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STEREOSELECTIVE TOTAL SYNTHESIS OF THE NONENOLIDE (+)-MICROCARPALIDE[#]

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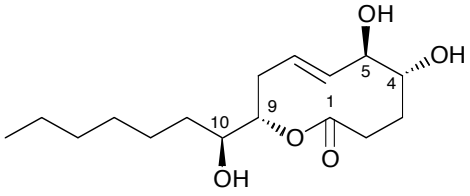
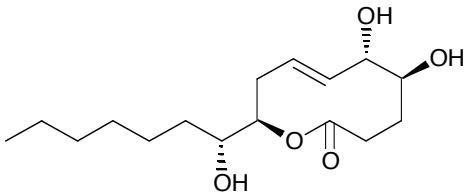
Abstract – The enantiomer [(+)-**1**] of the nonenolide natural product microcarpalide [(–)-**1**] has been prepared from (*S*)-malic acid (**3**) and 3-decyn-1-ol (**11**) *via* a sixteen step sequence involving, *inter alia*, two metathesis processes.

INTRODUCTION

In 2001 Hemscheidt *et al*. reported[1] the isolation of the nonenolide microcarpalide [(–)-**1**] from a thus far unidentified endophytic fungus found on plants growing in Hawaii. The compound displays anti-cytoskeletal activity in that it acts as a microfilament disrupting agent and yet it is only weakly cytotoxic to mammalian cells. As such the compound has therapeutic potential although this is only likely to be realized if effective synthetic protocols for accessing microcarpalide are developed. We have recently reported[2] a chemoenzymatic synthesis of the 12-membered macrolide cladospolide A that relied upon a ring closing metathesis (RCM) reaction to construct a nonenolide precursor which was then subject to a simple homologation sequence so as to provide the target compound. Such studies, as well as those of Fürstner,[3] prompted us to consider constructing the *E*-oxacyclodec-7-ene ring associated with **1** by the same means. The relevant substrate for the RCM process would be constructed by an esterification



(–)-**1**



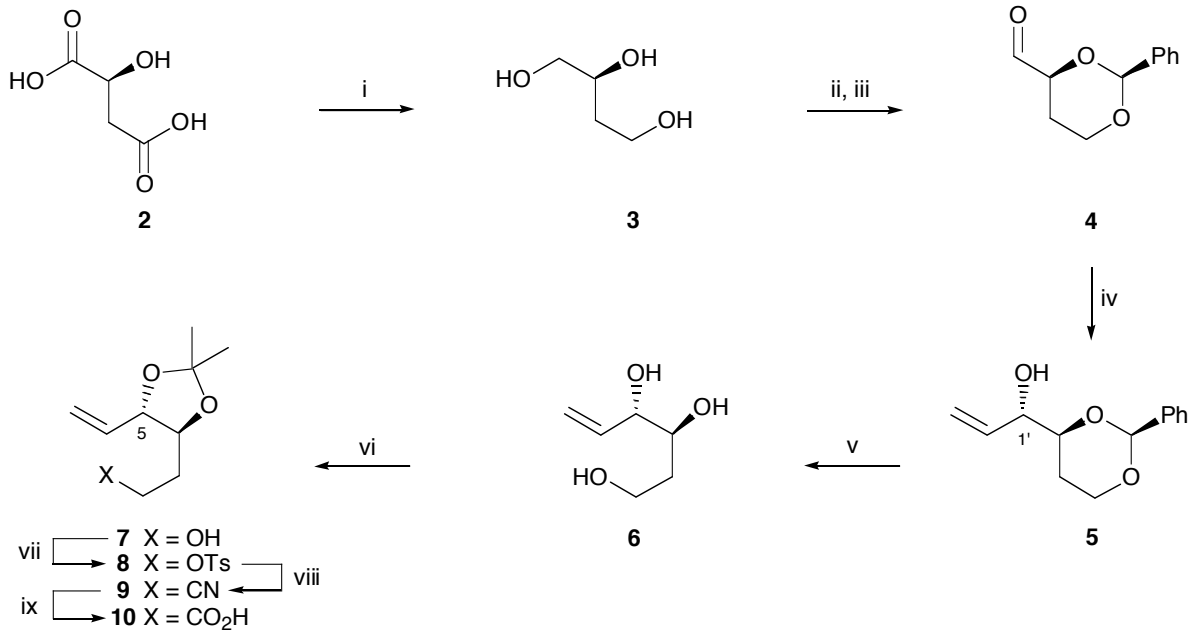
(+)-**1**

[#] *Dedicated to Professor L. A. Paquette on the occasion of his 70th birthday and in recognition of his seminal contributions to so many aspects of organic chemistry.*

reaction involving the coupling of a terminally unsaturated alcohol incorporating what would become the hydroxylatedheptanyl side-chain of **1** with a protected form of the relevant 4,5-dihydroxyhept-6-ene-carboxylic acid. Herein we describe the implementation of such ideas which have led to the synthesis of *ent*- or (+)-**1**. Whilst the synthetic protocols employed are such that (–)-**1** is equally accessible, we sought the unnatural enantiomer so as to undertake biological evaluation of this material and thus shed some light on the SAR within this interesting class of compound. During the course of our work two syntheses of (–)-microcarpalide were reported[4,5] and these also employ an RCM reaction as the key step. However, each of the reaction sequences used is somewhat longer than the one reported here.

RESULTS AND DISCUSSION

The synthesis of a suitably protected form of the 4,5-dihydroxyhept-6-enecarboxylic acid fragment required for the foreshadowed esterification reaction is shown in Scheme 1 and starts with readily available (*S*)-malic acid (**2**). This chiron was easily reduced, by established procedures,[6] to the known[6] triol (**3**) (100%) which was converted into the corresponding benzylidene acetal[7] and the remaining free hydroxyl group oxidized, using the oxammonium salt derived from 4-AcN-TEMPO,[8] to give the



Scheme 1. *Reagents and conditions*: (i) BH_3•DMS (0.3 mol equiv.), $B(OMe)_3$ (0.3 mol equiv.), THF, 0–18 °C, 16 h; (ii) PhCHO (1.4 equiv.), $(MeO)_3CH$ (1.4 mol equiv.), TFA (cat.), CH_2Cl_2, 18 °C, 24 h; (iii) 4-AcN-TEMPO (10 mol %), $PhI(OAc)_2$ (1.05 mol equiv.), CH_2Cl_2, 18 °C, 14 h; (iv) $(CH_2{=}CH)_2Zn$ (3.6 mol equiv.), THF, –50 °C, 20 h; (v) 1 M aq. HCl, THF, 18 °C, 2 h; (vi) 2,2-DMP (1.3 mol equiv.), *p*-TsOH (cat.), CH_2Cl_2, 18 °C, 2.5 h; (vii) *p*-TsCl (1.4 mol equiv.), pyridine, DMAP (20 mol %), 0–5 °C, 11 h; (viii) KCN (2 mol equiv.), DMF, 60 °C, 3 h; (ix) KOH (30 mol equiv.), 4 : 3 v/v MeOH–H_2O, 66 °C, 16 h.

previously reported[9] aldehyde (**4**) (70%). After considerable experimentation with a range of vinylating agents (Table 1) it was established that reaction of this latter compound with divinylzinc[10] proceeded with useful levels of diastereoselection to give an inseparable 3 : 1 mixture of allylic alcohol (**5**) and its C1'-epimer (92% combined yield). Oxidation of this mixture to the corresponding enone and 1,2-reduction of the latter (with DIBAL-H) gave material more highly enriched in compound (**5**) but the poor overall yields involved meant this was not a viable process. The acetal moiety associated with this mixture was cleaved under standard conditions and the resulting triol (**6**) and its epimer (87% combined yield) converted into the corresponding and chromatographically separable acetonide (**7**) (50%) and its C5-epimer (20%). The readily derived tosylate (**8**, 100%) of **7** was treated with potassium cyanide in DMF and the ensuing highly volatile nitrile (**9**) was then hydrolysed to the acid (**10**) (88% from **8**). The enantiomer of compound (**10**) has been prepared previously.[4,11]

Table 1. Vinylating agents employed in attempts to effect diastereoselective conversion of aldehyde (**4**) into allylic alcohol (**5**)

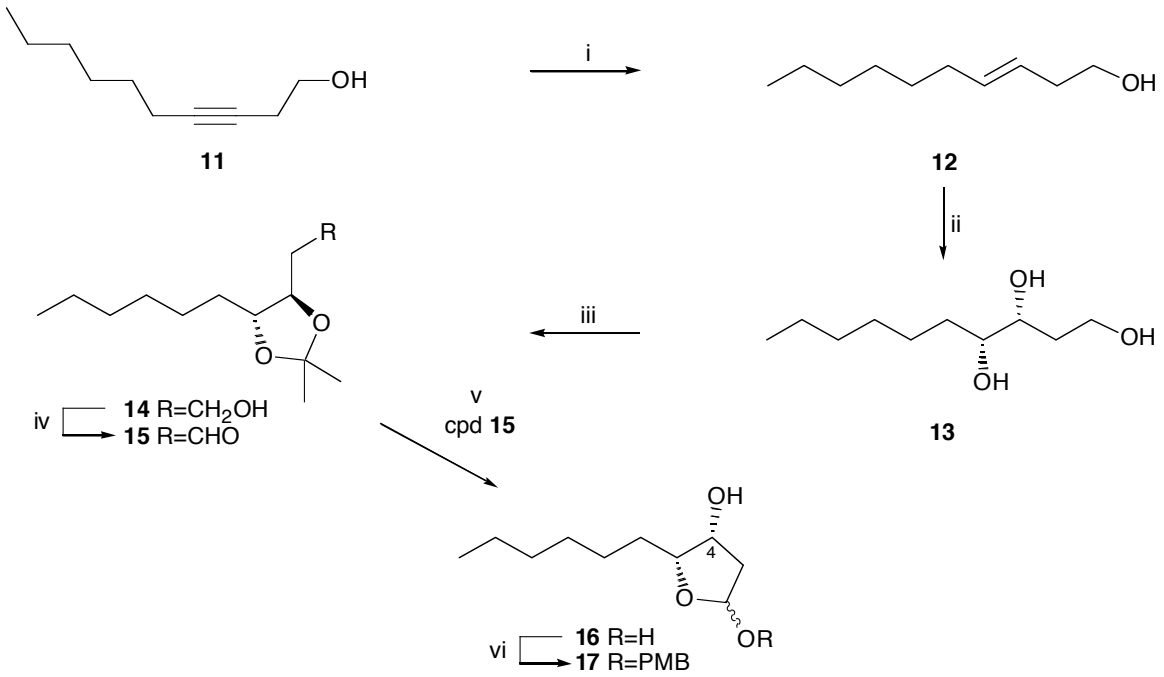
Entry	Reagent	Solvent	Temp. (°C)	Time (h)	Ratio of **5** : 1'-*epi* **5**[a]	Yield (%)
1	$BrMg(CH{=}CH_2)$	THF, Et_2O	–78 to –50	5	0.8 : 1	61
2	$Li(CH{=}CH_2)$	Et_2O	–100	8	0.3 : 1	67
3	$Cl_2Ce(CH{=}CH_2)$	THF	–50	2	0.7 : 1	52
4	$TiCl_4$, $(CH_2{=}CH)SnBu_3$	CH_2Cl_2	0	3	–	decomp
5	$BrMg(CH{=}CH_2)$, $CuBr{\bullet}S(CH_3)_2$	Et_2O	–78 to 18	16	–	complex mixture
6	$Zn(CH{=}CH_2)_2$	THF	–50	20	3 : 1	92[b]

