Synthesis of the Algicidal Allelochemical from *Lemna trisulca* (Duckweed)

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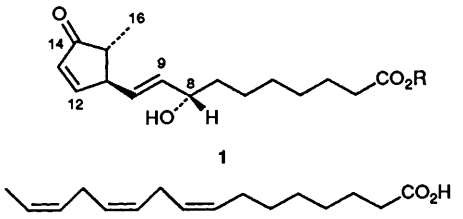
Synthesis [in (±)-form] of the allelochemical produced by duckweed, which inhibits algae growth, is reported. Michael addition of nitromethane to 2-methylcyclopent-2-enone followed by carbonyl protection and Nef reaction gives an aldehyde which is elaborated by Wittig reaction and reduction. The cyclopentenone double bond is introduced by selenation methods. A chiral side-chain intermediate is prepared from D-mannitol but its application in the Wittig reaction has not been successful. Comment is made on possible biogenetic routes from a methylene interrupted C_{16}-triene fatty acid.

During a study of the aquatic plant *Lemna trisulca*, a duckweed growing in still waters such as ponds and canals, Monaco and Previtera isolated the cyclopentenone **1** (R = H) along with its putative precursor the triene acid **2** having methylene interrupted conjugation.[1] The cyclopentenone shows good growth inhibition towards a variety of algae, presumably protecting the photosynthetic apparatus of *L. trisulca* from light exclusion by algae colonisation. We have been interested in the biosynthetic relationship between cyclopentenones and fatty acids[2,3] and this has prompted us to undertake a synthesis of the *Lemna* cyclopentenone **1** as its ethyl ester.



1 **2**

The synthetic approach to the (±)-compound is shown in Scheme 1. Michael addition of nitromethane to 2-methylcyclopent-2-enone **3** in the presence of benzyl(trimethyl)ammonium hydroxide ('Triton B')[4] at 65 °C gave the nitro ketone **4**[5] in excellent yield (86%), which was protected as the ethylene ketal **5** (82%).[6] Several variants of the Nef reaction were tried in order to convert the latter into the aldehyde **6** and best results were obtained by the McMurry conditions,[7] titanium(III) chloride buffered at pH 6.5, though yields were still only modest (42%). The oxophosphorane **11** was made by a one-pot procedure,[8] and Wittig reaction with the aldehyde **6** gave the alkene **7** (35%) which, as judged by the ^{1}H NMR spectrum, was formed exclusively in the (*E*)-configuration. Reduction of the carbonyl of (±)-compound **7** with *trans*-arrangement of side chains, introduces a new asymmetric centre. The reaction was carried out with sodium borohydride, no 1,4-reduction being observed, and the product **8**, which was not further separated at this stage, appeared to contain one predominant diastereoisomer. It was deprotected under acidic conditions in the usual way, the overall yield in the two stages being 79%.

The cyclopentanone **8** was converted into the required cyclopentenone using the procedure of Reich.[9] The anion[10] from **8** was formed using 2.1 equivalents of hexamethyldisilazane base and treated with benzeneselenenyl bromide to give **9**, oxidised to the selenoxide by hydrogen peroxide.[11] Elimination in the usual way gave the desired *Lemna* cyclopentenone structure as its ethyl ester. Because of difficulties in the final removal of the protecting group using tetrabutylammonium fluoride and other reagents, it was found unprofitable to block the hydroxy group as its *tert*-butyldimethylsilyl derivative prior to the phenylselenation.

