Synthesis of 12-Oxophytodienoic Acid (12-OxoPDA) and the Compounds of its Enzymic Degradation Cascade in Plants, OPC-8:0, -6:0, -4:0 and -2:0 (*epi*-Jasmonic Acid), as their Methyl Esters

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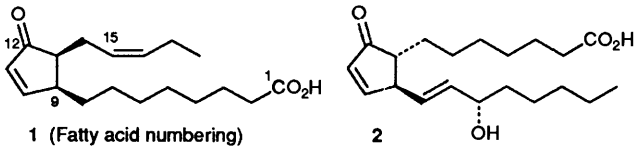
The synthesis of 12-Oxophytodienoic acid, and the compounds of its enzymic degradation sequence, OPC-8:0, -6:0, -4:0 and -2:0, important plant metabolites derived from linolenic acid, is reported. The syntheses use the known cyclopent-3-ene-1,2-diacetic acid as an early intermediate, and this is derived from the Cope rearrangement of 5-vinyltrinorborn-2-ene *via* bicyclo[4.3.0]nona-3,7-diene. Iodolactonisation and tributyltin hydride reduction provides the key intermediate (3-oxo-2-oxabicyclo[3.3.0]octan-6-yl)acetic acid for the OPC series, whilst phenylselenolactonisation and elimination provides the necessary unsaturated lactone (7-oxo-8-oxabicyclo[3.3.0]oct-2-en-4-yl)acetic acid for 12-oxoPDA. Members of the OPC-series were made by chain extending the saturated oxabicyclooctane acid: that for the OPC-4:0 involved double Arndt–Eistert reaction, whilst the intermediates for OPC-6:0 and -8:0 were made by Kolbe anodic crossed coupling. The lactones were then converted *via* their lactols, Wittig reaction, esterification and oxidation, into the compounds of the OPC ester series, including OPC-2:0 (methyl *epi*-jasmonate).

The unsaturated lactone 8-(7-oxo-8-oxabicyclo[3.3.0]oct-2-en-4-yl)octanoic acid required for 12-oxoPDA synthesis could also be prepared by anodic synthesis either from (7-oxo-8-oxabicyclo[3.3.0]oct-2-en-4-yl)acetic acid, or from its 2-phenylseleno-2,3-dihydro precursor as elimination occurred concomitantly during the reaction. Since yields were low, the unsaturated acid lactone was converted into its lactol and the (*Z*)-pent-2-enyl side-chain was inserted first. After TBDMS blocking of the cyclopentene hydroxy group, the side-chain was elaborated to give 5-(pent-2-enyl)cyclopent-2-enylacetaldehyde and chain extension carried out by a Grignard-demesylation procedure. Sequential desilylation and depyranylation, followed by oxidation of the diol, gave 12-oxoPDA, isolated as its methyl ester.

12-Oxophytodienoic acid (12-oxoPDA) **1** [1–3] is an important and widely distributed[4] plant metabolite bearing some structural resemblance to prostaglandin-A1 (PG-A1) **2**. Although it is formed from a fatty acid with methylene-interrupted conjugation *via* the hydroperoxide (13-hydroperoxylinolenic acid) **3**, its biosynthesis does not follow that established for mammalian systems but involves an epoxycarbonium ion **4** which loses a proton to form an allene epoxide **5**. Direct reaction of the latter short-lived intermediate with water leads to an α-**6** and a γ-ketol **7**, along with racemic 12-oxoPDA, formed *via* antarafacial electrocyclisation of the zwitterion **8** (*cf.* **5**).[5] Using [14,14-$^2H_2$]linolenic acid, we have devised a test for mass spectral discrimination between the plant and mammalian routes of biosynthesis.[5] In some plants the cyclisation is enzyme mediated, leading to (9*S*,13*S*,15*Z*)-12oxoPDA **1**.[6] The 9.13-*cis*-orientation of substituents, together with an easily epimerisable 13-centre, requires a synthetic approach different from those usually adopted to prepare *trans*-prostaglandins and this is discussed later.

12-OxoPDA is only the starting point for a series of important biochemical reactions. The 10-double bond in compound **1** is removed by enzymic reduction to form the enoic acid **9**, and a series of β-oxidations leads to chain-shortened acids (**10**; n = 5, 3, 1), the last member of the series being *cis*-(4*R*,5*S*,2′*Z*)-jasmonic (*epi*-jasmonic) acid **11**.[7,8] Natural jasmonic acid, valuable in perfumery (as its methyl ether), is usually known in the *trans*-(4*R*,5*R*,2′*Z*)-form **12** but it has been suggested that the valued odour is due to the presence of a small amount of stereoisomer **11**, *epi*- (or iso)jasmonic acid, in equilibrium with jasmonic acid **12**.[9,10] Jasmonic acid is an important plant-growth inhibitor and senescence inducer:[11–13] a related compound **13** has lately been identified as the tuber-



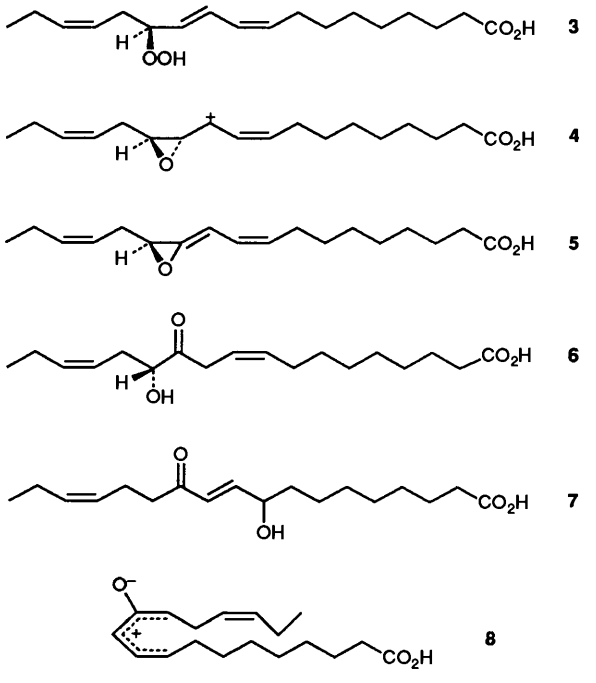
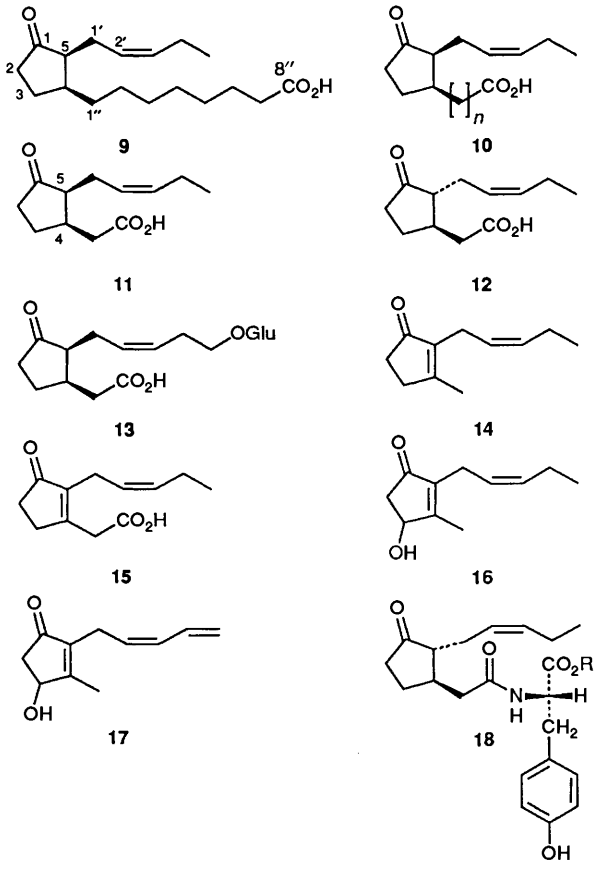


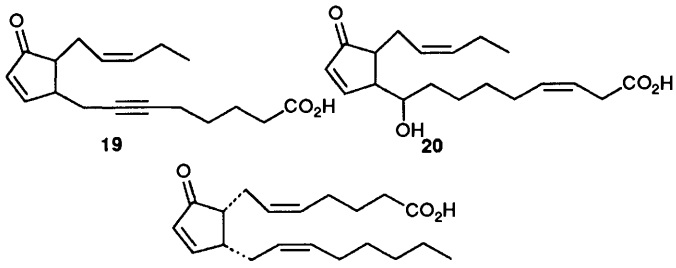
Table 1 Thermal rearrangement of commercial 5-vinyltrinorborn-2-ene at 200 lb in^{-2}