[a] Ratio determined by ^{1}H NMR spectral analysis

[b] Yield at 72% conversion

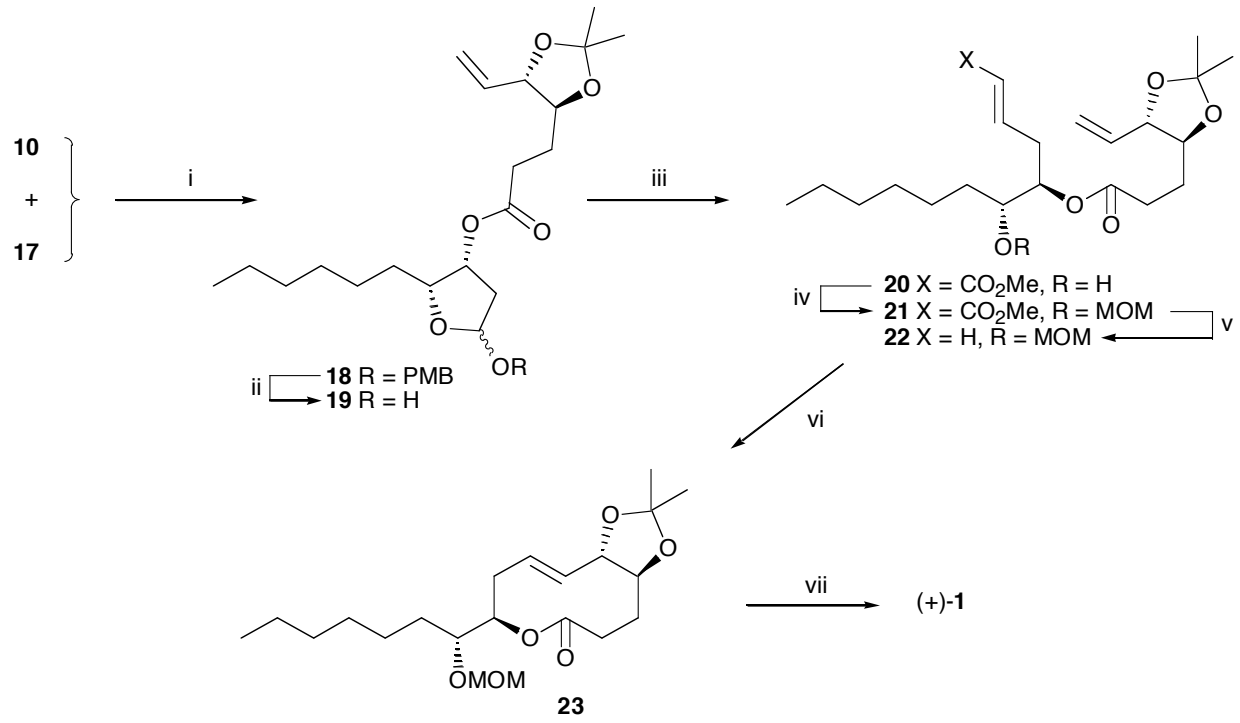
The alcohol required for coupling with acid (**10**) was prepared by the route shown in Scheme 2 which starts with the $LiAlH_4$-promoted and stereoselective reduction of commercially available alkyne (**11**) to the *E*-alkene (**12**)[12] (86%). Asymmetric dihydroxylation (AD)[13] of the latter compound using AD-mix-β afforded the crystalline triol (**13**) (94%). The ee of this compound could not be determined in any direct sense but was presumed to be rather high (>90%) by analogy with related conversions.[13] The absolute stereochemistries at the newly introduced stereogenic centres in compound (**13**) were initially assigned using the Sharpless mnemonic[13] and ultimately confirmed by the successful exploitation of this compound in the synthesis of target (+)-**1**. Conversion of compound (**13**) into the corresponding acetonide (**14**)

(77%) was accomplished by standard methods and the latter oxidized to aldehyde (**15**) (85%) using the oxammonium salt derived from 4-AcN-TEMPO.[8] Acid-catalysed hydrolysis of the latter material then afforded the lactol (**16**) (70%) which was obtained as a varying mixture of anomers. Attempts to acylate the C4 hydroxyl within compound (**16**) using various activated forms of acid (**10**) all failed because of competing reaction at its anomeric counterpart. Consequently, the anomeric hydroxyl group within lactol (**16**) was protected as the corresponding *p*-methoxybenzyl ether (**17**) (70% of a 2.5 : 1 mixture of chromatographically separable anomers) using the acid-catalysed glycosidation conditions recently described by Vidari *et al.*[14]



Scheme 2. *Reagents and conditions*: (i) $LiAlH_4$ (3.4 mol equiv.), 3 : 1 v/v diglyme–THF, 0–140 °C, 72 h; (ii) AD-mix-β (1.4 g/mmol), $MeSO_2NH_2$ (1 mol equiv.), 1 : 1 v/v *t*-BuOH–H_2O, 0 °C, 17 h; (iii) 2,2-DMP (1.05 mol equiv.), *p*-TsOH (cat.), CH_2Cl_2, 18 °C, 1.5 h; (iv) 4-AcN-TEMPO (7 mol %), $PhI(OAc)_2$ (1.1 mol equiv.), CH_2Cl_2, 18 °C, 2 h; (v) 13.5 : 2 : 1 v/v/v AcOH–H_2O–THF, 50 °C, 6 h; (vi) PMB-OH (2 mol equiv.), *p*-TsOH (cat.), CH_2Cl_2, –15 °C, 20 h.

The final stages of the synthesis of the title compound are shown in Scheme 3 and began with a DCC/DMAP-promoted coupling[15] of compound (**10**) and the separated anomeric forms of **17** thus affording the corresponding ester (**18**) (86% from major anomer of **17**, 81% from other anomer). Removal of the PMB-group within each of the anomeric forms of the last compound was accomplished with DDQ in the presence of water thus affording lactol (**19**) (90–92%). Various attempts to effect Wittig-type methylenation of the open-chain form of this latter compound and thereby install the second double bond required for participation in the planned RCM reaction failed because of elimination of the acyl group.



Scheme 3. *Reagents and conditions*: (i) DCC (2 mol equiv.), DMAP (3.3 mol equiv.), CH_2Cl_2, 0–18 °C, 18 h; (ii) DDQ (4.5 mol equiv.), 1 : 10 v/v pH 7 aqueous phosphate buffer–THF, 18 °C, 3.5 h; (iii) $Ph_3P{=}C(H)CO_2Me$ (1.7 mol equiv.), toluene, 0 °C, 36 h; (iv) MOM–Cl (46 mol equiv.), DMAP (36 mol %), Hünig's base (49 mol equiv.), CH_2Cl_2, 0–18 °C, 3 h; (v) Grubbs' 2nd-gen. cat. (21 mol %), $CH_2{=}CH_2$ (1 atm.), CH_2Cl_2, 18 °C, 25 h; (vi) Grubbs' 1st-gen. cat. (20 mol %), CH_2Cl_2, 40 °C, 24 h; (vii) $(CH_2SH)_2$ (4 mol equiv.), $BF_3{\bullet}Et_2O$ (1 mol equiv.), CH_2Cl_2, 0 °C, 1 h.

Related difficulties encountered by Pandit *et al.*[16] in their synthesis of castanospermine were solved by employing a stabilized ylide and then engaging the resulting α,β-unsaturated ester in the necessary RCM process. To that end lactol (**19**) was reacted with methyl (triphenylphosphoranylidene)acetate thus affording the diene (**20**) (93%) the free hydroxyl group of which was protected as the corresponding MOM-ether (**21**) (92%). Unfortunately, compound (**21**) would not engage in the required RCM process so methods for converting this into its counterpart lacking the carbomethoxy group, *viz.* diene (**22**), were sought. The most effective means for achieving this conversion involved reaction of ester (**21**) with Grubbs' 2nd-generation catalyst[17] in the presence of an atmosphere of ethylene and in this manner the olefin cross metathesis (OCM) product (**22**) (100% at 22% conversion) was obtained without any contamination from RCM-type products that might have been be expected[4] to incorporate a *Z*-configured alkene. Compound (**22**) is the enantiomeric form of an advanced intermediate in Marco's synthesis[4] of microcarpalide and the final two steps of the synthesis of (+)-**1** followed this earlier work. Thus, an RCM reaction of compound (**22**) using Grubbs' first generation catalyst[18] afforded nonenolide (**23**) (23%) which, in keeping with Marco's observations on *ent*-**23**,[1] exists as a *ca.* 4 : 1 mixture of rotamers in $CDCl_3$ at 25 °C. However, the more significant product of the reaction was the chomatographically

separable *Z*-isomer (31%) of compound (**23**). Presumably, this is the thermodynamically more stable species and may well be generated by isomerization of congener (**23**) under the reaction conditions.[19] Subjection of compound (**23**) to global deprotection using Marco's conditions[4] afforded (+)-**1** (89%) which was identical, as judged by the usual spectroscopic criteria, with the natural product (**1**). In particular, a comparison (Table 2) of the ^{13}C NMR spectral data reported[1] for natural (–)-microcarpalide with those recorded for synthetically-derived (+)-**1** provides strong indications that these compounds are identical. Furthermore, these data indicate that, like the natural product, (+)-microcarpalide is obtained as a *ca*. 3.2 : 1 mixture of conformers. Of course, the optical rotation recorded for the synthetic material is of essentially the same magnitude, but opposite sign, to that reported[1] for the natural product.

Table 2. Comparison of the ^{13}C NMR chemical shift data recorded for natural and synthetic samples of microcarpalide

Natural product [(–)-**1**][1,*a*]				Synthetic material [(+)-**1**][*b*]	
Major conformer		Minor conformer		Major conformer	Minor conformer
δ (ppm)	assignment[1]	δ (ppm)	assignment[1]	δ (ppm)	δ (ppm)
176.4	C1	173.5	C1	176.3	173.5
134.6	C6	133.8	C6	134.5	133.7
126.7	C7	130.0	C7	126.6	129.9
79.7	C9	79.5	C5	79.5	79.6
73.4	C4	77.0	C4	73.3	76.9
72.8	C10	76.5	C9	72.8	76.4
72.4	C5	73.8	C10	72.4	73.7
36.7	C8	36.0	C2	36.7	35.9
34.2	C11	33.9	C11	34.1	33.8
32.5	C14	32.3	C14	32.5	32.2
30.0	C13	32.2	C8	29.9	32.1
29.1	C2	30.0	C13	29.9	31.2
26.5	C3	ND	–	26.4	ND
26.1	C12	26.1	C12	26.1	26.1
23.3	C15	23.3	C15	23.3	23.3
14.4	C16	14.4	C16	14.3	14.3

[*a*] Data obtained at 100 MHz using CD_3CN as solvent

[*b*] Data obtained at 125 MHz using CD_3CN as solvent

ND = not detectable

CONCLUDING REMARKS

The synthetic studies described here provide a potentially useful route to both enantiomeric forms of microcarpalide as well as various analogues. As such, comprehensive SAR studies on this interesting microfilament disrupting agent can now be contemplated. Furthermore, the present work serves to emphasize the utility of OCM and RCM processes in chemical synthesis.

