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Synthesis of all four isomers of (*E*)-4,5-dihydroxydec-2-enal using osmium-catalysed asymmetric dihydroxylation

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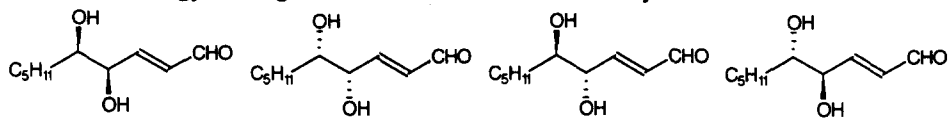
Abstract: The enantioselective synthesis of the four possible isomers of (*E*)-4,5-dihydroxydec-2-enal, a cytotoxic product formed in peroxidised liver microsomal lipids, is accomplished via a Sharpless AD reaction alone or associated as appropriate with a regioselective epimerisation of one of the introduced hydroxy groups. © 1997 Elsevier Science Ltd

(*E*)-4,5-Dihydroxydec-2-enals **1a–d** are cytotoxic aldehydes identified, apart from the stereochemistry, by Comporti and Esterbauer groups in liver microsomal lipids subjected to NADPH–Fe induced peroxidation.[1] Since these compounds are of interest in studying the damage consequent on the physiological or pathologic lipid peroxidation[2,3] and their synthesis have not been reported, we started a program to prepare them in quantities suitable for biological studies. As a result of our work we have already reported their preparation starting with a chiral pool of appropriate pentoses or of mannitol.[4,5] Here we report other new, convenient and general asymmetric syntheses of the hydroxyaldehydes **1a–d** based on a strategy of reagent-control of the stereochemistry.



4R, 5R **1a** *4S, 5S* **1b** *4S, 5R* **1c** *4R, 5S* **1d**

For obtaining the syn isomers directly, the Sharpless catalytic asymmetric dihydroxylation (AD) reaction[6] of appropriate achiral olefins was used. Similarly, for the preparation of the anti pair, an AD reaction, associated with a regioselective epimerisation of one of the stereogenic centres, proved successful. The epimerisation was accomplished by performing a Payne-type rearrangement on the cyclic sulphate of the syn diols and a nucleophilic trapping of the resulting epoxide.[7,8] All routes proceed satisfactorily giving the desired compounds with a good enantioselection, thus allowing the synthetic utility of the AD-reaction to be extended.

Results and discussion

In planning the asymmetric synthesis of aldehydes **1a–d** we considered that the more direct route for separately obtaining each enantiomer of the syn couple was the AD reaction of the (*E,E*)-2,4-decadienal which had permitted to Sharpless group to obtain the (*E*,4*R*,5*R*)-4,5-dihydroxydec-2-enal **1a**.[9] However, since the recovery of the compound from the reaction mixture was not completely satisfactory, we attempted an improvement of the yields by performing the reaction on the corresponding acetal **2** (Scheme 1).[10]

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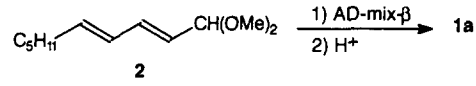
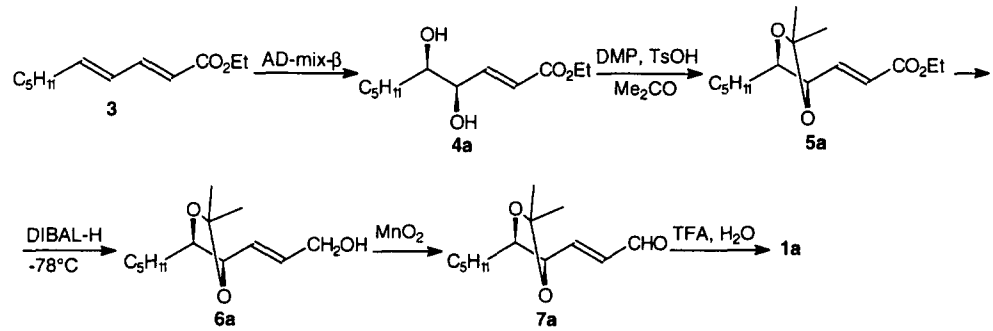


Scheme 1.

In effect, in this case, the AD reaction afforded the desired dihydroxyaldehydes **1a** and **1b** with high regio- and enantioselectivity and with better yields, but the recover of the aldehydes was still unsatisfactory. In parallel with this work, we decided to follow a different approach starting with ethyl (*E*,*E*)-deca-2,4-dienoate **3** (Scheme 2) which, subjected to an AD reaction using AD-mix-β,[11] permitted ethyl (*E*,4*R*,5*R*)-4,5-dihydroxydec-2-enoate (**4a**) in pure form and high enantiomeric excess (ee 98%) to be obtained.

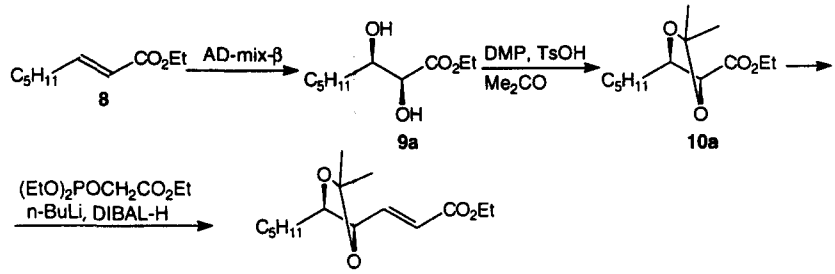


Scheme 2.

The diunsaturated ester **3** was prepared by a Wittig reaction of (*E*)-oct-2-enal and triethyl phosphonoacetate under conditions of low basicity[12] which allow it to be obtained accompanied only by 5% of the (2*Z*,4*E*)-isomer. The diol **4a** was then converted to the corresponding acetonide **5a**, using dimethoxypropane in acidic acetone, and reduced with diisobutylaluminium hydride (DIBAL–H; at −78°C). However, the reduction always afforded the corresponding alcohol **6a**, accompanied only by a minor amount (18%) of the desired aldehyde **7a** which however was obtained by oxidation of **6a** by manganese dioxide in hexane. Thus it was decided to perform the reduction under conditions affording the alcohol **6a** as a single compound, and to oxidise it to the aldehyde **7a**. By this route, after hydrolysis of the acetonide group of **7a**, the (*E*,4*R*,5*R*)-4,5-dihydroxydec-2-enal **1a** (ee 98%) was obtained. A parallel sequence of reactions, performing the hydroxylation of the ester **3** with AD-mix-α, afforded (*E*,4*S*,5*S*)-4,5-dihydroxydec-2-enal **1b** (ee 96%) via the dihydroxyester **4b**.

