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# 5-Methyl-4*H*-1,3-dioxins, new chiral building blocks: transformation into (*R*)- and (*S*)-4-hydroxymethyl-4-methyl-1,3-dioxolanes via oxidation and rearrangement and determination of the absolute configuration

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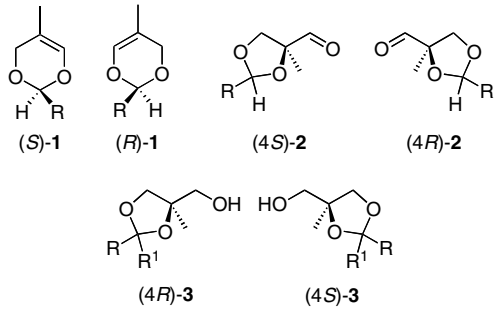
**Abstract**—5-Methyl-4*H*-1,3-dioxins obtained by asymmetric double-bond isomerization have been transformed into 4-hydroxymethyl-4-methyl-1,3-dioxolanes by *m*-chloroperbenzoic acid oxidation, ring contraction and reduction. The stereochemical course of this transformation has been studied, while the relative configuration of the intermediate oxidation product and the absolute configuration of the resulting camphanyl ester of 2-*tert*-butyl-4-hydroxymethyl-4-methyl-1,3-dioxolane was established by X-ray crystallography. From these results, the absolute configuration of the dioxins has been deduced.


## 1. Introduction

Previously, we have reported that optically active 5-methyl-4*H*-1,3-dioxins **1** can be obtained with high enantiomeric excess and in high yields by nickel-catalyzed asymmetric double-bond isomerization of 5-methylene-1,3-dioxanes **4**.[1] We have also reported that the one-pot *m*-CPBA oxidation/acid catalyzed rearrangement of dioxins **1** leads directly to 4-methyl-1,3-dioxolane-4-carbaldehydes **2**.[1,2]

Carbaldehydes **2** bearing a quarternary stereogenic centre in the 4-position and related compounds, for example, 4-hydroxymethyl-4-methyl-1,3-dioxolanes **3**, have been used as chiral building blocks in a variety of natural product and asymmetric syntheses.[2,3] Therefore, we have studied the stereochemical course of the latter transformation in order to establish the hitherto unknown absolute configuration of dioxins **1** and to demonstrate a practical route for the synthesis of both enantiomers of compounds **2** and **3** on a multigram scale.




## 2. Results and discussion

As a typical example, 2-*tert*-butyl-5-methylene-1,3-dioxane **4a** was used as the starting material. Compound **4a** was readily prepared from commercially available 5-methylene-1,3-propanediol and trimethylacetaldehyde by acid-catalyzed acetalization.[4] The isomerization of **4a** was performed with $NiBr_2$[(−)-Diop] as a precatalyst. The precatalyst was activated with lithium triethylborohydride at room temperature in ether and then reacted

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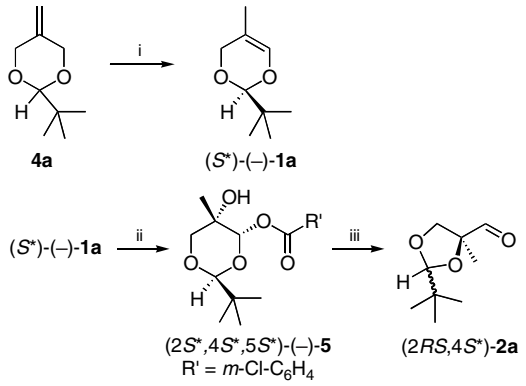
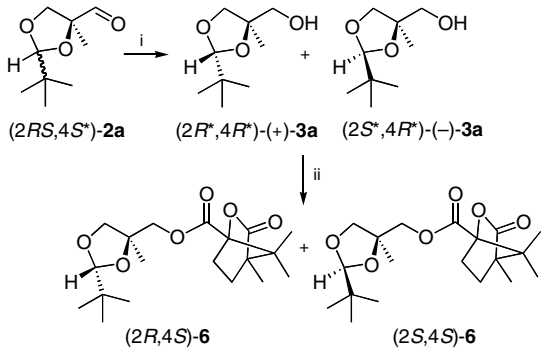



**Scheme 1.** Reagents and conditions: (i) 5 mol % $NiBr_2$[(−)-Diop], $LiBHEt_3$ (6 mol %, 1.0 M solution in THF), $Et_2O$, rt → −70 °C, addition of **4a**, 144 h, 85%, 92% ee; (ii) 1.2 equiv *m*-CPBA, THF, rt, 4 h, 84%; (iii) Lewatit® MonoPlus S 100 ($H^+$ form), $CHCl_3$, reflux, 1 h, 75%.

