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Stereoselective Synthesis of Enantiopure 4,5-Dihydroxy-2-Alkene Esters from Simple Allylic Alcohols

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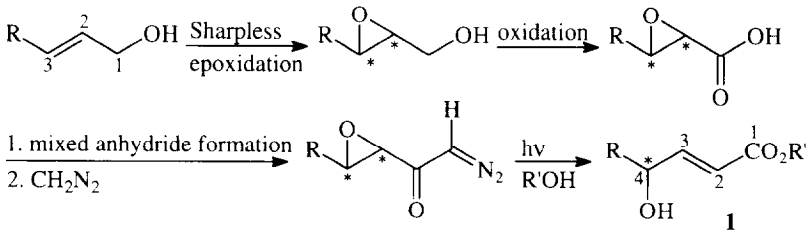
Abstract: *A general stereoselective synthesis of 4,5-dihydroxy-2-alkene esters is developed using the photo-induced rearrangement of α,β-epoxy diazomethyl ketones. Starting with readily available enantiopure allylic alcohols that contain a chiral center at C_4, i.e. a protected secondary alcohol function, a neighboring stereogenic center is introduced by irradiation of the mentioned diazo ketones. The configuration of this newly introduced center is determined by the chiral inductor used in the Sharpless epoxidation of the allylic alcohol and therefore can be selected at will.*

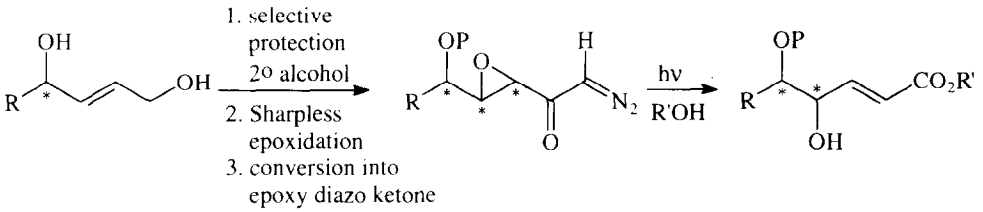
The photo-induced rearrangement of α,β-epoxy diazomethyl ketones constitutes an attractive synthetic method for the preparation of γ-hydroxy-α,β-unsaturated esters **1**[1,2]. The starting materials for epoxy diazo ketones are allylic alcohols which by Sharpless epoxidation[3] are converted into 2,3-epoxy alcohols. Subsequent oxidation of these alcohols gives oxirane-2-carboxylic acids of high enantiopurity. Transformation into the corresponding epoxy diazo ketones can readily be accomplished using a series of standard operations[4]. The photochemical conversion into γ-hydroxy-alkene esters is carried out in alcoholic solvents. It is of importance to note that the chiral integrity of the stereogenic center at C_3 of the starting material is retained in the product[2]. The sequence of events is depicted in scheme 1.



Scheme 1

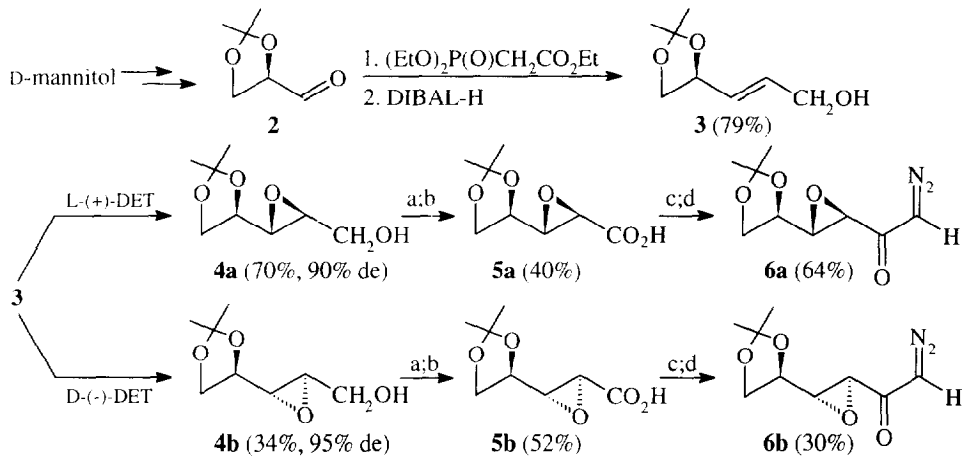
This methodology has been applied in the synthesis of several naturally occurring macrocyclic lactones, such as (+)-aspicilin[5], pyrenophorol[6], colletallol[7], patulolid C[8,9], isopatulolid C and analogues[9] and the macrocyclic subunit of cytochalasin B[10], all containing the 4-hydroxy-2-alkene ester moiety. Hydrogenation of

the γ-hydroxy-alkene esters **1** gives γ-hydroxy carboxylic esters, which readily give ring closure to yield enantiopure γ-lactones[4]. This spin-off of the preparation of γ-hydroxy-alkene esters has successfully been applied in the synthesis of the naturally occurring γ-lactone rubrenolide[11]. An interesting question arises whether it will be possible to introduce a new stereogenic center, adjacent to an already existing one, without affecting the chiral integrity of this neighboring center, by the method shown in scheme 1. The synthetic outline for this planned series of operations is depicted in scheme 2. To execute this plan it is convenient to start with suitably protected allylic alcohols, which already contain a stereogenic center, preferably a secondary hydroxyl function. By a proper choice of the chiral inductor in the Sharpless epoxidation the configuration of the newly introduced chiral center can be selected at will.



Scheme 2

D-Mannitol and L-malic acid were chosen as starting materials for the preparation of allylic alcohols containing a stereogenic center. (R)-isopropylidene glyceraldehyde **2** can readily be obtained from D-mannitol by a glycol cleavage procedure that is well documented[12,13]. Allylic alcohol **3** was prepared from this aldehyde in a two-step process, *viz.* a Wittig-Horner type chain elongation with triethyl phosphonoacetate[14] (E/Z-ratio 25:1), followed by a reduction with DIBAL-H (scheme 3). By following the sequence of reactions shown in

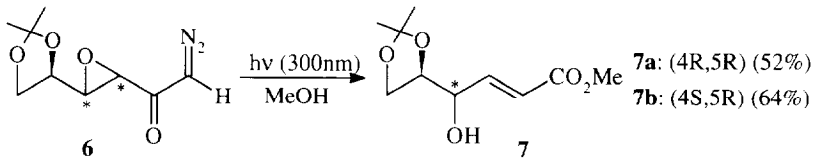


a. CrO_3/pyridine/CH_2Cl_2; b. PDC/DMF; c. $ClCO_2iBu/Et_3N$; d. CH_2N_2

Scheme 3

scheme 2, epoxy diazomethyl ketones **6a** and **6b** were synthesized. Asymmetric epoxidation of allylic alcohol **3** to the epoxy alcohols **4a** and **4b** was realized by using either L-(+)-DET or D-(-)-DET as chiral inductor[15,16,17]. Both epoxidations showed a high diastereomeric excess, as was determined by capillary gas chromatography (cf. ref.[18]). Catalytic one-step oxidation of **4** to **5**, employing RuO_4 in aqueous tetrachloromethane/acetonitrile[19], gave unsatisfactory results as undefined products in low yields were obtained. Therefore, the oxidation to the carboxylic acids **5** had to be performed in a two-step procedure using non-aqueous conditions because of the high water-solubility of compounds **4** and **5**[17]. It was found that Collins's reagent[20] is suitable for the conversion to the aldehyde and that pyridinium dichromate[21] gives satisfactory results in the second oxidation to the carboxylic acids **5**. For the preparation of the diazo ketones **6** the standard procedures[4] could be used successfully.