In order to confirm that both dihydroxyesters **4a** and **4b** possessed the stereochemistry predicted by using AD-mix-β and AD-mix-α respectively, and to establish the enantiomeric excess of each dihydroxyester, we prepared the Mosher's ester[13] of both hydroxy groups present in the molecule of these compounds. Their ^{1}H-NMR spectra established that both **4a** and **4b** possessed a high enantiomeric excess (98% and 96% respectively) but were not useful for confirming the absolute stereochemistry of the parent ester. However an unequivocal assignment of the stereochemistry was derived by the ^{1}H-NMR analysis of both possible Mosher monoesters obtained performing the esterification in the presence of one molar equivalent of Mosher's chloride per mole of diol. The stereochemistry was finally confirmed by comparison of the obtained dihydroxyaldehydes **1a** and **1b** with those previously prepared from known chiral precursors (by HPLC analysis on a chiral column, after dibenzoylation).[5]

A third alternative synthesis of the syn pair of dihydroxyaldehydes **1a** and **1b** was accomplished by AD reaction of ethyl (*E*)-oct-2-enoate **8** and adding the extra double bond at a later stage of the synthesis (Scheme 3).

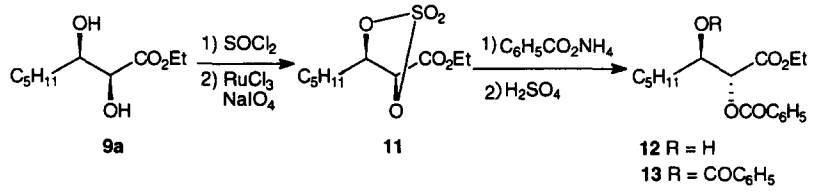


Scheme 3.

Reaction of the α,β-unsatured ester **8** with AD-mix-β afforded enantiomerically pure (2*S*,3*R*)-2,3-dihydroxyoctanoate[11b] **9a** (ee 95% detected by HPLC on a chiral column after dibenzoylation). The diol was then acetonised to afford **10a** which was subjected to a two-carbon homologation procedure using DIBAL–H and a Horner–Emmons reagent in a one pot procedure.[14] In this way, the protected (4*S*,5*R*)-4,5-dihydroxyester **5a** (a 92:8 mixture of *E* and *Z* isomers) was obtained and subjected to the reaction sequence described above for **5a** to afford the dihydroxyaldehyde **1a**.

A parallel sequence of reactions, starting with the ethyl (2*R*,3*S*)-2,3-dihydroxyoctanoate **9b**, afforded the dihydroxyaldehyde **1b**.

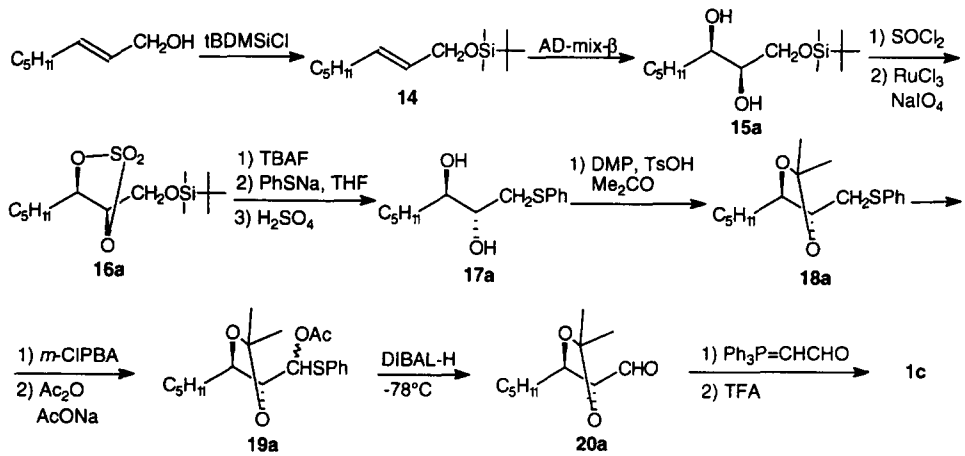
The dihydroxyester **9a** was also the starting material for an initial approach to the synthesis of the anti couple of dihydroxyaldehydes **1c** and **1d**, the diolic system of which, appeared obtainable by a regioselective epimerisation of the carbinol at C-2, using a cyclic sulphate ester as intermediate (Scheme 4).



Scheme 4.

In fact Sharpless and Gao[8b] have shown that cyclic sulphates of 2,3-dihydroxyesters react with a benzoate anion to afford, after hydrolysis, the dihydroxyester with a reversed stereochemistry at C-2. Thus the ethyl (2*S*,3*R*)-2,3-dihydroxyoctanoate **9a** was subjected to a sequence of reactions including: the transformation of the diolic system into a cyclic sulphate (by reaction with thionyl chloride in the presence of triethylamine followed by oxidation with catalytic RuO_4 and $NaIO_4$), the nucleophilic opening of the cyclic sulphate by an attack on C-2, (by means of ammonium benzoate in acetone and the selective hydrolysis of the sulphate ester). However, starting with a (2*S*,3*R*)-2,3-dihydroxyester **9a**, having a high enantiomeric excess (95%), the (2*S*,3*R*)-2,3-dibenzoyloxy isomer **13** was obtained with a decreased enantiomeric purity (ee 90%). This result could be rationalised assuming an incomplete regioselectivity (calculated as 97.3%) of the nucleophilic opening at C-2 of the sulphate. In fact, attack at C-3 with inversion of configuration results in the formation of the (2*R*,3*S*)-2,3-dihydroxyester, the enantiomer of the compound deriving from the expected attack at C-2. In effect, the formed intermediate (2*R*,3*S*)-2,3-dihydroxyester monobenzoate was a chromatographically inseparable mixture of 2- and 3-monobenzoates (66:34 ratio; ^{1}H-NMR analysis of the isolated product). The higher observed amount of 3-benzoate indicated however that a considerable C-2 to C-3 shift of the benzoyl group had also occurred after the opening of the cyclic sulphate, thus improving the quantity of 3-benzoyloxy regioisomer which however possessed stereogenic centers with the same absolute configuration of the C-2 benzoyloxy regioisomer. This was proved by HPLC analysis on a chiral column of the mixture

after complete benzoylation. On the other hand, all attempts to separate the 2-benzoyloxy derivative **12** from its racemic regioisomers, by column chromatography, were unsuccessful and so we decided to experiment with a route involving a Sharpless AD reaction of an appropriate TBDMS-protected (*E*)-allylic alcohol **14** followed by an irreversible Payne-type rearrangement as a key for the obtaining of the anti-pair of aldehydes **1c–d** (Scheme 5).[7,15]



Scheme 5.

Thus, the silylether **14** was dihydroxylated by AD-mix-β and the resulting syn diol **15a** (ee 96%) was converted into the cyclic sulphate **16a**. Desilylation of this compound was immediately followed by an irreversible rearrangement to an epoxy sulphate intermediate which, finally, was opened, by means of a benzenethiolate anion, to afford, after saponification, the (2*R*,3*R*)-1-phenylthiocta-2,3-diol **17a**. The formed benzensulfide **17a** was then acetonised, oxidised to the corresponding sulfoxide with m-chloroperoxybenzoic acid and subjected to the Pummerer rearrangement which afforded the corresponding acetoxysulfide **19a** as a diastereomeric mixture. Reduction of the acetoxysulphide **19a** with DIBAL–H afforded the (2*R*,3*R*)-aldehyde **20a** which was then transformed[5] into aldehyde **1c**. A similar sequence of reactions allowed to obtain the isomer **1d**.

In conclusion we have set-up a series of convenient asymmetric syntheses of all possible isomers of (*E*)-4,5-dihydroxydec-2-enals **1a–d** by routes which confirm and expand the synthetic utility of the AD reaction.