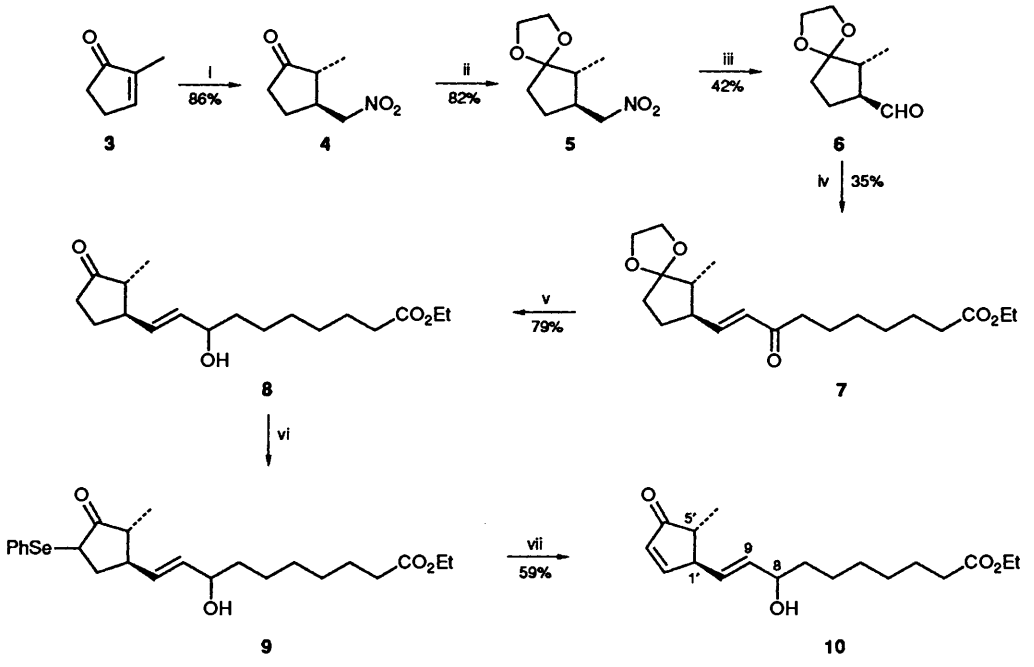
Table 1 ^{13}C NMR spectroscopic data for the natural *L. trisulca* algicide methyl ester **1** (R = Me) and the synthetic (±)-diastereoisomer of the ethyl ester **10**

	δ	
Carbon[a]	Natural **1** (R = Me)	Synthetic (±)-**10**
1	174.4	173.9
2	34.1	34.3
3	24.9	24.9
4	29.4	29.1
5	29.7	29.2
6	25.6	25.2
7	37.2	37.3
8	72.7	72.4
9	135.2	135.1
10	130.2	130.0
1′	52.0	52.5
2′	163.4	164.3
3′	133.0	133.0
4′	210.9	211.4
5′	47.1[b]	47.4
5′-Me	13.5	14.1

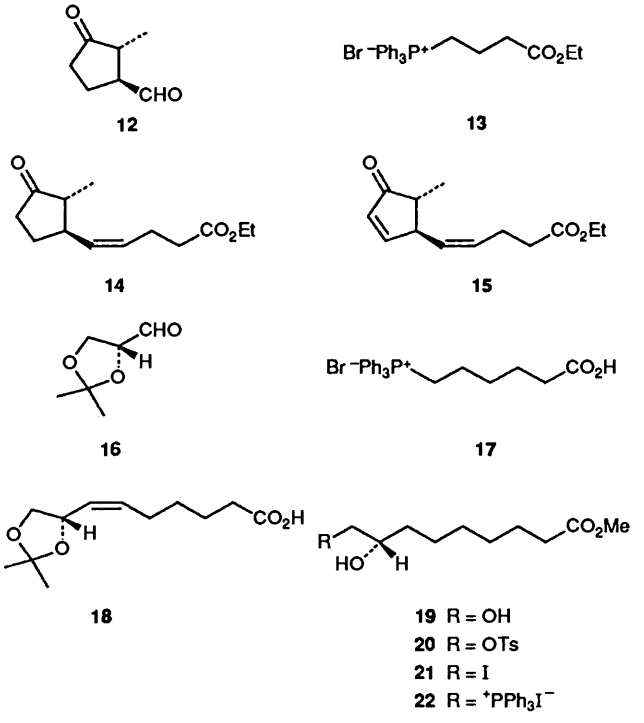
[a] For numbering see structure **10**. [b] Originally reported[1] in error as δ 45.1.

The synthetic cyclopentenone **10**, as isolated, consisted largely of one diastereoisomer (~85%) and comparison of the ^{13}C NMR spectrum of this with that published[1] for the natural *Lemna trisulca* compound as its methyl ester (Table 1) showed agreement within probable experimental error except for the C-5′ resonance where the natural material had a value of δ 45.1 as against 47.4. Initially this led us to suspect that whereas our material was *trans*- about the C-1′–C-5′ axis, the natural compound might be *cis*. However, on communicating these results to Professor Previtera he kindly informed us that the figure given is a misprint for 47.1 and so the two sets of data are in reasonable agreement throughout.