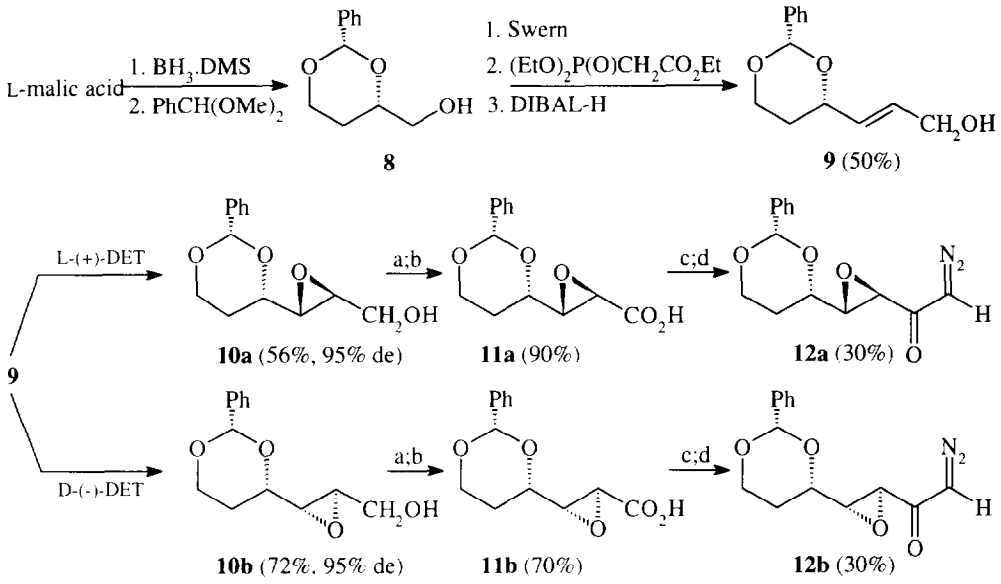
Irradiation of compounds **6** in methanol leads to alkene esters **7**, which both have two well-defined stereogenic centers (scheme 4). In the ^{1}H-NMR spectrum of the products **7a** and **7b** a difference was observed



Scheme 4

for the chemical shift of the C_4-protons. In **7a** this signal is part of the multiplet at 3.83-4.30 ppm, while in **7b** this signal appears at 4.48 ppm. Compound **7b** was synthesized previously by Regeling and Chittenden[22] from D-glucono-1,5-lactone. The spectral features are in full accordance. The spectra of the products **7** showed no signals of the other epimer, which means that the stereochemical configuration at C_4 is retained during the synthetic sequence starting with **4**. It should be noted that by starting from enantiomeric (S)-isopropylidene glyceraldehyde[23] the (4R,5S) and (4S,5S) diastereomers of **7** are also accessible.

As a second chiral substrate for this study, cyclic acetal **8** was selected (scheme 5). This compound can conveniently be obtained from L-malic acid by borane-dimethyl sulfide reduction according to Hanessian *et al.*[24], followed by a trans-acetalization with benzaldehyde dimethyl acetal. In this manner the six-membered ring acetal **8** is formed regioselectively (no five-membered ring product was present) displaying the (S)-configuration at the phenyl substituted carbon atom[25]. Swern oxidation[26] of **8** leads to an aldehyde suitable for chain elongation by a Wittig-Horner type reaction (E/Z-ratio 20:1). Reduction of the alkene ester obtained with DIBAL-H produces allylic alcohol **9**. This secondary hydroxyl protected compound is used as substrate for the synthetic plan shown in scheme 2. Sharpless epoxidation with either L-(+)-DET or D-(-)-DET as chiral inductors gave epoxy alcohols **10** (both reactions proceeded with high diastereomeric excess, as was determined by capillary gas chromatography), which in turn were converted into carboxylic acids **11**, using again a two-step procedure, *viz.* Swern oxidation[26b] to the aldehyde and subsequent oxidation with sodium chlorite[27] to the carboxylic acid. An attempted one-step oxidation of **10** using ruthenium tetroxide[19] did not give satisfactory results, due to oxidation of the phenyl ring. The two-step procedure mentioned above is different from that used for the conversion of **4** into **5**, due to the low solubility of **10** and **11** in water. During the work-up of **11**, acidification was very critical, because of the acid-sensitivity of the acetal function in the dioxane ring. This

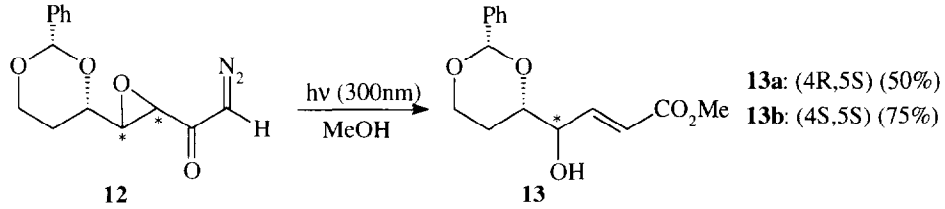


a. $(ClCO)_2$/DMSO; b. $NaClO_2/NaH_2PO_4$; c. $ClCO_2iBu/Et_3N$; d. CH_2N_2

Scheme 5

sensitivity towards acid also played a role during chromatography over silica gel. Diazo ketones **12**, which were synthesized from **11** without any difficulty, could be isolated but a considerable loss had to be accepted due to decomposition and rather large amounts of benzaldehyde were isolated as well.

Irradiation of **12** in methanol solution gave alkene esters **13** with defined stereogenic centers at C_4 and C_5 (scheme 6). In the ^{1}H-NMR spectra of **13a** and **13b** a considerable difference for the signals of the C_4 protons was observed. In **13a** this proton gives a multiplet at 4.41-4.53 ppm, whereas in **13b** it is part of the multiplet at 4.18-4.38 ppm. In comparison with **7a** and **7b**, the stereogenic center at C_5 of compounds **13a** and **13b** has an opposite absolute configuration. As a consequence the NMR spectrum for the C_4 and C_5 protons of **7a**



Scheme 6

resembles that of **13b** and the same holds for **7b** and **13a**. As with products **7**, the NMR spectra of compounds **13** show no signals of the other epimer, indicating that the configuration at C_4 is retained during the synthetic operations starting from **10**. It should be noted that when enantiomeric D-malic acid would be used as starting material the (4R,5R) and (4S,5R) diastereomers of **13** are accessible too.

As mentioned, in both sets of experiments the diastereomeric excess in the epoxidation reaction using either L-(+)-DET or D-(-)-DET is high. Using the same starting allylic alcohol and epoxidation method, Sharpless *et al.*[18] reported a diastereomeric excess of 95.6 and 98.9% for the epoxy alcohols **4a** and **4b**, respectively. However, no experimental details were reported. From synthetic point of view our results indicate that in the latter (D-(-)-DET) case the chiral center at C_4 of allyl alcohol **3** cooperates with the chiral auxiliary in the epoxidation reaction, whereas in the former (L-(+)-DET) case there is no significant influence of the chiral center at C_4 on the chiral induction.