EXPERIMENTAL

Unless otherwise specified, proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded on a Varian Gemini 300 or Varian Mercury 300 spectrometer operating at 300 MHz for proton and 75 MHz for carbon nuclei. Chemical shifts were recorded as δ values in parts per million (ppm). Spectra were acquired in deuterochloroform ($CDCl_3$) at 20 °C unless otherwise stated. For ^{1}H NMR spectra recorded in $CDCl_3$, the peak due to residual $CHCl_3$ (δ 7.26) was used as the internal reference while the central peak (δ 77.0) of the $CDCl_3$ triplet was used as the reference for proton-decoupled ^{13}C NMR spectra. ^{1}H NMR spectral data are recorded as follows: chemical shift (δ) [relative integral, multiplicity, coupling constant(s) *J* (Hz)] where multiplicity is defined as: s = singlet; d = doublet; t = triplet; q = quartet or quintet; septet; m = multiplet or combinations of the above. Infrared spectra (ν_{max}) were recorded on either a Perkin–Elmer 1800 Fourier Transform Infrared Spectrophotometer or a Perkin–Elmer Spectrum *One* instrument. Samples were analyzed as KBr discs (for solids) or as thin films on KBr plates (for liquids/oils). Low and high resolution MS spectra were recorded on an AUTOSPEC spectrometer or a Kratos Analytical Concept ISQ instrument, the latter being located at the University of Tasmania. Optical rotations were determined on a Perkin–Elmer 241 polarimeter at the sodium D line (598 nm) using spectroscopic grade chloroform (unless otherwise specified) at 20 °C and at the concentrations (*c*) (g/100 mL) indicated. Measurements were carried out in a cell with a path length of 1 dm. Mps were recorded on a Reichert hot-stage apparatus and are uncorrected. Elemental analyses were performed by the Australian National University Microanalytical Services Unit based in the Research School of Chemistry, The Australian National University, Canberra, Australia. Analytical thin layer chromatography (TLC) was conducted on aluminum-backed 0.2 mm thick silica gel 60 F_{254} plates (Merck) and the chromatograms were visualized under a 254 nm UV lamp and/or by treatment with an anisaldehyde–sulfuric acid–ethanol (3 mL : 4.5 mL : 200 mL) dip or, occasionally, with a phosphomolybdic acid–ceric sulfate–sulfuric acid–water (37.5 g : 7.5 g : 37.5 mL : 720 mL) dip, followed by heating. The quoted retardation factors (R_f) have been rounded to the first decimal place. Flash chromatography was conducted according to the method of Still and co-workers[20] using silica gel 60 (mesh size 0.040–0.063 mm) as the stationary phase and the analytical reagent (AR) grade solvents indicated. Many starting materials and reagents were available from the Aldrich Chemical Company or EGA–Chemie and were used as supplied or, in the case of stable

liquids, simply distilled. Drying agents and other inorganic salts were purchased from AJAX or BDH Chemicals. Reactions employing air- and/or moisture-sensitive reagents and intermediates were carried out under an atmosphere of dry, oxygen-free nitrogen in flame-dried apparatus. Tetrahydrofuran (THF) and ether were dried using sodium metal and then distilled, as required, from sodium benzophenone ketyl. Methanol was distilled from magnesium methoxide. Dichloromethane was distilled from calcium hydride. Ethylene glycol dimethyl ether (DME) was refluxed over calcium hydride then distilled, as required, from sodium benzophenone ketyl. *N*,*N*-dimethylformamide (DMF) was heated at reflux over calcium hydride for 16 h then distilled and stored over 3 Å molecular sieves. Organic solutions obtained from work-up of reaction mixtures were dried with magnesium sulfate ($MgSO_4$) then concentrated under reduced pressure on a rotary evaporator with the water bath temperature generally not exceeding 40 °C. Buffer solution of pH 7 was prepared by dissolving potassium dihydrogenphosphate (85 g) and sodium hydroxide (14.5 g) in water (950 mL).

(2*S*,4*S*)-2-Phenyl-1,3-dioxane-4-carboxaldehyde (4).

A magnetically stirred solution of (2*S*,4*S*)-2-phenyl-1,3-dioxane-4-methanol[7,9] (264 mg, 1.36 mmol) in dichloromethane (15 mL) maintained at 18 °C under a nitrogen atmosphere was treated with 4-acetamido-TEMPO (33 mg, 0.15 mmol) and phenyl iododiacetate (458 mg, 1.42 mmol). Stirring was continued for 14 h then the reaction mixture was quenched with $NaHCO_3$ (15 mL of a saturated aq. solution) and the separated aqueous layer extracted with dichloromethane (3 × 10 mL). The combined organic fractions were then dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a light-brown oil. Subjection of this material to flash chromatography (silica, 1 : 3 v/v ethyl acetate–hexane elution) and concentration of the relevant fractions (R_f 0.4 in 1 : 1 v/v ethyl acetate–hexane) gave the title aldehyde (**4**)[9] (182 mg, 70%) as a sticky brown gum, $[\alpha]_D$ –44° (*c* 0.7) (Found: $M^{+\bullet}$, 192.0788. $C_{11}H_{12}O_3$ requires $M^{+\bullet}$, 192.0786). ν_{max} (KBr/cm^{-1}) 3438, 2862, 1736, 1376, 1104, 1017, 757, 699; δ_H (300 MHz, $CDCl_3$) δ 9.72 (1H, br s), 7.57–7.52 (2H, complex m), 7.45–7.37 (3H, complex m), 5.60 (1H, s), 4.34 (2H, m), 3.99 (1H, dt, *J* 2.5 and 12.0 Hz), 2.04–1.88 (1H, complex m), 1.78 (1H, dm, *J* 13.3 Hz); δ_C (75 MHz, $CDCl_3$) 200.4 (CH), 137.6 (C), 129.1 (CH), 128.3 (CH), 126.0 (CH), 101.0 (CH), 80.2 (CH), 66.3 (CH_2), 25.8 (CH_2); *m*/*z* (SIMS) 194 (27%), 193 [$(M+H)^+$, 35], 163 (100), 105 (86).

(α*S*,2*S*,4*S*)-α-Ethenyl-2-phenyl-1,3-dioxane-4-methanol (5) and (α*R*,2*S*,4*S*)-α-Ethenyl-2-phenyl-1,3-dioxane-4-methanol (1'-*epi*-5).

Method A: A magnetically stirred solution of aldehyde (**4**) (1.00 g, 5.2 mmol) in THF (100 mL) maintained under a nitrogen atmosphere was cooled to –50 °C then treated, dropwise, with divinyl zinc[10] (38 mL of a 0.5 M solution in THF, 19 mmol). After 20 h at –50 °C the reaction mixture was quenched with NH_4Cl (100 mL of a saturated aq. solution) and the separated aqueous layer extracted with ether (4 ×

65 mL). The combined organic fractions were washed with water (1 × 50 mL) and brine (1 × 50 mL) before being dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a dark-grey and viscous oil. Subjection of this material to flash chromatography (silica, 3 : 7 v/v ethyl acetate–hexane elution) produced two fractions A and B.

Concentration of fraction A (R_f 0.5 in 1 : 1 v/v ethyl acetate–hexane) gave an inseparable 3 : 1 mixture of the *title compounds (**5**)* and *1'*-epi-***5*** (752 mg, 92% at 72% conversion) as a clear, colorless oil (Found: $M^{+\bullet}$, 220.1099. $C_{13}H_{16}O_3$ requires $M^{+\bullet}$, 220.1099). ν_{max} (KBr/cm^{-1}) 3435, 2925, 1661, 1456, 1398, 1216, 1101, 1069, 1025, 929, 759, 700; δ_C (75 MHz, $CDCl_3$) [for compound (**5**)] 138.2 (C), 135.4 (CH), 128.9 (CH), 128.2 (CH), 126.0 (CH), 118.2 (CH_2), 101.2 (CH), 79.7 (CH), 75.5 (CH), 66.5 (CH_2), 26.9 (CH_2); δ_C (75 MHz, $CDCl_3$) [for compound (1'-*epi*-**5**)] 138.3 (C), 135.6 (CH), 128.8 (CH), 128.2 (CH), 126.0 (CH), 117.0 (CH_2), 101.1 (CH), 79.3 (CH), 74.2 (CH), 66.7 (CH_2), 24.8 (CH_2); *m/z* (EI, 70 eV) 220 ($M^{+\bullet}$, 20%), 219 (20), 163 [$(M–C_3H_5O\cdot)^+$, 100%].

Concentration of fraction B (R_f 0.4 in 1 : 1 v/v ethyl acetate–hexane) gave the starting aldehyde (**4**) (284 mg, 28% recovery) that was identical, in all respects, with authentic material.

Method B: A magnetically stirred solution of a 3 : 1 mixture of compounds (**5**) and 1'-*epi*-**5** (57.0 mg, 0.26 mmol) in dichloromethane (3 mL) maintained under a nitrogen atmosphere at *ca.* 18 °C was treated with Dess–Martin periodinane (329 mg, 0.78 mmol). After 11 h the reaction mixture was quenched with $Na_2S_2O_3$ and $NaHCO_3$ (5 mL of 1 : 1 v/v mixture of saturated aq. solutions) then the biphasic mixture stirred vigorously at 18 °C for 1 h. The separated aqueous layer was extracted with dichloromethane (3 × 7 mL) and the combined organic fractions then dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a yellow oil. Subjection of this material to flash chromatography (silica, 1 : 4 v/v ethyl acetate–hexane elution) gave, after concentration of the relevant fractions (R_f 0.6 in 1 : 1 v/v ethyl acetate–hexane), (2'*S*,4'*S*)-1-(2-phenyl-[1,3]-dioxan-4-yl)propenone (36.5 mg, 64%) as a clear, colorless oil, $[\alpha]_D$ –63° (*c* 0.7) (Found: $M^{+\bullet}$, 218.0934. $C_{13}H_{14}O_3$ requires $M^{+\bullet}$, 218.0943). ν_{max} (KBr/cm^{-1}) 2969, 2857, 1701, 1610, 1454, 1401, 1303, 1239, 1215, 1124, 990, 699; δ_H (300 MHz, $CDCl_3$) 7.53 (2H, m), 7.40 (3H, m), 6.94 (1H, dd, *J* 10.5 and 17.3 Hz), 6.48 (1H, dd, *J* 1.8 and 17.3 Hz), 5.82 (1H, dd, *J* 1.8 and 10.5 Hz), 5.60 (1H, s), 4.50 (1H, dd, *J* 3.1 and 11.6 Hz), 4.36 (1H, ddd, *J* 1.3, 5.0 and 11.6 Hz), 4.04 (1H, td, *J* 2.8 and 11.9 Hz), 2.02 (1H, m), 1.86 (1H, dm, *J* 13.5 Hz); δ_C (75 MHz, $CDCl_3$) 197.3 (C), 137.9 (C), 130.6 (CH), 130.4 (CH), 129.0 (CH), 128.3 (CH), 126.0 (CH_2), 101.1 (CH), 80.8 (CH), 66.8 (CH), 27.3 (CH_2); (70 eV) *m/z* (EI, 70 eV) 218 ($M^{+\bullet}$, 2%), 217 [$(M–H\cdot)^+$, 9], 163 (100).

A magnetically stirred solution of (2'*S*,4'*S*)-1-(2-phenyl-[1,3]-dioxan-4-yl)propenone (36.5 mg, 0.17 mmol), prepared as described immediately above, in toluene (2 mL) maintained under a nitrogen atmosphere was cooled to –78 °C then treated, dropwise, with DIBAL-H (200 μL of a 1 M solution in hexanes, 0.200 mmol). After 1 h the reaction mixture was quenched by the addition of potassium sodium

tartrate (5 mL of a 1 M aq. solution) and the separated aqueous layer extracted with ether (3 × 7 mL). The combined organic fractions were washed with NH_4Cl (1 × 20 mL of a saturated aq. solution), water (1 × 20 mL) and brine (1 × 20 mL) before being dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a yellow oil. Subjection of this material to flash chromatography (silica, 3 : 7 v/v ethyl acetate–hexane elution) and concentration of the relevant fractions (R_f 0.4 in 1 : 1 v/v ethyl acetate–hexane) gave an inseparable 4 : 1 mixture of the *title compounds (**5**)* and *1*'-epi-***5*** (10.0 mg, 29%) as a clear, colorless oil. This material was identical, as judged by ^1H and ^{13}C NMR spectroscopy, with the samples of alcohols (**5**) and 1'-*epi*-**5** obtained *via* Method A.

