-(1-*tert*-Butyldimethylsilyloxy)hydroxymethyl-2,2-dimethyl-4-(1-phenyl)hydroxymethyl-1,3-dioxolane [*syn*- and *anti*-(26)]

Prepared from lactol **23**, in the absence of $ZnCl_2$, as a colourless oil and as a 6:4 *syn*-: *anti*- mixture (135 mg, 73% on a 0.484 mmol scale) following column chromatography (petrol/ethyl acetate, 10:1). Selected data for *anti*-**26**: δ_H (400 MHz, $CDCl_3$) 0.14 (6H, s, $SiMe_2$), 0.95 (9H, s, *t*-Bu), 1.24 and 1.38 (2×3H, 2×s, 2×CH_3), 3.47–3.51 (1H, m, OH), 3.72 (1H, dd, *J* 10.0, 6.9) and 3.95 (1H, d, *J* 10.0, 3.2, CH_2), 3.99–4.05 (1H, m, C*H*CH_2), 4.18 (1H, dd, *J* 9.7, 5.3, C*H*CHCH_2), 4.33 (1H, dd, *J* 9.5, 5.3, C*H*CHPh), 4.58–4.61 (1H, m, OH), 4.85 (1H, d, *J* 9.5, C*H*Ph), 7.26–7.50 (5H, m, Ph); δ_C (125 MHz, $CDCl_3$) −5.4 (CH_3), −5.3 (CH_3), 18.3 (C), 25.3 (CH_3), 25.9 (CH_3), 28.0 (CH_3), 64.4 (CH_2), 69.4 (CH), 71.6 (CH), 77.4 (CH), 81.3 (CH), 108.8 (C), 127.2 (CH), 127.8 (CH), 128.2 (CH), 141.3 (C).

3.21. General procedure for acetonide cleavage and benzylidene acetal formation from reduction products *anti*-(2) and *anti*-(12)

To a solution of alcohol *anti*-**2** or *anti*-**12** (1.0 mmol) in methanol (25 mL) at rt was added hydrochloric acid (20 μL, 37% solution, 0.22 mmol) and the mixture was stirred for 1 h. Triethylamine (0.139 mL, 1.0 mmol) was then added and the reaction mixture concentrated in vacuo. The crude triol (**14** or **15**) was then dissolved in dichloromethane (25 mL) and benzaldehyde dimethyl acetal (1.50 mL, 10.0 mmol) and *p*-toluenesulfonic acid (172 mg, 1.0 mmol; the monohydrate was heated at reflux in toluene for 2 h with Dean–Stark attachment then concentrated in vacuo to give 'anhydrous' reagent) were added, and the reaction stirred at rt for 18 h. Triethylamine (0.139 mL, 1.0 mmol) was added, the reaction was concentrated in vacuo, and the residue was purified by column chromatography to afforded the desired benzylidene acetal (**17** or **18**).

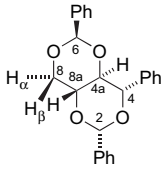
3.22. (2*R*,4*S*,5*R*,6*R*)-2,4-Diphenyl-6-vinyl-1,3-dioxan-5-ol (17)

Prepared from alcohol *anti*-**2**, the *title compound* (**17**) was obtained as a white solid (26 mg, 54% on a 0.17 mmol scale) following column chromatography (petrol/ethyl acetate, 10:1→4:1). R_f 0.28 (petrol/ethyl acetate, 4:1); mp 86 °C; $[\alpha]_D^{23}$ +48.0 (*c* 0.1, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3396br, 1455w, 1069m, 1028s, 759m, 700s; δ_H (400 MHz, $CDCl_3$) 1.72–1.75 (1H, br m, OH), 3.50 (1H, app td, *J* 9.0, 3.5, H-5), 4.24–4.29 (1H, m, H-6), 4.62 (1H, d, *J* 9.0, H-4), 5.37 (1H, dt, *J* 10.6, 1.1) and 5.55 (1H, *J* 17.2, 1.1, =CH_2), 5.85 (1H, s, H-2), 6.06 (1H, ddd, *J* 17.2, 10.6, 6.2, C*H*=CH_2), 7.34–7.44 (6H, m), 7.51–7.55 (2H, m) and 7.58–7.62 (2H, m, Ph); δ_C (100 MHz, $CDCl_3$) 71.1 (CH), 82.1 (CH), 83.5 (CH), 100.9 (CH), 118.8 (CH_2), 126.4 (CH), 127.5 (CH), 128.4 (CH), 128.6 (CH), 128.6 (CH), 129.0 (CH), 134.6 (CH), 137.6 (C), 138.2 (C); *m*/*z* (ESI^+) 305 (MNa^+, 100%); HRMS (ESI^+) found 305.1141, $C_{18}H_{18}NaO_3$ (MNa^+) requires 305.1148.