In conclusion, the two investigated allylic alcohols derived from D-glyceraldehyde and L-malic acid, both containing a protected secondary alcohol function as stereogenic center, can be stereoselectively converted into enantiopure 4,5-dihydroxy-2-alkene esters using the photo-induced rearrangement of α,β-epoxy diazomethyl ketones. This synthetic strategy may be useful in the constuction of molecules, for instance natural products, with hydroxy groups attached to two different stereogenic centers.

EXPERIMENTAL SECTION

General remarks:

^{1}H-NMR spectra were recorded on a Varian EM 390 (90 MHz, CW), a Bruker AC-100 (100 MHz, FT) or a Bruker AM-400 (400 MHz, FT) spectrometer with TMS as internal standard. ^{13}C-NMR spectra were recorded on a Bruker AM-400 (100 MHz, FT) spectrometer with $CHCl_3$ as internal standard. IR spectra were run on a Perkin-Elmer 298 spectrophotometer. Elemental analyses were standard carried out in triplicate on a Carlo Erba Instruments CHNSO EA 1108 element analyzer. For mass spectroscopy a double focusing VG 7070E was used. For the chemical ionization (CI) technique, methane was used as reacting gas. Melting points were measured on a Reichert Thermopan microscope and are uncorrected. Optical rotations were determined on a Perkin-Elmer 241 polarimeter. GC was performed on a Hewlett-Packard 5890 or a Hewlett-Packard 5890 Series II instrument, equipped with a capillary HP cross-linked methyl silicone (25 m x 0.31 mm) column, connected to a HP 5890 calculating integrator. For chromatography the flash technique was used with silica gel 60H (Merck) as stationary phase and a pressure of about 1.5 bar. Chromatography over florisil was performed under normal pressure. Chemical compounds were named using the Autonom® program, version 1.0. All solvents used were dried and distilled according to standard procedures. When diazomethane was used, proper safety precautions were taken.

E-*3-[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]-prop-2-en-1-ol* (**3**):

To a stirred suspension of oven-dried LiCl (6.9 g, 175 mmol) in dry acetonitrile (140 ml) were successively added triethyl phosphonoacetate (37.0 g, 175 mmol), N,N-diisopropylethylamine (DIPEA, 25.6 ml, 146 mmol) and aldehyde **2** (19.0 g, 146 mmol)[12,13] under nitrogen and at room temperature. During the addition of **2** the mixture became cloudy and warm. The reaction was followed by TLC and after 1 h the aldehyde had disappeared. Water was added until the solution became clear and acetonitrile was evaporated. The residue, a

cloudy oil, was taken up in water and extracted with ether (4x). After drying ($MgSO_4$) the combined organic layers were concentrated to give 33.98 g of crude product. Of this mixture 12.0 g was chromatographed (hexane/ethyl acetate 4:1) yielding pure *trans*-ester as an oil (8.54 g, 83%). ^{1}H-NMR ($CDCl_3$, 100 MHz): δ 1.22 (t, 3H, $CH_2C\underline{H}_3$, J 7.1 Hz), 1.34 and 1.41 (2s, 6H, $C(CH_3)_2$), 3.60 (dd, 1H, OCH$\underline{H}$CHO, J 8.4 Hz and 7.1 Hz), 4.11 (dd, 1H, OC$\underline{H}$HCHO, J 8.4 Hz and J 6.5 Hz), 4.14 (q, 2H, $C\underline{H}_2CH_3$, J 7.1 Hz), 4.60 (m, 1H, $OCH_2C\underline{H}O$), 6.02 (dd, 1H, CH=C$\underline{H}$CO, J 15.5 Hz and 1.3 Hz) and 6.82 (dd, 1H, C$\underline{H}$=CHCO, J 15.5 Hz and J 5.5 Hz) ppm. IR (CCl_4): ν 2980, 2940, 2870, 1720, 1660, 1380, 1370, 1300, 1250 cm^{-1}. Also pure *cis*-ester was isolated as an oil (0.62 g, 6%). The *trans*-ester (8.0 g, 40 mmol) was dissolved in dried ether (125 ml) under nitrogen at 0°C. DIBAL-H was added using a syringe (80 ml of a 1.0 M solution in hexane). After 15 min the ester had disappeared (TLC) and $Na_2SO_4.10H_2O$ was added until no further reaction took place. Stirring for one h was followed by filtration over hyflo. The residue was washed with warm ether (2x). The combined filtrates were washed with water. After drying ($MgSO_4$) the solvent was evaporated *in vacuo*, to yield pure **3** as an oil (6.0 g, 95%). ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.35 and 1.38 (2s, 6H, $C(CH_3)_2$), 2.01 (br s, 1H, OH), 3.55 (dd, 1H, OC$\underline{H}$HCHO), 4.10 (m, 3H, OCH$\underline{H}$CHO and $C\underline{H}_2$OH), 4.54 (m, 1H, C$\underline{H}$OCH=C), 5.80 (m, 2H, C$\underline{H}$=C$\underline{H}$) ppm. IR (CCl_4): ν 3600, 3450, 2980, 2940, 2875, 1380, 1370, 1210, 1060 cm^{-1}.

{(2S,3R)-3-[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]oxiran-2-yl}methanol (**4a**):

A suspension of finely powdered, activated molecular sieves (4Å, 0.5 g) in dry dichloromethane (20 ml) under nitrogen was cooled to −20°C and Ti(O*i*Pr)$_4$ (2.83 ml, 9.5 mmol) and L-(+)-diethyl tartrate (2.35 g, 11.4 mmol, dissolved in 3 ml of dry dichloromethane) were successively added. The mixture was stirred (20 min) and allylic alcohol **3** (1.5 g, 9.5 mmol dissolved in 10 ml of dry dichloromethane) was added over five min. After stirring (30 min) a *tert*-butyl hydroperoxide solution in 1,2-dichloroethane (5.40 ml of a 3.4 M solution, 2 equiv.) was added dropwise. The mixture was kept at −20°C overnight. The reaction was quenched by adding a solution of 3.4 g of $FeSO_4.7H_2O$ and 1.1 g of tartaric acid in 10 ml of water at 0°C. After stirring for 10 min the mixture was filtered over hyflo, the residue was washed with 25 ml of dichloromethane (3x). The filtrate layers were separated and the aqueous layer was extracted with ether (7x). The combined organic layers were stirred at 0°C for one h with 5 ml of a 30% NaOH (w/v) solution in saturated brine[3b], after which the layers were separated and the aqueous layer was washed with ether (3x). Drying of the combined organic layers ($MgSO_4$) and concentration gave 1.58 g of crude product. This was chromatographed (hexane/ethyl acetate 2:1), to give pure **4a** as an oil (1.16 g, 70%). $[\alpha]^{25}_D$ −20.5° (c 1.21, $CHCl_3$); lit.[14] $[\alpha]_D$ −21.5° (c 0.77, $CHCl_3$); lit.[20] $[\alpha]^{20}_D$ −26° (c 2.1, CH_2Cl_2). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.37 and 1.45 (2s, 6H, $C(CH_3)_2$), 2.40 (br s, 1H, OH), 3.06-3.11 (m, 2H, epox-H), 3.65-3.72 (m, 1H, OC$\underline{H}$HCHO), 3.88-3.98 (m, 3H, $OCH_2C\underline{H}O$), 4.10-4.14 (m, 1H, OCH$\underline{H}$CHO) ppm. ^{13}C-NMR (100 MHz): δ 25.2, 26.4, 55.2, 57.1, 61.0, 66.7, 75.2, 109.8 ppm. IR (CCl_4): ν 3600, 3480, 2990, 2935, 2875, 1380, 1370, 1210, 1060 cm^{-1}. MS (CI): *m/e* (%) 175 (12, M^++1), 159 (96), 117 (12, -$CH_3C(O)CH_3$), 101 (15, -$CHOCHCH_2OH$), 99 (41), 84 (17), 69 (33).