Experimental section

Nuclear magnetic resonance spectra were recorded as $CDCl_3$ solution at 303 K on Bruker AM-500 spectrometer operating at 500.13 MHz for ^1H and 125.76 MHz for ^{13}C. All chemical shifts are reported in ppm relative to $CHCl_3$ fixed at 7.24 ppm for the ^1H spectra and relative to $CDCl_3$ fixed at 77.00 ppm for the ^{13}C spectra. Signal multiplicity was designated according to the following abbreviations: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet. All reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60 F_{254}) using UV light or 50% sulphuric acid and heat as developing agent. E Merck 230–400 mesh silica gel was used for flash column chromatography.[16] Optical rotations were measured for 1% $CHCl_3$ solutions.

All AD reactions were carried out using AD-mix-α or AD-mix-β,[11b] which was purchased from Aldrich. The enantiomeric purities of the diol products by AD reaction and of the final aldehydes **1a–d** were measured by NMR analysis of the corresponding Mosher diesters and/or by HPLC analysis of their dibenzoates on a chiral column (LiChroCART 250-4 (*R*,*R*)-Whelk-01, 5μm, Merck, eluent hexane/2-propanol, 94:6, v/v, 1 mL/min, λ 222 nm). Usual work-up refers to diluting with brine,

extraction with an organic solvent, washing the organic layer with water, drying over anhydrous Na_2SO_4 and evaporating the solvent under reduced pressure.

General procedure for AD reaction

AD reactions were performed on 1–5 mmol scale of olefins using for each mmol the following experimental conditions reported by Sharpless.

A mixture of *tert*-butyl alcohol (5 mL), water (5 mL) and AD-mix-α or β (1.4 g) was stirred for few minutes at room temperature until two clear phases were produced. Methanesulphonamide (95 mg; 1 mmol) was then added and the mixture was cooled to −5°C before adding the olefin (1 mmol). The mixture was then stirred at −5°C for 20 h. Sodium metabisulphite (1.5 g) was then added to the cold reaction mixture and the suspension was warmed to room temperature and stirred for 30 min. Usual work-up and purification afforded the final diol.

General procedure for acetonisation of diols

Diols (2 mmol) and *p*-toluenesulfonic acid (10 mg) were dissolved in a 1:1 mixture (20 mL) of 2,2-dimethoxypropane and acetone and stirred at room temperature for 12 h. Saturated aqueous $NaHCO_3$ was added and the mixture was worked-up to afford the crude acetonides.

*General procedure for regeneration of dihydroxy groups of (*E*)-4,5-dihydroxydec-2-enals (**1a–d**)*

The regeneration of diolic system was performed treating each acetonide (226 mg; 1 mmol) with aqueous trifluoroacetic acid (2 mL; 90%; v/v) at −25°C for 30 min. The solution was then poured into a mixture of ice and aqueous saturated $NaHCO_3$ solution and worked-up to give, after rapid column chromatography (eluting with hexane/ethyl acetate; 6:4; v/v), each pure dihydroxyaldehyde **1a–d**.

*Synthesis of (*E,E*)-1,1-dimethoxydeca-2,4-diene 2*

(*E,E*)-Deca-2,4-dienal (1g; 6.6 mmol) was stirred with a suspension of the K-10 montmorillonite/trimethyl orthoformate reagent[10] (2.8 g) in dichloromethane (8.4 mL) at room temperature for 2 h. Filtration on Celite, washing the filtrate with saturated $NaHCO_3$ solution and usual work-up afforded, after distillation, the acetal **2** (800 mg; Y 61%): an oil; ^{1}H-NMR δ 6.26 (1H, dd, *J*=15.0, 11.0 Hz, H-3), 6.00 (1H, dd, *J*=15.0, 11.0 Hz, H-4), 5.72 (1H, dt, *J*=15.0, 7.0 Hz, H-5), 5.45 (1H, dd, *J*=15.0, 5.0 Hz, H-2), 4.76 (1H, d, *J*=5.0 Hz, H-1), 3.26 (6H, s, 2×-OC*H*$_3$), 2.04 (2H, dt, *J*=8.0, 7.0 Hz, H_2-6), 0.84 (3H, t, *J*=8.0 Hz, H_3-10).

*Synthesis of (*E,4R,5R*)- and (*E,4S,5S*)-4,5-dihydroxydec-2-enals **1a** and **1b***

Acetal **2** (198 mg; 1 mmol) was reacted with AD-mix-β to afford a crude diol which was dissolved in moist acetone (10 mL) and treated with ion exchange resin (Dowex 50W×8 -200; 600 mg) for 30 min at room temperature. Filtration and usual work-up afforded, after flash chromatography (eluting with hexane/ethyl acetate; 6:4; v/v), the (*E,4R,5R*)-4,5-dihydroxydec-2-enal (**1a**; 96 mg; Y 52%, ee 90%): an oil; $[\alpha]_D^{20}$=+46.8, lit[5,9] +52.3 and +40.7; ^{1}H-NMR δ 9.52 (1H, d, *J*=7.5 Hz, H-1), 6.82 (1H, dd, *J*=15.5, 5.0 Hz, H-3), 6.34 (1H, ddd, *J*=15.5, 7.5, 1.5 Hz, H-2), 4.21 (1H, ddd, *J*=5.0, 5.0, 1.5 Hz, H-4), 3.56 (1H, ddd, *J*=8.5, 5.0, 5.0 Hz, H-5), 0.85 (3H, t, *J*=7.0 Hz, H_3-10); ^{13}C-NMR δ 193.66 (C1), 156.27 (C3), 132.30 (C2), 73.98, 73.85, 33.14, 31.62, 25.20, 22.47, 13.90. Anal. Calcd. for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.52; H, 9.70.

A parallel AD reaction, performed on acetal **2** with AD-mix-α, afforded the (*E,4S,5S*)-4,5-dihydroxydec-2-enal (**1b**; 100 mg; Y 54%, ee 87%): an oil; $[\alpha]_D^{20}$=−45.5, lit[5] −52.0; ^{1}H and ^{13}C-NMR spectra are superimposable with those of **1a**. Anal. Calcd. for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.58; H, 9.64.

*Synthesis of ethyl (*E,E*)-deca-2,4-dienoate 3*

A mixture of (*E*)-oct-2-enal (1 mL; 7 mmol), K_2CO_3 (1.8 g; 13 mmol), triethyl phosphonoacetate (1.6 mL; 7.8 mmol) and water (1.4 mL) was stirred for 48 h at room temperature. After water dilution and usual work-up the ethyl (*E,E*)-deca-2,4-dienoate (**3**; 1.2 g; Y 85%) was obtained: an oil; b.p. 85°C

(0.6 mmHg); ^{1}H-NMR δ 7.22 (1H, dd, *J*=15.4, 9.8 Hz, H-3), 6.14 (1H, dd, *J*=15.4, 9.8 Hz, H-4), 6.08 (1H, dt, *J*=15.4, 7.0 Hz, H-5), 5.74 (1H, d, *J*=15.4 Hz, H-2), 4.16 (2H, q, *J*=7.2 Hz, -OC*H*$_2$CH$_3$), 2.13 (2H, dt, *J*=7.0, 7.0 Hz, H$_2$-6), 1.40 (2H, tt, *J*=7.0, 7.0 Hz, H$_2$-7), 1.32–1.27 (4H, overlapping; 2×CH$_2$), 1.25 (3H, t, *J*=7.2 Hz, -OCH$_2$C*H*$_3$), 0.86 (3H, t, *J*=7.0 Hz, H$_3$-10); mass spectrum m/z 196 (1.32), 97 (100%).