(4*S*-*trans*)-5-Ethenyl-2,2-dimethyl-1,3-dioxolane-4-ethanol (7) and (4*S*-*cis*)-5-Ethenyl-2,2-dimethyl-1,3-dioxolane-4-ethanol (5-*epi*-7).

A magnetically stirred solution of a *ca.* 3 : 1 mixture of acetals (**5**) and 1'-*epi*-**5** (1.31 g, 5.9 mmol) in THF (30 mL) maintained at 18 °C was treated with HCl (30 mL of a 1 M aq. solution) and after 2 h quenched with $NaHCO_3$ (10 g). Silica gel type 60 (5 g) was added and the ensuing mixture evaporated to dryness. The resulting lumpy white powder was added to the top of a flash chromatography column which was then subject to elution with 1 : 9 v/v methanol–chloroform. Concentration of the relevant fractions (R_f 0.4) afforded a *ca.* 3 : 1 mixture of triol (**6**) and its C3-epimer (675 mg, 87%). A magnetically stirred suspension of this material in dichloromethane (50 mL) was treated with 2,2-dimethoxypropane (940 μL, 7.6 mmol) then *p*-TsOH (13.7 mg, 0.07 mmol). The resulting mixture was allowed to stir at 18 °C for 13 h then quenched with triethylamine (500 μL) and concentrated under reduced pressure to give a light-yellow oil. Subjection of this material to flash chromatography (silica, 1 : 4 v/v ethyl acetate–hexane elution) gave two fractions, A and B.

Concentration of fraction A (R_f 0.23 in 3 : 7 v/v ethyl acetate–hexane) afforded alcohol (**7**) (508 mg, 50%) as a light–yellow oil, $[\alpha]_D$ –27° (*c* 0.2) [Found: $(M–CH_3\cdot)^+$, 157.0862. $C_9H_{16}O_3$ requires $(M–CH_3\cdot)^+$, 157.0865]. ν_{max} (KBr/cm^{-1}) 3402, 2987, 2937, 1376, 1239, 1057, 873; δ_H (300 MHz, $CDCl_3$) 5.79 (1H, ddd, *J* 7.3, 10.3 and 17.3 Hz), 5.36 (1H, ddd, *J* 1.0, 1.5, and 17.3 Hz), 5.25 (1H, ddd, *J* 0.7, 1.5 and 10.3 Hz), 4.04 (1H, tm, *J* 8.0 Hz), 3.82 (1H, td, *J* 3.5 and 8.3 Hz), 3.78 (2H, t, *J* 5.6 Hz), 2.45 (1H, br s), 1.90–1.67 (2H, complex m), 1.41 (3H, s), 1.40 (3H, s); δ_C (75 MHz, $CDCl_3$) 134.7 (CH), 119.3 (CH_2), 109.0 (C), 82.6 (CH), 79.4 (CH), 60.5 (CH_2), 33.6 (CH_2), 27.2 (CH_3), 26.9 (CH_3); *m/z* (EI, 70 eV) 171 [$(M–H\cdot)^+$, 2%], 157 [$(M–CH_3\cdot)^+$, 65], 98 (100), 97 (69).

Concentration of fraction B (R_f 0.17 in 3 : 7 v/v ethyl acetate–hexane) afforded alcohol (5-*epi*-**7**) 203 mg, 20%) as a light-yellow oil, $[\alpha]_D$ –19° (*c* 1.5) [Found: $(M–CH_3\cdot)^+$, 157.0865. $C_9H_{16}O_3$ requires $(M–CH_3\cdot)^+$, 157.0865]. ν_{max} (KBr/cm^{-1}) 3399, 2987, 2937, 1428, 1376, 1248, 1217, 1165, 1054, 929, 871; δ_H (300 MHz, $CDCl_3$) 5.78 (1H, ddd, *J* 7.6, 10.3 and 17.3 Hz), 5.30 (1H, ddd, *J* 1.0, 1.6 and 17.1 Hz), 5.23 (1H,

m), 4.53 (1H, tm, *J* 6.4 Hz), 4.33 (1H, ddd, *J* 3.5, 6.5 and 10.1 Hz), 3.76 (2H, m), 2.44 (1H, br s), 1.78–1.54 (2H, complex m), 1.48 (3H, s), 1.35 (3H, s); δ_C (75 MHz, $CDCl_3$) 133.9 (CH), 118.5 (CH_2), 108.5 (C), 79.6 (CH), 76.9 (CH), 60.7 (CH_2), 32.9 (CH_2), 28.0 (CH_3), 25.5 (CH_3); *m/z* (EI, 70 eV) 171 [$(M–H\cdot)^+$, 1%], 157 [$(M–CH_3\cdot)^+$, 38%], 98 (73), 58 (100), 57 (80).

(4*S*-*trans*)-5-Ethenyl-2,2-dimethyl-1,3-dioxolane-4-ethanol 4-Methylbenzenesulfonate (8).

A magnetically stirred solution of alcohol (**7**) (402 mg, 2.3 mmol) in pyridine (1 mL) maintained under a nitrogen atmosphere was cooled to 0 °C then treated sequentially with *p*-toluenesulfonyl chloride (635 mg, 3.33 mmol) and DMAP (54 mg, 0.44 mmol). The reaction mixture was maintained at 5 °C for 11 h then diluted with water (20 mL) and the separated aqueous layer extracted with ether (3 × 40 mL). The combined organic fractions were washed with copper(II) sulfate (3 × 10 mL of a 0.5 M aq. solution), water (3 × 10 mL) and brine (1 × 10 mL) then dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a pale-yellow oil. Subjection of this material to flash chromatography (silica, 5 : 95 → 3 : 7 v/v ethyl acetate–hexane gradient elution) and concentration of the relevant fractions (R_f 0.08 in 1 : 9 v/v ethyl acetate–hexane) gave *tosylate (**8**)* (831 mg, 100%) as a clear, colorless oil, $[\alpha]_D$ –5.9° (*c* 0.9) (Found: $M^{+\bullet}$, 326.1174. $C_{16}H_{22}O_5S$ requires $M^{+\bullet}$, 326.1188). ν_{max} (KBr/cm^{-1}) 2986, 2931, 1598, 1456, 1361, 1175, 923, 662; δ_H (300 MHz, $CDCl_3$) 7.75 (2H, dm, *J* 8.4 Hz), 7.32 (2H, dm, *J* 8.4 Hz), 5.69 (1H, ddd, *J* 7.5, 10.3 and 17.1 Hz), 5.29 (1H, ddd, *J* 0.9, 1.5 and 17.1 Hz), 5.19 (1H, ddd, *J* 0.9, 1.5 and 10.3 Hz), 4.20–4.06 (2H, complex m), 3.92 (1H, dm, *J* 8.3 Hz), 3.64 (1H, td, *J* 3.4 and 8.3 Hz), 2.41 (3H, s), 1.92 (1H, m), 1.78 (1H, m), 1.30(3) (3H, s), 1.29(8) (3H, s); δ_C (75 MHz, $CDCl_3$) 144.7 (C), 134.3 (CH), 132.7 (C), 129.7 (CH), 127.8 (CH), 119.4 (CH_2), 108.8 (C), 82.3 (CH), 76.2 (CH), 67.2 (CH_2), 30.9 (CH_2), 27.0 (CH_3), 26.7 (CH_3), 21.5 (CH_3); *m/z* (EI, 70 eV) 326 ($M^{+\bullet}$, 0.4%), 311 [$(M–CH_3\cdot)^+$, 1], 270 (6), 155 (46), 98 (100), 97 (69).

(4*S*-*trans*)-5-Ethenyl-2,2-dimethyl-1,3-dioxolane-4-propanoic Acid (10).

A magnetically stirred solution of tosylate (**8**) (803 mg, 2.3 mmol) in DMF (10 mL) maintained under a nitrogen atmosphere was treated with potassium cyanide (302.5 mg, 4.65 mmol) and resulting mixture heated to 60 °C for 3 h. The cooled reaction mixture was then diluted with water (10 mL) and extracted with ether (3 × 10 mL). The combined organic fractions were washed with water (1 × 20 mL) and brine (1 × 20 mL) then dried ($MgSO_4$), filtered and concentrated at atmospheric pressure to give the volatile *nitrile (**9**)* (371 mg, 89%) as a beige-colored oil. δ_H (300 MHz, $CDCl_3$) 5.07 (1H, ddd, *J* 7.3, 10.3 and 17.6 Hz), 4.65 (1H, ddd, *J* 1.3, 2.3 and 17.1 Hz), 4.55 (1H, ddd, *J* 0.9, 1.5 and 10.3 Hz), 3.29 (1H, tm, *J* 8.4 Hz), 3.01 (1H, td, *J* 3.4 and 8.4 Hz), 1.90–1.70 (2H, complex m), 1.28–1.03 (2H, complex m), 0.67 (6H,

s); δ_C (75 MHz, $CDCl_3$) 134.1 (CH), 119.1 (CH_2), 118.8 (C), 108.7 (C), 81.7 (CH), 77.9 (CH), 65.3 (CH_2), 30.9 (CH_2), 26.6 (CH_3), 26.4 (CH_3).

A magnetically stirred solution of the nitrile (**9**) (371 mg, 2.04 mmol) in methanol–water (24 mL of a 4 : 3 v/v mixture) was treated with potassium hydroxide (3.8 g, 68 mmol) and the ensuing mixture heated at 66 °C for 16 h then cooled, acidified to pH 4.5 by careful addition of HCl (1 M aq. solution) and extracted with dichloromethane (5 × 70 mL). The combined organic phases were dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the *title acid (**10**)* (409 mg, 88% from **8**) as a light-yellow oil, $[\alpha]_D$ –7.5° (*c* 0.4) {lit.,[11] $[\alpha]_D$ (for *ent*-**10**) +6.8° (*c* 0.6, $CHCl_3$)} [Found: $(M–H\cdot)^+$, 199.0969. $C_{10}H_{16}O_4$ requires $(M–H\cdot)^+$, 199.0970]. ν_{max} (KBr/cm^{-1}) 3087, 2988, 2935, 2875, 1712, 1427, 1374, 1241, 1166, 1113, 1068, 872; δ_H (300 MHz, $CDCl_3$) 5.70 (1H, ddd, *J* 7.5, 10.3 and 17.3 Hz), 5.37 (1H, ddd, *J* 0.7, 1.5 and 17.3 Hz), 5.26 (1H, ddd, *J* 0.7, 1.5 and 10.3 Hz), 4.01 (1H, tm, *J* 8.4 Hz), 3.70 (1H, td, *J* 3.8 and 8.4 Hz), 2.66–2.40 (2H, complex m), 1.96 (1H, m), 1.82 (1H, m), 1.40 (6H, s) (resonance due to OH not observed); δ_C (75 MHz, $CDCl_3$) 179.2 (C), 134.8 (CH), 119.4 (CH_2), 108.9 (C), 82.4 (CH), 79.3 (CH), 30.4 (CH_2), 27.1 (CH_3), 26.9 (CH_3), 26.4 (CH_2); *m/z* (EI, 70 eV) 199 [$(M–H\cdot)^+$, 5%], 185 [$(M–CH_3\cdot)^+$, 57], 125 (91), 98 (100), 83 (67), 69 (92), 59 (59).