During preliminary work directed to making the *Lemna* compound **1** in optically active form, it was established that a Wittig reaction between the unprotected formyl ketone **12** and the unstabilised ylide from **13** satisfactorily gave the olefin **14** with a (*Z*)-olefinic linkage, and the latter was dehydrogenated to **15** by the selenation–elimination procedure given above.

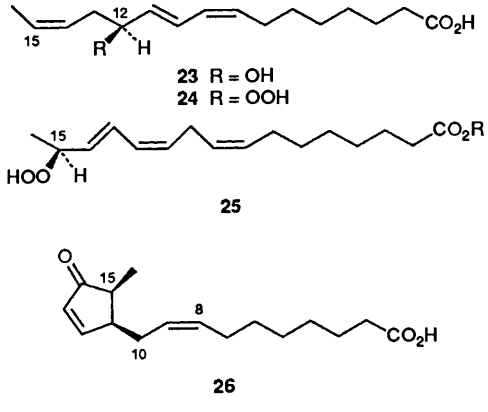


Scheme 1 Synthesis of the (±)-*Lemna trisulca* algicide *Reagents and conditions:* i, $MeNO_2$/Triton B; ii, $HO[CH_2]_2OH$/PTSA; iii, $TiCl_3$, pH 6.5; iv, $Ph_3P{=}CHCO[CH_2]_6CO_2Et$ **11**; v, $NaBH_4/H^+$; vi, LiHMDS/ PhSeBr; vii, 30% H_2O/Py



Since alkylated chiral β-oxido ylides are reported to undergo the Wittig reaction with formation of an (*E*)-olefinic linkage,[12] the necessary chiral synthon **22** for application to our example was made. (*R*)-2,3-Isopropylideneglyceraldehyde **16** was prepared in good yield from D-mannitol[13] and treated with a Wittig reagent from **17**, made from 6-bromohexanoic acid,[14] to give olefin **18** which was catalytically hydrogenated and then deprotected to produce the (*S*)-diol **19**. A crystalline toluene-*p*-sulfonate **20** was formed at the primary alcohol and Finkelstein exchange then gave the desired iodide **21**. Using the (*R*)-(+)-form of Mosher's acid as a chiral probe, an ester was formed at the 8-OH of the iodide **21** and the product was examined by ^1H NMR. The 8-H (methine) signal, initially observed as a multiplet, formed a single clean triplet when decoupled from the 9-CH_2, suggesting that compound **21** was enantiomerically pure as expected. On treatment with triphenylphosphine, a phosphonium salt **22** was formed in a slow reaction, but, using a selection of bases to produce the ylide, we have not been able to carry out a successful olefin-forming reaction with the aldehyde function of **12**. Further work is needed to complete a synthesis of **1** in optically active form.

It has been suggested[1] that the biosynthetic origin of the *L. trisulca* compound **1** lies in the prostaglandin-like endoperoxide pathway, and indeed the isolation of the hydroxy acid **23** as a companion substance in *L. trisulca* lends support as **24** would be the initiating hydroperoxide. On the other hand, the allene epoxide (12-oxoPDA) type of route,[2] using the 15-hydroperoxide **25**, could lead directly to **26**, *cis* about the 1′,5′-axis. This



is a biosynthetic process used by many plants.[15] Epimerisation at C-5′ (C-15 on fatty acid numbering), together with allylic hydroxylation (along with accompanying rearrangement and stereomutation of the olefin) could give **1**. Further work is needed to distinguish between these two pathways.

Experimental

NMR Spectra were recorded using Bruker AM400, WM.250

and WP80SY spectrometers in $CDCl_3$ (unless stated otherwise). *J*-Values are given in Hz. Mass spectra were recorded on an MS902 or a VG 7070E mass spectrometer.

2-Methyl-3-nitromethylcyclopentanone **4**.—2-Methylcyclopent-2-enone (5 g, 52 mmol) and 'Triton B' (0.5 cm^3, 40% solution in methanol) in dry nitromethane (10 cm^3) were heated to 65 °C under nitrogen and stirred for 5 h. The product was poured into water and worked up by diethyl ether extraction. Distillation gave the title cyclopentanone **4** (7.01 g, 86%), an oil, b.p. 150 °C/1.0 mmHg (Found: C. 53.65; H, 7.2; N, 8.75%; M^+, 157.076. $C_7H_{11}NO_3$ requires C, 53.5; H, 7.0; N, 8.9%; *M*, 157.078); δ_H(250 MHz) 1.13 (3 H, d, *J* 7.7, Me), 1.66 (1 H, m, CH), 1.95 (1 H, m, CH), 2.26 (2 H, m, CH_2), 2.49 (2 H, m, CH_2CO) and 4.55 (2 H, m, CH_2NO_2); ν_{max}(film)/cm^{-1} 1735 (C=O), 1555 and 1380 (NO).