with **4a** at −70 °C to give (−)-**1a** with 92% ee in 85% yield (Scheme 1).[2]

Oxidation of (−)-**1a** with purified *m*-chloroperbenzoic acid[5,6] in THF led to a 95:2.3:2.3:0.4 mixture of diastereomers **5** in a virtually quantitative yield. After recrystallization from light petroleum, the main diastereomer could be isolated from the mixture in a diastereomerically pure form in 84% yield. The relative configuration was determined by NMR spectroscopy and unambiguously established by X-ray crystallography as (2*S**, 4*S**,5*S**)-configuration (Fig. 1).[7]

Ring contraction was achieved by refluxing (2*S**, 4*S**,5*S**)-**5** in either diethyl ether or chloroform in the presence of a cationic exchange resin, which afforded a 1:1 and 3:1 mixture, respectively, of carbaldehydes (2*S**,4*S**)-**2a** and (2*R**,4*S**)-**2a** (Scheme 1). Subsequent reduction of the mixtures gave the corresponding alcohols (2*S**,4*R**)-**3a** and (2*R**,4*R**)-**3a** (Scheme 2). For the determination of the enantiomeric purity, diastereomers (2*S**,4*R**)-**3a** and (2*R**,4*R**)-**3a** were isolated by column chromatography. By separating on a β-cyclodex




**Scheme 2.** Reagents and conditions: (i) $LiAlH_4$, $Et_2O$, reflux, 2 h, 95%; (ii) (1*S*)-camphanic chloride, pyridine, THF, rt, 3 h, 86%.

capillary column, each of the diastereomers was obtained as a 96:4 mixture of enantiomers (92% ee).[9] This indicates that ring contraction and the following reduction proceeds without the loss of enantiomeric purity.

Coupling of (2*S**,4*R**)-(−)-**3a** with (1*S*)-camphanic chloride afforded ester (2*S*,4*S*)-**6** as a crystalline white solid, whose absolute configuration was characterized by X-ray crystallography (Fig. 2).[10]

In the same way, treatment of a 1:1-mixture of (2*RS*,4*R**)-**3a** with (1*S*)-camphanic chloride led to a mixture of camphanyl esters **6**. Interestingly, it was shown by X-ray crystallography that both diastereomers crystallize in a single cell, and the absolute configuration was determined as (2*R*,4*S*)- and (2*S*,4*S*)-configurations (Fig. 3).[11]

Furthermore, the diastereomeric mixture of alcohols **3a** was transformed into the corresponding benzyl ethers **7** and then into diol (*S*)-(+)-**8** by acetal ring cleavage. Comparison of the specific rotation with the literature confirmed the absolute configuration (Scheme 3).[3,12]

At least, the (*R*)-enantiomer of diol **8** was prepared by the same reaction sequence as described above but

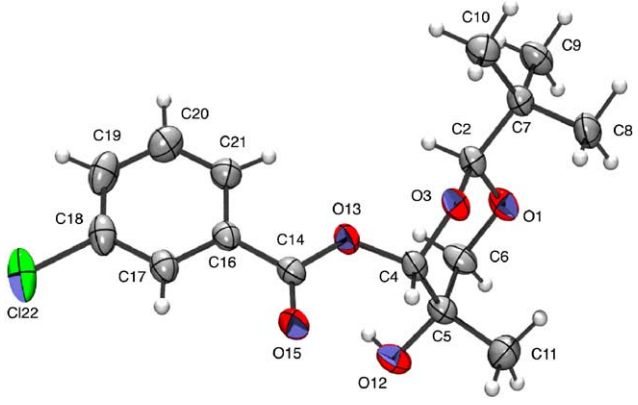



**Figure 1.** ORTEP[8] representation of (2*S**,4*S**,5*S**)-(−)-**5** with atomic labelling scheme showing 40% ellipsoids. H atoms are drawn as small spheres of arbitrary radii.

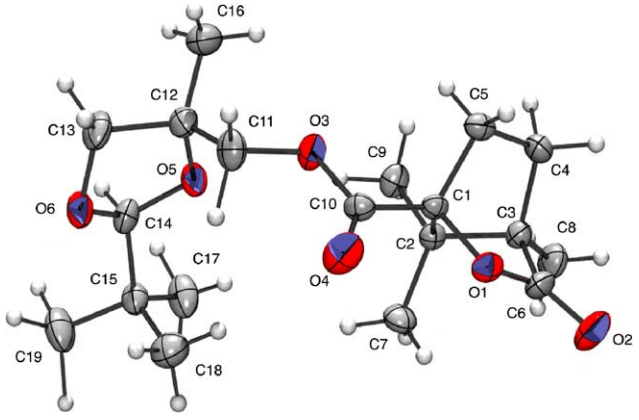



**Figure 2.** ORTEP[8] representation of (2*S*,4*S*)-**6** with atomic labelling scheme showing 40% ellipsoids. H atoms are drawn as small spheres of arbitrary radii.