The compound was contaminated by trace amount (5%) of the (2*Z*,4*E*)-isomer (^{1}H-NMR).

*Synthesis of ethyl (*E,*4*R,*5*R*)- and (*E,*4*S,*5*S*)-4,5-dihydroxydec-2-enoate **4a** and **4b***

AD reaction was performed on the ester **3** (588 mg; 3 mmol) with AD-mix-β to afford, after chromatographic purification (eluting with hexane/ethyl acetate; 6:4; v/v), the ethyl (*E*,4*R*,5*R*)-4,5-dihydroxydec-2-enoate (**4a**; 607 mg; Y 88%, ee 98%): m.p. 83–85°C (from diisopropyl ether); $[\alpha]_D^{20}$=+29.5; ^{1}H-NMR δ 6.91 (1H, dd, *J*=16.1, 5.6 Hz, H-3), 6.12 (1H, dd, *J*=16.1, 1.4 Hz, H-2), 4.19 (2H, q, *J*=7.0 Hz, -OC*H*$_2$CH$_3$), 4.11 (1H, ddd, *J*=5.6, 4.9, 1.4 Hz, H-4), 3.54 (1H, ddd, *J*=8.4, 4.9, 4.2 Hz, H-5), 1.56–1.42 (2H, m, H$_2$-6), 1.39–1.22 (6H, overlapping, 3×CH$_2$), 1.27 (3H, t, *J*=7.0 Hz, -OCH$_2$C*H*$_3$), 0.87 (3H, t, *J*=7.0 Hz, H$_3$-10); mass spectrum m/z 130 (100); 102 (45), 84 (78), 3 (29), 55 (44). Anal. Calcd. for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found: C, 62.61; H, 9.56.

A parallel AD reaction performed using AD-mix-α afforded the ethyl (*E*,4*S*,5*S*)-4,5-dihydroxydec-2-enoate **4b** (573 mg; Y 83%, ee 96%): an oil $[\alpha]_D^{20}$=−27.9; its ^{1}H-NMR spectrum was superimposable with that of **4a**. Anal. Calcd. for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found: C, 62.69; H, 9.76.

*Synthesis of ethyl (*E,*4*R,*5*R*) and (*E,*4*S,*5*S*)-4,5-isopropylidenedioxydec-2-enoate **5a** and **5b***

Acetonisation of the dihydroxyester **4a** (460 mg; 2 mmol), according to the general procedure, afforded the ethyl (*E*,4*R*,5*R*)-4,5-isopropylidenedioxydec-2-enoate **5a** (460 mg; Y 85%): an oil; $[\alpha]_D^{20}$=+12.0; ^{1}H-NMR δ 6.81 (1H, dd, *J*=16.0, 6.5 Hz, H-3), 6.06 (1H, dd, *J*=16.0, 1.5 Hz, H-2), 4.16 (2H, q, *J*=7.5 Hz, OC*H*$_2$CH$_3$), 4.09 (1H, ddd, *J*=8.5, 6.5, 1.5 Hz, H-4), 3.68 (1H, dt, *J*=8.5, 6.0 Hz, H-5), 1.55 (2H, dt, *J*=9.0, 6.0 Hz, H$_2$-6), 1.40 (2H, tt, *J*=7.0, 7.0 Hz, H$_2$-7), 1.32–1.27 (4H, overlapping, 2×CH$_2$), 1.38, 1.36 (2×3H, 2×s, C(C*H*$_3$)$_2$), 1.25 (3H, t, *J*=7.5 Hz, OCH$_2$C*H*$_3$), 0.82 (3H, t, *J*=7.5 Hz, H$_3$-10); mass spectrum m/z 130 (100); 102 (49), 84 (95), 73 (40), 55 (56). Anal. Calcd. for $C_{15}H_{26}O_4$: C, 66.64; H, 9.69. Found: C, 66.77; H, 9.62.

A parallel acetonisation of the dihydroxyester **4b** (460 mg; 2 mmol) afforded the ethyl (*E*,4*S*,5*S*)-4,5-isopropylidenedioxydec-2-enoate **5b** (465 mg; Y 86%): an oil; $[\alpha]_D^{20}$=−11.2; ^{1}H-NMR spectrum was superimposable with that of **5a**. Anal. Calcd. for $C_{15}H_{26}O_4$: C, 66.64; H, 9.69. Found: C, 66.58; H, 9.75.

*Synthesis of (*E,*4*R,*5*R*) and (*E,*4*R,*5*R*)-4,5-isopropylidenedioxydec-2-enal **7a** and **7b***

*i. By DIBAL–H reduction of the ester **5a***

The ester **5a** (1.28 g; 4.7 mmol), dissolved in toluene (10 mL), was treated with DIBAL–H (5.2 mL of a 1M solution in hexane) at −78°C for 2 h. At this time acetone and water were added in the sequence and the mixture was warmed to room temperature. Usual work-up afforded a mixture which, after flash chromatography (eluting with hexane/ethyl acetate; 7:3; v/v), afforded first the (*E*,4*R*,5*R*)-4,5-isopropylidenedioxydec-2-enal **7a** (193 mg; Y 18%): an oil; $[\alpha]_D^{20}$=+12.3, lit[5] +13.1; ^{1}H-NMR δ 9.58 (1H, d, *J*=7.7 Hz, H-1), 6.72 (1H, dd, *J*=15.5, 5.5 Hz, H-3), 6.35 (1H, ddd, *J*=15.5, 7.7 1.5 Hz, H-2), 4.25 (1H, ddd, *J*=8.5, 5.5, 1.5 Hz, H-4), 3.76 (1H, ddd, *J*=8.5, 8.0, 7.5 Hz, H-5), 1.43 (3H, s, C(C*H*$_3$)$_2$), 1.40 (3H, s, C(C*H*$_3$)$_2$), 1.40 (2H, tt, *J*=7.0, 7.0 Hz, H$_2$-7), 1.32–1.27 (4H, overlapping, 2×CH$_2$), 0.86 (3H, t, *J*=7.0 Hz, H$_3$-10). Anal. Calcd. for $C_{13}H_{22}O_3$: C, 68.99; H, 9.79. Found: C, 69.26; H, 9.78.

Further elution afford the (*E*,4*R*,5*R*)-4,5-isopropylidenedioxydec-2-enol **6a** (573 mg; Y 53%): an oil; $[\alpha]_D^{20}$=+7.3; ^{1}H-NMR δ 5.92 (1H, dt, *J*=15.5, 5.0 Hz, H-2), 5.66 (1H, ddt, *J*=15.5, 8.0, 2.0 Hz, H-3), 4.13 (2H, dd, *J*=5.0, 2.0 Hz, H$_2$-1), 3.98 (1H, dd, *J*=8.0, 8.0 Hz, H-4), 3.64 (1H, dt, *J*=8.0, 6.0 Hz, H-5), 1.79 (1H, s, -OH), 1.51 (2H, dt, *J*=7.5, 6.0 Hz, H$_2$-6), 1.48–1.39 (2H, m, H$_2$-7), 1.38 (3H,

s, $C(CH_3)_2$), 1.37 (3H, s, $C(CH_3)_2$), 1.36–1.22 (4H, overlapping, $2\times CH_2$), 0.82 (3H, t, J=7.5 Hz, H_3-10). Anal. Calcd. for $C_{13}H_{24}O_3$: C, 68.38; H, 10.59. Found: C, 68.56; H, 9.81.