Temperature (T/°C)	Heating time (t/min)	Yield (%)	Reactant recovery (%) **25**/**24** unchanged
250	64	50.0	1.7
250	32	45.9	3.7
250	22	39.2	5.3
230	107	43.0	5.3
206	107	40.6	18.7
200	107	35.9	27.3
200	64	25.6	44.3
180	107	10.4	62.1



inducing factor in the potato plant.[14] Aside from these plant regulatory functions, it is likely that this pathway provides biogenetic clues on the origins of a number of other natural products. Jasmone **14** can be envisaged as being formed from 12-oxoPDA through processes of β-oxidation and migration of the ring double bond into the thermodynamically stable position **15**. Jasmone is then formed by decarboxylation of this vinylogous β-keto acid.[15] The pyrethrin ketols jasmolone **16** and pyrethrolone **17** probably arise in a similar fashion:[15] it has been shown that microbiological hydroxylation and dehydrogenation of the type required for this further elaboration is reasonable.[16,17] Jasmonic acid itself is sometimes found in higher plants or microbiological sources where it is conjugated with amino acids, *e.g.* jasmonyltyrosine **18**.[18,19]

Other natural products likely to originate *via* the 12-oxoPDA (allene epoxide) type of pathway are *Dicranium* (moss) extractives, *e.g.* compound **19**,[20] and the algae-inhibiting cyclopentenones, *e.g.* compound **20** of *Eleocharis microcarpa*,[21] a freshwater rush. The eicosanoid preclavulone-A **21**, found in coral (an animal), is now known to follow the allene epoxide pathway.[22,23] The oxygenated cyclopentanoids of *Lemna* (duckweed) may also have relationships with this pathway.[24]

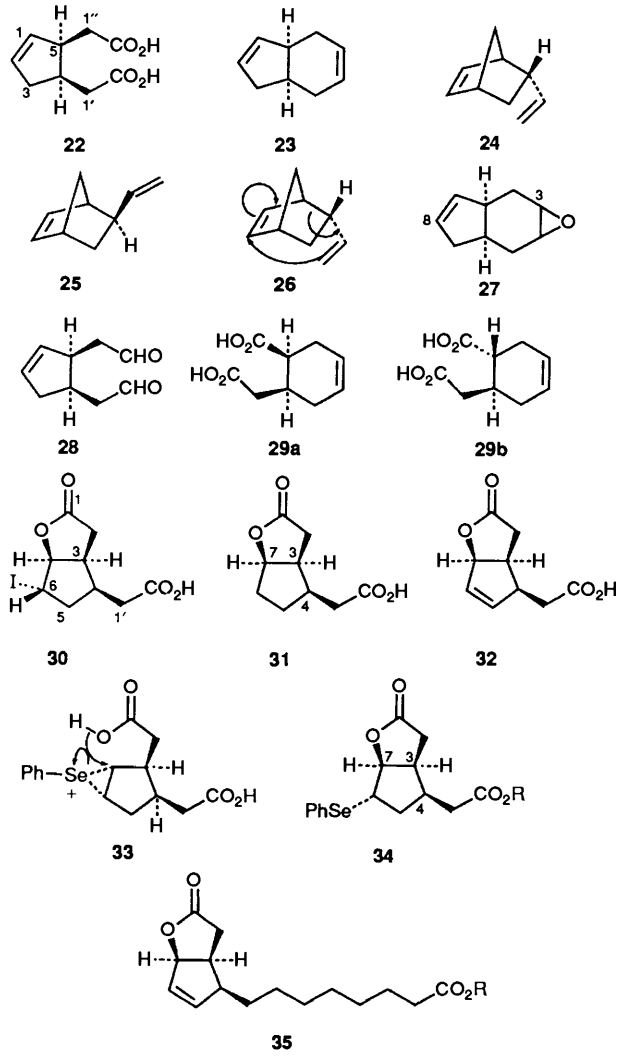


This paper describes the synthesis of 12-oxoPDA and the cascade of products formed by 10,11-reduction and successive β-oxidations.[25] These are OPC-8 **9** [the acronym is derived from the name 8-{3-oxo-2-*cis*-[(*Z*)-pent-2-enyl]cyclopentyl}-octanoic acid], OPC-6 (**10**; $n = 5$), OPC-4 (**10**; $n = 3$) and OPC-2 [*cis*-(2*Z*)-*epi*-jasmonic acid] **11**. As pointed out above, the syntheses have stricter stereochemical requirements than the usual prostaglandin syntheses because of the epimerisable *cis* attachments to the cyclopentanoid ring. Additionally, in the OPC series the synthetic approach was designed to allow easy isotopic labelling by insertion of the invariant (*Z*)-pentenyl at a late stage using a labelled Wittig reagent. Although the synthetic work carried out with racemic products, test optical resolutions of the key intermediate lactonic acids showed that it could be readily modified to produce chiral products if required.

The pivotal intermediate chosen for the synthesis was the *cis*-cyclopentenediacetic acid **22** made available by Stevens and Hrib who studied the selective oxidation of bicyclo[4.3.3]nona-3,7-diene **23** and employed it in a synthesis of jasmonic acid.[26] Unfortunately the diene **23** was not commercially available to us and our work therefore began with an examination of the thermal rearrangement of 5-vinyltrinorborn-2-ene,[27] which is commercially available as a mixture of *endo* (**24**) and *exo* (**25**) isomers (ratio 67:33). Since the rearrangement is a [3,3]-sigmatropic one (see structure **26**), only the *endo* isomer would be expected to participate. Table 1 shows the formation of diene **23** from the heating of commercial 5-vinyltrinorborn-2-ene in an autoclave at 200 lb in^{-2} for various periods of time at various temperatures. Monitoring was by GLC, the bicyclic product **23** being isolated by careful vacuum distillation from polymeric material. The best conversion was attained at 250 °C with a residence time of 64 min at 200 lb in^{-2}: this gave a yield of 50%. On the basis that only the *endo*-isomer rearranges, this is equivalent to a yield of 75%. Evidence that the latter is a reasonable assumption was obtained by heating of 5-vinyltrinorborn-2-ene neat at 206 °C/200 lb in^{-2} for 40 min, when examination of the recovered starting material showed that it was almost pure *exo*-form **25**. Although the possibility of *endo*/*exo* conversion exists, *via* retro-Diels–Alder reaction, no positive evidence for this was found and less stringent conditions led to unchanged starting material, whilst more stringent conditions led to formation of polymeric material.

Differential oxidation at the cyclohexane double bond in structure **23** was achieved by the Stevens–Hrib approach of differential functionalisation through formation of the epoxide **27**, using hypobromous acid generated from *N*-bromosuccinimide (NBS) in wet dimethyl sulphoxide (DMSO).[26] The bromohydrin, isolated in 50–55% yield, but not distilled, was treated with potassium t-butoxide in tetrahydrofuran (THF) to give the epoxide **27** in 80–90% yield. Oxidation using chromium trioxide in THF then gave the *cis*-dicarboxylic acid **22** in 30–33% yield.[26] A number of variations on the reaction did not

improve the yields. The epoxide **27** could be readily cleaved to the sensitive dialdehyde **28** by using sodium periodate but oxidation of this under neutral conditions with pyridinium dichromate (PDC) in dimethylformamide (DMF) gave diacid **22** in only 27% yield. Ozonisation of diene **23** was unselective, giving diacids **22** and (**29a** + **29b**) in a 1:3 ratio: various modifications such as addition of acid or pyridine failed to improve selectivity and our main supply of the *cis*-dicarboxylic acid **22** was obtained by the oxidation of the selectively epoxidised product **27**.



The diacid **22** was now iodolactonised with sodium hydrogen carbonate–iodine/potassium iodide in the dark, giving the crystalline iodo lactone **30** in 75–80% yield. Deiodination [tributyltin hydride–azoisobutyronitrile (AIBN) in THF] gave the lactone **31**,[26] m.p. 86–87 °C (80%), which is the key intermediate for the OPC-series. The hydrogens at carbons 3, 4 and 7 lie on the same face of the molecule as was shown by NOE experiments. Thus, irradiation at 7-H (δ 5.10) caused enhancement at 3-H (δ 3.15, 3.4%), and irradiation at 3-H caused enhancement at 7-H (4.7%) and 4-H (δ 2.43, 5.3%).