3.23. (2*R*,4*S*,5*R*,6*R*)-4-(2-Methoxyphenyl)-2-phenyl-6-vinyl-1,3-dioxan-5-ol (18)

Prepared from alcohol *anti*-**12**, the *title compound* (**18**) was obtained as a colourless oil (16 mg, 75% on a 0.068 mmol scale) following column chromatography (petrol/ethyl acetate, 5:1). R_f 0.26 (petrol/ethyl acetate, 4:1); $[\alpha]_D^{25}$ +45.7 (*c* 0.7, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3474br,1603w, 1495m, 1463w, 1395w, 1288w, 1249s, 1072s, 1028s, 925w, 757m, 701m; δ_H (500 MHz, $CDCl_3$) 2.51 (1H, d, *J* 3.6, OH), 3.48–3.54 (1H, m, H-5), 3.91 (3H, s, OCH_3), 4.25–4.30 (1H, m, H-6), 5.20 (1H, d, *J* 9.1, H-4), 5.35 (1H, dt, *J* 10.7, 1.4) and 5.55 (1H, dt, *J* 17.3, 1.4, =CH_2), 5.84 (1H, s, H-2), 6.09 (1H, ddd, *J* 17.3, 10.7, 6.0, C*H*=CH_2), 6.95 (1H, d, *J* 8.4), 7.06 (1H, td, *J* 7.5, 0.8), 7.30–7.40 (4H, m) and 7.57–7.63 (3H, m, Ph and Ar); δ_C (125 MHz, $CDCl_3$) 55.8 (CH_3), 72.4 (CH), 76.2 (CH), 82.5 (CH), 101.0 (CH), 110.6 (CH), 118.2 (CH_2), 121.6 (CH), 126.4 (CH), 127.2 (CH), 127.8 (C), 128.2 (CH), 128.9 (CH), 129.0 (CH), 134.7 (CH), 137.7 (C), 156.4 (C); *m*/*z* (ESI^+) 647 (M_2Na^+, 100%), 376 (80), 335 (MNa^+, 30); HRMS (ESI^+) found 335.1251, $C_{19}H_{20}NaO_4$ (MNa^+) requires 335.1254.

3.24. (2*S*,4*S*,4a*S*,6*R*,8a*R*)-2,4,6-Triphenyltetrahydro-[1,3]dioxino[5,4-*d*][1,3]dioxine (19)



A solution of *anti*-**13** (22 mg, 0.063 mmol) in aqueous acetic acid (0.5 mL, 80%) was stirred at rt for 18 h. The solvents were removed in vacuo and the residue, the crude tetraol **16**, was dissolved in dichloromethane (1.0 mL). The reaction then proceeded according to the general procedure for generation of benzylidene acetals **17** and **18**. The final product, a complex mixture of benzylidene isomers, was purified by column chromatography to give a sample (5 mg) of the *title compound* (**19**), a pale yellow oil, that was contaminated with some residual benzaldehyde dimethyl acetal, but which provided clear ^1H NMR data. R_f 0.69 (petrol/ether, 10:1); δ_H (500 MHz, $CDCl_3$) 3.80 (1H, app t, *J* 9.2, H-4a), 3.94 (1H, app t, *J* 10.3, H-8α), 4.14 (1H, ddd, *J* 10.3, 9.2, 4.7, H-8a), 4.45 (1H, dd, *J* 10.3, 4.7, H-8β), 4.95 (1H, d, *J* 9.2, H-4), 5.56 and 5.95 (2×1H, 2×s, H-2 and H-6), 7.30–7.62 (15H, m, 3×Ph).