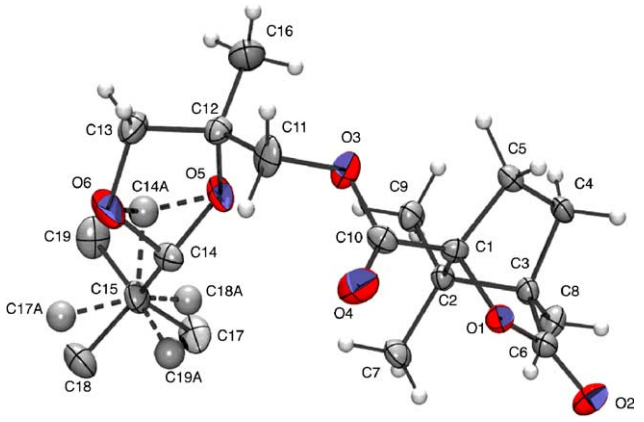
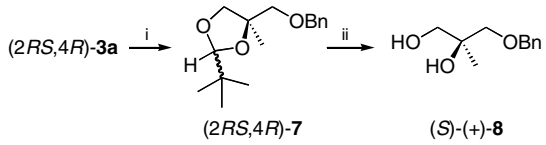
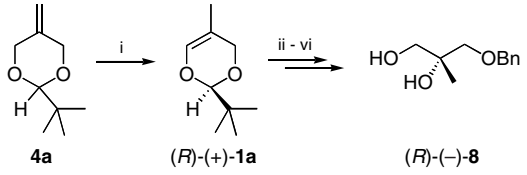



**Figure 3.** ORTEP[8] representation of (2*R*,4*S*)-**6** in a mixed crystal of diastereomers (2*RS*,4*S*)-**6** with atomic labelling scheme showing 40% ellipsoids. H atoms are drawn as small spheres of arbitrary radii. The second splitting position (50% probability) representating diastereomer (2*S*,4*S*)-**6** is indicated with dashed bonds and C atoms are drawn as spheres of arbitrary radii. H atom positions of the disordered group are not refined.




**Scheme 3.** Reagents and conditions: (i) NaH, THF, 0 °C → rt, BnBr, $Bu_4NI$, 24 h, 85%; (ii) HCl (10%), THF, 50 °C, 12 h, 85%.




**Scheme 4.** Reagents and conditions: (i) 5 mol % $NiBr_2$[(+)-Diop], $LiBHEt_3$ (6 mol %, 1.0 M solution in THF), $Et_2O$, rt → −70 °C, addition of **4a**, 144 h, 85%, 91% ee; (ii) 1.2 equiv *m*-CPBA, THF, rt, 4 h, 82%; (iii) Lewatit® MonoPlus S 100 ($H^+$-form), $CHCl_3$, reflux, 1 h, 76%; (iv) $LiAlH_4$, $Et_2O$, reflux, 2 h, 96%; (v) NaH, THF, 0 °C → rt, BnBr, $Bu_4NI$, 24 h, 85%; (vi) HCl (10%), THF, 50 °C, 12 h, 85%.

starting from (+)-**1a**. Dioxin (+)-**1a** was obtained by the asymmetric double bond isomerization of **4a** using $NiBr_2$[(+)-Diop] as a precatalyst (Scheme 4).

## 3. Conclusions

The absolute configuration of alcohol (2*S*,4*R*)-(−)-**3a** derived from 5-methyl-4*H*-1,3-dioxin (−)-**1a** and *m*-chlorobenzoic ester **5a** was confirmed by X-ray crystallography of the corresponding camphanyl ester. Since the quaternary stereogenic centre in the 5-position of ester **5a** and in the 4-position of aldehyde **2a**, respectively, is not affected during the rearrangement and reduction, *m*-chlorobenzoic ester **5a** must have a (2*S*,4*S*,5*S*)-configuration. Hence, together with the known relative configuration of **5a**, the absolute configuration of (−)-**1a** can be established as an (*S*)-configuration. This result was confirmed by transformation of alcohol **3a** into benzyl ether (*S*)-(+)-**8** and comparison of the specific rotation with the literature values.[3,12] The reaction sequence used for the determination of the absolute configuration of 5-methyl-4*H*-1,3-dioxins also demonstrates that these compounds are useful chiral building blocks for a multigram scale synthesis of homochiral compounds such as (*S*)- and (*R*)-benzyloxy-2-methylpropane-1,2-diol.