The key intermediate for 12-oxoPDA, the unsaturated lactone **32**, was also prepared from diacid **22** *via* selenolactonisation. Treatment with benzeneselenenyl chloride in dry THF at −79 °C gave crystalline lactone **34** (75–80%) *via* intermediate **33**. Irradiation of 3-H (δ 3.35) caused enhancement to 4-H (δ 2.95, 6.3%) and 7-H (δ 4.99, 5.6%): irradiation at 4-H gave a NOE enhancement of 6.4% at 3-H. Direct oxidative elimination of the phenylseleno group proved unsatisfactory, but the difficulty was readily overcome by esterification (CH_2N_2) followed by treatment with hydrogen peroxide in THF, when the desired unsaturated ester was obtained in 96% yield, and was then hydrolysed by cold methanolic potassium hydroxide to afford the unsaturated lactone **32**, m.p. 68–69 °C.

All the synthetic intermediates and products in this paper are recemic unless mentioned otherwise, but it seemed desirable to ascertain if, should it be required, the compounds could be obtained in optically pure form. This could be achieved by optical resolution of the bicyclic lactones **31** and **32**. Each lactone was esterified with (−)-borneol and for each case the pair of diastereoisomeric products could be satisfactorily resolved by HPLC as described in the Experimental section.

For further elaboration of the unsaturated lactone **32** towards 12-oxoPDA, a six-carbon homologation of the side-chain was required and an electrolytic method was selected.[28] Electrolysis of the lactonic acid **32** with methyl hydrogen suberate (3 mol equiv.) in methanol under Kolbe anodic conditions gave the required ester **35**; R = Me, though in disappointing yield (17%) after separation from a complex product by preparative TLC (PLC), followed by HPLC. NOE Experiments showed that the 3-, 4- and 7-protons lay on the same face of the cyclopentene ring. Since it was thought that side reactions might result from generation of the radical from compound **32** close to its unsaturated site (*cf.* structures 36, 37), it was decided to move the radical site one further carbon away. The unsaturated lactone **32** was converted into its acid chloride and homologated by the Arndt–Eistert procedure[29] to give the methyl ester of the acid **38**, which was then hydrolysed to the crystalline acid **38**, m.p. 104–106 °C. Its relative stereochemistry was verified by the NOE method described above [irradiation of 3-H (δ 2.87) caused enhancement of 4-H (δ 3.20, 4.7%) and 7-H (δ 5.48, 4.5%): irradiation of 4-H enhanced 3-H (4.1%)], and confirmed by an X-ray structure determination carried out in our laboratory by Dr. M. J. Begley.

Kolbe electrolysis of compound **38** with methyl hydrogen pimelate again gave a complex mixture, the desired product **35** being isolated in 18% yield after extensive chromatography. Since these results were distinctly poorer, both with regard to product complexity and yield, than examples containing a saturated cyclopentane ring (see later), the seleno lactone **34** was tried in the reaction and gave the homologated unsaturated lactone **35** with deselenation. Although this procedure combined two desired oxidative steps, yields were again poor (15%) and so a method other than the Kolbe method was examined.

Unsaturated lactone **32** was reduced with diisobutylaluminium hydride (DIBAL) to give the lactol **39** which was used crude although TLC indicated a very high conversion. Wittig reaction employing the ylide derived from triphenyl(propyl)phosphonium bromide and dimsyl sodium in dry DMSO at 75 °C gave the hydroxy acid **40**; R = H, which was methylated to prevent lactonisation. ^{13}C NMR analysis, however, showed that the newly formed double bond was not stereochemically homogeneous but an ~80:20 (*Z*/*E*) mixture. The hydroxy ester was protected as the t-butyldimethylsilyl (TBDMS) ether **41** and GLC then showed a 85:15 (*Z*/*E*) ratio. At this stage the (*E*)-isomer was removed by chromatography on silica impregnated with silver nitrate (15% w/w) and elution with ethyl acetate–benzene (1:10). The purified (*Z*)-ester **41** was now reduced further with DIBAL to give the alcohol **42**; R = H (94%), which was in turn converted into the tosate **42**; R = Ts (82%) by treatment with tosyl chloride and pyridine at 0 °C.

The tosylated product **42**; R = Ts was allowed to react with a Grignard reagent prepared from the pyranylated bromide **43** in refluxing THF for 25 h; the reaction was followed by observing the disappearance of the starting tosate. The product, however, was not the desired bis ether **44** but the bromide **45** (74%).

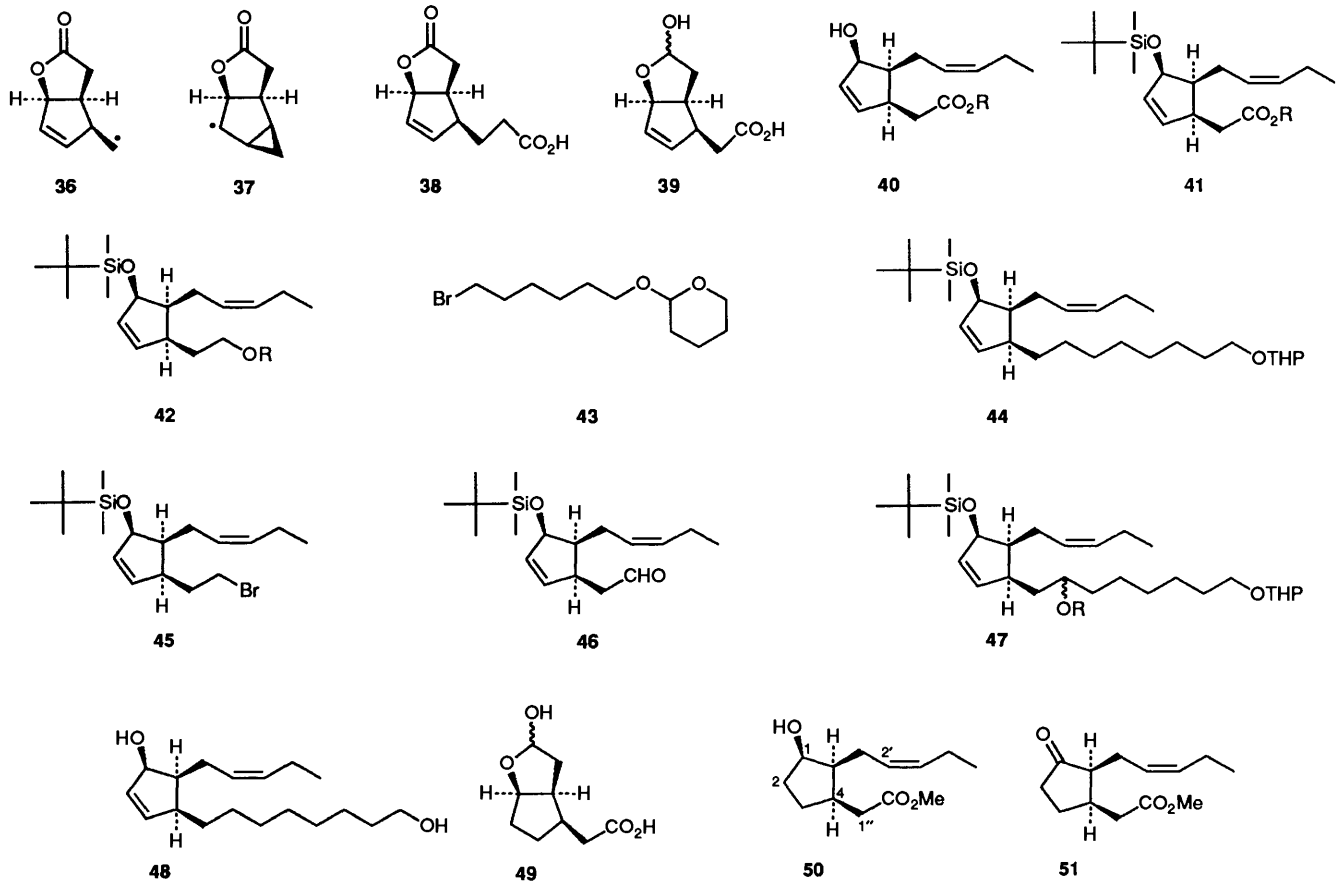


Fig. 1 Appearance of olefinic ^{1}H NMR signals for the (*Z*) and (*E*) isomers of compound **50**

Employment of dilithium tetrachlorocuprate in THF did not catalyse a reaction at low temperature, and on heating (69 °C) only the bromide **45** (88%) was obtained. Since other attempts to catalyse the desired reaction failed, the alcohol **42** was oxidised to the aldehyde **46** (78%) by PDC in dichloromethane. Compound **46** now reacted with the Grignard reagent from the bromide **43** to give the secondary alcohol **47**; R = H in high (92%) yield. The product consisted of two diastereoisomers, separable chromatographically and designated A and B.