2'-Methyl-3'-nitromethylspiro[1,3-*dioxolane*-2,1'-*cyclopentane*] **5**.—The cyclopentanone **4** (1.77 g, 11.3 mmol), ethylene glycol (930 mg, 15 mmol) and toluene-*p*-sulfonic acid monohydrate (20 mg) in benzene (20 cm^3) were heated under reflux in a Soxhlet apparatus containing 3Å molecular sieves for 5 h. Work-up, washing with sodium hydrogen carbonate solution, drying ($MgSO_4$) and evaporation gave an oil which was purified by chromatography on silica gel (eluent: ethyl acetate–light petroleum, b.p. 60–80 °C, 3:17). The title acetal **5** (1.85 g, 82%) was an oil (Found: *m/z* 141.091. $C_9H_{15}NO_4 - CH_2NO_2$ requires 141.092); δ_H(80 MHz) 3.90 (4 H, s, OCH_2CH_2O) and 4.20–4.70 (2 H, m, CH_2NO_2); ν_{max}(film)/cm^{-1} 1550 (NO).

2'-Methylspiro[1,3-*dioxolane*-2,1'-*cyclopentane*]-3'-*carbaldehyde* **6**.—The acetal **5** (1.7 g, 8.5 mmol) in THF (42 cm^3) was added to a stirred 30% titanium(III) chloride solution (17.5 cm^3, 34 mmol) and ammonium acetate (15.7 g) in water (75 cm^3) under nitrogen. The initially dark blue solution was stirred (10 h) and water (350 cm^3) was added. Work-up by extraction with chloroform gave the title acetal carbaldehyde **6** (602 mg, 42%) (Found: M^+, 170.095. $C_9H_{14}O_3$ requires *M*, 170.095); δ_H(80 MHz) 0.97 (3 H, d, *J* 6.4, Me), 1.72–1.98 (4 H, m, 2 × CH_2), 2.08–2.58 (2 H, m, 2 × CH_2), 3.93 (4 H, s, OCH_2CH_2O) and 9.63 (1 H, d, *J* 1.9, CHO); ν_{max}/cm^{-1} 1720 (C=O).

Ethyl 10-(2'-*Methylspiro*[1,3-*dioxolane*-2,1'-*cyclopentan*-3'-*yl*])-8-*oxodec*-9-*enoate* **7** *by Wittig Reaction*.—Methyltriphenylphosphonium iodide (8.08 g, 20 mmol) in dry ether (50 cm^3) at 0 °C was treated under nitrogen with butyllithium (1.6 mol dm^{-3} in hexane; 12.5 cm^3) for 1 h and then added to ethyl 7-chloroformylheptanoate (4.41 g, 20 mmol) in ether (10 cm^3) at 0 °C. The mixture was stirred at room temperature for 1 h when the solvent was removed and the residue extracted with chloroform (200 cm^3). After washing with sodium hydroxide (2 mol dm^{-3}), and drying ($MgSO_4$), the chloroform was evaporated and the residue was chromatographed on silica gel (eluent: chloroform–methanol, 19:1) to give the phosphorane **11** (4.1 g, 44%) which was used immediately.

A solution of the aldehyde **6** (400 mg, 2.3 mmol) and the stabilised phosphorane **11** (4.1 g) in dry dichloromethane (20 cm^3, deacidified by running through an alumina column) was stirred at room temperature under nitrogen for 24 h. The solvent was removed and the residue was thoroughly extracted with ether. Work-up gave an oil which was chromatographed on silica gel (eluent: ethyl acetate–light petroleum, b.p. 60–80 °C, 1:5) to give the spiroacetal **7** (223 mg, 35%) (Found: M^+, 352.224. $C_{20}H_{32}O_5$ requires *M*, 352.222); δ_H(80 MHz) 0.89 (3 H, d, *J* 6.6, Me), 1.24 (3 H, t, OCH_2Me), 1.20–2.00 (12, m, 6 × CH_2), 2.10–2.60 (6 H, m, 2 × CH_2, 2 × CH), 3.92 (4 H, s, OCH_2CH_2O), 4.11 (2 H, q, OCH_2Me), 6.35 (1 H, d, *J* 15.9, 9-H) and 6.70 (1 H, dd, *J* 15.9, 8.0, 10-H); ν_{max}(film)/cm^{-1} 1730 (ester C=O), 1690 (ketone) and 1625 (C=C).