(*E*)-Dec-3-en-1-ol (12).

A magnetically stirred mixture of lithium aluminium hydride (2.20 g, 58 mmol), THF (10 mL) and diglyme (30 mL) maintained under a nitrogen atmosphere was heated to 140 °C until no distillable material remained. The residual grey slurry was then cooled to 0 °C and a solution of alkyne (**11**) (3 mL, 17 mmol, ex. Aldrich Chemical Co.) in diglyme (10 mL) added dropwise. The resulting mixture was heated at 140 °C for 72 h then cooled, quenched with ice-cold and degassed water (100 mL) then acidified with HCl (~100 mL of a 1 M aq. solution). The separated aqueous layer was extracted with pentane (6 × 50 mL) and the combined organic fractions washed with water (1 × 200 mL) and brine (1 × 200 mL) before being dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a yellow-grey oil. Kugelrohr distillation (150 °C/2 mmHg) of this material gave the *title alkene (**12**)*[12] (2.27 g, 86%) as a clear, colorless oil (Found: $M^{+\bullet}$, 156.1514. $C_{10}H_{20}O$ requires $M^{+\bullet}$, 156.1514). ν_{max} (KBr/cm^{-1}) 3338, 2926, 2856, 1462, 1048, 967; δ_H (300 MHz, $CDCl_3$) 5.57–5.46 (1H, complex m), 5.40–5.28 (1H, complex m), 3.58 (2H, t, *J* 6.4 Hz), 2.22 (2H, m), 2.20–1.93 (3H, complex m), 1.35–1.23 (7H, br m), 0.85 (3H, t, *J* 6.4 Hz) (resonance due to OH not observed); δ_C (75 MHz, $CDCl_3$) 134.1 (CH), 125.6 (CH), 61.9 (CH_2), 35.9 (CH_2), 32.6 (CH_2), 31.6 (CH_2), 29.3 (CH_2), 28.8 (CH_2), 22.5 (CH_2), 14.0 (CH_3); *m/z* (EI, 70 eV) 156 ($M^{+\bullet}$, 2%), 138 [$(M–H_2O)^{+\bullet}$, 32], 110 (42), 109 (40), 55 (100).

(3*R*,4*R*)-Decane-1,3,4-triol (13).

A magnetically stirred slurry of AD-mix β (6.6 g, 1.4 g/mmol[13]) and methanesulfonamide (450 mg, 4.73 mmol) in *t*-BuOH–H_2O (40 mL of a 1 : 1 v/v mixture) was cooled to 0 °C then treated, dropwise, with a solution of alkene (**12**) (738 mg, 4.72 mmol) in *t*-BuOH–H_2O (10 mL of a 1 : 1 v/v mixture). The resulting slurry was maintained at 0 °C for 17 h then quenched with Na_2SO_3 (~5 g) and the mixture this obtained was stirred vigorously for 0.5 h then diluted with ether (50 mL). The separated aqueous fraction was extracted with ether (2 × 50 mL) and the combined organic fractions washed with KOH (1 × 200 mL of a 2 M aq. solution), water (1 × 100 mL) and brine (1 × 100 mL) before being dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a viscous and dark-yellow oil. Filtration of this material through a short column of silica gel (1 : 1 v/v ethyl acetate–hexane elution) and concentration of the relevant fractions (R_f 0.1 in 1 : 9 v/v MeOH–$CHCl_3$) gave the *triol (**13**)* (837 mg, 94%) as an off-white solid which was used in the next step of the reaction sequence. Recrystallization (methanol–dichloromethane) of a small sample of this material afforded an analytically pure sample of compound (**13**) as white plates, mp 65 °C, $[\alpha]_D$ +18° (*c* 1.3) [Found: $(M+H)^+$, 191.1644; C, 63.19; H, 11.86. $C_{10}H_{22}O_3$ requires $(M+H)^+$, 191.1647; C, 63.12; H, 11.65%]. ν_{max} (KBr/cm^{-1}) 3350, 2928, 2857, 1460, 1056; δ_H (300 MHz, $CDCl_3$) 3.92–3.80 (2H, complex m), 3.69 (1H, m), 3.46 (1H, m), 2.75 (3H, br s), 1.76 (2H, m), 1.47 (2H, m), 1.40–1.23 (8H, m), 0.89 (3H, m); δ_C (75 MHz, $CDCl_3$) 74.6 (CH), 74.1 (CH), 61.0 (CH_2), 35.0 (CH_2), 33.4 (CH_2), 31.8 (CH_2), 29.3 (CH_2), 25.6 (CH_2), 22.6 (CH_2), 14.1 (CH_3); *m/z* (EI, 70 eV) 191 [$(M+H)^+$, 0.8%], 173 [$(M–HO\cdot)^+$, 3.7], 155 (5), 145 (48), 115 (44), 97 (76), 58 (100).
cis-Dihydroxylation of alkene (**12**) in the manner described above but using AD-mix-α gave *ent*-**13** (69%), $[\alpha]_D$ –18° (*c* 0.9). This material was identical, as judged by ^1H and ^{13}C NMR spectroscopy, with triol (**13**).

(4*R*,5*R*)-5-Hexyl-2,2-dimethyl-1,3-dioxolane-4-ethanol (14).

A magnetically stirred mixture of triol (**13**) (711 mg, 3.8 mmol) and *p*-toluenesulfonic acid (7 mg, 0.04 mmol) in dichloromethane (40 mL) maintained under a nitrogen atmosphere was treated with 2,2-dimethoxypropane (490 μL, 3.98 mmol) and the resulting solution kept at 18 °C for 1.5 h then quenched by addition to $NaHCO_3$ (50 mL of a saturated aq. solution). The separated aqueous layer extracted with dichloromethane (3 × 15 mL) and the combined organic fractions were then washed with water (1 × 30 mL) and brine (1 × 30 mL) before being dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a light-yellow oil. A solution of this material in ethyl acetate was passed through a plug of silica gel (ethyl acetate elution) and the filtrate concentrated under reduced pressure to give the *title compound (**14**)* (671 mg, 77%) as a pale-yellow oil, $[\alpha]_D$ +34° (*c* 1.0) [Found: $(M–CH_3\cdot)^+$, 215.1649. $C_{13}H_{26}O_3$ requires $(M–CH_3\cdot)^+$, 215.1647]. ν_{max} (KBr/cm^{-1}) 3496, 2987, 2932, 2859, 1459, 1378, 1241, 1215, 1185, 1168, 1080, 1057, 857; δ_H (300 MHz, $CDCl_3$) 3.77–3.65 (3H, complex m), 3.61 (1H, m), 2.82 (1H, br s),

1.72 (2H, m), 1.45 (2H, m), 1.34 (3H, s), 1.33 (3H, s), 1.30–1.23 (8H, br m), 0.83 (3H, m); δ_C (75 MHz, $CDCl_3$) 108.1 (C), 80.9 (CH), 79.7 (CH), 60.5 (CH_2), 34.9 (CH_2), 32.5 (CH_2), 31.7 (CH_2), 29.4 (CH_2), 27.2 (CH_3), 27.1 (CH_3), 26.0 (CH_2), 22.5 (CH_2), 14.1 (CH_3); *m/z* (EI, 70 eV) 215 [$(M–CH_3\cdot)^+$, 68%], 155 (73), 59 (100).

(4*R*,5*R*)-5-Hexyl-2,2-dimethyl-1,3-dioxolane-4-acetaldehyde (15).

A magnetically stirred solution of alcohol (**14**) (671 mg, 2.90 mmol) in dichloromethane (30 mL) maintained at 18 °C under a nitrogen atmosphere was treated sequentially with 4-acetamido-TEMPO (42 mg, 0.20 mmol) and phenyl iododiacetate (999 mg, 3.10 mmol). The resulting solution was stirred for 2 h at 18 °C then quenched with $NaHCO_3$ (20 mL of a saturated aq. solution) and extracted with dichloromethane (3 × 15 mL). The combined organic fractions were then dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a yellow oil. Subjection of this material to flash chromatography (silica, 1 : 9 v/v ethyl acetate–hexane elution) and concentration of the relevant fractions (R_f 0.2) afforded the *title compound (**15**)* (513 mg, 85%) as a light-yellow oil, $[\alpha]_D$ +36° (*c* 1.1) [Found: $(M–CH_3\cdot)^+$, 213.1492. $C_{13}H_{24}O_3$ requires $(M–CH_3\cdot)^+$, 213.1491]. ν_{max} (KBr/cm^{-1}) 2930, 2860, 1728, 1459, 1375, 1238, 1089, 860; δ_H (300 MHz, $CDCl_3$) 9.78 (1H, m), 4.04 (1H, m), 3.64 (1H, m), 2.59 (2H, m), 1.52 (2H, m), 1.37 (3H, s), 1.35 (3H, s), 1.30–1.26 (8H, br m), 0.85 (3H, m); δ_C (75 MHz, $CDCl_3$) 199.8 (CH), 108.6 (C), 80.6 (CH), 75.4 (CH), 46.5 (CH_2), 32.3 (CH_2), 31.7 (CH_2), 29.3 (CH_2), 27.3 (CH_3), 27.1 (CH_3), 26.0 (CH_2), 22.6 (CH_2), 14.1 (CH_3); *m/z* (EI, 70 eV) 213 [$(M–CH_3\cdot)^+$, 33%], 184 (17), 171 (21), 153 (100).

(2*R*,4*R*,5*R*)- and (2*S*,4*R*,5*R*)-5-Hexyltetrahydrofurane-2,4-diol (16).

A magnetically stirred solution of compound (**15**) (541.7 mg, 2.37 mmol) in a mixture of glacial acetic acid (13.5 mL), water (2 mL) and THF (1 mL) was maintained under a nitrogen atmosphere and heated at 50 °C for 6 h. The cooled reaction mixture was diluted with ether (30 mL) and the separated aqueous layer extracted with ether (3 × 50 mL). The combined organic phases were washed with NaOH (1 × 100 mL of a 1 M aq. solution) and brine (1 × 100 mL) before being dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a yellow oil. Subjection of this material to flash chromatography (silica, 1 : 1 v/v ethyl acetate–hexane elution) and concentration of the relevant fractions (R_f 0.2 in 7 : 3 v/v ethyl acetate–hexane) afforded the *title diol (**16**)* (312 mg, 70%) as a white solid, mp 79–82 °C, $[\alpha]_D$ –29° (*c* 0.2, acetone) (Found: $M^{+\bullet}$, 188.1420. C, 63.82; H, 10.68. $C_{10}H_{20}O_3$ requires $M^{+\bullet}$, 188.1412; C, 63.80; H, 10.71%). ν_{max} (KBr/cm^{-1}) 3346, 2918, 2853, 1456, 1277, 1087, 1013; δ_H (300 MHz, $CDCl_3$) (major anomer) 5.68 (1H, m), 4.29 (1H, m), 4.05 (1H, td, *J* 3.1 and 6.5 Hz), 2.70 (1H, br s), 2.29–2.05 (2H, complex m), 1.78–1.55 (3H, complex m), 1.47–1.25 (8H, complex m), 0.88 (3H, m); δ_H (300 MHz, $CDCl_3$) (minor anomer) 5.48 (1H, t, *J* 5.3 Hz), 4.16 (1H, m), 3.86 (1H, td, *J* 3.4 and 7.2 Hz), 3.22 (1H,

m), 2.51 (1H, d, *J* 8.1 Hz), 2.29–2.05 (2H, complex m), 1.78–1.55 (3H, complex m), 1.47–1.25 (7H, complex m), 0.88 (3H, m); δ_C (75 MHz, acetone-d_6) 97.6 (CH), 81.5 (CH), 72.4 (CH), 45.0 (CH_2), 32.4 (CH_2), 30.1 (CH_2), 29.4 (CH_2), 26.9 (CH_2), 23.1 (CH_2), 14.2 (CH_3); *m/z* (EI, 70 eV) 188 ($M^{+\bullet}$, <1%), 171 92), 113 (15), 97 (35), 74 (100).