The diastereoisomers were individually mesylated in high yield (92% and near theoretical) and, on reductive demesylation with lithium aluminium hydride in refluxing diethyl ether, both gave the same product **44**, although in differing yields (A, 92%; B, 78%). An attempt at double deprotection in one step with acetic acid–water–THF gave poor results, so the TBDMS group was removed in near theoretical yield by using t-butylammonium fluoride. This was now followed by removal of the tetrahydropyran (THP) group (58%) using pyridinium toluene-*p*-sulphonate (PPTS). The diol **48** thus obtained was now oxidised at the primary and secondary hydroxy sites by treatment with PDC in DMF at 20 °C. After work-up and methylation (CH_2N_2) the methyl ester of 12-oxoPDA was isolated (20%). Its ^{1}H NMR spectrum, mass spectrum and TLC characteristics agreed well with those of the methyl ester of 12-oxoPDA isolated from enzyme sources in our laboratory by Dr. D. O. Morgan.

Attention was now turned to the series of compounds formed in nature from the enzymic 10,11-reduction and β-oxidation of 12-oxoPDA, *i.e.* compounds OPC-8:0, -6:0, -4:0 and -2:0 (the last being *epi*-jasmonic acid). Reduction of the saturated lactone **31** with DIBAL (3 mol equiv.) at −75 °C gave the lactol **49**, which was used crude after being carefully washed to remove traces of mineral acid in order to avoid dimerisation. The lactol was now treated with the ylide prepared from triphenyl(propyl)-phosphonium bromide (above), followed by work-up and esterification to give the hydroxy ester **50** (74%). ^{13}C NMR and GLC analysis of the t-butyldimethylsilyl ether again showed an 85:15 (*Z*)/(*E*) ratio although separation was readily effected by chromatography on silver nitrate-impregnated (15%) silica gel, with benzene–ethyl acetate (4:1) for elution. The separated isomers were homogeneous as judged by ^{13}C NMR spectroscopy and the (*Z*)-isomer was recovered in 80% yield.

In this group of compounds the use of ^{1}H *J*-values to diagnose olefinic stereochemistry is complicated as the chemical shifts of the 2′,3′-protons are close; nonetheless the appearance of the olefinic protons as a triplet pattern for the (*Z*)-isomer relative to a quartet pattern of the (*E*)-isomer (Fig. 1) can be a useful guide. The most useful criteria are the ^{13}C chemical shifts of the carbons flanking the double bond, since the more compressed (*Z*)-methylenes lie at higher field relative to those in the (*E*)-isomer [*e.g.*, (*Z*)-**50** δ_C 20.7, 23.0; (*E*)-**50** δ_C 25.6, 28.5].

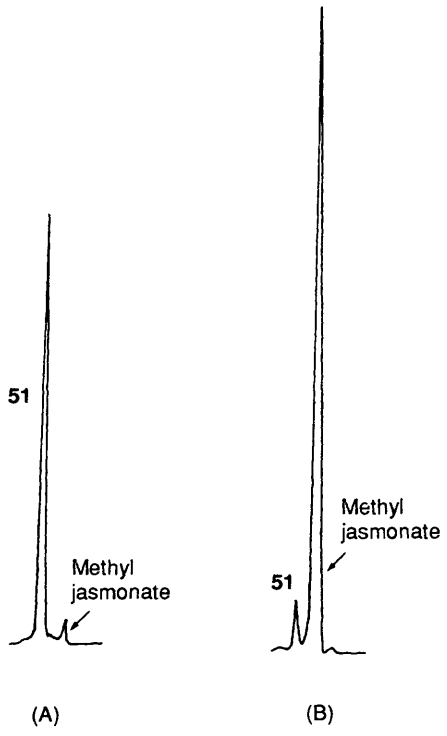


Fig. 2 GLC traces of methyl *epi*-jasmonate **51** before (A) and after (B) epimerisation. GLC conditions: OV17 capillary column, injector block 100 °C, detector 200 °C, temperature programme 120 °C ⟶ (4 °C min^{-1}) ⟶ 200 °C.

Table 2 ^{13}C NMR data (δ_C) for methyl *epi*-jasmonate **51** and methyl jasmonate **12** (CO_2Me instead of CO_2H)

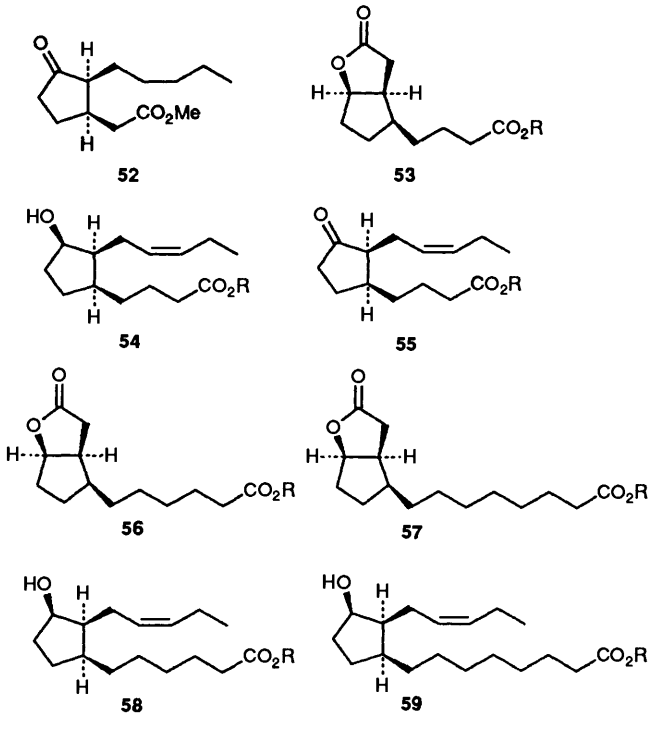
Carbon	Signal	Methyl *epi*-jasmonate	Methyl jasmonate
C-1	C	219.0	218.7
C-2″	C	172.9	172.4
C-3′	CH	133.5	134.0
C-2′	CH	125.5	125.0
C-5	CH	52.7	54.0
C-3″	Me	51.8	51.5
C-4	CH_2	35.6	38.1
C-2	CH_2	35.3	38.8
C-1″	CH_2	33.7	37.7
C-3	CH_2	25.7	27.2
C-1′	CH_2	23.0	25.6
C-4′	CH_2	20.7	20.6
C-5″	Me	14.1	14.0

The small shifts between the two olefinic carbons can also be of (limited) use.

Oxidation of compound **50** with PDC in dichloromethane now gave methyl *epi*-jasmonate (OPC-2:0) **51** (80%). As judged from its ^{13}C NMR spectrum the sample appeared very pure with no sign of the epimer, but on GLC a small amount of 4,5-*trans*-contaminant was revealed (Fig. 2) and is thought to have been formed by thermal isomerisation on the column. Upon treatment with methanolic HCl, epimerisation to methyl jasmonate took place, establishing the 4,5-*cis*-nature of the product (Fig. 2). These findings were confirmed by ^{13}C and ^{1}H NMR comparison of methyl *epi*-jasmonate and methyl jasmonate. The 4,5-cyclopentanone ^{13}C signals in methyl 4,5-*cis* *epi*-jasmonate lie upfield of those of methyl 4,5-*trans*-jasmonate by ~2.5 and ~1.3 ppm (Table 2), providing a useful stereochemical criterion additional to the demonstration of acid-catalysed 5-epimerisation which was effected on all the OPC-samples. This spectral correlation is supported by data for other members of the series. These carbons at C-5 and C-4 in *cis*-OPC-4:0 (**10**; $n = 3$) resonate at δ_C 53.5 and 38.6 whilst in the *trans*-isomer they resonate at δ_C 54.9 and 41.0. Similarly, the figures for *cis*-OPC-6:0 (**10**; $n = 5$) are δ_C 53.7 and 38.7 as against δ_C 55.0 and 41.1 in the corresponding *trans*-compound. Methyl dihydro-*epi*-jasmonate **52**, of perfumery interest, was made by catalytic hydrogenation, and epimerised to methyl dihydrojasmonate. A synthesis of methyl *epi*-jasmonate is recorded in the literature,[30] as is one of methyl dihydro-*epi*-jasmonate.[31]

The synthesis of OPC-4:0 was effected from the lactonic acid intermediate **31** using a double Arndt–Eistert reaction.[29] The acid chloride was made by the oxalyl dichloride procedure and the diazo ketone formed from diazomethane in 89% yield. Wolff rearrangement using silver benzoate in methanolic triethylamine gave the homologous methyl ester (92%). The stereochemistry was not disturbed during the homologation, as shown by irradiation at 3-H (δ 3.0) which caused NOE enhancement of 4-H (δ 1.94, 5.0%) and 7-H (δ 5.04, 5.5%). Hydrolysis gave the corresponding acid (95%) which, taken through a similar Arndt–Eistert cycle, gave diazo ketone (91%), which was rearranged to the methyl ester of the OPC-4:0 precursor **53**; R = Me (89%), and this was then hydrolysed to the acid in almost quantitative yield.