3.25. (4*S*,5*R*,1′*R*,1″*R*)-5-(1,2-Dihydroxyethyl)-2,2-dimethyl-4-(1-phenyl)hydroxymethyl-1,3-dioxolane (27)

From *syn*-**25**. Palladium on carbon (3.2 mg, 10%) was added to a solution of diol *syn*-**25** (32 mg, 0.089 mmol) in methanol (2.5 mL). The flask was briefly evacuated and filled with Ar (×3) then evacuated and filled with H_2 (×3) and stirring continued at rt for 2 h. The H_2 atmosphere was replaced with Ar (three evacuation/filling cycles) and the reaction mixture filtered through Celite® and concentrated in vacuo to afford *triol* **27** as a colourless oil (24 mg, 100%).

R_f 0.15 (ethyl acetate); $[\alpha]_D^{25}$ −31.0 (*c* 0.4, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3385br, 1495w, 1455m, 1382s, 1260s, 1216s, 1164w, 1064s, 886w; δ_H (400 MHz, $CDCl_3$) 1.34 and 1.53 (2×3H, 2×s, 2×CH_3), 2.60 (1H, br s, OH), 3.00 (2H, br s, 2×OH), 3.65–3.70 (1H, m) and 3.87 (1H, br d, *J* 10.7, CH_2), 4.09–4.14 (2H, m, *CH*CH_2 and C*H*CHPh), 4.39–4.43 (1H, m, C*H*CHCH_2), 5.03–5.12 (1H, m, C*H*Ph), 7.27–7.45 (5H, m, Ph); δ_C (125 MHz, $CDCl_3$) 25.0 (CH_3), 27.3 (CH_3), 64.7 (CH_2), 69.7 (CH), 70.7 (CH), 77.2 (CH), 80.0 (CH), 108.7 (C), 126.6 (CH), 127.9 (CH), 128.5 (CH), 141.6 (C); *m*/*z* (ESI^+) 559 (M_2Na^+, 100%), 332 (80), 291 (MNa^+, 30), 193 (40); HRMS (ESI^+) found 291.1200, $C_{14}H_{20}NaO_5$ (MNa^+) requires 291.1203.

From *syn*-**26**. To a stirred solution of diol *syn*-**26** (116 mg, 0.303 mmol) in THF (1.5 mL) at rt was added dropwise TBAF (0.33 mL, 1.0 M solution in THF, 0.33 mmol). After 10 min the solution was diluted with ether (10 mL), washed with aq NH_4Cl solution (5.0 mL, saturated), dried over $MgSO_4$, and the residue was purified by column chromatography (solvent system) to afforded *triol* **27** as a colourless oil (46 mg, 57%). Data as above.

3.26. (4*R*,4′*R*,5′*S*)-2′,2′-Dimethyl-5′-[(1*R*)-(phenyl)]hydroxymethyl-4,4′-bi(1,3-dioxolane)-2-thione (28)