(2*R*,3*R*,5*S*)- and (2*R*,3*R*,5*R*)-2-Hexyl-5-[(4-methoxyphenyl)methoxy]tetrahydrofuran-3-ol (17).

A magnetically stirred mixture of compound (**16**) (159.3 mg, 0.846 mmol) and dichloromethane (17 mL) maintained under a nitrogen atmosphere was cooled to –20 °C and treated, sequentially, with *p*-methoxybenzyl alcohol (211 μL, 1.69 mmol) and *p*-toluenesulfonic acid (1 mg, 0.005 mmol). The resulting mixture was stirred at –15 °C for 20 h then quenched with $NaHCO_3$ (~500 mg). Additional $NaHCO_3$ (5 mL of a saturated aq. solution) was added at –15 °C and after 5 min of vigorous stirring, the mixture was warmed to 18 °C. The separated aqueous layer was extracted with ether (3 × 20 mL) and the combined organic phases were washed with water (1 × 50 mL) and brine (1 × 50 mL) before being dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a yellow oil. Subjection of this material to flash chromatography (silica, 3 : 7 v/v ethyl acetate–hexane elution) produced two fractions, A and B.

Concentration of fraction A (R_f 0.4 in 1 : 1 v/v ethyl acetate–hexane) afforded the major anomeric form of *compound (**17**)* (133 mg, 50%) as a light-yellow oil, $[\alpha]_D$ –64° (*c* 0.6) (Found: $M^{+\bullet}$, 308.1989. $C_{18}H_{28}O_4$ requires $M^{+\bullet}$, 308.1988). ν_{max} (KBr/cm^{-1}) 3523, 2929, 2858, 1613, 1514, 1462, 1301, 1249, 1176, 1084, 1030, 936, 827, 771; δ_H (300 MHz, $CDCl_3$) 7.25 (2H, d, *J* 8.8 Hz), 6.88 (2H, d, *J* 8.8 Hz), 5.19 (1H, d, *J* 4.2 Hz), 4.70 (1H, d, *J* 11.3 Hz), 4.40 (1H, d, *J* 11.3 Hz), 4.12 (1H, m), 3.93 (1H, td, *J* 3.8 and 7.0 Hz), 3.80 (3H, s), 2.88 (1H, d, *J* 11.4 Hz), 2.17 (1H, d, *J* 13.2 Hz), 2.09 (1H, dt, *J* 4.4 and 13.2 Hz), 1.72 (2H, m), 1.50–1.25 (8H, complex m), 0.89 (3H, m); δ_C (75 MHz, $CDCl_3$) 159.2 (C), 129.5(9) (C), 129.5(7) (CH), 113.8 (CH), 102.1 (CH), 85.2 (CH), 71.5 (CH), 68.4 (CH_2), 55.2 (CH_3), 41.5 (CH_2), 31.7 (CH_2), 30.6 (CH_2), 29.4 (CH_2), 26.1 (CH_2), 22.6 (CH_2), 14.1 (CH_3); *m/z* (EI, 70 eV) 308 ($M^{+\bullet}$, 17%), 194 (5), 163 (21), 121 (100).

Concentration of fraction B (R_f 0.5 in 1 : 1 v/v ethyl acetate–hexane) afforded the minor anomeric form of *compound (**17**)* (53 mg, 20%) as a light-yellow oil, $[\alpha]_D$ +79° (*c* 1.3) (Found: $M^{+\bullet}$, 308.1988. $C_{18}H_{28}O_4$ requires $M^{+\bullet}$, 308.1988). ν_{max} (KBr/cm^{-1}) 3400, 2927, 2857, 1613, 1514, 1463, 2248, 1095, 1026, 822; δ_H (300 MHz, $CDCl_3$) 7.27 (2H, d, *J* 8.8 Hz), 6.88 (2H, d, *J* 8.6 Hz), 5.33 (1H, dd, *J* 3.7 and 5.3 Hz), 4.68 (1H, d, *J* 11.3 Hz), 4.43 (1H, d, *J* 11.3 Hz), 4.24 (1H, br m), 3.92 (1H, td, *J* 3.1 and 6.6 Hz), 3.80 (3H, s), 2.20 (2H, m), 1.80–1.54 (3H, complex m), 1.43–1.26 (8H, complex m), 0.91 (3H, m); δ_C (75 MHz, $CDCl_3$) 159.1 (C), 130.1 (C), 129.5 (CH), 113.7 (CH), 101.6 (CH), 80.8 (CH), 72.3 (CH), 69.2 (CH_2),

55.2 (CH_3), 43.5 (CH_2), 31.7 (CH_2), 29.4 (CH_2), 28.2 (CH_2), 26.3 (CH_2), 22.6 (CH_2), 14.1 (CH_3); *m/z* (EI, 70 eV) 308 ($M^{+\bullet}$, 16%), 194 (5), 163 (17), 122 (42), 121 (100).

(2*R*,3*R*,5*S*)- and (2*R*,3*R*,5*R*)-2-Hexyl-5-[(4-methoxyphenyl)methoxy]tetrahydrofuran-3-yl Esters of (4*S*-*trans*)-5-Ethenyl-2,2-dimethyl-1,3-dioxolane-4-propanoic Acid (18).

A magnetically stirred solution of the major anomeric form of compound (**17**) (12.8 mg, 0.042 mmol) and acid (**10**) (12.6 mg, 0.063 mmol) in dichloromethane (0.5 mL) maintained under a nitrogen atmosphere was cooled to 0 °C and treated with DMAP (17.1 mg, 0.140 mmol) then DCC (84 μL of a 1 M solution in dichloromethane, 0.084 mmol). The resulting mixture was allowed to warm to 18 °C over 18 h and the resulting slurry filtered through a pad of Celite and the filter cake washed with dichloromethane (3 × 5 mL). Concentration of the combined filtrates, subjection of the residue so-obtained to flash chromatography (silica, 15 : 85 → 30 : 70 v/v ethyl acetate–hexane gradient elution) and concentration of the relevant fractions (R_f 0.3 in 3 : 7 v/v ethyl acetate–hexane) gave the major anomeric form of *compound (**18**)* (17.8 mg, 86%) as a pale-yellow oil, $[\alpha]_D$ –65° (*c* 0.2) (Found: $M^{+\bullet}$, 490.2915. $C_{28}H_{42}O_7$ requires $M^{+\bullet}$, 490.2931). ν_{max} (KBr/cm^{-1}) 2927, 1733, 1613, 1514, 1459, 1428, 1216, 1132, 996, 757, 668; δ_H (500 MHz, $CDCl_3$) 7.27 (2H, d, *J* 8.8 Hz), 6.87 (2H, d, *J* 8.8 Hz), 5.78 (1H, ddd, *J* 7.3, 10.3 and 17.6 Hz), 5.33 (1H, d, *J* 17.6 Hz), 5.25 (2H, m), 5.17 (1H, dd, *J* 1.5 and 5.9 Hz), 4.72 (1H, d, *J* 11.7 Hz), 4.42 (1H, d, *J* 11.7 Hz), 4.06 (1H, m), 3.97 (1H, t, *J* 7.8 Hz), 3.80 (3H, s), 3.68 (1H, td, *J* 3.4 and 8.5 Hz), 2.55 (1H, m), 2.45 (1H, m), 2.35 (1H, m), 2.09 (1H, dm, *J* 14.6 Hz), 1.94 (1H, m), 1.80 (1H, m), 1.70 (1H, m), 1.51 (1H, m), 1.40 (3H, s), 1.39 (3H, s), 1.36–1.26 (8H, m), 0.88 (3H, m); δ_C (125 MHz, $CDCl_3$) 172.8 (C), 159.1 (C), 135.0 (CH), 130.3 (C), 129.4 (CH), 119.2 (CH_2), 113.7 (CH), 108.8 (C), 101.6 (CH), 82.4 (CH), 81.7 (CH), 79.5 (CH), 73.0 (CH), 68.8 (CH_2), 55.2 (CH_3), 39.5 (CH_2), 31.8 (CH_2), 30.8 (CH_2), 30.2 (CH_2), 29.7 (CH_2), 29.3 (CH_2), 27.2 (CH_3), 26.9 (CH_3), 26.7 (CH_2), 22.6 (CH_2), 14.1 (CH_3); *m/z* (EI, 70 eV) 490 ($M^{+\bullet}$, <1%), 475 [$(M–CH_3\cdot)^+$, 0.5], 153 (70), 121 (100).

Condensation of the minor anomeric form of compound (**17**) (140.5 mg, 0.456 mmol) and acid (**10**) (91 mg, 0.454 mmol) in the manner detailed immediately above afforded a yellow oil on work-up. Subjection of this material to flash chromatography (silica, 5 : 95 → 20 : 80 v/v ethyl acetate–hexane gradient elution) and concentration of the relevant fractions (R_f 0.6 in 1 : 1 v/v ethyl acetate–hexane) gave the minor anomeric form of compound (**18**) (182 mg, 81%) as a pale-yellow oil, $[\alpha]_D$ +43° (*c* 1.00) (Found: $M^{+\bullet}$, 490.2930. $C_{28}H_{42}O_7$ requires $M^{+\bullet}$, 490.2931). ν_{max} (KBr/cm^{-1}) 2986, 2929, 2861, 1735, 1613, 1514, 1460, 1373, 1300, 1246, 1169, 1093, 1069, 1032, 933, 873, 820; δ_H (300 MHz, $CDCl_3$) 7.26 (2H, d, *J* 8.8 Hz), 6.87 (2H, d, *J* 8.8 Hz), 5.79 (1H, ddd, *J* 7.5, 10.3 and 17.4 Hz), 5.37 (1H, m), 5.31 (1H, m), 5.26 (1H, dm, *J* 10.3 Hz), 4.68 (1H, d, *J* 11.4 Hz), 4.43 (1H, d, *J* 11.4 Hz), 4.05 (1H, ddd, *J* 3.7, 5.1 and 7.8 Hz), 3.99 (1H, t, *J* 7.5 Hz), 3.79 (3H, s), 3.69 (1H, td, *J* 3.5 and 8.4 Hz), 2.55–2.37 (2H, m), 2.31 (1H,

ddd, *J* 2.9, 6.3 and 15.2 Hz), 2.16 (1H, ddd, *J* 1.6, 7.5 and 15.1 Hz), 1.98–1.89 (1H, complex m), 1.85–1.74 (1H, complex m), 1.65–1.53 (2H, complex m), 1.39 (3H, s), 1.38 (3H, s), 1.34–1.24 (8H, complex m), 0.87 (3H, m); δ_C (75 MHz, $CDCl_3$) 172.5 (C), 159.2 (C), 134.9 (CH), 129.9 (C), 129.5 (CH), 119.3 (CH_2), 113.8 (CH), 108.8 (C), 101.5 (CH), 82.4 (CH), 79.4 (CH), 79.3 (CH), 74.4 (CH), 69.2 (CH_2), 55.2 (CH_3), 41.0 (CH_2), 31.7 (CH_2), 30.7 (CH_2), 29.3 (CH_2), 28.3 (CH_2), 27.2 (CH_3), 26.9 (CH_3), 26.7 (CH_2), 26.2 (CH_2), 22.6 (CH_2), 14.0 (CH_3); *m/z* (EI, 70 eV) 490 ($M^{+\bullet}$, 3%), 153 (18), 122 (27), 121 (100), 98 (21).