*ii. By DIBAL–H reduction of the esters **5a** and **5b** followed by oxidation with MnO_2.*

The ester **5a** (1.3 g; 4.8 mmol) dissolved in THF (10 mL) was treated with DIBAL–H (10.2 mL of a 1M solution in hexane) at −78°C for 2 h. The mixture was then warmed to room temperature and worked-up to afford the allylic alcohol **6a** (1 g) as a crude oil which was dissolved in hexane (50 mL) and treated with MnO_2 (2.9 g; 33.4 mmol) under vigorous stirring for 24 h. Filtration and evaporation of the solvent afforded, after chromatographic purification the aldehyde **7a** (946 mg; Y 87%); $[\alpha]_D^{20}$=+12.8; identical in all respects with that reported above.

A parallel sequence of DIBAL–H reduction and MnO_2 oxidation starting with the ester **5b** (1.25 g; 4.63 mmol), afforded the (*E*,4*S*,5*S*)-4,5-isopropylidenedioxydec-2-enal **7b** (921 mg; Y 88%): an oil; $[\alpha]_D^{20}$=−12.7, lit[5] −13.0; ^{1}H-NMR spectrum was superimposable with that of its enantiomer **7a**. Anal. Calcd. for $C_{13}H_{22}O_3$: C, 68.99; H, 9.79. Found: C, 68.87; H, 9.84.

The hydrolysis of the acetonide group of the obtained aldehydes **7a** and **7b**, performed as described in general procedure, afford the corresponding dihydroxyaldehydes **1a** (467 mg; Y 60%; ee 98%) and **1b** (470 mg; Y 62%; ee 96%): $[\alpha]_D^{20}$ +52.5 for **1a** and $[\alpha]_D^{20}$=−51.9 for **1b**.

*Synthesis of ethyl (2S,3R)- and (2R,3S)-dihydroxyoctanoate **9a** and **9b***

AD reaction was performed on ethyl (*E*)-oct-2-enoate **8** (510 mg; 3 mmol) with AD-mix-β to afford, after chromatographic purification (eluting with hexane/ethyl acetate; 6:4; v/v), the ethyl (2*S*,3*R*)-2,3-dihydroxyoctanoate (**9a**; 544 mg; Y 89%, ee 95%): an oil; $[\alpha]_D^{20}$ +10.2; ^{1}H-NMR δ 4.26 (2H, q, J=7.0 Hz, OCH_2CH_3), 4.05 (1H, d, J<2.0 Hz, H-2), 3.85 (1H, ddd, J=8.0, 8.0, 2.0 Hz, H-3), 1.62–1.54 (2H, AB system, H-4a and H-4b), 1.5–1.26 (6H, overlapping, H_2-5, H_2-6 and H_2-7), 1.39 (3H, t, J=7.0 Hz, OCH_2CH_3), 0.87 (3H, t, J=7.0 Hz, H_3-8). Anal. Calcd. for $C_{10}H_{20}O_4$: C, 58.80; H, 9.87. Found: C, 59.04; H, 9.75.

A parallel AD reaction performed using AD-mix-α afford, after chromatographic purification, ethyl (2*R*,3*S*)-2,3-dihydroxyoctanoate **9b** (532 mg; Y 87%, ee 95%): an oil; $[\alpha]_D^{20}$=−9.8; ^{1}H-NMR spectrum was superimposable with that of its enantiomer **9a**. Anal. Calcd. for $C_{10}H_{20}O_4$: C, 58.80; H, 9.87. Found: C, 58.68; H, 9.80.

Both these compounds were synthesised by Sharpless who tentatively assigned their stereochemistry by comparison of their specific rotations with those of closely related diols and comparing the retention time of their bis-MTPA esters.[11b]

*Synthesis of ethyl (2S,3R)- and (2R,3S)-2,3-isopropylidenedioxyoctanoate **10a** and **10b***

Acetonisation of the dihydroxyester **10a** (408 mg; 2 mmol) according to the general procedure afforded the ethyl (2*S*,3*R*)-2,3-isopropylidenedioxyoctanoate **10a** (429 mg; Y 88%): an oil; ^{1}H-NMR δ 4.26–4.17 (2H, AB system, OCH_2CH_3), 4.11–4.06 (2H, AB system, H-2 and H-3), 1.72 (1H, ddt, J=6.0, 6.0, 4.0 Hz, H-4a), 1.66 (1H, ddt, J=6.0, 6.0, 2.0 Hz, H-4b) 1.44 (3H, s, $C(CH_3)_2$), 1.41 (3H, s, $C(CH_3)_2$), 1.27 (3H, dd, J=7.0, 7.0 Hz, OCH_2CH_3), 0.87 (3H, t, J=7.0 Hz, H_3-8). Anal. Calcd. for $C_{13}H_{24}O_4$: C, 63.91; H, 9.90. Found: C, 63.96; H, 9.82.

A parallel acetonisation of the dihydroxyester **10b** (408 mg; 2 mmol) afforded the ethyl (2*R*,3*S*)-2,3-isopropylidenedioxyoctanoate **10b** (415 mg; Y 85%): an oil; ^{1}H-NMR spectrum was superimposable with that of its enantiomer **10a**. Anal. Calcd. for $C_{13}H_{24}O_4$: C, 63.91; H, 9.90. Found: C, 63.84; H, 10.12.

*Homologation of the ethyl (2S,3R)- and (2R,3S)-2,3-isopropylidenedioxyoctanoate **10a** and **10b***

n-BuLi (2 mL of a 2.5M solution in hexane; 5 mmol) was added dropwise to a solution of triethyl phosphonoacetate (655 mg; 2.9 mmol) in dry dichloromethane (20 mL) at −78°C, the mixture was then stirred at the same temperature for 30 min. A solution of the ester **10a** (244 mg; 1 mmol) in dichloromethane (2 mL) was then added slowly and the mixture was stirred for 1 h. At this time

DIBAL–H (5.6 mL of a 1M solution in hexane; 5.6 mmol) was added dropwise. The mixture was stirred for 12 h at −78°C, warmed up to room temperature and then refluxed for 1 h. After a quenching with saturated aqueous NH_4Cl, it was worked-up and the product purified by flash chromatography (eluting with hexane/ethyl acetate; 7:3; v/v) to give the ethyl (*E*,4*R*,5*R*)-4,5-isopropylidenedioxydec-2-enoate **5a** (195 mg; Y 72%): an oil; $[\alpha]_D^{20}$=+12.5; ^{1}H-NMR spectrum was identical in all respects with that reported above. Compound **5a** was transformed, as previously described, into dihydroxyaldehyde **1a**: $[\alpha]_D^{20}$=+52.5, ee 95%.