To a solution of triol **27** (33 mg, 0.123 mmol) in THF (1.0 mL) at rt was added thiocarbonyl diimidazole (22 mg, 0.123 mmol) and the mixture was stirred for 24 h then concentrated in vacuo. The residue was purified by column chromatography (petrol/ethyl acetate, 3:1) to afford the *title compound* (**28**) as a pale yellow oil (22 mg, 58%). R_f 0.51 (petrol/ethyl acetate, 1:1); $[\alpha]_D^{25}$ −42 (*c* 0.25, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3420br, 2931w, 1471w, 1294s, 1164m, 957m, 859w, 702w; δ_H (400 MHz, $CDCl_3$) 1.37 and 1.56 (2×3H, 2×s, 2×CH_3), 2.54 (1H, d, *J* 8.4, OH), 4.46 (1H, dd, *J* 7.1, 6.0, *CH*CHCH_2), 4.57 (1H, dd, *J* 7.1, 1.8, C*H*CHPh), 4.76 (2H, app d, *J* 7.3, CH_2), 4.91 (1H, dd, *J* 8.4, 1.8, C*H*Ph), 5.40 (1H, app td, *J* 7.3, 6.0, C*H*CH_2), 7.33–7.44 (5H, m, Ph); δ_C (125 MHz, $CDCl_3$) 24.3 (CH_3), 26.4 (CH_3), 70.5 (CH), 71.5 (CH_2), 76.3 (CH), 79.0 (CH), 80.0 (CH), 109.8 (C), 126.5 (CH), 128.3 (CH), 128.7 (CH), 140.6 (C), 191.5 (C); *m*/*z* (ESI^+) 953 (M_3Na^+, 40%), 948 ($M_3NH_4^+$, 20), 643 (M_2Na^+, 50), 638 ($M_2NH_4^+$, 100), 311 (MH^+, 80), 279 (40); HRMS (ESI^+) found 333.0768, $C_{15}H_{18}NaO_5S$ (MNa^+) requires 333.0767.

3.27. (4*S*,5*R*,1′*R*)-2,2-Dimethyl-4-(1-phenyl)hydroxymethyl-5-vinyl-1,3-dioxolane [*syn*-(2)]

A solution of thionocarbonate **28** (15 mg, 0.048 mmol) in trimethylphosphite (1.0 mL) was heated at reflux for 72 h and then cooled and concentrated in vacuo. The product was sufficiently pure for NMR confirmation that the *anti*- diastereomer of alcohol **2** was not present and the structure of *syn*-**2** was assigned both on this basis and on the basis of the following Mitsunobu sequence from *anti*-**2**. To a solution of alcohol *anti*-**2** (39 mg, 0.167 mmol) in benzene (2.0 mL) at rt was added triphenylphosphine (66 mg, 0.251 mmol) followed by *p*-nitrobenzoic acid (42 mg, 0.251 mmol) and then diisopropyl azodicarboxylate (49.4 μL, 0.251 mmol) dropwise. Stirring was continued for 18 h then the mixture was concentrated in vacuo and the residue purified by column chromatography (petrol/ethyl acetate, 5:1) to afford a mixture of *p*-nitrobenzoate esters (55:45, *anti*-: *syn*-) (19 mg, 34%) as a colourless