## 4. Experimental

### 4.1. General

Solvents were purified according to standard procedures. Analytical TLC was performed using silica gel 60 $F_{254}$ plates. Column chromatography was performed using silica gel 60 (0.063–0.200 mm). *m*-CPBA was purchased from Acros. Melting points are uncorrected and were measured in open glassware. $^1H$ and $^{13}C$ NMR spectra were recorded on a Varian Unity INOVA 500 spectrometer. Chemical shifts are reported in ppm and coupling constants in Hz. Optical rotations were measured on a Perkin–Elmer 241 polarimeter in 1 or 10 cm cells. Microanalyses were carried out on a Vario El analyzer and were in good agreement with the calculated values. IR spectra were recorded on a Bio-Rad FTS 40a spectrometer. GC analysis of the enantiomeric excess of **1a** and **3a**: GC 8000 Top Serie (CE Instruments), column 30 m × 0.32 mm ID, Rt-βDEXcst™ (Restek GmbH).[9]

### 4.2. 2-*tert*-Butyl-5-methyl-4*H*-1,3-dioxin (*S*)-1a

$NiBr_2$[(−)-Diop] (1.15 g, 1.6 mmol) was dissolved in abs. $Et_2O$ at room temperature and activated with $LiBHEt_3$ (1.92 mmol, 1.92 mL, 1 M in THF). After cooling to −70 °C, a solution of **4a** (5 g, 32 mmol) in abs. $Et_2O$ (25 mL) was added and the mixture left at this temperature in a deep freezer for 144 h. The conversion of **4a** was monitored by GC. After complete conversion, the mixture was allowed to warm up to room temperature and quenched with saturated $NH_4Cl$ solution (50 mL). The organic layer was separated and the aqueous layer extracted three times with ether. The combined organic layers were dried ($MgSO_4$). After removal of the solvent, the residue was distilled in vacuo to give (*S*)-(−)-**1a** as a colourless liquid (4.25 g, 27.2 mmol, 85%). Bp 56 °C/12 Torr. $[\alpha]_D^{20} = -91.1$ (*neat*); 92% ee (GC). $^1H$ NMR ($CDCl_3$): $\delta$ 0.95 (s, 9H, $C(CH_3)_3$); 1.51 (q, 3H, $J = 1.3$, CH=C–$CH_3$); 4.03 (ddq, 1H, $J = 2.0$, $J = 1.0$, O–$CH_2$); 4.24 (dqui, 1H, $J = 15.1$, $J = 1.3$, O–$CH_2$); 4.33 (s, 1H, O–CHR–O); 6.34 (sext, 1H, $J = 1.3$, $CH$=C–$CH_3$). $^{13}C$ NMR ($CDCl_3$): $\delta$ 13.8 (1C, CH=C–$CH_3$); 24.4 (3C, $C(CH_3)_3$); 34.3 (1C, $C(CH_3)_3$); 68.13 (1C, O–$CH_2$); 103.9 (1C, O–CHR–O); 109.5 (1C, $C$=CH); 138.5 (1C, C=$CH$). IR (film): $\nu = 940\ cm^{-1}$, 955, 990, 1070, 1095, 1115, 1125, 1155, 1215, 1240, 1285, 1365, 1380, 1405, 1440, 1460, 1485, 1650, 1685, 1725, 2670, 2700, 2745, 2845, 2880, 2940, 2960, 2985, 3075. Anal.

Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.15; H, 10.30.

The enantiomer (*R*)-**1a** was obtained by the same procedure from **4a** (5 g, 32 mmol) and $NiBr_2$[(+)-Diop] (1.15 g, 1.6 mmol) as a colourless liquid (4.25 g, 27.2 mmol, 85%). $[\alpha]_D^{20} = +90.1$ (*neat*); 91% ee (GC).