{(2R,3R)-3-[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]oxiran-2-yl}carbaldehyde:

CrO_3 (3.0 g, 33 mmol) was suspended in dry dichloromethane (55 ml), followed by the addition of pyridine (4.80 ml, 30 mmol). The mixture was stirred for 10 min after which epoxy alcohol **4a** (870 mg, 5.0 mmol dissolved in 6 ml of dry dichloromethane) was added. After 20 min the reaction was complete according to TLC

and ether (55 ml) was added, followed by stirring for 15 min. The organic layer was decanted, the residue was washed with ether (2x) and with warm ether (3x). The combined organic layers were chromatographed (ether) over a 15 cm florisil column, giving after concentration crude aldehyde (622 mg, 73%), which was immediately converted into acid **5a**. ^{1}H-NMR (100 MHz, $CDCl_3$), δ 1.36 and 1.42 (2s, 6H, $C(CH_3)_2$), 3.33-3.43 (m, 2H, epox-H), 3.85-4.11 (m, 3H, $OC\underline{H}_2CH$ and $OCH_2C\underline{H}$), 9.06 (d, 1H, $CHOC\underline{H}(O)$, J 6 Hz) ppm. IR (CCl_4): ν 2990, 2930, 2890, 1735, 1380, 1370, 1070 cm^{-1}.

{(2R,3R)-3-[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]oxiran-2-yl}carboxylic acid (**5a**):
Pyridinium dichromate (PDC, 2.6 g, 7.2 mmol) was dissolved in dry DMF (3.5 ml). The mixture was stirred for 4 min after which the aldehyde (620 mg, 3.6 mmol dissolved in 4 ml of dried DMF) was added quickly. Stirring was continued for 75 min and then ether (20 ml) was added, followed by another 15 min. of stirring. The organic solvent was decanted, the residue was washed with warm ether (4x). The combined organic solvents were filtered (hyflo) and concentrated until constant weight, yielding crude acid **5a** (350 mg, 52%). IR (CCl_4): ν 3500-2500, 2980, 2930, 2880, 1680, 1380, 1370 cm^{-1}. For instability reasons the product was immediately converted into diazo ketone **6a**.

1-{(2R,3R)-3-[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]oxiran-2-yl}-2-diazo-ethanone (**6a**):
Crude glycidic acid **5a** (350 mg, 1.86 mmol) was dissolved in dry ether (30 ml) under nitrogen at 0°C. *Iso*-butyl chloroformate (276 µl, 1.86 mmol) was added, followed by dried triethylamine (404 µl, 2.88 mmol). A white solid appeared, which was filtered off (under nitrogen) after one h of stirring. To the filtrate was added a 0.3 M diazomethane solution in ether (20 ml). After stirring for 2 h excess diazomethane was evaporated and the mixture was concentrated and chromatographed (hexane/ethyl acetate 3:2), to give pure diazo ketone **6a** as an oil (252 mg, 64%). ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.36 and 1.43 (2s, 6H, $C(CH_3)_2$), 3.11 (dd, 1H, $C\underline{H}CHC(O)$, J 5 Hz, 1.7 Hz), 3.44 (d, 1H, $CHC\underline{H}C(O)$, J 1.7 Hz), 3.84-4.16 (m, 3H, $C\underline{H}_2CH$ and $CH_2C\underline{H}$), 5.53 (s, 1H, CHN_2) ppm. IR (CCl_4): ν 3120, 2980, 2930, 2880, 2105, 1645, 1380, 1370 cm^{-1}.

Methyl E-*4-[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]-4-(R)-hydroxy-but-2-enoate* (**7a**):
Diazo ketone **6a** (100 mg, 0.47 mmol, dissolved in 45 ml of absolute methanol) was irradiated under nitrogen at 300 nm. The progress of the reaction was monitored by IR. After 75 min the diazo peak had disappeared. Concentration of the mixture gave 92 mg of crude product, which was chromatographed (hexane/ethyl acetate 2:1), yielding unsaturated ester **7a** as a solid (53 mg, 52%). M.p. (pentane) 74-74.5°C. ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.37 and 1.46 (2S, 6H, $C(CH_3)_2$), 2.60 (d, 1H, OH, J 7 Hz), 3.75 (s, 3H, OCH_3), 3.83-4.30 (m, 4H, $OC\underline{H}_2CH$, $CH_2C\underline{H}O$ and $C\underline{H}(OH)C$), 6.17 (dd, 1H, C=CHC(O), J 16 Hz and 1.6 Hz), 6.88 (dd, 1H, $C\underline{H}$=CHC(O), J 16 Hz and 4.5 Hz) ppm. IR (CCl_4): ν 3600-3300, 2980, 2940, 2880, 1725, 1660, 1380, 1370 cm^{-1}. MS (CI): *m/e* (%) 217 (30, $M^+ + 1$), 201 (39, $-CH_3$), 199(10, $-H_2O$), 185 (3), 169 (8), 159 (28, $-CO_2Me$), 141 (19, $-CO_2Me$, $-H_2O$), 127 (32, $-H_2O$, $-CHCO_2Me$), 101 (100, $-CH(OH)CH{=}CHCO_2Me$). EI/HRMS: *m/e* calcd. for $C_{10}H_{16}O_5$ 216.09977, found 216.09962 ± 0.00082 a.m.u. Calcd. for $C_{10}H_{16}O_5$: C 55.55, H 7.46%, found C 54.91, H 7.26%.

{(2R,3S)-3-[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]oxiran-2-yl}methanol (**4b**):

Epoxy alcohol **4b** was prepared following the procedure for epoxy alcohol **4a**, using D-(-)-diethyl tartrate as chiral inductor, as crude product. No extensive extractions were performed (cf. compound **4a**), consequently the yield was relatively low. After chromatography (hexane/ethyl acetate 2:1) pure **4a** was obtained as an oil (34% yield). $[\alpha]^{25}_D$ +35.8° (c 1.07, $CHCl_3$); lit.[14] $[\alpha]_D$ +38° (c 1.45, $CHCl_3$); lit.[20] $[\alpha]^{20}_D$ +29° (c 3.2, CH_2Cl_2). ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.37 and 1.45 (2s, 6H, $C(CH_3)_2$), 1.62 (s, 1H, OH), 3.05-3.20 (m, 2H, epox-H), 3.50-4.20 (m, 5H, $OC\underline{H}_2CH$, $CH_2C\underline{H}O$ and $C\underline{H}_2OH$) ppm. IR (CCl_4): ν 3600, 3480, 2990, 2870, 1380, 1370, 1210, 1060 cm^{-1}. MS (CI): *m/e* (%) 175 (6, M^++1), 159 (96), 117 (14, $-CH_3C(O)CH_3$), 101 (29, $-CHOCHCH_2OH$), 99 (50), 69 (37).