A parallel reaction of the dihydroxyester **10b** (244 mg; 1 mmol) afforded the ethyl (*E*,4*S*,5*S*)-4,5-isopropylidenedioxydec-2-enoate **5b** (190 mg; Y 70%): an oil; $[\alpha]_D^{20}$=−12.3 and then the dihydroxyaldehyde **1b**: $[\alpha]_D^{20}$=−52.1, ee 95%.

*Synthesis of ethyl (2S,3R)-dihydroxyoctanoate cyclic sulfate **11***

The dihydroxyester **9a** (408 mg; 2 mmol), dissolved in dichloromethane (23 mL) containing triethylamine (0.6 mL; 4.6 mmol), was cooled in an ice bath, and thionyl chloride (0.2 mL; 2.5 mmol) was added. The mixture was stirred for 10 min and the reaction was quenched by adding water (15 mL). The organic phase was separated and the aqueous phase was extracted with dichloromethane (3×30 mL). The crude cyclic sulphite obtained after usual work-up was then dissolved in a solution of CCl_4, MeCN and H_2O (20 mL; 2:2:3; v/v/v) and $RuCl_3$ $3H_2O$ (29 mg; 0.11 mmol) was added followed by $NaIO_4$ (0.82 g; 3.8 mmol). The mixture was stirred at 0°C for 1 h and then worked-up and filtered through a short column of silica to afford the pure cyclic sulphate **11** (468 mg; Y 88%): an oil $[\alpha]_D^{20}$=+48.8.

*Opening of the cyclic sulfate **11** with ammonium benzoate*

To a solution of the cyclic sulfate **11** (266 mg; 1 mmol) in acetone (10 mL), ammonium benzoate (278 mg; 2 mmol) was added and the resulting mixture was stirred at room temperature for 48 h. After evaporation of the solvent under reduced pressure, the residue was stirred with diethylether (10 mL) and aqueous sulfuric acid (10 mL; 20%) at room temperature for 12 h. Usual work-up afforded, after chromatographic purification (eluting with hexane/ethyl acetate, 6:4; v/v), an unseparable mixture of 2 and 3 benzoyl derivatives (66:34; ^{1}H-NMR) of ethyl (2*R*,3*R*)-2,3-dihydroxyoctanoate **12** (290 mg; Y 94%): ^{1}H-NMR (2-benzoyl derivative) δ 5.24 (1H, d, *J*=4.3 Hz, H-2), 4.15 (1H, ddd, *J*=8.5, 4.3, 4.3 Hz, H-3); (3-benzoyl derivative) δ 5.30 (1H, ddd, *J*=8.5, 4.3, 4.3 Hz, H-3), 4.38 (1H, d, *J*=4.3 Hz, H-2).

A sample of the obtained product was transformed in the corresponding dibenzoate **13** which, by chiral HPLC analysis, showed a enantiomeric excess of 90%.

*Synthesis of (E)-1-[(tert-butyldimethylsilyl)oxy]oct-2-ene **14***

A solution of 2-octen-1-ol (2 g; 15.6 mmol) in dichloromethane (60 mL) containing triethylamine (4 mL) and 4-dimethylaminopyridine (20 mg) was treated with *tert*-butyldimethylchlorosilane (3.5 g; 23 mmol) for 24 h at room temperature. After usual work-up, the (*E*)-1-[(*tert*-butyldimethylsilyl)oxy]oct-2-ene **14** (3.58 g; Y 95%) was obtained: an oil; ^{1}H-NMR, δ 5.61 (1H, dt, *J*=15.0, 7.0 Hz, H-3), 5.50 (1H, dt, *J*=15.0, 5.0 Hz, H-2), 4.10 (2H, d, *J*=5.0 Hz, H_2-1), 2.00 (2H, dt, *J*=7.0, 7.5 Hz, H-4), 1.30 (2H, tt, *J*=15.0, 7.5 Hz, H-5), 1.29–1.21 (4H, m, 2×CH_2), 0.89 (9H, s, $Si(CH_3)_2C(CH_3)_3$), 0.86 (3H, t, *J*=6.0 Hz, H_3-8), 0.10 (6H, s, $Si(CH_3)_2C(CH_3)_3$. Anal. Calcd. for $C_{14}H_{30}OSi$: C, 69.35; H, 12.47. Found: C, 69.68; H, 12.61.

*Synthesis of (2R,3R)- and (2S,3S)-1-[(tert-butyldimethylsilyl)oxy]octane-2,3-diol **15a** and **15b***

AD reaction was performed on (*E*)-1-[(*tert*-butyldimethylsilyl)oxy]oct-2-ene **14** (726 mg; 3 mmol) with AD-mix-β to afford, after usual work-up and chromatographic purification (eluting with hexane/ethyl acetate; 7:3; v/v), the (2*R*,3*R*)-1-[(*tert*-butyldimethylsilyl)oxy]octane-2,3-diol **15a** (762 mg; Y 92%; ee 96%, detected by chiral HPLC after dibenzoylation.): an oil $[\alpha]_D^{20}$=+8.5; ^{1}H-NMR δ 3.75 (1H, dd, *J*=10.0, 5.0 Hz, H-1a), 3.67 (1H, dd, *J*=10.0, 5.0 Hz, H-1b), 3.64–3.59 (1H, m, H-3),

3.48–3.44 (1H, m, H-2), 1.22 (3H, t, *J*=7.0 Hz, H_3-8), 0.89 (9H, s), 0.10 (6H, s). Anal. Calcd. for $C_{14}H_{32}O_3Si$: C, 60.82; H, 11.67. Found: C, 60.78; H, 11.52.

A parallel reaction of the silyloxyalkene **14** (726 mg; 3 mmol) with AD-mix-α, afforded the (2*S*,3*S*)-1-[(*tert*-butyldimethylsilyl)oxy]octane-2,3-diol **15b** (745 mg; Y 90%; ee 95%): an oil $[\alpha]_D^{20}=-8.7$; ^{1}H-NMR spectrum was superimposable with those of **15a**. Anal. Calcd. for $C_{14}H_{32}O_3Si$: C, 60.82; H, 11.67. Found: C, 60.54; H, 11.80.

*Synthesis of (2R,3R)- and (2S,3S)-1-[(tert-butyldimethylsilyl)oxy]-octane-2,3-diol cyclic sulphate **16a** and **16b***

The silyloxydiol **15a** (612 mg; 2 mmol), dissolved in dichloromethane (23 mL) containing triethylamine (0.64 mL; 4.6 mmol), was cooled in an ice bath, and thionyl chloride (0.2 mL; 2.5 mmol) was added. The mixture was stirred for 10 min and the reaction was quenched by adding water (15 mL). The organic phase was separated and the aqueous phase was extracted with dichloromethane (3×30 mL). The crude cyclic sulphite obtained after usual work-up was then dissolved in a solution of CCl_4, MeCN and H_2O (20 mL; 2:2:3; v/v/v) and $RuCl_3$ $3H_2O$ (29 mg; 0.11 mmol) was added followed by $NaIO_4$ (0.82 g; 3.8 mmol). The mixture was stirred at 0°C for 1 h and then worked-up and filtered through a short column of silica to afford the pure cyclic sulphate **16a** (581 mg; Y 86%): an oil $[\alpha]_D^{20}=+27.9$; ^{1}H-NMR δ 4.82 (1H, ddt, *J*=8.4, 7.7, 4.2 Hz, H-3), 4.52 (1H, ddt, *J*=4.9, 4.2, 7.7 Hz, H-2), 3.90 (1H dd, *J*=11.9, 4.9 Hz, H-1a), 3.87 (1H, dd, *J*=11.9, 4.2 Hz, H-1b), 1.89 (1H, ddt, *J*=19.0, 4.9, 10.0 Hz, H-4a), 1.76 (1H, ddt, *J*=10.0, 6.0, 4.2 Hz, H-4b), 0.88 (9H, s), 0.09 (3H, s), 0.08 (3H, s). Anal. Calcd. for $C_{14}H_{30}O_5SSi$: C, 49.67; H, 8.93. Found: C, 49.73; H, 8.86.