### 4.3. 2-*tert*-Butyl-5-hydroxy-5-methyl-1,3-dioxan-4-yl 3-chlorobenzoate (2*S*,4*S*,5*S*)-5

Acid free *m*-CPBA (14.88 g, 60.4 mmol) dissolved in THF (180 mL) was added dropwise at room temperature to a solution of (−)-**1a** (7.86 g, 50.3 mmol) in THF (50 mL). After stirring for 4 h, the mixture was evaporated in vacuo to dryness. Recrystallization of the residue from light petroleum (40–60 °C) afforded the pure diastereomer (2*S*,4*S*,5*S*)-**5** as a colourless solid (13.91 g, 42.3 mmol, 84%). Mp 98 °C. $[\alpha]_D^{20} = -110.1$ (*c* 5, $CHCl_3$). $^1$H NMR ($CDCl_3$): $\delta$ 0.90 (s, 9H, $C(CH_3)_3$); 1.53 (d, 3H, $J = 0.8$, $CH_3$); 2.56 (s, 1H, OH); 3.73 (dd, 1H, $J = 10.8$, $J = 1.6$, O–$CH_2$eq); 3.95 (dq, 1H, $J = 10.8$, $J = 0.8$, O–$CH_2$ax); 4.95 (s, 1H, O–CHR–O); 6.13 (d, 1H, $J = 1.6$, O–CH–O–CO); 7.39 (ddd, 1H, $J = 7.7$, $J = 8.0$, $J = 0.4$, Ph–H, C5); 7.55 (ddd, 1H, $J = 8.0$, $J = 1.1$, $J = 2.2$, Ph–H, C4); 7.94 (ddd, 1H, $J = 7.7$, $J = 1.7$, $J = 1.1$, Ph–H, C6); 7.99 (ddd, 1H, $J = 1.6$, $J = 2.1$, $J = 0.4$, Ph–H, C2). $^{13}$C NMR ($CDCl_3$): $\delta$ 23.1 (3C, C(*C*$H_3$)$_3$); 24.3 (1C, *C*$(CH_3)_3$); 34.2 (1C, $CH_3$); 65.5 (1C, O–$CH_2$); 71.1 (1C, *C*$(CH_3)$(OH)); 96.4 (1C, O–*C*H–O–CO); 100.9 (1C, O–CHR–O); 127.8 (1C, Ph, C6); 129.6 (1C, Ph, C5); 129.8 (1C, Ph, C2); 131.2 (1C, Ph, C1); 133.4 (1C, Ph, C4); 134.6 (1C, Ph, C3); 164.2 (1C, COOR). IR (ATR): $\nu = 581\ cm^{-1}$, 672, 744, 810, 882, 918, 1074, 1105, 1163, 1186, 1259, 1281, 1345, 1429, 1485, 1577, 1692, 1728, 2874, 2964, 3401, 3464. Anal. Calcd for $C_{16}H_{21}ClO_5$: C, 58.45; H, 6.44. Found: C, 58.51; H 6.44. X-ray data: CCDC 153216.

The enantiomer (2*R*,4*R*,5*R*)-**5** was obtained by the same procedure from (+)-**1a** (4.25 g, 27.2 mmol) as a pure diastereomer after recrystallization from light petroleum (40–60 °C). Colourless solid (7.33 g, 22.3 mmol, 82%).

### 4.4. 2-*tert*-Butyl-4-methyl-1,3-dioxolane-4-carbaldehyde (2*RS*,4*S*)-2a

(2*S*,4*S*,5*S*)-**5** (13.91 g, 42.3 mmol) dissolved in $CHCl_3$ or $Et_2O$ (250 mL) was heated under reflux for 1 h in the presence of catalytic amounts of a strong acid cation resin (Lewatit® MonoPlus 100, $H^+$ form). After cooling to room temperature, the ion exchange resin was removed by filtration and the reaction mixture washed three times with saturated $NaHCO_3$ solution and dried over $MgSO_4$. After filtration and evaporation of the solvent, the residue was distilled in vacuo to afford the aldehydes as a colourless liquid. (2*RS*,4*S*)-**2a** (5.46 g, 31.7 mmol, 75%). Bp 56 °C/11 Torr; (2*S*,4*S*)-**2a**/(2*R*,4*S*)-**2a**: 75:25 (from $CHCl_3$); 52:48 (from $Et_2O$). (2*S*,4*S*)-**2a** $^1$H NMR ($CDCl_3$): $\delta$ 0.96 (s, 9H, $C(CH_3)_3$); 1.34 (s, 3H, $CH_3$); 3.59 (d, 1H, $J = 9.0$, O–$CH_2$); 4.30 (d, 1H, $J = 9.0$, O–$CH_2$); 4.74 (s, 1H, O–CHR–O); 9.62 (s, 1H, CHO). $^{13}$C NMR ($CDCl_3$): $\delta$ 18.4 (1C, $CH_3$); 24.3 (3C, C(*C*$H_3$)$_3$); 34.0 (1C, *C*$(CH_3)_3$); 72.8 (1C, O–$CH_2$); 83.4 (1C, *C*–CHO); 111.0 (1C, O–CHR–O); 201.8 (1C, CHO). (2*R*,4*S*)-**2a** $^1$H NMR ($CDCl_3$): $\delta$ 0.95 (s, 9H, $C(CH_3)_3$); 1.37 (s, 3H, $CH_3$); 3.65 (d, 1H, $J = 8.4$, O–$CH_2$); 4.05 (d, 1H, $J = 8.4$, O–$CH_2$); 4.69 (s, 1H, O–CHR–O); 9.70 (s, 1H, CHO). $^{13}$C NMR ($CDCl_3$): $\delta$ 19.1 (1C, $CH_3$); 24.2 (3C, C(*C*$H_3$)$_3$); 34.4 (1C, *C*$(CH_3)_3$); 70.7 (1C, O–$CH_2$); 84.1 (1C, *C*–CHO); 111.1 (1C, O–CHR–O); 202.0 (1C, CHO).