The lactone **53**; R = H was reduced to the corresponding lactol by the DIBAL method; Wittig reaction followed by methylation then gave ester **54**; R = Me (53%). (*E*)-Contaminant was removed from the predominantly (*Z*)-product by silver chromatography and the secondary alcohol was oxidised to the ketone OPC-4:0 **55**; R = Me (81%) by PDC. Treatment of the *cis*-compound with methanolic HCl caused epimerisation at C-5 to give the *trans*-compound.



The approach adopted for the remaining two metabolites, OPC-6:0 and OPC-8:0, employed Kolbe chain-extension from the intermediate **31**, using a three-fold excess of methyl hydrogen adipate or methyl hydrogen suberate as appropriate. Electrolysis was carried out in dry methanol containing enough sodium methoxide to neutralise 5–6% of the acid present. Simple equipment was employed (parallel plate platinum electrodes, 2.5 × 1.5 cm, 3–4 mm apart, 150 V) and the

electrolysis was monitored by following the pH. When the latter changed from acidic to alkaline, the reaction was considered complete and the mixture was worked up by chromatography. In this way the lactonic esters **56**; R = Me and **57**; R = Me were obtained in yields of 25 and 38%, respectively. Each lactonic acid (**56**; R = H and **57**; R = H) was reduced to the lactol by DIBAL and then, without further purification, this was in turn converted into enoate esters **58**; R = Me and **59**; R = Me by Wittig reaction followed by methylation. Once again silver nitrate/silica chromatography was needed to obtain pure (*Z*)-materials. Finally, oxidation of the two secondary alcohols with PDC gave OPC-6:0 and OPC-8:0 in yields of 71 and 56%.

Since publication of our preliminary communications on the synthesis of 12-oxoPDA,[25] a second synthesis has been briefly described.[32]

Experimental

Unless stated otherwise NMR spectra are measured in deuteriochloroform. NMR spectra were recorded using a Bruker WP 80 SY (^{1}H, 80.13; ^{13}C, 20.15 MHz), a Bruker WM 250 (^{1}H, 250.13; ^{13}C, 62.89 MHz), a Bruker AM 400 (^{1}H, 400.13; ^{13}C 100.62 MHz) and a JEOL FX 90Q (^{1}H, 89.9; ^{13}C, 22.5 MHz). *J*-Values are given in Hz.

Cyclopent-3-ene-1,2-diacetic acid **22**.—5-Vinyltrinorborn-2-ene (*endo* **24**/*exo* **25**: 67:33) (484 g) was heated at 250 °C at 200 lb in^{-2} for 32 min. Fractional distillation under vacuum gave bicyclo[4.3.0]nona-3,7-diene **23** (227 g, 47%), b.p. 93 °C/93 mmHg (Found: M$^+$, 120.0947. Calc. for C_9H_{12}: M, 120.0939); δ_H(250 MHz) 1.84–1.90 (2 H, m), 1.93–2.05 (1 H, m), 2.10–2.30 (2 H, m), 2.30–2.60 (2 H, m), 2.75–2.90 (1 H, m), 5.60–5.70 (2 H, m) and 5.80–5.90 (2 H, m).

The diene **23** (61.5 g, 0.51 mol) and water (10 cm^3) were added to DMSO (600 cm^3) to give a clear solution and NBS (46.9 g, 0.26 mol) was added in portions during 90 min to the stirred solution. The mixture was stirred (90 min) and was then poured into water (300 cm^3) and extracted with diethyl ether. The extracts were dried ($MgSO_4$) and evaporated to give an orange oil, which was chromatographed on dry column silica with hexane as eluent, the polarity being gradually increased by the addition of ethyl acetate. The bromohydrin (33.7 g, 59%) had *m/z* 137.0921 [Calc. for (M − Br), $C_9H_{13}O$: *m/z*, 137.0967].

A solution of the bromohydrin (33.4 g, 154 mmol) in dry THF (20 cm^3) was added dropwise to a solution of potassium t-butoxide (29.2 g, 250 mmol) in dry THF under nitrogen, the temperature being maintained at or below 45 °C. The mixture was stirred for 90 min, when formic acid (50% aq. solution) was added to complete the formation of a buff precipitate, which was filtered off and washed with dry diethyl ether. The organic filtrates were combined, dried ($MgSO_4$), and evaporated to give an oil, which was chromatographed on silica and eluted with diethyl ether–hexane (1:4) to give the epoxide **27** (19.5 g, 93%) (Found: M$^+$, 136.0890. Calc. for $C_9H_{12}O$: M, 136.0885); δ_H(250 MHz) 1.7–2.6 (7 H, m), 2.71 (1 H, m), 3.14 (2 H, m) and 5.57 (2 H, m); δ_C(90 MHz) 134.8, 127.6, 50.1, 49.2 (d, C-9, -8, -3, -4), 39.9 (t, C-7) and 38.0, 31.1 (d, C-1, -6), 25.6, 25.7 (t, C-2, -5).

A chromium trioxide solution was prepared from chromium trioxide (18.25 g, 182 mmol), conc. sulphuric acid (15 cm^3) and water (100 cm^3). This solution (115 cm^3) was added dropwise to a stirred mixture of the epoxide **27** (4.06 g, 29.9 mmol) in THF (150 cm^3) at 0 °C, and the mixture was stirred for 3 h after which it was allowed to attain room temperature overnight. The dark green reaction mixture separated into two phases and the aq. phase was separated and thoroughly extracted with diethyl ether. The organic phases were combined, washed with brine, dried ($MgSO_4$) and evaporated. The semi-solid was chromatographed on silica and eluted first with diethyl ether–chloroform (1:1), then with pure diethyl ether, to give the cyclopentene dicarboxylic acid **22** (1.62 g, 30%), m.p. 167–169 °C (lit.,[26] 168–170 °C) (Found: C, 58.7; H, 6.55. Calc. for $C_9H_{12}O_4$: C, 58.4; H, 6.55%) [Found: *m/z*, 166.0271. Calc. for (M − H_2O), $C_9H_{10}O_3$: *m/z*, 166.0220]; δ_C([$^2H_6$]acetone) 174.2, 173.9 (s, C-2′, -2″), 134.4, 130.3 (d, C-1, -2), 43.3, 37.5 (d, C-4, -5) and 37.3, 34.5, 34.0 (t, C-3, -1′, -1″).

Iodolactonic Acid **30**.—The dicarboxylic acid **22** (1.20 g, 6.52 mmol) was dissolved in a solution of sodium carbonate (2.5 g) in water (120 cm^3) and was cooled to 0 °C. Potassium iodide (14.4 g) and iodine (3.9 g) were added and the mixture was kept in the dark and stirred for 6 h at 0 °C and then for 48 h at room temperature. After acidification with dil. hydrochloric acid, the mixture was extracted with diethyl ether–ethyl acetate (1:1). The extracts were washed successively with brine and aq. sodium 'metabisulphite' ($Na_2S_2O_5$), and was then evaporated to give crude iodo lactone **30** (1.93 g, 96%). Crystallisation from chloroform–diethyl ether gave the iodo lactone as crystals, m.p. 109–110 °C (lit.,[26] 106–109 °C) (Found: C, 34.95; H, 3.55. Calc. for $C_9H_{11}IO_4$: C, 34.85; H, 3.5%) [Found: *m/z*, 291.9606. Calc. for (M − H_2O), $C_9H_9IO_3$: *m/z*, 291.9605]; ν_{max}(KBr)/cm^{-1} 1700 and 1780.