Ethyl 8-*Hydroxy*-10-(2'-*methyl*-3'-*oxocyclopentyl*)*dec*-9-*enoate* **8**.—The spiro acetal **7** (220 mg, 0.62 mmol) in ethanol (10 cm^3) at 0 °C was treated with sodium borohydride (30 mg, 0.79 mmol). After stirring (1 h) at 0 °C the product was acidified (HCl; 4 mol dm^{-3}), stirred (1 h) and worked-up. Purification by column chromatography on silica gel (eluent: ethyl acetate–light petroleum, b.p. 60–80 °C, 2:3) gave the hydroxycyclopentanone **8** (152 mg, 79%) (Found: *m/z* 292.202. $C_{18}H_{30}O_4 - H_2O$ requires 292.201); δ_H(400 MHz) 1.06 (3 H, m, Me), 1.25 (3 H, t, OCH_2Me), 1.33 (6 H, br s, 4,5,6-H_2), 1.41–1.70 (6 H, m, 3,7,5'-H_2), 1.75–1.90 (1 H, m, 2'-H), 2.05–2.20 (2 H, m, 4'-H_2), 2.28 (2 H, t, *J* 7.4, 2-H_2), 2.30–2.43 (1 H, m, 1'-H), 4.07–4.14 (1 H, m, C*H*OH), 4.13 (2 H, q, OCH_2Me) and 5.55–5.68 (2 H, m, 9,10-H_2); ν_{max}(film)/cm^{-1} 3600–3200 (OH) and 1730 (ester and ketone).

(±)-*Ethyl* 8-*Hydroxy*-10-(5'-*methyl*-4'-*oxocyclopent*-2-*enyl*)-*dec*-9-*enoate* **10** *by Phenylselenation*.—Cyclopentanone **8** (40 mg, 0.13 mmol) in anhydrous THF (2 cm^3) was stirred with lithium hexamethyldisilazide (1.0 mol dm^{-3} in THF; 0.28 cm^3) under nitrogen at −78 °C for 15 min. Benzeneselenenyl bromide (30.5 mg, 0.13 mmol) in THF (0.1 cm^3) was then added, stirring at −78 °C for 20 min. After warming to room temperature, ether (20 cm^3) was added and the mixture was worked-up to give the α-phenylselenocyclopentanone **9** (60 mg) as an oil which was dissolved in dichloromethane (5 cm^3) and added to a solution of pyridine (10 drops), hydrogen peroxide (2 cm^3, 30%) and water (2 cm^3). The two phase system was stirred vigorously at 20 °C for 2 h and diethyl ether (20 cm^3) was then added. Work-up by ether extraction followed by chromatographic purification on silica gel (eluent: ethyl acetate–light petroleum, b.p. 68–80 °C, 7:13) gave the ethyl ester **10** of the (±)-*L. trisulca* cyclopentenone (23.5 mg, 59%) as a colourless oil (Found: *m/z* 290.189. $C_{18}H_{28}O_4 - H_2O$ requires 290.189); δ_H(400 MHz) 1.20 (3 H, d, *J* 7.4, Me), 1.25 (3 H, t, OCH_2Me), 1.33 (6 H, br s, 4,5,6-H_2), 1.41–1.64 (4 H, m, 3,7-H_2), 1.78 (1 H, br s, OH), 2.04–2.11 (1 H, m, 5'-H), 2.29 (2 H, t, 2-H_2), 3.10 (1 H, m, 1'-H), 4.10–4.15 (1 H, m, C*H*OH), 4.12 (2 H, q, OCH_2Me), 5.62 (2 H, m, 9,10-H_2), 6.17 (1 H, dd, *J* 5.7, 2.1, 3'-H) and 7.48 (1 H, dd, *J* 5.7, 2.3, 2'-H); for δ_C see Table 1; ν_{max}(film)/cm^{-1} 3600–3620 (OH), 1720 (ester C=O), 1705 (C=O), 1650 (C=C) and 1585 (conj. C=C).