oil. δ_H (500 MHz, $CDCl_3$) 1.36 (3H, s, CH_3, *anti*), 1.44 (3H, s, CH_3, *syn*), 1.49 (3H, s, CH_3, *anti*), 1.66 (3H, s, CH_3, *syn*), 4.62–4.70 (3H, m, C*HCH*CHPh, *anti*, C*H*CHPh, *syn*), 4.83 (1H, dd, *J* 7.4, 5.5, C*H*CH=, *syn*), 5.11 (1H, d, *J* 10.4, =C*H*H′, *syn*), 5.18 (1H, d, *J* 10.6, =C*H*H′, *anti*), 5.25 (1H, d, *J* 17.0, =CH*H*′, *syn*), 5.37 (1H, d, *J* 17.0, =CH*H*′, *anti*), 5.79 (1H, ddd, *J* 17.0, 10.6, 6.8, CH=, *anti*), 5.89 (1H, d, *J* 9.0, C*H*Ph, *anti*) overlapping 5.90 (1H, ddd, *J* 17.0, 10.4, 7.4, CH=, *syn*), 5.95 (1H, d, *J* 5.2, C*H*Ph, *syn*), 7.31–7.40 (6H, m) and 7.44–7.50 (4H, m, *Ph*CH, *syn* and *anti*), 8.15–8.18 (4H, m) and 8.25–8.31 (4H, m, ArCO, *syn* and *anti*); δ_C (125 MHz, $CDCl_3$) *anti*- isomer: 25.3 (CH_3), 27.8 (CH_3), 74.9 (CH), 78.8 (CH), 79.0 (CH), 109.4 (C), 118.6 (CH_2), 123.6 (CH), 127.8 (CH), 128.5 (CH), 128.7 (CH), 130.9 (CH), 132.4 (CH), 135.3 (C), 136.6 (C), 150.6 (C), 162.9 (C); *syn*- isomer: 25.4 (CH_3), 27.5 (CH_3), 75.9 (CH), 78.4 (CH), 79.7 (CH), 109.4 (C), 119.3 (CH_2), 123.5 (CH), 128.0 (CH), 128.5 (CH), 128.8 (CH), 130.7 (CH), 132.6 (CH), 135.8 (C), 137.4 (C), 150.5 (C), 163.8 (C). A sample of this crude mixture (8.0 mg) was dissolved in methanol (0.1 mL) and added dropwise at rt to a stirred solution of NaOH (1.0 mg, 0.025 mmol) in methanol (0.6 mL). After 1 h the mixture was diluted with ether (2.0 mL), washed with brine (1.0 mL) and then concentrated in vacuo to afford a mixture of alcohols *anti*-**2** and *syn*-**2** (55:45 ratio). The product was sufficiently pure for NMR analysis to enable full correlation of resonances with those of authentic material synthesised by the routes described above. NMR data for *syn*-**2**: δ_H (500 MHz, $CDCl_3$) 1.42 and 1.61 (2×3H, 2×s, 2×CH_3), 2.75 (1H, d, *J* 4.6, OH), 4.42 (1H, dd, *J* 6.6, 5.5, C*H*CHOH), 4.54–4.51 (1H, m, C*H*CH=), 4.64–4.66 (1H, m, C*H*OH), 5.27 (1H, ddd, *J* 10.2, 1.4, 1.2) and 5.30 (1H, dt, *J* 17.4, 1.4, =CH_2), 5.97 (1H, ddd, *J* 17.4, 10.2, 7.4, C*H*=CH_2), 7.30–7.39 (5H, m, Ph); δ_C (125 MHz, $CDCl_3$) 25.1 (CH_3), 27.5 (CH_3), 72.2 (CH), 78.9 (CH), 81.4 (CH), 108.9 (C), 119.2 (=CH_2), 127.3 (CH), 128.0 (CH), 128.4 (CH), 133.7 (=CH), 140.4 (C).