{(2S,3S)-3-[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]oxiran-2-yl}carbaldehyde:

This aldehyde was prepared following the method for the (2R,3S)-diastereomer. Starting with epoxy alcohol **4b** (450 mg, 2.6 mmol), crude aldehyde was synthesized as an oil (289 mg, 65%). ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.35 and 1.42 (2s, 6H, $C(CH_3)_2$), 3.25-3.35 (m, 2H, epox-H), 3.86-4.21 (m, 3H, $OC\underline{H}_2CH$ and $CH_2C\underline{H}$), 9.06 (d, 1H, $C\underline{H}(O)$, J 6 Hz) ppm. IR(CCl_4): ν 2990, 2935, 2880, 1735, 1380, 1370, 1065 cm^{-1}. This aldehyde was immediately converted into acid **5b**.

{(2S,3S)-3-[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]oxiran-2-yl}carboxylic acid (**5b**):

Following the procedure for the preparation of glycidic acid **5a**, compound **5b** was synthesized as an oil (80% yield). IR (CCl_4): ν 3600-2500, 2980, 2930, 2870, 1680, 1380, 1370 cm^{-1}. The product was immediately converted into diazoketone **6b**.

1-{(2S,3R)-3-[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]oxiran-2-yl}-2-diazo-ethanone (**6b**):

Starting with glycidic acid **5b** (300 mg, 1.60 mmol) and following the procedure for compound **6a**, pure epoxy diazo ketone **6b** (chromatographed with hexane/ethyl acetate 2:1) was obtained as an oil (80 mg, 25%). ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.36 and 1.45 (2s, 6H, $C(CH_3)_2$), 3.09 (dd, 1H, $C\underline{H}CHC(O)$, J 4.4 Hz and 1.8 Hz), 3.35 (d, 1H, $CHC\underline{H}C(O)$, J 1.8 Hz), 3.77-4.13 (m, 3H, $OC\underline{H}_2CH$ and $CH_2C\underline{H}$), 5.50 (s, 1H, CHN_2) ppm. IR (CCl_4): ν 3120, 2980, 2940, 2880, 2105, 1645, 1380, 1370 cm^{-1}.

Methyl E-*4-[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]-4-(S)-hydroxy-but-2-enoate* (**7b**):

Starting with diazoketone **6b** (80 mg, 0.38 mmol) and following the procedure for compound **7a**, pure ester **7b** was obtained as an oil (52 mg, 64%) after chromatography (hexane/ethyl acetate 2:1). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.37 and 1.46 (2s, 6H, $C(CH_3)_2$), 2.45 (br s, 1H, OH), 3.76 (s, 3H, OCH_3), 3.89 (dd, 1H, $OCH\underline{H}CHO$, J 8.5 Hz and 6.2 Hz), 3.95 (dd, 1H, $OC\underline{H}HCHO$, J 8.5 Hz and 6.6 Hz), 4.16 (m, 1H, $CH_2C\underline{H}O$), 4.48 (m, 1H, $C\underline{H}(OH)C$), 6.19 (dd, 1H, $CH{=}C\underline{H}C(O)$, J 15.7 Hz and 1.9 Hz), 6.92 (dd, 1H, $C\underline{H}{=}CHC(O)$, J 15.7 Hz and 4.1 Hz) ppm. IR (CCl_4): ν 3600-3300, 2990, 2940, 2880, 1725, 1665, 1380, 1370 cm^{-1}. MS (CI): *m/e* (%) 217 (27, M^++1), 201 (33, $-CH_3$), 199 (8, $-H_2O$), 185 (12), 169 (11), 159 (24, $-CO_2Me$), 141 (11, $-CO_2Me$, $-H_2O$), 127

(34, -H_2O, -$CHCO_2Me$), 101 (100, -CH(OH)CH=$CHCO_2Me$). EI/HRMS: *m/e* calcd. for $C_{10}H_{16}O_5$ 216.09977, found 216.09983 ± 0.00082 a.m.u.

(2S,4S)-2-Phenyl-1,3-dioxane-4-carbaldehyde:

To a stirred solution of freshly distilled oxalyl chloride (3.84 ml, 44 mmol) in dry dichloromethane (100 ml) dimethyl sulfoxide (6.9 ml, 80 mmol dissolved in 15 ml of dry dichloromethane) was added at −78°C under nitrogen. The white suspension was stirred for 10 min, after which alcohol 8 was added (7.68 g, 39.6 mmol), to give a clear solution. Stirring for 40 min was followed by addition of diisopropylethylamine (35 ml, 195 mmol). The mixture was allowed to reach room temperature, after which it was washed with water. The organic layer was extracted successively with 1% HCl, 5% Na_2CO_3 and brine. After drying ($MgSO_4$) the mixture was concentrated *in vacuo* to give the crude aldehyde (7.12 g, 94%), which was reacted further without purification. ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.60-2.10 (m, 2H, $OCH_2C\underline{H}_2CH$), 3.60-4.35 (m, 3H, $OC\underline{H}_2CH_2CH$ and $OCH_2CH_2C\underline{H}$), 5.60 (s, 1H, CHPh), 7.30-7.64 (m, 5H, Ph), 9.72 (s, 1H, CHC(O)$\underline{H}$) ppm. IR (CCl_4): ν 3090, 3065, 3040, 2970, 2930, 2850, 2820, 1740, 1370 cm^{-1}.

Ethyl E-*3-[(2S,4S)-2-phenyl-1,3-dioxan-4-yl]prop-2-enoate*:

To a suspension of oven-dried LiCl (1.855 g, 43.75 mmol) in dry acetonitrile (200 ml) under nitrogen and at room temperature was added triethyl phosphonoacetate (9.8 g, 43.74 mmol) and diisopropylethylamine (6.33 ml, 36.46 mmol). Stirring for 5 min was followed by the addition of crude aldehyde (described above, 7.0 g, 36.36 mmol) in dry CH_3CN (50 ml). The mixture was stirred for 2 h (progress of reaction monitored by TLC), after which water was added until all salts had dissolved. Acetonitrile was evaporated and the residue was taken up in water and washed with ether (3x). The combined ethereal layers were dried ($MgSO_4$) and concentrated *in vacuo* to yield a yellow solid as crude product (11.12 g). This was chromatographed (hexane/ethyl acetate 4:1), giving pure *trans* ester as a solid (6.12 g, 65%). M.p. (pentane) 67.5-68°C. $[\alpha]^{25}_D$ −22.6° (*c* 1.5, $CHCl_3$), lit.[25a] $[\alpha]^{23}_D$ −23.8° (*c* 1.8, $CHCl_3$). ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.29 (t, 3H, CH_3, J 7.2 Hz), 1.58-2.12 (m, 2H, $OCH_2C\underline{H}_2CH$), 3.86-4.40 (m, 2H, $OC\underline{H}_2CH_2CH$), 4.41-4.67 (m, 1H, $C\underline{H}OCH$=C), 4.21 (q, 2H, $OC\underline{H}_2CH_3$, J 7.1 Hz), 5.59 (s, 1H, CHPh), 6.13 (dd, 1H, C=C$\underline{H}$C(O), J 15.7 Hz and 1.8 Hz), 6.97 (dd, 1H, C$\underline{H}$=CHC(O), J 15.7 Hz and 4.1 Hz), 7.29-7.58 (m, 5H, Ph) ppm. IR (CCl_4): ν 3090, 3065, 3040, 2980, 2960, 2920, 2850, 1720, 1660, 1540, 1300 cm^{-1}. MS (CI): *m/e* (%) 263 (39, M^++1), 217 (42, -EtOH), 157 (61, -PhC(O)H), 139 (44, -PhC(O)H, -H_2O), 127 (58, -EtOH, -PhCH), 111 (67, -PhC(O)H, -EtOH), 107 (62, $PhC(O)H^+$+1), 106 (46, $PhC(O)H^+$), 105 (100, $PhC(O)^+$), 94 (57), 83 (47), 67 (55). Calcd. for $C_{15}H_{18}O_4$: C 68.69, H 6.92%, found C 67.72, H 6.81%.

E-*3-[(2S,4S)-2-phenyl-1,3-dioxan-4-yl]prop-2-en-ol* (**9**):

Allylic alcohol **9** was synthesized from the α,β-unsaturated ester described above, following the procedure for the preparation of allylic alcohol **3**. Starting with the ester (3.0 g, 11.45 mmol) *trans*-alcohol **9**, purified by chromatography (hexane/ethyl acetate 3:1), was prepared as an oil (1.88 g, 75%). ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.41-1.60 (br d, 1H, $OCH_2C\underline{H}H$, J 13 Hz), 1.93 (dq, 1H, $OCH_2C\underline{H}HCH$, J 11 Hz and 4.9 Hz), 2.76 (br s, 1H, OH), 3.83-4.27 (m, 4H, $OC\underline{H}_2CH_2CHO$ and $C{=}CC\underline{H}_2OH$), 4.28-4.47 (m, 1H, $OCH_2CHC\underline{H}O$), 5.55 (s, 1H,

CHPh), 5.81-5.91 (m, 2H, C<u>H</u>=C<u>H</u>), 7.27-7.57 (m, 5H, Ph) ppm. IR (CCl_4): ν 3610, 3440, 3190, 3160, 3140, 2980, 2950, 2920, 2850, 1550 cm^{-1}. MS (CI): *m/e* (%) 221 (41, M^++1), 203 (19, -H_2O), 163 (6, -CH=CHCH_2OH), 149 (15), 134 (19), 115 (21), 107 (35, PhC(O)H^++1), 106 (20, PhC(O)H^+), 105 (45), 97 (100, -PhC(O)H, -H_2O), 91 (26), 80 (39), 69 (27), 49 (29). EI/HRMS: *m/e* calcd. for $C_{13}H_{16}O_3$ 220.10994, found 220.10990 ± 0.00088 a.m.u.

{(2S,3R)-3-[(2S,4S)-2-phenyl-1,3-dioxan-4-yl]oxiran-2-yl}methanol (**10a**):

Compound **10a** was prepared following the procedure for epoxy alcohol **4a**. Starting with allylic alcohol **9** (950 mg, 4.3 mmol) and using L-(+)-DET as chiral inductor, crude epoxide was obtained as a white solid (965 mg), which was recrystallized from ether at −20°C, yielding epoxy alcohol **10a** (568 mg, 56%). M.p. 84-84.5°C. $[\alpha]^{25}_D$ −8.85° (*c* 1.17, $CHCl_3$). ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.50-1.77 (m, 2H, CH_2C<u>H</u>HCHO and OH), 2.01 (dq, 1H, CH_2CH<u>H</u>CHO, J 11.5 Hz and 4.9 Hz), 3.15 (dd, 1H, C<u>H</u>OCHOCH_2OH, J 4.3 Hz and 2.0 Hz), 3.25 (dt, 1H, CHOC<u>H</u>OCH_2OH, J 6.0 Hz and 2.0 Hz), 3.65 (ddd, 1H, CHOC<u>H</u>HOH, J 12 Hz, 7.5 Hz and 4.0 Hz), 3.80-4.12 (m, 3H C<u>H</u>$_2$CH_2CHO and CHOCH<u>H</u>OH), 4.33 (ddd, 1H, CH_2CH_2C<u>H</u>OCHO, J 11.5 Hz, 6.0 Hz and 1.6 Hz), 5.50 (s, 1H, CHPh), 7.31-7.50 (m, 5H, Ph) ppm. IR (CCl_4): ν 3500, 2960, 2870, 1120 cm^{-1}. MS (CI): *m/e* (%) 237 (4, M^++1), 236 (24 ,M^+), 235 (47, M^+-1), 163 (67, -CHOCHCH_2OH), 131 (13, -PhC(O)H), 113 (55, -PhC(O)H, -H2O), 107 (81, PhC(O)H^++1), 106 (32, PhC(O)H^+), 105 (PhC(O)$^+$), 95 (24), 91 (50), 87 (72), 83 (61), 79 (52), 77 (46), 71 (73), 67 (41), 55 (50), 41 (100). EI/HRMS: *m/e* calcd. for $C_{13}H_{16}O_4$ 236.1049, found 236.10496 ± 0.00046 a.m.u. Calcd. for $C_{13}H_{16}O_4$: C 66.09, H 6.83%, found C 66.66, H 6.92%.

{(2R,3R)-3-[(2S,4S)-2-phenyl-1,3-dioxan-4-yl]oxiran-2-yl}carboxylic acid (**11a**):