Ethyl 5-(2'-*Methyl*-3'-*oxocyclopentyl*)*pent*-4(Z)-*enoate* **14**.—Lithium hexamethyldisilazide (1.0 mol dm^{-3} in THF; 0.87 cm^3) was added to a stirred suspension of 3-(ethoxycarbonyl)propyl(triphenyl)phosphonium bromide **13** (379 mg, 0.87 mmol) in anhydrous THF (5 cm^3) at −78 °C under nitrogen. The mixture was warmed to −30 °C over 20 min and then cooled to −78 °C. Formylcyclopentanone **12** (100 mg, 0.79 mmol) in THF (1 cm^3) was added over 10 min and the temperature was maintained at −78 °C for 10 min before warming to 0 °C over 1 h. The product was poured into citric acid solution (20 cm^3, 5%) and thoroughly extracted with ether. Work-up gave an oil which was chromatographed on silica gel (eluent: ethyl acetate–light petroleum, b.p. 60–80 °C) to give the (*Z*)-cyclopentanone **14** (65 mg, 35%). (Found: M^+, 224.143. $C_{13}H_{20}O_3$ requires *M*, 224.144); δ_H(400 MHz) 1.02 (3 H, d, *J* 6.9, Me), 1.26 (3 H, t, *J* 7.1, OCH_2Me), 1.57 (1 H, m, 5'-H), 1.81 (1 H, m, 5'-H), 2.10 (2 H, m, 4'-H_2), 2.37 (5 H, m, 2 × CH_2 and 2'-H), 2.62 (1 H, m, 1'-H), 5.32 (1 H, dd, *J* 10.6, 9.4, 5-H) and 5.50 (1 H, dt, *J* 10.6, 6.8, 4-H); ν_{max}(film)/cm^{-1} 1730 (ester and ketone) and 1650 (C=C).

Ethyl 5-(5'-*Methyl*-4'-*oxocyclopent*-2-*enyl*)*pent*-4(Z)-*enoate* **15**.—Lithium hexamethyldisilazide (1.0 mol dm^{-3} in THF; 0.27

cm^3) was added to the stirred cyclopentanone **14** (60 mg, 0.27 mmol) in dry THF (3 cm^3) at −78 °C under nitrogen. The mixture was stirred at −78 °C for 15 min when benzeneselenenyl bromide (64 mg, 0.27 mmol) was added over 5 min. The reaction mixture was kept at −78 °C for 10 min and then warmed to room temperature. Acidification with hydrochloric acid (0.5 mol dm^{-3}) and extraction with diethyl ether gave the α-phenylseleno ether as an oil (45 mg, 45%).

The latter (45 mg) was dissolved in dichloromethane (4 cm^3) and stirred vigorously with pyridine (5 drops), hydrogen peroxide (30%; 0.5 cm^3) and water (1 cm^3) as above. Work-up followed by chromatography on silica gel (eluent: ethyl acetate–light petroleum, b.p. 60–80 °C, 3:17) gave the (*Z*)-cyclopentenone **15** (15 mg, 25% overall) (Found: M^+, 222.124. $C_{13}H_{18}O_3$ requires *M*, 222.123); δ_H(400 MHz) 1.21 (3 H, d, *J* 7.4, Me), 1.27 (3 H, t, OCH_2Me), 2.03 (1 H, qd, *J* 7.4, 2.7, 5′-H), 2.39–2.55 (4 H, m, 2,3-H_2), 3.47 (1 H, ddd, 1′-H), 4.15 (2 H, q, OCH_2Me), 5.28 (1 H, dd, *J* 10.6, 9.9, 5-H), 5.52 (1 H, dt, *J* 10.6, 7.1, 4-H), 6.17 (1 H, dd, *J* 5.6, 2.1, 3′-H) and 7.39 (1 H, dd, *J* 5.6, 2.4, 2′-H); ν_{max}(film)/cm^{-1} 1740 (ester), 1705 (C=O), 1650 (C=C) and 1580 (conj. C=C).