(4*S*-*trans*)-5-Ethenyl-2,2-dimethyl-1,3-dioxolane-4-propanoic Acid (2*R*,3*R*,5*S*/*R*)-2-Hexyl-5-hydroxytetrahydrofuran-3-yl Ester (19).

A magnetically stirred solution of the major anomeric form of compound (**18**) (39 mg, 0.080 mmol) in dichloromethane (10 mL) was treated with pH 7 phosphate buffer (1 mL) and the resulting biphasic mixture stirred vigorously at 18 °C for 3 min. After this time DDQ (83 mg, 0.366 mmol) was added, the mixture kept at 18 °C for 3.5 h then filtered through a short plug of Celite and the filter cake washed with dichloromethane (3 × 5 mL). The combined filtrates were concentrated under reduced pressure and subjection of the residue to flash chromatography (silica, 1 : 17 v/v ethyl acetate–hexane elution) followed by concentration of the relevant fractions (R_f 0.2 in 3 : 7 v/v ethyl acetate–hexane) afforded the *title compound (**19**)* (27 mg, 92%) as a light-yellow oil, $[\alpha]_D$ +7.2° (*c* 0.6) [Found: $(M–CH_3\cdot)^+$, 355.2119 $C_{20}H_{34}O_6$ requires $(M–CH_3\cdot)^+$, 355.2121]. ν_{max} (KBr/cm^{-1}) 3449, 2928, 2858, 1735, 1437, 1374, 1241, 1168, 1069, 874; δ_H (300 MHz, $CDCl_3$) 5.78 (1H, ddd, *J* 7.3, 10.3 and 17.3 Hz), 5.64 (0.66H, t, *J* 4.8 Hz), 5.43–5.22 (3.33H, complex m), 4.17 (0.66H, ddd, *J* 3.7, 5.6 and 7.6 Hz), 3.96 (1H, m), 3.92 (0.33H, m), 3.69 (1H, m), 3.34 (1H, br s), 2.57–2.27 (2H, complex m), 2.20 (2H, m), 2.10–1.72 (2H, complex m), 1.68–1.46 (2H, complex m), 1.39 (3H, s), 1.38 (3H, s), 1.30–1.20 (8H, complex m), 0.86 (3H, m); δ_C (75 MHz, $CDCl_3$) 172.5 (C), 134.8 (CH), 119.3 (CH_2), 108.8 (C), 97.0 (CH), 82.4 (CH), 79.6 (CH), 79.4 (CH), 74.6 (CH), 41.6 (CH_2), 31.6 (CH_2), 30.7 (CH_2), 29.2 (CH_2), 28.5 (CH_2), 27.1 (CH_3), 26.9 (CH_3), 26.7 (CH_2), 26.1 (CH_2), 22.5 (CH_2), 14.0 (CH_3); *m/z* (EI, 70 eV) 355 [$(M–CH_3\cdot)^+$, 8%], 311 (21), 171 (55), 125 (100), 98 (88).

Subjection of the minor anomeric form of compound (**18**) to the reaction conditions defined immediately above afforded lactol (**19**) in 90% yield.

(2*E*,5*R*,6*R*)-5-[(4*S*-*trans*)-5-Ethenyl-2,2-dimethyl-1,3-dioxolane-4-propanoyl]oxy-6-hydroxy-2-dodecenoic Acid Methyl Ester (20).

A magnetically stirred solution of lactol (**19**) (112.1 mg, 0.302 mmol) in toluene (3 mL) maintained under a nitrogen atmosphere was cooled to 0 °C and treated with methylene triphenylphosphoranylideneacetate (125.6 mg, 0.376 mmol) over a period of 1 h. The resulting solution was maintained at 0 °C for 12 h and

then an additional portion of the ylide (50 mg, 0.150 mmol) was added. The mixture was then warmed to 18 °C, maintained at this temperature for 12 h then re-cooled to 0 °C. After 12 h at the latter temperature the reaction mixture was diluted with pH 7 phosphate buffer (7 mL) and the separated aqueous layer extracted with ether (3 × 7 mL). The combined organic fractions were washed with water (1 × 20 mL) and brine (1 × 20 mL) before being dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a yellow oil. Subjection of this material to flash chromatography (silica, 1 : 4 v/v ethyl acetate–hexane elution) and concentration of the relevant fractions (R_f 0.2 in 3 : 7 v/v ethyl acetate–hexane) gave the *title* bis-*ester (**20**)* (120.2 mg, 93%) as a yellow oil, $[\alpha]_D$ +3.2° (*c* 0.7) [Found: $(M–C_2H_2O_2)^{+\bullet}$, 368.2562. $C_{23}H_{38}O_7$ requires $(M–C_2H_2O_2)^{+\bullet}$, 368.2563]. ν_{max} (KBr/cm^{-1}) 3479, 2930, 2858, 1729, 1659, 1437, 1373, 1223, 1168, 1067, 986, 873; δ_H (300 MHz, $CDCl_3$) 6.87 (1H, dt, *J* 7.6 and 15.6 Hz), 5.89 (1H, dt, *J* 1.5 and 15.6 Hz), 5.78 (1H, ddd, *J* 7.6, 10.3 and 17.3 Hz), 5.37 (1H, ddd, *J* 0.9, 1.5 and 17.3 Hz), 5.26 (1H, ddd, *J* 0.9, 1.5 and 10.3 Hz), 4.93 (1H, ddd, *J* 4.2, 5.6 and 7.2 Hz), 3.98 (1H, dd, *J* 7.5 and 8.4 Hz), 3.72 (3H, s), 3.67 (1H, td, *J* 3.7 and 8.4 Hz), 3.59 (1H, m), 2.64–2.42 (5H, complex m), 1.99–1.76 (4H, complex m), 1.40 (3H, s), 1.38 (3H, s), 1.29–1.24 (8H, complex m), 0.87 (3H, m); δ_C (75 MHz, $CDCl_3$) 172.4 (C), 166.4 (C), 143.6 (CH), 134.8 (CH), 123.8 (CH), 119.4 (CH_2), 108.9 (C), 82.4 (CH), 79.6 (CH), 74.8 (CH), 72.0 (CH), 51.5 (CH_3), 33.6 (CH_2), 33.4 (CH_2), 31.7 (CH_2), 31.0 (CH_2), 29.1 (CH_2), 27.1 (CH_3), 26.9 (CH_3), 26.6 (CH_2), 25.4 (CH_2), 22.5 (CH_2), 14.0 (CH_3); *m/z* (EI, 70 eV) 368 [$(M–C_2H_2O_2)^{+\bullet}$, 1%], 353 (12), 269 (11), 185 (47), 126 (67), 125 (100), 98 (88).

(2*E*,5*R*,6*R*)-5-[(4*S*-*trans*)-5-Ethenyl-2,2-dimethyl-1,3-dioxolane-4-propanoyl]oxy-6-methoxymethoxy-2-dodecenoic Acid Methyl Ester (21).

A magnetically stirred solution of MOM-Cl (1.0 mL, 13 mmol) and DMAP (12.9 mg, 0.1 mmol) in Hünig's base (2.35 mL, 13.8 mmol) maintained at 0 °C under a nitrogen atmosphere was treated, *via* cannula, with a solution of alcohol (**20**) (118.2 mg, 0.28 mmol) in dichloromethane (1.0 mL). The resulting mixture was kept at 0 °C for 0.5 h then warmed to 18 °C and after 2.5 h quenched with $NaHCO_3$ (2 mL of a saturated aq. solution). The resulting mixture was extracted with ether (3 × 10 mL) and the combined organic fractions washed with water (1 × 30 mL) and brine (1 × 30 mL) before being dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a yellow oil. Subjection of this material to flash chromatography (silica, 1 : 9 v/v ethyl acetate–hexane elution) and concentration of the relevant fractions (R_f 0.3) gave *compound (**21**)* (119.6 mg, 92%) as a pale-yellow oil, $[\alpha]_D$ –3.8° (*c* 0.6) (Found: $M^{+\bullet}$, 470.2878. $C_{25}H_{42}O_8$ requires $M^{+\bullet}$, 470.2880). ν_{max} (KBr/cm^{-1}) 2930, 1731, 1659, 1373, 1225, 1167, 1036; δ_H (300 MHz, $CDCl_3$) 6.86 (1H, ddd, *J* 6.9, 7.7 and 15.5 Hz), 5.86 (1H, dm, *J* 15.7 Hz), 5.76 (1H, m), 5.37 (1H, dm, *J* 17.4 Hz), 5.26 (1H, dd, *J* 0.7 and 10.3 Hz), 5.07 (1H, m), 4.65 (2H, ABq, *J* 2.6 Hz), 3.98 (1H, dd, *J* 7.4 and 8.2 Hz), 3.70 (3H, s), 3.65 (1H, m), 3.57 (1H, m), 3.37 (3H, s), 2.62–2.36

(4H, complex m), 2.02–1.72 (2H, complex m), 1.46 (2H, m), 1.38 (3H, s), 1.37 (3H, s), 1.31–1.20 (8H, complex m), 0.86 (3H, m); δ_C (75 MHz, $CDCl_3$) 172.4 (C), 166.4 (C), 144.2 (CH), 134.9 (CH), 123.6 (CH), 119.2 (CH_2), 108.8 (C), 96.7 (CH_2), 82.4 (CH), 79.3 (CH), 77.8 (CH), 72.7 (CH), 55.9 (CH_3), 51.5 (CH_3), 32.7 (CH_2), 31.7 (CH_2), 30.6 (CH_2), 30.2 (CH_2), 29.3 (CH_2), 27.2 (CH_3), 26.9 (CH_3), 26.7 (CH_2), 25.2 (CH_2), 22.5 (CH_2), 14.0 (CH_3); *m/z* (EI, 70 eV) 470 ($M^{+\bullet}$, 0.3%), 455 [$(M–CH_3\cdot)^+$, 1.4], 229 (17), 125 (100), 98 (38).

(4*S*-*trans*)-5-Ethenyl-2,2-dimethyl-1,3-dioxolane-4-propanoic Acid (1*R*,2*R*)-2-Methoxymethoxy-1-(2-propenyl)octyl Ester (22).

Grubbs' second-generation catalyst[17] (35.0 mg, 0.04 mmol, 21 mol %) was added, in one portion, to a magnetically stirred solution of compound (**21**) (94 mg, 0.20 mmol) in deoxygenated dichloromethane (100 mL) maintained under a nitrogen atmosphere. A balloon of ethylene was attached and the reaction mixture flushed with ethylene then stirred vigorously at 18 °C for 25 h. The resulting dark-brown solution was filtered through a short plug of silica gel and the filtrate concentrated under reduced pressure to give a dark-brown oil. This material was subjected to flash chromatography (silica, 1 : 9 → 1 : 4 v/v ethyl acetate–hexane gradient elution) thereby affording two fractions A and B.