Glycidic acid **11a** was synthesized in a two-step procedure from epoxy alcohol **10a** via the aldehyde. Starting with the alcohol (500 mg, 2.12 mmol) and following the procedure for the synthesis of *(2S,4S)-2-phenyl-1,3-dioxan-4-carbaldehyde* (*vide supra*), crude aldehyde was prepared as an oil (623 mg). ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.59 (br d, 1H, CH_2C<u>H</u>HOCH, J 13.1 Hz), 1.99 (dq, 1H, CH_2CH<u>H</u>OCH, J 11.4 Hz and 5.2 Hz), 3.35 (dd, 1H, epox-H, J 3.9 Hz and 1.9 Hz), 3.47 (dd, 1H, epox-H, J 6.0 Hz and 1.9 Hz), 3.81-4.13 (m, 2H, OC<u>H</u>$_2$CH_2CH), 4.31 (ddd, 1 H, CH_2C<u>H</u>OCHO, J 11.6 Hz, 5.2 Hz and 1.5 Hz), 5.55 (s, 1H, CHPh), 7.20-7.53 (m, 5H, Ph), 9.05 (d, 1H, CHO, J 6.0 Hz) ppm. IR (CCl_4): ν 3090, 3070, 3040, 2980, 2960, 2920, 2850, 2820, 1735, 1110, 700 cm^{-1}. The aldehyde was immediately dissolved in a mixture of *tert*-butyl alcohol (40 ml), 2-methyl-2-butene (12 ml) and dichloromethane (3 ml, to raise the solubility of the aldehyde), to which a solution of $NaClO_2$ (1.7 g, 18.8 mmol) and NaH_2PO_4 (1.7 g, 14.2 mmol) in water (17 ml) was added. The slightly yellow mixture was stirred overnight, after which the volatile solvents were evaporated. Acidification to pH 5, followed by extraction with ether (4x), drying of the combined ethereal layers ($MgSO_4$) and concentration *in vacuo* yielded crude glycidic acid **11a** (529 mg), which was immediately converted into diazo ketone **12a**. ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.49-1.74 (m, 1H, CH_2C<u>H</u>HCHO), 1.80-2.23 (m, 1H, CH_2CH<u>H</u>CHO), 3.36 (dd, 1H, epox-H, J 3.9 Hz and 1.8 Hz), 3.58 (d, 1H, epox-H, J 1.8 Hz), 3.80-4.12 (m, 2H, OC<u>H</u>$_2$CH_2CHO), 4.22-4.55 (m, 1H, CH_2CH_2C<u>H</u>O), 5.49 (s, 1H, CHPh), 7.30-7.65 (m, 5H, Ph) ppm. IR (CCl_4): ν 3600-2500, 2920, 2860, 1725 cm^{-1}.

1-[(2R,3R)-3-[(2S,4S)-2-phenyl-1,3-dioxan-4-yl]oxiran-2-yl]-2-diazo-ethanone (**12a**):
Starting with crude acid **11a** (530 mg, 2.12 mmol) and following the procedure for the synthesis of diazoketone **5a**, crude product was synthesized (475 mg). This was chromatographed (hexane/ethyl acetate 1:1), yielding compound **12a** as an oil (170 mg, 30%). The low yield is due to decomposition on the silica gel column, as was indicated by the isolation of benzaldehyde. ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.52 (br d, 1H, $CH_2C\underline{H}HCHO$, J 13.1 Hz), 1.70-2.20 (m, 1H, $CH_2CH\underline{H}CHO$), 3.20 (dd, 1H, epox-H, J 3.3 Hz and 2.0 Hz), 3.54 (d, 1H, epox-H, J 2.0 Hz), 3.92-4.18 (m, 2H, $OC\underline{H}_2CH_2CHO$), 4.30 (ddd, 1H, $CH_2CH_2C\underline{H}O$, J 10.5 Hz, 5.2 Hz and 1.3 Hz), 5.49 (s, 2H, CHN_2 and CHPh), 7.31-7.53 (m, 5H, Ph) ppm. IR (CCl_4): ν 3120, 3060, 2960, 2920, 2850, 2110, 1645, 1110, 910, 700 cm^{-1}. MS (CI): *m/e* (%) 275 (1, M^++1), 273 (23, M^+-1), 197 (5), 163 (35), 131 (11), 124 (7), 107 (22, $PhC(O)H^+$+1), 106 (15, $PhC(O)H^+$), 105 (100, $PhC(O)^+$-1), 91 (32), 83 (22), 77 (19), 69 (23), 55 (24), 43 (23), 41 (41). EI/HRMS: *m/e* calcd. for $C_{14}H_{14}N_2O_4$ 274.09536, found 274.09523 ± 0.00081 a.m.u.

Ethyl E-*4-[(2S,4S)-2-phenyl-1,3-dioxan-4-yl]-4-(R)-hydroxy-but-2-enoate* (**13a**):
Following the procedure for the synthesis of unsaturated ester **7a** and starting with epoxy diazo ketone **12a** (160 mg, 0.60 mmol dissolved in 50 ml of methanol), crude ester was synthesized (133 mg). After chromatography (hexane/ethyl acetate 4:1) pure compound **13a** was isolated as an oil (80 mg, 50%). ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.41 (br d, 1H, $OCH_2C\underline{H}HCHO$), 2.04 (dq, 1H, $OCH_2CH\underline{H}CHO$, J 13 Hz and 5.3 Hz), 2.61 (d, 1H, OH, J 4.0 Hz), 3.75 (s, 3H, OCH_3), 3.91 (t, 1H, $OC\underline{H}HCH_2CHO$, J 2.4 Hz), 4.03 (t, 1H, $OCH\underline{H}CH_2CHO$, J 2.8 Hz), 4.23-4.36 (m, 1H, $OCH_2CH_2C\underline{H}O$), 4.41-4.53 (m, 1H, $CHOC\underline{H}(OH)CH$), 5.55 (s, 1H, CHPh), 6.18 (dd, 1H, $CH=C\underline{H}C(O)$, J 15.6 Hz and 1.8 Hz), 6.97 (dd, 1H, $C\underline{H}=CHC(O)$, J 15.6 Hz and 4.3 Hz), 7.32-7.54 (m, 5H, Ph) ppm. IR (CCl_4): ν 3590, 3060, 3030, 2965, 2950, 2870, 1725, 1665, 1435, 1310, 1170, 1110, 700 cm^{-1}. MS (CI): *m/e* (%) 279 (7, M^++1), 247 (3, -MeOH), 173 (18, -PhC(O)H), 163 (100), 155 (43, -PhC(O)H, -H_2O), 141 (21, -PhC(O)H, -MeOH), 123 (10, -PhC(O)H, -MeOH, -H_2O), 107 (20), 91 (24), 79 (14), 57 (11), 41 (22). EI/HRMS: *m/e* calcd. for $C_{15}H_{18}O_5$ 278.11542, found 278.11544 ± 0.00081 a.m.u.

[(2R,3S)-3-[(2S,4S)-2-phenyl-1,3-dioxan-4-yl]oxiran-2-yl]methanol (**10b**):
Starting with allylic alcohol **9** (0.95 g, 4.3 mmol), following the procedure for the synthesis of **4a** and using D-(-)-DET as chiral inductor, crude epoxy alcohol was prepared (1.013 g), which was recrystallized from ether at 4°C, to give pure **10b** (0.737 g, 72%). $[\alpha]^{25}_D$ +29.5° (*c* 1.08, $CHCl_3$). M.p. 98.5-99°C. ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.42-1.82 (m, 2H, $OCH_2CH\underline{H}CHO$ and OH), 2.05 (dq, 1H, $OCH_2C\underline{H}HCHO$, J 12 Hz and 5.2 Hz), 3.17-3.24 (m, 2H, epox-H), 3.50-4.10 (m, 4H, $OC\underline{H}_2CH_2CHO$ and $CHOC\underline{H}_2OH$), 4.32 (ddd, 1H, $OCH_2CH_2C\underline{H}O$, J 11.5 Hz, 4.6 Hz and 1.4 Hz), 5.52 (s, 1H, CHPh), 7.31-7.55 (m, 5H, Ph) ppm. IR (CCl_4): ν 3600, 3400, 3050, 2970, 2930, 2870, 1110 cm^{-1}. MS (CI): *m/e* (%) 237 (7, M^++1), 236 (33, M^+), 235 (48, M^+ -1), 163 (65, -$CHOCHCH_2OH$), 131 (8, -PhC(O)H)), 113 (45, -PhC(O)H, -H_2O), 107 (71, $PhC(O)H^+$+1), 106 (30, $PhC(O)H^+$), 105 (100, $PhC(O)^+$), 95 (23), 91 (42), 87 (63), 83 (61), 79 (47), 77 (46), 71 (63), 67 (35), 57 (46), 41 (57). EI/HRMS: *m/e* calcd. for $C_{13}H_{16}O_4$ 236.1049, found 236.10496 ± 0.00046 a.m.u. Calcd. for $C_{13}H_{16}O_4$: C 66.09, H 6.83%, found C 66.53, H 6.88%.