A parallel reaction of the silyloxydiol **15b** (552 mg; 2 mmol) afforded cyclic sulphate **16b** (595 mg; Y 88%): an oil $[\alpha]_D^{20}=-27.5$; ^{1}H-NMR spectrum was superimposable with that of **16a**. Anal. Calcd. for $C_{14}H_{30}O_5SSi$: C, 49.67; H, 8.93. Found: C, 49.42; H, 9.04.

*Synthesis of (2R,3R)- and (2S,3S)-1-(phenylthio)-2,3-octanediol **17a** and **17b***

The cyclic sulphate **16a** (676 mg; 2 mmol) was dissolved in THF (20 mL) and tetrabutylammonium fluoride trihydrate (650 mg; 2 mmol) was added. The mixture was stirred at room temperature under argon. After 30 min, a THF solution of PhSNa (prepared from PhSH [0.28 mL; 2.7 mmol] and NaH [60%, 109 mg; 2.7 mmol] in THF [10 mL]) was added. The mixture was stirred for 2 h at room temperature. Concentrated sulphuric acid (0.1 mL; 3.6 mmol) was then added. After stirring for 30 min at room temperature, usual work-up and chromatographic purification (eluting with hexane/ethyl acetate; 7:3; v/v), afforded the (2*R*,3*R*)-1-(phenylthio)-2,3-octanediol **17a** (437 mg; Y 86%): m.p. 96–98°C; $[\alpha]_D^{20}=-37.7$; ^{1}H-NMR δ 7.39–7.21 (5H, m), 3.74 (1H, dt, *J*=6.0, 3.5 Hz, H-3), 3.57 (1H, ddt, *J*=10.0, 3.5, 3.5 Hz, H-2), 3.21 (1H dd, *J*=14.0, 3.5 Hz, H-1a), 2.95 (1H, dd, *J*=14.0, 10.0 Hz, H-1b), 1.45–1.40 (2H, m, H_2-4), 0.86 (3H, t, *J*=7.0 Hz, H_3-8). Anal. Calcd. for $C_{14}H_{22}O_2S$: C, 66.10; H, 8.72. Found: C, 66.14; H, 8.86.

A parallel reaction of the cyclic sulphate **16b** (676 g; 2 mmol) afforded (2*S*,3*S*)-1-(phenylthio)-2,3-octanediol **17b** (427 mg; Y 84%): m.p. 96–98°C; $[\alpha]_D^{20}=+36.5$; ^{1}H-NMR spectrum was superimposable with that of **17a**. Anal. Calcd. for $C_{14}H_{22}O_2S$: C, 66.10; H, 8.72. Found: C, 66.25; H, 8.58.

*Synthesis of (2R,3R)- and (2S,3S)-1-(phenylthio)-2,3-isopropylidenedioxyoctane **18a** and **18b***

Acetonisation of the diol **17a** (508 mg; 2 mmol) according to the general procedure afforded, after column chromatography (eluting with hexane/ethyl acetate; 9:1; v/v), the (2*R*,3*R*)-1-(phenylthio)-2,3 isopropylidenedioxyoctane **18a** (506 mg; Y 86%): an oil; $[\alpha]_D^{20}=+6.2$; ^{1}H-NMR, δ 7.39–7.21 (5H, m), 4.19 (1H, ddd, *J*=7.0, 7.0, 1.4 Hz, H-2), 4.11 (1H, dt, *J*=7.0, 5.6 Hz, H-3), 3.05 (1H, dd, *J*=13.3, 7.7 Hz, H-1a), 2.98 (1H, dd, *J*=13.3, 5.6 Hz, H-1b), 1.44 (3H, s), 1.32 (3H, s). Anal. Calcd. for $C_{17}H_{26}O_2S$: C, 69.34; H, 8.90. Found: C, 69.45; H, 8.81.

A parallel acetonisation of the diol **17b** (508 mg; 2 mmol) afforded the (2*S*,3*S*)-1-(phenylthio)-2,3 isopropylidenedioxyoctane **18** (506 mg; Y 86%): an oil; $[\alpha]_D^{20}=-6.0$; ^{1}H-NMR spectrum was

superimposable with that of its enantiomer **18a**. Anal. Calcd. for $C_{17}H_{26}O_2S$: C, 69.34; H, 8.90. Found: C, 69.18; H, 8.98.

*Synthesis of (2R,3R)- and (2S,3S)-1-acetoxy-1-(phenylthio)-2,3-isopropylidenedioxyoctane **19a** and **19b***

A solution of *m*-chloroperoxybenzoic acid (344 mg; 2 mmol) in dichloromethane (5 mL) was added dropwise to a solution of compound **18a** (588 mg; 2 mmol) in dichloromethane (20 mL) at −78°C. After 2 h the reaction was quenched by aqueous NaOH (5 mL of a 1M solution) and worked-up to afford the crude (2*R*,3*R*)-2,3-isopropylidenedioxyoctilphenylsulphoxide (580 mg). This crude sulphoxide, dissolved in acetic anhydride (20 mL) containing sodium acetate (1.3 g; 15.8 mmol), was refluxed under a argon atmosphere for 24 h. The mixture was concentrated under reduced pressure, diluted with dichloromethane (20 mL) and filtered. Usual work-up and column chromatography (eluting with hexane/ethyl acetate; 6:4; v/v) afforded the (2*R*,3*R*)-1-acetoxy-1-(phenylthio)-2,3-isopropylidenedioxyoctane **19a** (626 mg; Y 89%) as a diastereomeric mixture: an oil; ^{1}H-NMR (major diastereomer) δ 7.39 (2H, d, *J*=7.0 Hz), 7.27 (2H, dd, *J*=7.0, 7.0 Hz), 7.21 (1H, ddd, *J*=7.0, 7.0, 1.4 Hz,), 6.06 (1H, d, *J*=7.0 Hz, H-1), 4.19 (1H, dd, *J*=7.0, 5.5 Hz, H-2), 4.16–4.10 (1H, m, H-3), 2.07 (3H, s, -OCOC*H*$_3$), 1,43 (3H, s, C(C*H*$_3$)$_2$), 1.29 (3H, s, C(C*H*$_3$)$_2$), 0.88 (3H, t, *J*=7.0 Hz, H$_3$-8); (minor diastereomer) δ 7.59–7.47 (2H, m), 7.32–7.27 (3H, m), 6.05 (1H, d, *J*=5.0 Hz, H-1), 4.16–4.10 (2H, overlapping, H-2 and H-3), 2.02 (3H, s, OCOC*H*$_3$), 1.48 (3H, s, C(C*H*$_3$)$_2$), 1.31 (3H, s, C(C*H*$_3$)$_2$), 0.86 (3H, t, *J*=7.0 Hz, H$_3$-8). Anal. Calcd. for $C_{19}H_{28}O_4S$: C 64.74, H 8.01. Found: C 64.48, H 8.13.