The enantiomers (2*RS*/4*R*)-**2a** were obtained from (2*R*,4*R*,5*R*)-**5** (7.33 g, 22.3 mmol) as a colourless liquid (2.93 g, 17.0 mmol, 76%). Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.84; H, 9.48.

### 4.5. 2-*tert*-Butyl-4-hydroxymethyl-4-methyl-1,3-dioxolane (2*RS*,4*R*)-3a

Aldehydes (2*RS*,4*S*)-**2a** (5.46 g, 31.73 mmol) dissolved in dry $Et_2O$ (30 mL) were added dropwise at room temperature to a suspension of $LiAlH_4$ (0.328 g, 8.63 mmol) in dry $Et_2O$ (50 mL). After complete addition, the reaction mixture was heated to reflux for 2 h. After cooling to 0 °C, the excess $LiAlH_4$ was destroyed by adding water. The solid was removed by filtration and washed with $Et_2O$. The combined organic layers were dried over $MgSO_4$. Removal of the solvent afforded the diastereomers **3a** as a colourless oil (5.25 g, 30.14 mmol, 95%), which was used in the next step (transformation into benzylethers **7**) without further purification. For the preparation of camphanoates **6**, the diastereomers were separated by column chromatography (silica, light petroleum/EtOAc, 85:15). (2*S*,4*R*)-**3a** $^1$H NMR ($CDCl_3$): $\delta$ 0.94 (s, 9H, $C(CH_3)_3$); 1.29 (s, 3H, $CH_3$); 2.30 (br s, 1H, OH); 3.46 (d, 1H, $J = 11.3$, $CH_2OH$); 3.56 (d, 1H, $J = 8.1$, O–$CH_2$); 3.58 (d, 1H, $J = 11.3$, $CH_2$–OH); 3.97 (d, 1H, $J = 8.1$, O–$CH_2$); 4.62 (s, 1H, O–CHR–O). $^{13}$C NMR ($CDCl_3$): $\delta$ 20.7 (1C, $CH_3$); 24.3 (3C, C(*C*$H_3$)$_3$); 34.2 (1C, *C*$(CH_3)_3$); 67.5 (1C, $CH_2OH$); 72.4 (1C, O–$CH_2$); 80.6 (1C, *C*–$CH_2OH$); 109.2 (1C, O–CHR–O). $[\alpha]_D^{20} = -9.30$ (*c* 5, $CHCl_3$); 92% ee (GC). Anal. Calcd for $C_9H_{18}O_3$: C, 62.04; H, 10.41. Found: C, 61.94; H, 10.53. (2*R*,4*R*)-**3a** $^1$H NMR ($CDCl_3$): $\delta$ 0.93 (s, 9H, $C(CH_3)_3$); 1.26 (s, 3H, $CH_3$); 2.30 (br s, 1H, OH); 3.57 (m, 1H, C*H*$_2$OH); 3.57 (m, 1H, C*H*$_2$–OH); 3.68 (d, 1H, $J = 8.0$, O–$CH_2$); 3.86 (d, 1H, $J = 8.0$, O–$CH_2$); 4.65 (s, 1H, O–CHR–O). $^{13}$C NMR ($CDCl_3$): $\delta$ 22.0 (1C, $CH_3$); 24.2 (3C, C(*C*$H_3$)$_3$); 33.9 (1C, *C*$(CH_3)_3$); 66.2 (1C, $CH_2OH$); 72.2 (1C, O–$CH_2$); 80.4 (1C, *C*–$CH_2OH$); 111.1 (1C, O–CHR–O). $[\alpha]_D^{20} = +7.9$ (*c* 5, $CHCl_3$); 92% ee (GC).

The enantiomers (2*RS*,4*S*)-**3a** were obtained by the same procedure from (2*RS*,4*R*)-**2a** (2.93 g, 17 mmol) as a colourless liquid (2.84 g, 16.3 mmol, 96%).

### 4.6. 2-*tert*-Butyl-4-methyl-1,3-dioxolane-4-ylmethyl camphanoate (2*S*,4*S*)-6

(1*S*)-(−)-Camphanic chloride (1.24 g, 5.47 mmol) was added slowly to a solution of alcohol (2*S*,4*R*)-**3a** (1.0 g, 5.74 mmol) and pyridine (0.486 mL, 6.27 mmol)