{(2S,3S)-3-[(2S,4S)-2-phenyl-1,3-dioxan-4-yl]oxiran-2-yl}carboxylic acid (**11b**):

Glycidic acid **11b** was prepared following the procedure for the synthesis of compound **11a**. Starting with epoxy alcohol **10b** (500 mg, 2.12 mmol) crude aldehyde was prepared (610 mg). ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.56 (br d, 1H, $OCH_2C\underline{H}HCHO$, J 13 Hz), 2.05 (dq, 1H, $OCH_2CH\underline{H}CHO$, J 11.7 and 5.2 Hz), 3.41-3.48 (m, 2H, epox-H), 3.83-4.09 (m, 2H, $OC\underline{H}_2CH_2CHO$), 4.33 (ddd, 1H, $OCH_2CH_2C\underline{H}O$, J 11.6 Hz, 5.2 Hz and 1.4 Hz), 5.51 (s, 1H, CHPh), 7.31-7.54 (m, 5H, Ph), 9.06 (d, 1H, C(O)H, J 6 Hz) ppm. IR (CCl_4): ν 3090, 3070, 3030, 2970, 2920, 2850, 1735, 700, 650 cm^{-1}. The aldehyde (600 mg) was oxidized in a mixture of *tert*-butyl alcohol (50 ml), 2-methyl-2-butene (12 ml) and dichloromethane (2 ml, *cf.* compound **11a**), yielding acid **11b** as a yellow oil (250 mg), which was immediately converted into the epoxy diazo ketone. ^{1}H-NMR (90 MHz, $CDCl_3$): δ 1.45 (br d, 1H, $OCH_2C\underline{H}HCHO$, J 12 Hz), 1.63-2.17 (m, 1H, $OCH_2CH\underline{H}CHO$), 3.30-3.60 (m, 2H, epox-H), 3.65-4.05 (m, 2H, $OC\underline{H}_2CH_2CHO$), 4.05-4.33 (m, 1H, $OCH_2CH_2C\underline{H}O$), 5.46 (s, 1H, CHPh), 7.30-7.55 (m, 5H, Ph), 8.77 (br s, 1H, CO_2H) ppm. IR (CCl_4): ν 3600-2700, 2950, 2920, 2860, 1725 cm^{-1}.

1-{(2S,3S)-3-[(2S,4S)-2-phenyl-1,3-dioxan-4-yl]oxiran-2-yl}-2-diazo-ethanone (**12b**):

Following the procedure for the synthesis of compound **5a**, crude diazo ketone **12b** was prepared (137 mg), starting from crude glycidic acid **11b** (180 mg). Chromatography of the crude product (hexane/ethyl acetate 1:1) yielded diazo compound **12b** as an oil (58 mg, 30%). The low yield was due to decomposition on the silica gel column (isolation of benzaldehyde). ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.47-1.65 (br d, 1H, $OCH_2C\underline{H}HCHO$, J 13 Hz), 2.04 (dq, 1H, $OCH_2CH\underline{H}CHO$, J 11.5 Hz and 5.2 Hz), 3.20 (dd, 1H, $C\underline{H}OCHCH(O)$, J 5 Hz and 2 Hz), 3.51 (d, 1H, $CHOC\underline{H}CH(O)$, J 2 Hz), 3.76-3.90 (m, 1H, $OC\underline{H}HCH_2CHO$), 4.01 (dd, 1H, $OCH\underline{H}CH_2CHO$, J 11.8 Hz and 2.7 Hz), 4.31 (ddd, 1H, $OCH_2CH_2C\underline{H}O$, J 11.4 Hz, 5.1 Hz and 1.3 Hz), 5.50 (s, 2H, CHPh and CHN_2), 7.31-7.53 (m, 5H, Ph) ppm. IR (CCl_4): ν 3120, 3070, 3040, 2960, 2930, 2860, 2110, 1645, 1370 cm^{-1}. MS (CI): *m/e* (%) 275 (14, M^++1), 273 (M^+-1), 197 (6), 163 (18), 131 (7), 124 (12), 107 (20, $PhC(O)H^+$+1), 106 (14, $PhC(O)H^+$), 105 (100, $PhC(O)^+$), 91 (19), 83 (25), 77 (19), 69 (23), 55 (26), 43 (20), 41 (40). EI/HRMS: *m/e* calcd. for $C_{14}H_{14}N_2O_4$ 274.09536, found 274.09550 ± 0.00081 a.m.u.

Ethyl E-*4-[(2S,4S)-2-phenyl-1,3-dioxan-4-yl]-4-(S)-hydroxy-but-2-enoate* (**13b**):

Starting with diazo ketone **12b** (58 mg, 0.21 mmol) and following the procedure for the synthesis of compound **7a**, unsaturated ester **13b** was obtained as an oil (52 mg, 75%) in absolute methanol as the solvent. ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.52 (br d, 1H, $OCH_2C\underline{H}HCHO$, J 13 Hz), 1.98 (dq, 1H, $OCH_2CH\underline{H}CHO$, J 11.6 Hz and 5.2 Hz), 2.82 (d, 1H, OH, J 4.1 Hz), 3.75 (s, 3H, OCH_3), 3.76-3.86 (m, 1H, $OCH\underline{H}CH_2CHO$), 3.99 (dd, 1H, $OC\underline{H}HCH_2CHO$, J 11.9 Hz and 2.8 Hz), 4.18-4.38 (m, 2H, $OCH_2CH_2C\underline{H}O$ and $CHOC\underline{H}(OH)$), 5.53 (s, 1H, CHPh), 6.21 (dd, 1H, $CH{=}C\underline{H}C(O)$, J 15.6 Hz and 1.7 Hz), 6.95 (dd, 1H, $C\underline{H}{=}CHC(O)$, J 15.6 Hz and 4.8 Hz), 7.32-7.54 (m, 5H, Ph) ppm. IR (CCl_4): ν 3620, 3400, 2970, 2920, 2880, 1725 cm^{-1}. MS (CI): *m/e* (%) 279 (2, M^++1), 247 (2, -MeOH), 223 (2), 163 (47, $-CH(OH)CH{=}CHCO_2Me$), 155 (31, -PhC(O)H, $-H_2O$), 149 (32), 141 (53, -PhC(O)H, -MeOH), 123 (18, -PhC(O)H, -MeOH, $-H_2O$), 116 (25), 105 (36, $PhC(O)^+$), 86 (51), 75 (16), 57 (36), 41 (100). EI/HRMS: *m/e* calcd. for $C_{15}H_{18}O_5$ 278.11542, found 278.11517 ± 0.00081 a.m.u.

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