Lactone Acid **31**.—Tributyltin hydride (25.4 g, 85 mmol) was added dropwise under nitrogen to a mixture of the iodo lactone **30** (13.8 g, 44 mmol) and AIBN (110 mg) in dry THF (600 cm^3) and the mixture was refluxed (80 min) and then stirred at room temperature overnight. The reaction mixture was concentrated under reduced pressure, treated with potassium hydroxide (4.0 g) in methanol (110 cm^3) and stirred (20 min). Excess of methanol was evaporated off and the white suspension was extracted with diethyl ether after addition of water (100 cm^3). The ethereal extracts were discarded, along with gelatinous material. The aq. phase was acidified with hydrochloric acid, saturated with sodium chloride and extracted with chloroform (4 × 30 cm^3). The extracts were washed with brine, dried ($MgSO_4$) and evaporated to give the lactonic acid **31**, which after crystallisation from diethyl ether–hexane (6.31 g, 77%) had m.p. 86–87 °C (lit.,[26] 85–87 °C) (Found: C, 58.6; H, 6.7%; M$^+$, 184.0740. Calc. for $C_9H_{12}O_4$: C, 58.7; H, 6.55%; M, 184.0735); ν_{max}(KBr)/cm^{-1} 1690 and 1750; δ_C 178.0, 177.7 (s, C-1, -2′), 86.1, 40.2, 38.5 (d, C-7, -3, -4) and 35.1, 32.7, 29.1, 28.7 (t, C-1′, -2, -5, - 6).

Lactol Acid **49**.—A solution of the lactone **31** (220 mg, 1.2 mmol) in dry THF (40 cm^3) at −30 °C under nitrogen was treated with DIBAL (2.8 cm^3, 3.8 mmol under toluene), stirred for 1 h, and quenched with water. Acidification (Congo Red) was followed by saturation with sodium chloride and thorough extraction with diethyl ether. After washing (water), the ethereal extracts were evaporated and the residue was crystallised from diethyl ether (153 mg, 69%), m.p. 98.5–99.0 °C (lit.,[26] 83–85 °C) [Found: *m/z*, 168.0773. Calc. for (M − H_2O), $C_9H_{12}O_3$: *m/z*, 168.0786].

(*Z*)-*Hydroxycyclopentylacetate Ester* **50** *and its* (E)-*Isomer*.—A mixture of sodium hydride (100 mg, 4.2 mmol) in dry DMSO (4 cm^3) was heated and stirred under nitrogen (90 min), cooled to room temperature and triphenyl(propyl)phosphonium bromide (1.7 g, 4.4 mmol) was added together with dry DMSO (3 cm^3). After the mixture had been stirred at 20 °C for 1 h, a solution of lactol **49** (144 mg, 0.77 mmol) in dry DMSO was added under nitrogen and the mixture was stirred and heated at 70 °C for 24 h. After cooling, the mixture was quenched with aq. sodium carbonate (210 mg in 30 cm^3) and extracted with ethyl acetate. The aq. phase was acidified and extracted with ethyl

acetate (5 × 15 cm^3) and these extracts were dried ($MgSO_4$), evaporated and esterified by the addition of ethereal diazomethane. The ester was passed through a plug of Florisil (100–200 mesh) and chromatographed on dry column silica gel, with ethyl acetate–hexane (1:4) as eluent, to give a mixture of (*Z*)/(*E*) stereoisomers of compound **50** (130 mg, 74%). After trimethylsilylation, GLC analysis indicated the (*Z*):(*E*) ratio to be 85:15. Separation of the two stereoisomers was achieved by PLC on HF_{254} Kieselgel impregnated with 15% w/w of silver nitrate, with ethyl acetate–benzene (1:4) as developing solvent. To achieve satisfactory separation, the plates were run twice. Isolation of the more polar component gave the (*Z*)-isomer **50** (97 mg, 55%) [Found: *m/z*, 208.1461. ($M^+ - H_2O$) $C_{13}H_{20}O_2$, requires *m/z*, 208.1464]; ν_{max}(film)/cm^{-1} 1730; δ_C 174.6 (s, C-2″), 132.6, 127.7, 74.8 (d, C-2′, -3′, -1), 51.5 (q, OMe), 47.7 (d, C-5), 36.6 (t, C-1″), 36.4 (d, C-4), 33.3, 29.5, 23.0, 20.7 (t, C-2, -3, -1′, -4′) and 14.2 (q, C-5′). Isolation of the less polar isomer gave the corresponding (*E*)-compound (17.1 mg, 10%); ν_{max}(film)/cm^{-1} 1750; δ_C 174.6 (s, C-2″), 133.2, 128.1, 74.8 (d, C-2′, -3′, -1), 51.4 (q, OMe), 47.6 (d, C-5), 36.7 (t, C-1″), 36.6 (d, C-4), 33.4, 29.6, 28.5, 25.6 (t, C-2, -3, -1′, -4′) and 13.9 (q, C-5′).

Methyl 5-epi-*Jasmonate* (*OPC*-2:0 *ester*) **51** *and Methyl Jasmonate* **12** (*Me Ester*).—A solution of the secondary alcohol **50** (97 mg) in dry dichloromethane (8 cm^3) was stirred with PDC (550 mg) for 24 h under nitrogen. Dry diethyl ether (6 cm^3) was added and the brown precipitate formed was filtered off and washed well with diethyl ether. The united solvents were evaporated and the residual yellow oil was chromatographed on dry column silica, with diethyl ether–hexane (1:4) as eluent, to give *methyl* epi-*jasmonate* **51** (81 mg, 85%) (Found: M^+, 224.1411. $C_{13}H_{20}O_3$ requires M, 224.1413). OPC-2:0 Methyl ester had *m/z* 224 (34.7%, M^+), 193 (9.7, $M^+ - OMe$), 156 (19.6, $M^+ - C_5H_8$), 151 (34.8, $M^+ - CH_2CO_2Me$) and 83 [100, $M^+ - (C_5H_8 + CH_2CO_2Me)$] [lit.,[8] (corrected for $C=^{18}O$) *m/z*, 224 (13%), 193 (9), 156 (13), 151 (26) and 83 (100)]; ν_{max}(film)/cm^{-1} 1720; δ_H 0.96 (3 H, t, *J* 7.5), 1.75–1.90 (1 H, m), 1.95–2.10 (4 H, m), 2.10–2.18 (1 H, dd, *J* 15.5 and 10.3), 2.18–2.30 (2 H, m), 2.30–2.53 (3 H, m), 2.75–2.90 (1 H, m), 3.70 (3 H, s, OMe) and 5.23–5.52 (2 H, m, 2′- and 3′-H); δ_C 219.0, 172.9 (s, C-1, -2″), 133.5, 125.5 (d, C-2′, -3′), 52.7 (d, C-5), 51.75 (q, OMe), 35.6 (d, C-4), 35.3, 33.7, 25.7, 23.0, 20.7 (t, C-1″, -2, -3, -1′, -4′) and 14.1 (q, C-5′).

Methyl *epi*-jasmonate 2.7 mg) was stirred in methanol (2 cm^3) containing a drop of conc. hydrochloric acid for 13 h. The reaction was followed by GLC (Fig. 2). Work-up gave methyl jasmonate (2.2 mg) which co-eluted with an authentic specimen on GLC.

Methyl Dihydro-epi-*jasmonate* **52** *and Methyl Dihydrojasmonate*.—Secondary alcohol **50** (mixed *E* and *Z* isomers) (46 mg) was hydrogenated over palladium on carbon (10%) in ethyl acetate (4 cm^3), the progress of the reaction being followed by TLC. When complete, the catalyst was filtered off (Celite) and the filtrate was evaporated. Chromatography on silica, with ethyl acetate–hexane (1:4) as eluent, gave the dihydro alcohol (45 mg, 97%); ν_{max}(film)/cm^{-1} 1735; δ_C 174.7 (s, C-2″), 74.8 (d, C-1), 51.3 (q, OMe), 48.0 (d, C-5), 36.7 (t, C-1″), 36.5 (d, C-4), 33.8, 32.3, 29.5, 28.3, 25.1, 22.7 (t, C-2-1′, -3, -2′, -3′, -4′) and 14.0 (q, C-5′).