in THF (17 mL). After stirring for 3 h, $Et_2O$ (20 mL) was added. The resulting solid was filtered off and washed with small amounts of $Et_2O$. Concentration of the combined filtrates afforded the ester as colourless crystals (1.84 g, 5.1 mmol, 89%). Mp 100 °C. $^1$H NMR ($CDCl_3$): $\delta$ 0.91 (s, 9H, $C(CH_3)_3$); 0.97 (s, 3H, $CH_3$); 1.08 (s, 3H, $CH_3$); 1.12 (s, 3H, $CH_3$); 1.36 (s, 3H, $CH_3$); 1.70 (ddd, 1H, $J = 13.4$, $J = 9.4$, $J = 4.3$, $CH_2$); 1.94 (ddd, 1H, $J = 13.4$, $J = 10.7$, $J = 4.6$, $CH_2$); 2.05 (ddd, 1H, $J = 13.4$, $J = 9.4$, $J = 4.6$, $CH_2$); 2.44 (ddd, 1H, $J = 13.4$, $J = 10.7$, $J = 4.3$, $CH_2$); 3.56 (dd, 1H, $J = 8.7$, $J = 0.9$, O–$CH_2$ax); 3.93 (d, 1H, $J = 9.7$, O–$CH_2$eq); 4.05 (d, 1H, $J = 10.9$, $CH_2$–O–CO); 4.16 (dd, 1H, $J = 10.9$, $J = 0.9$, $CH_2$–O–CO); 4.62 (s, 1H, O–CHR–O). $^{13}$C NMR ($CDCl_3$): $\delta$ 9.7 (1C, $CH_3$); 16.7 (2C, $CH_3$); 21.1 (1C, $CH_3$); 24.3 (3C, C($CH_3$)$_3$); 28.9 (1C, $CH_2$); 30.6 (1C, $CH_2$); 33.7 (1C, $C(CH_3)_3$); 54.2 (1C, $C(CH_3)_2$); 54.7 (1C, $C$–$CH_3$); 68.9 (1C, $CH_2$–O–CO); 73.2 (1C, O–$CH_2$); 78.0 (1C, $C$–$CH_2$–O–CO); 91.0 (1C, O(CO)–$C$–O); 110.0 (1C, O–CHR–O); 167.1 (1C, C–O–CO); 178.0 (1C, $CH_2$–O–CO). IR (film): $\nu = 443\ cm^{-1}$, 479, 511, 584, 641, 667, 738, 793, 843, 898, 933, 971, 993, 1019, 1044, 1067, 1106, 1167, 1224, 1272, 1312, 1378, 1402, 1461, 1559, 1650, 1748, 1792, 2361, 2730, 2877, 2972, 3480, 3565, 3651, 3676, 3748. Anal. Calcd for $C_{19}H_{30}O_6$: C, 64.38; H, 8.53. Found: C, 64.45; H, 8.49. X-ray data: CCDC 153217.

A 1:1 mixture of camphanyl esters **6** (1.75 g, 4.94 mmol, 86%) was obtained from a 1:1 mixture of the corresponding alcohols **3a**.

(2*R*,4*S*)-**6** $^1$H NMR ($CDCl_3$): $\delta$ 0.90 (s, 9H, $C(CH_3)_3$); 0.97 (s, 3H, $CH_3$); 1.08 (s, 3H, $CH_3$); 1.13 (s, 3H, $CH_3$); 1.34 (s, 3H, $CH_3$); 1.70 (ddd, 1H, $J = 13.3$, $J = 9.3$, $J = 4.2$, $CH_2$); 1.94 (ddd, 1H, $J = 13.3$, $J = 10.6$, $J = 4.5$, $CH_2$); 2.06 (ddd, 1H, $J = 13.3$, $J = 9.3$, $J = 4.5$, $CH_2$); 2.44 (ddd, 1H, $J = 13.3$, $J = 10.6$, $J = 4.2$, $CH_2$); 3.67 (d, 1H, $J = 8.2$, O–$CH_2$); 3.82 (d, 1H, $J = 8.2$, O–$CH_2$); 4.12 (d, 1H, $J = 11.3$, $CH_2$–O–CO); 4.34 (d, 1H, $J = 11.3$, $CH_2$–O–CO); 4.67 (s, 1H, O–CHR–O). $^{13}$C NMR ($CDCl_3$): $\delta$ 9.7 (1C, $CH_3$); 16.7 (2C, $CH_3$); 22.2 (1C, $CH_3$); 24.1 (3C, C($CH_3$)$_3$); 28.9 (1C, $CH_2$); 30.6 (1C, $CH_2$); 34.2 (1C, $C(CH_3)_3$); 54.3 (1C, $C(CH_3)_2$); 54.8 (1C, $C$–$CH_3$); 67.6 (1C, $CH_2$–O–CO); 72.6 (1C, O–$CH_2$); 78.6 (1C, $C$–$CH_2$–O–CO); 91.1 (1C, O–CO–$C$–O); 110.8 (1C, O–CHR–O); 167.2 (1C, C–O–CO); 178.1 (1C, $CH_2$–O–CO). X-ray data: CCDC 153218.