3-*Formyl*-2-*methylcyclopentanone* **12**.—Using the procedure employed above for the protected ketone **5**, the nitro ketone **4** (2 g, 12.7 mmol) furnished the title aldehyde **12** (640 mg, 40%), b.p. 100–110 °C/0.9 mmHg (Found: M^+, 126.068. $C_7H_{10}O_2$ requires *M*, 126.069); δ_H(80 MHz) 1.15 (3 H, d, *J* 6.7, Me), 1.80–2.80 (6 H, m, 2 × CH_2, 2 × CH) and 9.77 (1 H, d, *J* 2.2, CHO); ν_{max}(film)/cm^{-1} 1740 (ketone) and 1720 (aldehyde).

Methyl (8S)-8,9-*Dihydroxynonanoate* **19**.—(*R*)-2,3-*O*-Isopropylideneglyceraldehyde **16** (4.1 g, 82%) was prepared from the lead tetraacetate cleavage of 1,2,5,6-di-*O*-isopropylidene-D-mannitol (m.p. 122–123 °C),[13] and had b.p. 44–45 °C/15 mmHg (lit.,[16] b.p. 39 °C/15 mmHg); $[\alpha]_D^{25}$ +61.1 (*c* 0.1, benzene) {lit.,[15] $[\alpha]_D^{25}$ +64 (*c* 0.1, benzene)}; δ_H(80 MHz) 9.71 (1 H, d, *J* 1.8, CHO).

Carboxypentyl(triphenyl)phosphonium bromide **17** was prepared (11.2 g, 96%) by refluxing (16 h) 6-bromohexanoic acid (5 g, 25.6 mmol) with triphenylphosphine (7.3 g, 28.2 mmol) in acetonitrile (30 cm^3) under nitrogen. It had m.p. 198–199 °C (Found: C, 62.9; H, 5.9. $C_{24}H_{26}BrO_2P$ requires C, 63.0; H, 5.7%).

Sodium hydride (1.10 g, 46 mmol) and anhydrous dimethyl sulfoxide (15 cm^3) were heated at 80 °C under nitrogen for 2 h, cooled to room temperature, and added to a solution of the phosphonium bromide **17** (10 g, 21.8 mmol) in DMSO (10 cm^3) over 1 h, followed by stirring for 30 min. The glyceraldehyde **16** (3.0 g, 23 mmol) in THF (3 cm^3) was added to the ylide over 2 h, when the mixture was stirred (1 h) and poured into water. The aqueous layer was extracted with ether and the extracts were discarded. The aqueous layer was acidified with citric acid (to pH 4.5) and thoroughly extracted with ether. Washing, drying and evaporation gave an oil, purified by chromatography on silica gel (eluent: ethyl acetate–light petroleum, b.p. 60–80 °C, 1:4). This gave (8*S*)-8,9-*O*-isopropylidenenon-6(*Z*)-enoic acid **18** (1.59 g, 33%); $[\alpha]_D^{25}$ +5.25 (*c* 2.4, $CHCl_3$) (Found: M^+, 228.134. $C_{12}H_{20}O_4$ requires *M*, 228.131); δ_H(250 MHz) 1.40, 1.43 (6 H, d, 2 × Me), 1.65 (2 H, m, $CH_2CH_2CO_2H$), 2.12 (2 H, m, CH=CHCH_2), 2.36 (2 H, t, CH_2CO_2H), 3.52 (1 H, dd, *J* 8.1, 9-H_A), 4.07 (1 H, dd, *J* 8.1, 6.1, 9-H_B), 4.82 (1 H, m, 8-H), 5.45 (1 H, m, 7-H) and 5.63 (1 H, dtd, *J* 10.9, 7.4, 0.4, 6-H); ν_{max}(film)/cm^{-1} 1710 (acid CO_2H).

The non-6(*Z*)-enoic acid **18** (1.55 g, 6.8 mmol) was hydrogenated over 10% palladium on carbon (100 mg) in ethanol (100 cm^3). Filtration and evaporation gave an oil which was dissolved in methanol (50 cm^3) and concentrated sulfuric acid (4 drops) and refluxed (2 h). Work-up gave, after chromatography on silica gel (eluent: ethyl acetate–light petroleum, b.p. 60–80 °C, 2:3 then 3:2), the title nonanoate **19** (0.96 g, 70%), a white oily solid, $[\alpha]_D^{25}$ +2.5 (*c* 2.8, $CHCl_3$) (Found: *m/z* 173.118. $C_{10}H_{20}O_4 - OCH_3$ requires *m/z* 173.119); δ_H(80 MHz) 1.10–1.80 (10 H, m, 5 × CH_2), 2.31 (2 H, t, CH_2CO_2H), 2.75 (2 H, br s, 2 × OH), 3.41–3.49 (3 H, m, CH_2OH, CHOH), 3.67 (3 H, s, OMe); ν_{max}(film)/cm^{-1} 1740 (ester).