The dihydroalcohol (78 mg) was oxidised as above with PDC (495 mg) in dry dichloromethane (10 cm^3) for 44 h. Work-up and chromatography on silica with ethyl acetate–hexane (1:5) as eluent gave methyl dihydro-*epi*-jasmonate **52** (72 mg, 93%) (Found: M^+, 226.1568. Calc. for M, 226.1569); ν_{max}/cm^{-1} 1720; δ_C 220.2, 172.8, (s, C-1, -2″), 52.5 (d, C-5), 51.5 (q, OMe), 35.7 (d, C-4), 35.0, 33.7, 31.8, 27.0, 25.6, 24.6, 22.3 (t, C-1″, -2, -1′, -2′, -3, -3′, -4′) and 139.9 (q, C-5′). A solution of the dihydro-*epi*-jasmonate (2 mg) in methanol containing a drop of hydrochloric acid was stirred overnight at room temperature. Analysis by GLC (see Fig. 2) showed that it had epimerised to methyl dihydrojasmonate.

Butanoic Lactone **53**; R = H.—The lactone acid intermediate **31** (1 g) was treated with excess of oxalyl dichloride (2.4 cm^3) in dry benzene (15 cm^3) and refluxed under nitrogen (2 h). After evaporation under reduced pressure the acid chloride, a pale yellow solid, was taken up in dry benzene (4 cm^3) and added to excess of diazomethane in diethyl ether under nitrogen. After storage at 20 °C for 1 h, volatiles were removed by evaporation under reduced pressure and the oily residue was chromatographed on silica with ethyl acetate–hexane (3:2) as eluent to give the diazo ketone (1.02 g, 89%) as the polar component (Found: M^+, 208.0870. $C_{10}H_{12}N_2O_3$ requires M, 208.0848); ν_{max}(film)/cm^{-1} 1640, 2120 (diazo ketone) and 1770 (lactone).

Silver benzoate (125 mg) in dry triethylamine (2 cm^3) was added dropwise to a solution of the diazo ketone (1 g) in dry methanol (50 cm^3) under nitrogen and the mixture was stirred (3 h). The black reaction mixture was concentrated and the product was adsorbed onto dry silica, after extraction with diethyl ether–chloroform, and chromatographed on silica with ethyl acetate–hexane (3:2) as eluent to give the homologated lactonic ester (934 mg, 92%) [Found: *m/z*, 181.0877. ($M - OMe$), $C_{10}H_{13}O_3$, requires *m/z*, 181.0885].

The latter compound (934 mg) was hydrolysed using potassium hydroxide (950 mg) in methanol (20 cm^3). Work-up gave the homologated lactonic acid (830 mg, 95%), m.p. 89–90 °C [Found: *m/z*, 180.0786. ($M^+ - H_2O$), $C_{10}H_{12}O_3$ requires *m/z*, 180.0786].

The homologated acid (825 mg) and excess of oxalyl dichloride (1.8 cm^3) in dry benzene (10 cm^3) were refluxed for 24 h. Volatile material was removed under reduced pressure and the solid crude acid chloride, dissolved in dry benzene (10 cm^3), was added to excess of dry ethereal diazomethane. Work-up as above, followed by chromatography on dry silica with ethyl acetate–hexane (1:1) then neat ethyl acetate as eluent, gave the methyl ester of the homologated acid as a side-product (28 mg, 8%). The diazo ketone from the homologated acid (839 mg, 91%) was then eluted (UV-active); ν_{max}(film)/cm^{-1} 1630, 2100 (diazo ketone) and 1760 (lactone) [Found: *m/z*, 194.1000. ($M - N_2$), $C_{11}H_{14}O_3$, requires *m/z*, 194.0943].

Silver benzoate (90 mg) in dry triethylamine (1.8 cm^3) was added dropwise to a solution of the diazo ketone of the homologated acid (830 mg) in dry methanol (20 cm^3) under nitrogen and the mixture was stirred (2 h) then concentrated and the product was taken up in diethyl ether–chloroform and passed down a short column of dry column silica, and eluted with ethyl acetate–hexane (1:1, then 3:2), to give the methyl ester of the *butanoic homologue* **53**; R = Me (Found: M^+, 226.1213. $C_{12}H_{18}O_4$ requires M, 226.1205).

The latter (753 mg) was then hydrolysed to the corresponding acid with potassium hydroxide (720 mg) in methanol (20 cm^3) and stirred for 18 h at 20 °C. Work-up and extraction gave the acid **53**; R = H (705 mg, near theoretical) which solidified on storage, m.p. 65.5–66.5 °C; ν_{max}(KBr)/cm^{-1} 1700, 1765 [Found: *m/z*, 194.0938. ($M - H_2O$), $C_{11}H_{14}O_3$ requires *m/z*, 194.0943]; δ_C 178.0, 177.7 (s, C-1, -4′), 85.8, 41.9, 39.8 (d, C-7, -3, -4) and 33.4, 32.4, 29.5, 28.3, 28.2, 23.1 (t, C-3′, -2, -5, -6, -1′, -2′).

Methyl Ester of OPC-4:0 **54**; R = Me.—DIBAL in toluene (1.5 cm^3, 1.5 mmol) was added dropwise to a solution of stirred lactone **53**; R = H (93 mg, 0.44 mmol) in dry THF (6 cm^3) under nitrogen at −73 °C. Work-up as previously gave the lactol (bis-homologue of **49**) as an oil (99 mg). A Wittig reagent

was prepared as before from sodium hydride (60 mg, 2.5 mmol), DMSO (2 cm^3) and triphenyl(propyl)phosphonium bromide (1 g, 2.6 mmol), the lactol acid (99 mg, 0.44 mmol) was added, and the mixture was heated at 80 °C for 18 h. Work-up followed by diazomethane esterification as before was followed by chromatography on dry silica, with chloroform–diethyl ether–hexane (1:2:3) which gave the (*Z*)-isomer **54**; R = Me along with (*E*)-contaminant (59 mg, 53%). The stereoisomers were separated by PLC on HF_{254} silica impregnated with silver nitrate (15%), with ethyl acetate–benzene (1:3) as eluent. The more polar (*Z*)-**54**; R = Me (24.2 mg, 22% overall from the lactonic acid) had ν_{max}(film)/cm^{-1} 1730; δ_C 174.3 (s, C-4″), 132.2, 128.5, 75.2 (d, C-2′, -3′, -1), 51.5 (q, OMe), 47.8, 39.7 (d, C-5, -4), 34.3, 33.2, 31.3, 28.8, 24.2, 22.7, 20.7 (t, C-3″, -2, -2″, -3, -1″, -1′, -4′) and 14.2 (q, C-5′).

The (*Z*)-alcohol **54**; R = Me (22 mg) was stirred in dichloromethane (2 cm^3) with excess (124 mg) of PDC under nitrogen at room temperature for 18 h. Work-up and chromatography gave the *methyl ester* of *OPC*-4:0 **55**; R = Me (177 mg, 81%) (Found: M^+, 252.1712. $C_{15}H_{24}O_3$ requires M, 252.1726). OPC-4:0 Methyl ester had *m/z*, 252 (5.1%, M^+), 221 (2.3, $M^+ - OMe$), 184. (7.0, $M^+ - C_5H_8$), 151 ($M^+ - [CH_2]_3CO_2Me$) and 83 {100, $M^+ - (C_5H_8 + [CH_2]CO_2Me)$} [lit.,[8] (corrected for C=^{18}O) *m/z*, 252 (2%), 221 (2), 184 (7), 151 (24) and 83 (100)]; ν_{max}(film)/cm^{-1} 1745; δ_C 219.8, 173.8 (s, C-1, -4″), 133.1, 126.0, 53.5 (d, C-2′, -3′, -5), 51.6 (q, OMe), 38.6 (d, C-4), 35.3, 34.0, 27.7, 24.8, 23.1, 22.6, 20.7 (t, C-3″, -2, -2″, -3, -1′, -1″, - 4′) and 14.2 (q, C-5′); δ_H 0.93–1.00 (3 H, t, *J* 7.5), 1.03–1.15 (1 H, m), 1.37–1.47 (1 H, m), 1.53–1.66 (1 H, m), 1.72–1.82 (1 H, m), 1.82–2.0 (2 H, m), 2.00–2.13 (3 H, m), 2.17–2.24 (2 H, t, *J* 8.0), 2.25–2.40 (5 H, m), 3.67 (3 H, s, OMe) and 5.28–5.47 (2 H, m, 2′- and 3′-H).