### 4.7. 4-Benzyloxymethyl-2-*tert*-butyl-4-methyl-1,3-dioxolane (2*RS*,4*R*)-7

Under an inert atmosphere, alcohols **3a** (dr 3:1, 5.25 g, 30.14 mmol) were dissolved in dry THF (100 mL) and the resulting solution added to NaH (0.796 g, 33.15 mmol) at 0 °C. The reaction mixture was allowed to warm up to room temperature and BnBr (6.24 g, 36.47 mmol) and $Bu_4NI$ (3.31 g, 8.95 mmol) added. After stirring for a further 18 h, the reaction was quenched by the addition of water (50 mL). Extracting with EtOAc (100 mL), drying over $MgSO_4$ and removal of the solvent under reduced pressure afforded crude **7**, which was purified by column chromatography (silica, light petroleum/EtOAc, 95:5; dr 3:1, 6.39 g, 25.62 mmol, 85%). Main diastereomer (2*S*,4*R*)-**7** $^1$H NMR ($CDCl_3$): $\delta$ 0.92 (s, 9H, $C(CH_3)_3$); 1.36 (s, 3H, $CH_3$); 3.53 (d, 1H, $J = 8.3$, CHR–O–$CH_2$); 3.35 (d, 1H, $J = 9.0$, $CH_2$); 3.39 (d, 1H, $J = 9.0$, $CH_2$); 3.98 (d, 1H, $J = 8.3$, CHR–O–$CH_2$); 4.57 (m, 2H, O–$CH_2$–Ph); 4.63 (s, 1H, O–CHR–O); 7.34 (m, 5H, Ph–H). $^{13}$C NMR ($CDCl_3$): $\delta$ 21.3 (1C, $CH_3$); 24.4 (3C, C($CH_3$)$_3$); 33.8 (1C, $C(CH_3)_3$); 73.4 (1C, $CH_2$); 73.6 (1C, $CH_2$); 74.9 (1C, $CH_2$); 79.5 (1C, O–$C$–$CH_3$); 109.6 (1C, O–CHR–O); 127.5 (2C, Ph); 127.6 (1C, Ph); 128.3 (2C, Ph); 138.3 (1C, Ph). Minor diastereomer (2*R*,4*R*)-**7** $^1$H NMR ($CDCl_3$): $\delta$ 0.93 (s, 9H, $C(CH_3)_3$); 1.31 (s, 3H, $CH_3$); 3.45 (m, 2H, $CH_2$); 3.65 (d, 1H, $J = 8.0$, CHR–O–$CH_2$); 3.88 (d, 1H, $J = 8.0$, CHR–O–$CH_2$); 4.58 (m, 2H, O–$CH_2$–Ph); 4.67 (s, 1H, O–CHR–O); 7.34 (m, 5H, Ph–H). $^{13}$C NMR ($CDCl_3$): $\delta$ 22.5 (1C, $CH_3$); 24.3 (3C, C($CH_3$)$_3$); 34.1 (1C, $C(CH_3)_3$); 72.3 (1C, $CH_2$); 73.4 (1C, $CH_2$); 74.0 (1C, $CH_2$); 79.9 (1C, O–$C$–$CH_3$); 110.6 (1C, O–CHR–O); 127.5 (2C, Ph); 127.6 (1C, Ph); 128.4 (2C, Ph); 138.2 (1C, Ph). Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 72.48; H, 9.23.

The enantiomers (2*RS*,4*S*)-**7** were obtained by the same procedure from alcohols (2*RS*,4*S*)-**3a** (dr 3:1, 2.84 g, 16.3 mmol) as an oil (dr 3:1, 3.66 g, 13.85 mmol, 85%).

### 4.8. 3-Benzyloxy-2-methylpropane-1,2-diol (*S*)-8

HCl (10% aqueous solution, 25 mL) was added to a solution of (2*RS*,4*R*)-**7** (6.39 g, 25.62 mmol) in THF (100 mL) and the reaction mixture was heated to 50 °C for 12 h. After cooling to room temperature, the mixture was concentrated in vacuo and extracted three times with EtOAc (30 mL). The combined organic layers were dried ($MgSO_4$), concentrated and purified by column chromatography (light petroleum/$Et_2O$, 3:1) to afford (*S*)-**8** as a colourless oil (4.27 g. 21.78 mmol, 85%), which solidifies on standing. $[\alpha]_D^{25} = +7.0$ (*c* 1.1, $CH_2Cl_2$).

The enantiomer (*R*)-**8** was obtained from benzyl ether (2*RS*,4*S*)-**7** (3.66 g, 13.85 mmol) by the same procedure as a colourless oil (2.31 g, 11.77 mmol, 85%). $[\alpha]_D^{25} = -6.92$ (*c* 1.1, $CH_2Cl_2$).

All spectral data were in good agreement with the literature.[3,12]

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