Concentration of fraction A (R_f 0.5 in 30 : 70 v/v ethyl acetate–hexane) gave the *title compound (**22**)* (18.3 mg, 100% at 22% conversion) as a pale-yellow oil, $[\alpha]_D$ –4.2° (*c* 0.5) {lit.,[4] $[\alpha]_D$ (for *ent*-**22**) +4.2° (*c* 1.0, $CHCl_3$)} (Found: $M^{+\bullet}$, 412.2820. $C_{23}H_{40}O_6$ requires $M^{+\bullet}$, 412.2825). ν_{max} (KBr/cm^{-1}) 2927, 2856, 1737, 1457, 1373, 1240, 1165, 1039, 920, 875; δ_H (500 MHz, $CDCl_3$) 5.77 (2H, m), 5.37 (1H, d, *J* 17.6 Hz), 5.26 (1H, d, *J* 10.3 Hz), 5.09 (1H, dd, *J* 1.5 and 17.6 Hz), 5.05 (2H, m), 4.68 (2H, ABq, *J* 3.4 Hz), 3.99 (1H, t, *J* 7.8 Hz), 3.69 (1H, td, *J* 3.4 and 8.3 Hz), 3.58 (1H, m), 3.40 (3H, s), 2.53 (1H, m), 2.44 (2H, m), 2.33 (1H, m), 1.94 (1H, m), 1.81 (1H, m), 1.49 (2H, m), 1.41 (3H, s), 1.39 (3H, s), 1.31–1.27 (8H, complex m), 0.88 (3H, t, *J* 6.8 Hz); δ_C (125 MHz, $CDCl_3$) 172.6 (C), 135.0 (CH), 133.9 (CH), 119.2 (CH_2), 117.7 (CH_2), 108.8 (C), 96.6 (CH_2), 82.4 (CH), 79.4 (CH), 78.0 (CH), 73.6 (CH), 55.9 (CH_3), 34.7 (CH_2), 31.7 (CH_2), 30.7 (CH_2), 30.5 (CH_2), 29.4 (CH_2), 27.2 (CH_3), 26.9 (CH_3), 26.8 (CH_2), 25.3 (CH_2), 22.6 (CH_2), 14.1 (CH_3); *m/z* (EI, 70 eV) 412 ($M^{+\bullet}$, 0.6%), 397 [$(M–CH_3\cdot)^+$, 1.9], 229 (42), 125 (100), 98 (85).

Concentration of fraction B (R_f 0.3 in 30 : 70 v/v ethyl acetate–hexane) gave the starting ester (**21**) (73 mg, 78% recovery) as a pale-yellow oil and identical, in all respects, with authentic material.

(3a*S*,8*R*,10*E*,11a*S*)-3a,4,5,8,9,11a-Hexahydro-8-[(1*R*)-1-methoxymethoxyheptyl]-2,2-dimethyl-6*H*-1,3-dioxolo[4,5-*e*]oxecin-6-one (23) and (3a*S*,8*R*,10*Z*,11a*S*)-3a,4,5,8,9,11a-Hexahydro-8-[(1*R*)-1-methoxymethoxyheptyl]-2,2-dimethyl-6*H*-1,3-dioxolo[4,5-*e*]oxecin-6-one.

Grubbs' first-generation catalyst[18] (17 mg, 0.021 mmol, 20 mol %) was added to a magnetically stirred solution of diene (**22**) (38.4 mg, 0.104 mmol) in deoxygenated dichloromethane (100 mL) maintained under a nitrogen atmosphere. The resulting mixture was brought to and maintained at reflux for 24 h then cooled and filtered through a short pad of TLC-grade silica gel. Concentration of the filtrate and subjection of the residue to flash chromatography (silica, 5 : 95 → 15 : 85 v/v ethyl acetate–hexane gradient elution) provided two fractions, A and B.

Concentration of fraction A (R_f 0.4 in 3 : 7 v/v ethyl acetate–hexane) gave *compound (**23**)* (8.8 mg, 23%) as a pale-yellow oil and a 4 : 1 mixture (as judged by ^{1}H NMR spectral analysis) of conformers, $[\alpha]_D$ +35° (*c* 0.9) {lit.,[4] $[\alpha]_D$ (for *ent*-**23**) –18.1° (*c* 0.6, $CHCl_3$)}. ν_{max} (KBr/cm^{-1}) 2930, 2858, 1733, 1452, 1370, 1236, 1165, 1065, 1039; δ_H (500 MHz, $CDCl_3$) (major conformer) 5.77 (1H, ddd, *J* 4.6, 11.3 and 15.9 Hz), 5.34 (1H, dd, *J* 9.4 and 15.9 Hz), 4.84 (1H, ddd, *J* 2.5, 3.8 and 8.8 Hz), 4.70 (2H, t, *J* 6.5 Hz), 3.94 (1H, t, *J* 8.8 Hz), 3.68–3.59 (2H, complex m), 3.42 (3H, s), 2.66 (1H, m), 2.55 (1H, dt, *J* 3.8 and 14.0 Hz), 2.44 (1H, dm, *J* 12.8 Hz), 2.39–2.27 (2H, complex m), 2.09 (1H, dt, *J* 4.8 and 14.9 Hz), 1.99 (1H, m), 1.61 (2H, m), 1.42 (6H, s), 1.34–1.26 (7H, complex m), 0.89 (3H, m); δ_H (500 MHz, $CDCl_3$) (minor conformer) 5.92 (1H, ddd, *J* 5.9, 9.9 and 15.7 Hz), 5.75 (1H, m, partially obscured), 5.10 (1H, dt, *J* 3.3 and 9.4 Hz), 4.73 (2H, t, *J* 4.8 Hz), 3.87 (1H, dd, *J* 6.5 and 9.0 Hz), 3.77 (1H, td, *J* 4.8 and 10.7 Hz), 3.65 (1H, m, partially obscured), 3.41 (3H, s), 2.66 (1H, m), 2.55 (1H, dt, *J* 3.8 and 14.0 Hz), 2.44 (1H, dm, *J* 12.8 Hz), 2.39–2.27 (2H, complex m), 2.09 (1H, dt, *J* 4.8 and 14.9 Hz), 1.99 (1H, m), 1.61 (2H, m), 1.47 (6H, s), 1.34–1.26 (7H, complex m), 0.89 (3H, m); δ_C (75 MHz, $CDCl_3$) (major conformer) 171.8 (C), 130.1 (CH), 129.3 (CH), 108.8 (C), 96.4 (CH_2), 84.4 (CH), 79.8 (CH), 79.2 (CH), 73.5 (CH), 56.0 (CH_3), 34.2 (CH_2), 31.7 (CH_2), 30.8 (CH_2), 30.5 (CH_2), 29.4 (CH_2), 27.1 (CH_3), 26.9 (CH_3), 25.4 (CH_3), 25.3 (CH_2), 22.6 (CH_2), 14.0 (CH_3); *m/z* (EI, 70 eV) 384 ($M^{+\bullet}$, <1%), 369 [$(M–CH_3\cdot)^+$, 5], 237 (40), 220 (45), 113 (78), 85 (88), 45 (100).

Concentration of fraction B (R_f 0.3 in 3 : 7 v/v ethyl acetate–hexane) gave the Z-*isomer of compound (**23**)* (11.9 mg, 31%) as a clear, colorless oil, $[\alpha]_D$ –3.5° (*c* 1.1) [Found: $(M–CH_3OCH_2O\cdot)^+$, 323.2224. $C_{21}H_{36}O_6$ requires $(M–CH_3OCH_2O\cdot)^+$, 323.2222]. ν_{max} (KBr/cm^{-1}) 2929, 2858, 1736, 1452, 1371, 1240, 1157, 1035; δ_H (300 MHz, $CDCl_3$) (major conformer) 5.77 (1H, td, *J* 7.7 and 10.8 Hz), 5.52 (1H, t, *J* 10.8 Hz), 5.06 (1H, ddd, *J* 2.1, 4.4 and 11.9 Hz), 4.68 (2H, m), 4.51 (1H, t, *J* 8.4 Hz), 3.67 (2H, m), 3.41 (3H, s) 2.67 (2H, m), 2.50–2.00 (6H, complex m), 1.39 (6H, m), 1.35–1.26 (8H, complex m), 0.89 (3H, m); δ_C (75 MHz, $CDCl_3$) (major conformer) 170.8 (C), 130.9 (CH), 130.3 (CH), 107.7 (C), 96.4 (CH_2), 81.4 (CH), 78.3 (CH), 77.1 (CH), 72.9 (CH), 55.9 (CH_3), 32.1 (CH_2), 31.7 (CH_2), 30.9 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 28.1 (CH_2), 27.1 (CH_3), 26.9 (CH_3), 25.1 (CH_2), 22.6 (CH_2), 14.1 (CH_3); *m/z* (LSIMS) 323 [$(M–CH_3OCH_2O\cdot)^+$, 32%], 265 (100), 207 (86).

(+)-Microcarpalide [(+)-1].

A magnetically stirred solution of compound (**23**) (8.8 mg, 0.024 mmol) in dichloromethane (1 mL) maintained under a nitrogen atmosphere was cooled to 0 °C and treated with BF_3•Et_2O (5 μL, 0.024 mmol) and ethanedithiol (8 μL, 0.095 mmol). The resulting mixture was stirred at 0 °C for 1 h then quenched with $NaHCO_3$ (1 mL of a saturated aq. solution) and the separated aqueous layer extracted with ether (3 × 7 mL). The combined organic fractions were washed with water (1 × 20 mL) and brine (1 × 20 mL) before being dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a light-yellow residue. Subjection of this material to column chromatography (silica, 1 : 1 → 7 : 3 v/v ethyl acetate–hexane then 1 : 9 v/v methanol–chloroform gradient elution) and concentration of the relevant fractions (R_f 0.2 in 1 : 9 v/v methanol–chloroform) gave (+)-microcarpalide [(+)-**1**] (6.1 mg, 89%) as a clear, colorless oil and a 3.2 : 1 mixture (as judged by ^{1}H NMR spectral analysis) of conformers, $[\alpha]_D$ +20° (*c* 0.6, methanol) {lit.,[1] $[\alpha]_D$ [for (–)-**1**] –22° (*c* 0.7, methanol)}. ν_{max} (KBr/cm^{-1}) 3369, 2926, 2856, 1711, 1436, 1225, 1155, 1064; δ_H (500 MHz, CD_3CN) (major conformer) 5.70 (1H, dd, *J* 15.6 and 2.5 Hz), 5.51 (1H, dddd, *J* 2.2, 5.0, 10.2 and 15.6 Hz), 4.82 (1H, ddd, *J* 3.2, 5.0 and 11.4 Hz), 4.11 (1H, br s), 3.78 (1H, br s), 3.54 (1H, br s), 2.84 (2H, br s) 2.48 (1H, ddd, *J* 1.5, 10.6 and 15.3 Hz), 2.27 (1H, m), 2.22–2.05 (3H, complex m), 1.75 (1H, m), 1.48–1.38 (3H, complex m), 1.35–1.28 (8H, complex m), 0.87 (3H, m); δ_H (500 MHz, CD_3CN) (minor conformer) 5.68 (1H, ddd, *J* 5.4, 10.6 and 16.9 Hz), 5.06 (1H, dd, *J* 9.6 and 15.8 Hz), 4.61 (1H, ddd, *J* 2.5, 4.3 and 8.4 Hz), 3.62 (1H, t, *J* 8.9 Hz), 3.55 (1H, m), 3.25 (1H, t, *J* 7.7 Hz), 3.10 (2H, br s), 2.55 (1H, dd, *J* 2.2 and 3.5 Hz), 2.52 (1H, dd, *J* 2.3 and 7.0 Hz), 2.32 (1H, m), 2.15 (1H, m), 2.01 (1H, dd, *J* 2.0 and 7.4 Hz), 1.48–1.38 (2H, m), 1.35–1.28 (8H, complex m), 0.87 (3H, m); δ_C (125 MHz, CD_3CN) (major and minor conformers) see Table 2. In accordance with the report of Heimscheidt,[1] no satisfactory mass spectral data could be recorded for (+)-microcarpalide.

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