Methyl (8S)-8-*Hydroxy*-9-*tosyloxynonanoate* **20**.—Compound **20** (950 mg, 59%) was made by stirring the nonanoate **19** (925 mg, 4.5 mmol) with toluene-*p*-sulfonyl chloride (907 mg, 4.7 mmol) in dry pyridine (8 cm^3) at −30 °C under nitrogen for 5 h. Stirring was continued at 0 °C for a further 20 h. The compound was purified chromatographically on flash silica (eluent: ethyl acetate–light petroleum, b.p. 60–80 °C, 1:3), m.p. 45–46 °C, $[\alpha]_D^{25}$ +2.75 (*c* 2.0, $CHCl_3$) (Found: $M^+ - C_9H_{13}O_4S$, 141.092. $C_8H_{13}O_2$ requires 141.092); δ_H(80 MHz) 1.10–1.70 (10 H, m, 5 × CH_2), 2.29 (2 H, t, CH_2CO_2Me), 2.44 (3 H, s, ArMe), 3.65 (3 H, s, OMe), 3.75–4.01 (3 H, m, CH_2OTs, CHOH), 7.34 (2 H, d, *J* 8, ArH_2) and 7.80 (2 H, d, *J* 8, ArH_2); ν_{max}($CHCl_3$)/cm^{-1} 3600–3300 (br OH), 1740 (ester) and 1600 (Ar).

2-*Hydroxy*-8-(*methoxycarbonyl*)*octyl*(*triphenyl*)*phosphonium Iodide* **22** *and Treatment of its Ylide with the Cyclopentanone Aldehyde* **12**.—Compound **20** (907 mg, 2.53 mmol) was refluxed in acetone (30 cm^3) for 2 h with sodium iodide (3 g, 20 mmol). Work-up gave methyl (8*S*)-8-hydroxy-9-iodononanoate **21** (756 mg, 95%), m.p. 55–57 °C (Found: $M^+ - C_2H_3O$, 271.021. $C_8H_{16}IO_2$ requires 271.022); δ_H(80 MHz) 1.10–1.80 (10 H, m, 5 × CH_2), 2.15 (1 H, br s, OH), 2.31 (2 H, t, CH_2CO_2H), 3.10–3.70 (3 H, m, CH_2I, CHOH) and 3.66 (3 H, s, OMe); ν_{max}($CHCl_3$)/cm^{-1} 3600–3300 (br, OH) and 1740 (ester).

The (*R*)-(+)-Mosher's ester derivative showed the C-8 methine proton (CHOR) at δ_H(400 MHz) 4.97 (1 H, tt, *J* 6.0, 5.4). When decoupled from the C-9 methylene protons a clean triplet was observed with no sign of doubling of the signal.

The iodide (327 mg, 1.04 mmol) was heated under nitrogen in benzene (20 cm^3) with triphenylphosphine (545 mg, 2.08 mmol) at 45 °C for 20 days. Work-up gave the β-hydroxyphosphonium iodide **22** (420 mg, 70%) as an amorphous oily solid. The latter (336 mg, 0.583 mmol) in dry THF (2 cm^3) at −78 °C and under nitrogen was treated with lithium hexamethyldisilazide (1.0 mol dm^{-3} in THF; 1.2 cm^3) over 3 min. The red reaction mixture was warmed to −50 °C over 10 min and then cooled back to −78 °C. A solution of the cyclopentanone aldehyde **12** (75 mg, 0.58 mmol) in THF (0.5 cm^3) was added slowly over 5 min and the product was kept at −78 °C for 15 min, then warmed to room temperature over 1 h. The reaction mixture was poured into 10% citric acid solution (10 cm^3) and worked-up with ether to give an oil. TLC comparisons with our (±)-material (above) indicated that none of the desired product had been formed. Chromatography on silica gel (eluent: ethyl acetate–light petroleum, b.p. 60–80 °C, 1:20) afforded three major products, none of which was the desired product as indicated by ^1H NMR examination. Generation of the ylide by methyllithium or butyllithium gave similar results.

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