A parallel reaction sequence on the diol **18b** (588 mg; 2 mmol) afforded the (2*S*,3*S*)-1-acetoxy-1-(phenylthio)-2,3-isopropylidenedioxyoctane **19b** (605 mg; Y 86%) ^{1}H-NMR spectrum was superimposable with that of **19a**. Anal. Calcd. for $C_{19}H_{28}O_4S$: C 64.74, H 8.01. Found: C 64.83, H 7.89.

*Synthesis of (2R,3R)- and (2S,3S)-2,3-isopropylidenedioxyoctanal **20a** and **20b***

To a solution of compound **19a** (704 mg; 2 mmol) in dichloromethane (30 mL), DIBAL–H (4.3 mL of a 1M solution in hexane; 4.3 mmol) was added at −78°C and the resulting mixture was stirred for 2 h. Then aqueous saturated NH_4Cl solution was added and the mixture was allowed to warm to room temperature. Usual work-up afforded, after column chromatography (eluting with hexane/ethyl acetate; 8:2; v/v), the (2*R*,3*R*)-2,3-isopropylidenedioxyoctanal **20a** (365 mg; Y 89%): an oil; $[\alpha]_D^{20}$=+7.2; the specific rotation of this aldehyde changes fast on standing in solution and slowly when stored as pure oil at −20°C; ^{1}H NMR δ 9.61 (1H, s, *J*=3.5 Hz, H-1), 4.31 (1H, ddd, *J*=8.5, 7.0, 4.5 Hz, H-3), 4.22 (1H, dd, *J*=7.0, 3.5 Hz, H-2), 1.57 (3H, s, C(C*H*$_3$)$_2$), 1.39 (3H, s, C(C*H*$_3$)$_2$), 0.87 (3H, t, *J*=7.0 Hz, H$_3$-9).

A parallel reaction sequence on the compound **19b** (704 mg; 2 mmol) afforded the (2*S*,3*S*)-2,3-isopropylidenedioxyoctanal **20b** (348 mg; Y 87%): an oil; $[\alpha]_D^{20}$=−7.0; ^{1}H-NMR spectrum was superimposable with that of **20a**.

*Synthesis of (E,4S,5R)- and (E,4R,5S)-4,5-dihydroxydec-2-enals **1c** and **1d***

The aldehyde **20a** (300 mg; 1.5 mmol) was homologised by Wittig reaction with (formylmethylene)triphenylphosphorane as described previously[5] to afford, after regeneration of the diolic system, the (*E*,4*S*,5*R*)-4,5-dihydroxydec-2-enal **1c** (145 mg; Y 52%, ee 96%): an oil; $[\alpha]_D^{20}$=−33.1, lit[5] −33.5; ^{1}H-NMR δ 9.52 (1H, d, *J*=7.5 Hz, H-1), 6.85 (1H, dd, *J*=15.5, 5.0 Hz, H-3), 6.36 (1H, ddd, *J*=15.5, 7.5, 1.5 Hz, H-2), 4.38 (1H, ddd, *J*=5.0, 5.0, 1.5 Hz, H-4), 3.78 (1H, ddd, *J*=8.0, 4.5, 4.5 Hz, H-5), 0.85 (3H, t, *J*=7.0 Hz, H$_3$-10); ^{13}C-NMR, δ 193.63 (C1), 154.81 (C3), 132.72 (C2), 74.171 (C4 and C5), 32.11, 31.62, 25.45, 22.46, 13.90. Anal. Calcd. for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.61; H, 9.67.

A similar sequence of reaction, starting from aldehyde **20b**, afforded the (*E*,4*R*,5*S*)-4,5-dihydroxydec-2-enal **1d** (148 mg; Y 53%, ee 95%): an oil; $[\alpha]_D^{20}$=+33.2, lit[5] +33.9; ^{1}H-NMR

spectrum was superimposable with that of **1c**. Anal. Calcd. for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.58; H, 9.89.

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References

1. Benedetti, A.; Comporti, M.; Fulceri, R.; Esterbauer, H. *Biochem. Biophys. Acta*, **1984**, *792*, 172.
2. Esterbauer, H.; Zollner, H.; Schaur, R.J. *Membrane Lipid Oxidation*; Vigo-Pelfrey, C.; Boca Raton, FL: CRC Press; **1990**; *Vol 1*, 239.
3. Esterbauer, H.; Schaur, R.J.; Zollner, H. *Free Radical Biol. and Med.*, **1991**, *11*, 81.
4. Allevi, P.; Cajone, F.; Ciuffreda, P.; Anastasia, M. *Tetrahedron Lett.*, **1995**, *36*, 1347.
5. Allevi, P.; Ciuffreda, P.; Tarocco, G.; Anastasia, M. *Tetrahedron: Asymmetry*, **1995**, *6*, 2357.
6. For a recent review on the asymmetric dihydroxylation see: (a) Becker, H.; Soler, M.A.; Sharpless, K.B. *Tetrahedron*, **1995**, *51*, 1345. (b) Kolb, H.C.; VanNieuwenhze, M.S.; Sharpless, K.B. *Chem. Rev.*, **1994**, *94*, 2483.
7. Ko, S.Y.; Lerpiniere, J. *Tetrahedron Lett.*, **1995**, *36*, 2101. (b) Ko, S.Y.; Malik, M.; Dickinson, A.F. *J. Org. Chem.*, **1994**, *59*, 2570.
8. Kim, B.M.; Sharpless, K.B. *Tetrahedron Lett.*, **1989**, *30*, 655. (b) Gao, Y.; Sharpless, K.B. *J. Am. Chem. Soc.*, **1988**, *110*, 7538.
9. Becker, H.; Soler, M.A.; Sharpless, K. B. *Tetrahedron*, **1995**, *51*, 1345.
10. Taylor, E.C.; Chiang, C.-S. *Synthesis*, **1977**, 467.
11. Sinha, S.C.; Sinha-Bagchi, A.; Keinan, E. *J. Org. Chem.*, **1993**, *58*, 7789. (b) Sharpless, K.B.; Amberg, W.; Bennani, Y.L.; Crispino, G.A.; Hartung, J.; Jeong, K.S.; Kwong, H.L.; Morikawa, K.; Wang, Z.M.; Xu, D.; Zhang, X.L. *J. Org. Chem.*, **1992**, *57*, 2768.
12. Villieras, J.; Rambaud, M. *Synthesis*, **1983**, 300.
13. Dale, J.A.; Dull, D.L.; Mosher, H.S. *J. Org. Chem.*, **1969**, *34*, 2543. (b) Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.*, **1991**, *113*, 4092.
14. Takacs, J.M.; Helle, M.A.; Seely, F.L. *Tetrahedron Lett.*, **1986**, *27*, 1257.
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16. Still, W.C.; Kahn, M.; Mirta, A. *J. Org. Chem.*, **1978**, *43*, 2923.

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