3.28. (3a*R*,6*R*,6a*R*)-6-Benzyloxymethyl-2,2-dimethyl-4-(2-methoxyphenyl)tetrahydrofuro[3,4-*d*][1,3]dioxol-4-ol (37)

To a solution of 2-bromoanisole (0.495 mL, 3.97 mmol) in THF (38 mL) at −78 °C was added *tert*-butyllithium (5.14 mL, 1.7 M solution in hexanes, 8.74 mmol) and the solution was stirred for 30 min. The resulting organolithium solution was then transferred dropwise by cannula into a solution of lactone **20** (920 mg, 3.31 mmol) in THF (19 mL) at −78 °C, and stirring continued at this temperature for 90 min. The reaction was then quenched by the addition of brine (10 mL), allowed to warm to rt and then extracted with ethyl acetate (3×20 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo. Purification by column chromatography (petrol/ethyl acetate, 10:1) afforded the *title compound* (**37**) as a pale yellow oil, comprising a mixture of anomers (A:B, 2:1) as a pale yellow oil (614 mg, 48%). R_f 0.40 (petrol/ethyl acetate, 5:1); $[\alpha]_D^{20}$ −32 (*c* 0.7, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3411br, 1603w, 1492m, 1464w, 1372w, 1245s, 1211m, 1079s, 1028s, 873w, 755m, 699w; δ_H (400 MHz, $CDCl_3$) 1.23 and 1.27 (2×3H, 2×s, 2×CH_3, A), 1.42 and 1.68 (2×3H, 2×s, 2×CH_3, B), 3.64–3.75 (4H, m, CH_2OBn, A & B), 3.78 (3H, s, OCH_3, B), 3.91 (3H, s, OCH_3, A), 4.40–4.44 (1H, m, *CH*CH_2, B), 4.45–4.50 (1H, m, C*H*CH_2, A), 4.58 (2H, s, CH_2Ph, B), 4.62 and 4.67 (2×1H, 2×d, *J* 12.0, CH_2Ph, A), 4.77 (2H, m, OH, A, and *CH*CHCH_2, B), 4.86 (1H, br s, OH, B), 4.89–4.92 (2H, m, C*H*CHCH_2, A, and C*H*C(OH)Ar, B), 5.00 (1H, d, *J* 5.7, C*H*C(OH)Ar, A), 6.88–6.99 (4H, m, Ar, both), 7.27–7.39 (12H, m, Ar, both), 7.69 (1H, dd, *J* 7.6, 1.6, C*H*C(OMe), A), 7.75 (1H, dd, *J* 7.7, 1.6, C*H*C(OMe), B); δ_C (100 MHz, $CDCl_3$) anomer A: 25.7 (CH_3), 26.6 (CH_3), 56.1 (CH_3), 71.4 (CH_2), 73.6 (CH_2), 82.6 (CH), 84.4 (CH), 87.6 (CH), 111.4 (CH), 112.4 (CH), 120.4 (CH), 137.3 (C), 156.1 (C); anomer B: 25.2 (CH_3), 26.8 (CH_3), 55.4 (CH_3), 69.6 (CH_2), 73.4 (CH_2), 81.1 (CH), 82.1 (CH), 84.9 (CH), 111.3 (CH), 115.4 (CH), 120.3 (CH), 138.1 (C), 156.6 (C); additional resonances at 101.6 (2×C), 106.9 (2×C), 127.3 (CH), 127.6 (2×CH), 127.7 (CH), 128.0 (2×CH), 128.3 (CH), 128.5 (CH), 129.5 (CH) and 129.8 (CH) were not attributed to individual anomers; *m*/*z* (ESI^+) 795 (M_2Na^+, 100%), 790 ($M_2NH_4^+$, 100), 445 ($M{\cdot}CH_3CN{\cdot}NH_4^+$, 100), 409 ($MNa^+$, 80), 369 (90); HRMS ($ESI^+$) found 409.1615, $C_{22}H_{26}NaO_6$ (MNa^+) requires 409.1622.

3.29. (4*S*,5*R*,1′*R*,1″*R*)-5-(1-Benzyloxymethyl)hydroxymethyl-2,2-dimethyl-4-[1-(2-methoxyphenyl)]hydroxymethyl-1,3-dioxolane [*syn*-(38)]

Prepared from lactol **37**, following the general procedure for L-Selectride reduction in the presence of $ZnCl_2$, with the

following modification. After the addition of aq H_2O_2 and aq NaOH the mixture was allowed to stir for 1 h before continuing the work-up. The product (*syn*-**38**) was obtained as a colourless oil (29 mg, 69% on a 0.109 mmol scale) following column chromatography (petrol/ethyl acetate, 10:1→4:1). R_f 0.19 (petrol/ethyl acetate, 2:1); $[\alpha]_D^{22}$ −31 (*c* 0.6, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3344br, 1603w, 1492m, 1457m, 1379m, 1241s, 1065s, 753w, 699w; δ_H (400 MHz, $CDCl_3$) 1.33 and 1.55 (2×3H, 2×s, 2×CH_3), 3.66 (1H, dd, *J* 9.6, 6.2) and 3.79 (1H, d, *J* 9.6, 2.9, CH_2OBn), 3.82 (3H, s, OCH_3), 4.21 (1H, dd, *J* 8.6, 6.3, C*H*CHCH_2), 4.38 (1H, ddd, *J* 8.6, 6.2, 2.9, C*H*CH_2), 4.45 (1H, dd, *J* 6.3, 1.6, C*H*CHAr), 4.62 (2H, s, CH_2Ph), 5.52–5.53 (1H, m, C*H*Ar), 6.87 (1H, d, *J* 8.3), 6.97–7.02 (1H, m), 7.25–7.40 (6H, m) and 7.47 (1H, dd, *J* 7.6, 1.4, Ph and Ar); δ_C (100 MHz, $CDCl_3$) 24.9 (CH_3), 27.0 (CH_3), 55.4 (CH_3), 65.6 (2×CH), 71.9 (CH_2), 73.4 (CH_2), 76.9 (CH), 78.8 (CH), 108.4 (C), 110.3 (CH), 120.6 (CH), 127.3 (CH), 127.7 (CH), 127.8 (CH), 128.4 (2×CH), 130.2 (C), 138.0 (C), 155.9 (C); *m*/*z* (ESI^+) 799 (M_2Na^+, 100%), 794 ($M_2NH_4^+$, 90), 777 (M_2H^+, 50), 447 ($M{\cdot}CH_3CN{\cdot}NH_4^+$, 100), 411 ($MNa^+$, 70); HRMS ($ESI^+$) found 411.1779, $C_{22}H_{28}NaO_6$ (MNa^+) requires 411.1778.

3.30. (4*S*,5*R*,1′*R*,1″*S*)-5-(1-Benzyloxymethyl)hydroxymethyl-2,2-dimethyl-4-[1-(2-methoxyphenyl)]hydroxymethyl-1,3-dioxolane [*anti*-(38)]

Prepared from lactol **37**, following the general procedure for L-Selectride reduction in the absence of $ZnCl_2$, with the following modification. The product was purified by chromatography on basic alumina (petrol/ethyl acetate, 4:1→1:1) rather than on silica. The product (*anti*-**38**) was obtained as a colourless oil (38 mg, 47% on a 0.207 mmol scale). R_f 0.18 (petrol/ethyl acetate, 2:1); $[\alpha]_D^{21}$ −20 (*c* 0.3, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3385br, 1602w, 1495m, 1455w, 1369w, 1246s, 1071s, 916w, 754m, 699w; δ_H (500 MHz, $CDCl_3$) 1.27 and 1.34 (2×3H, 2×s, 2×CH_3), 3.68 (1H, dd, *J* 9.8, 6.3) and 3.85–3.88 (1H, m, CH_2OBn) overlaying 3.86 (3H, s, OCH_3), 4.22–4.27 (1H, m, C*H*CH_2), 4.32 (1H, dd, *J* 9.6, 5.2, C*H*CHCH_2), 4.57 (1H, dd, *J* 9.8, 5.2, C*H*CHAr), 4.63 and 4.67 (2×1H, 2×d, *J* 12.1, CH_2Ph), 5.10 (1H, d, *J* 9.8, C*H*Ar), 6.92 (1H, d, *J* 8.2), 6.99 (1H, app t, *J* 7.4) and 7.27–7.40 (7H, m, Ph and Ar); δ_C (100 MHz, $CDCl_3$) 25.4 (CH_3), 27.7 (CH_3), 55.4 (CH_3), 68.7 (CH), 68.8 (CH), 71.9 (CH_2), 73.5 (CH_2), 77.7 (CH), 79.1 (CH), 108.6 (C), 110.9 (CH), 120.9 (CH), 127.6 (CH), 127.7 (CH), 128.4 (CH), 128.6 (C), 129.1 (CH), 129.2 (CH), 138.2 (C), 157.2 (C); *m*/*z* (ESI^+) 799 (M_2Na^+, 100%), 794 ($M_2NH_4^+$, 30), 777 (M_2H^+, 10), 490 (90), 447 ($M{\cdot}CH_3CN{\cdot}NH_4^+$, 60), 411 ($MNa^+$, 30); HRMS ($ESI^+$) found 411.1777, $C_{22}H_{28}NaO_6$ (MNa^+) requires 411.1778.

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12. It was found that the crude product mixture in reductions of substrate **37** contained large amounts of what appeared to be a boron-containing complex of the product(s) that was not rapidly oxidised. For this reason, the oxidation during the work-up was allowed to proceed for 1 h, rather than a few minutes; even so, in the $ZnCl_2$-free case the unidentified 'complex' was still present and could only be removed (although not isolated) when chromatography was performed on basic alumina.
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