Kolbe Synthesis of Lactone Acid **56**; R = H.—Lactone acid **31** (148 mg, 0.80 mmol), methyl hydrogen adipate (270 mg, 1.69 mmol) and sodium methoxide (8 mg) were cooled together to 0 °C and electrolysed between parallel platinum plate electrodes (2.5 × 1.5 cm^2, 3–4 mm apart) at 150 V and a current of 0.8 A (direction reversed every minute) for 44 min (when the reaction mixture became alkaline). The reaction mixture was evaporated and the residue was dissolved in chloroform (10 cm^3), washed with dil. aq. sodium carbonate, dried ($MgSO_4$) and evaporated. Chromatography on dry column silica, with diethyl ether–hexane (1:1) as eluent, gave the *lactonic ester* **56**: R = Me as an oil (51 mg, 25%); ν_{max}($CHCl_3$)/cm^{-1} 1730 and 1760; δ_C 177.9, 174.1 (s, C-1, -6′), 86.1 (d, C-7), 51.5 (q, OMe), 42.7, 40.4 (d, C-3, -4) and 33.9, 33.0, 30.5, 29.2, 28.9, 28.7, 28.2, 24.8 (t, C-5′, -2, -5, -6, -4′, -3′, -2′, -1′).

The ester (469 mg) was hydrolysed using potassium hydroxide (420 mg) in methanol (8 cm^3), stirred for 15 h at room temperature. After work-up, the crude acid **56**, R = H was chromatographed on silica with chloroform–diethyl ether (1:1) (400 cm^3 containing 1% glacial acetic acid) to give the purified acid as an oil (390 mg, 88%) [Found: *m/z*, 222.1242. ($M - H_2O$), $C_{13}H_{18}O_3$ requires *m/z* 222.1256]; δ_C 178.5, 178.0 (s, C-1, -6′), 86.0 (d, C-7), 42.2, 40.1 (d, C-3, -4) and 33.5, 32.6, 30.0, 28.7, 28.5, 28.3, 27.7, 24.2 (t, C-5′, -2, -5, -6, -4′, -3′, -2′, -1′).

Kolbe Synthesis of the Lactone Acid **57**; R = H.—The lactone acid **31** (141 mg), methyl hydrogen suberate (308 mg) and sodium methoxide (7 mg) in methanol (30 cm^3) were electrolysed as described above at 5 °C for 22 min. The reaction mixture was worked up as above, the product being chromatographed on dry-column silica, with ethyl acetate–hexane (1:3) as eluent, to give the *ester* **57**; R = Me (82 mg, 38%) (Found: M^+, 282.1826. $C_{16}H_{26}O_4$ requires M, 282.1831); ν_{max}(film)/cm^{-1} 1725 and 1760; δ_C 177.4, 173.6 (s, C-1, -8′), 85.7 (d, C-7), 50.9 (q, OMe), 42.3, 40.1 (d, C-3, -4) and 33.7, 32.6, 30.3, 29.2, 28.7, 28.3, 28.1, 24.5 (t, C-7′, -2, -5, -6, -6′, -5′, -4′, -3′, -2′, -1′) (lines at 28.3 and 28.1 are each apparently doubled).

The ester (362 mg) was stirred overnight with potassium hydroxide (330 mg) in methanol (20 cm^3) and on work-up gave the *lactone acid* **57**; R = H as an oil (294 mg, 85%) [Found: *m/z*, 250.1587. ($M - H_2O$), $C_{15}H_{22}O_3$ requires *m/z* 250.1569]; ν_{max}($CHCl_3$)/cm^{-1} 1710 and 1760.

Methyl Ester of OPC-6:0 (**10**; *n* = 5).—DIBAL in toluene (0.9 cm^3, 0.9 mmol) was added to a solution of the lactone acid **56**; R = H (67 mg, 0.28 mmol) in dry THF (12 cm^3) at −74 °C under nitrogen and the mixture was kept for 40 min. Work-up as before gave the lactol acid (84 mg), used without further purification.

A Wittig reagent was prepared from sodium hydride (60.2 mg, 2.51 mmol), dry DMSO (2 cm^3) and triphenyl(propyl)-phosphonium bromide (1.1 g, 2.36 mmol). The ylide was added to the lactol acid (106 mg, 0.40 mmol) and heated at 75 °C for 18 h under nitrogen. Proceeding as described above gave, on work-up, esterification by diazomethane, and chromatography by PLC on silica, with chloroform–diethyl ether–hexane (1:2:3) as eluent, crude compound **58** as a mixture of (*Z*) and (*E*) stereoisomers. These were separated on 15% silver nitrate–silica as before. The more polar component was (*Z*)-**58** (8.3 mg, 7% from **56**; R = H), δ_C 174.4 (s, C-6″), 132.2, 128.7 (d, C-2′, -3′), 75.4 (d, C-1), 51.5 (q, OMe), 47.8, 40.0 (d, C-4, -5), 34.2, 33.2, 31.6, 29.4, 28.9, 28.4, 25.1, 22.7, 20.8 (t, C-5″, -2, -4″, -3, -3″, -2″, -1″, -1′, -4′) and 14.3 (q, C-5′). The minor component was again the (*E*)-isomer of **58** (2.4 mg).

The (*Z*)-isomer (8.6 mg) and excess of PDC (62 mg) were stirred together overnight in dichloromethane (2 cm^3). Work-up gave OPC-6:0 (**10**; *n* = 5) (6.1 mg, 71%) as its methyl ester (Found–M^+, 280.2033. $C_{17}H_{28}O_3$ requires M, 280.2038). OPC-6:0 Methyl ester had *m/z*, 280 (3.2%, M^+), 249 (3.8, $M^+ - OMe$), 212 (11.5, $Me^+ - C_5H_8$), 151 (34.8, $M^+ - [CH_2]_5CO_2Me$) and 83 {100, $M^+ - (C_5H_8 + [CH_2]_5CO_2Me)$}, [lit.,[8] (corrected for C=^{18}O) *m/z*, 280 (5%), 249 (6), 212 (33), 151 (75) and 83 (100)]; ν_{max}(film)/cm^{-1} 1730; δ_C 220.1 (s, C-1), 174.2 (s, C-6″), 133.0, 126.1 (d, C-2′, -3′), 53.7 (d, C-5), 51.5 (q, OMe), 38.7 (d, C-4), 35.3, 34.0, 29.3, 28.0, 27.4, 24.9, 24.8, 22.6, 20.6 (t, C-5″, -2, -4″, -3″, -2″, -3, -1″, -2′, -5′) and 14.15 (q, C-5′); δ_H 0.94–1.00 (3 H, t, *J* 7.5), 1.0–1.10 (1 H, m), 1.22–1.47 (6 H, m), 1.58–1.67 (2 H, m), 1.78–1.98 (2 H, m), 1.99–2.13 (3 H, m), 2.15–2.23 (2 H, m), 2.23–2.40 (4 H, m), 3.67 (3 H, s, OMe) and 5.40 (2 H, m, 2′- and 3′-H).

Methyl Ester of OPC-8:0 (**10**; *n* = 7).—DIBAL in toluene (1.6 cm^3, 1.6 mmol) was added to a solution of the lactone acid **57**; R = H (126 mg, 0.49 mmol) in dry THF (8 cm^3) at −73 °C under nitrogen. Proceeding as described above gave the lactol acid (130 mg), used without further purification.

A Wittig reagent was prepared from sodium hydride (62 mg, 2.56 mmol), DMSO (2 cm^3) and triphenyl(propyl)phosphonium bromide (1.09 g, 2.33 mmol) in DMSO (3 cm^3) and was added to the lactol acid (130 mg, 0.47 mmol) as described earlier. Work-up and esterification gave the secondary alcohol **59**; R = Me as a (*Z*)/(*E*) mixture (47 mg, 32%). This was separated by TLC on silica containing 15% silver nitrate, with ethyl acetate–benzene (1:4) as developing agent. The polar isomer was the (*Z*)-isomer **59**; R = Me (25 mg, 17%); δ_C 174.4 (s, C-8″), 132.1, 128.7 (d, C-2′, -3′), 75.4 (d, C-1), 51.4 (q, OMe), 47.8, 40.4 (d, C-5, -4), 34.1, 33.1, 31.7, 29.7, 29.3, 29.2, 28.9, 28.7, 25.0, 22.7, 20.7 (t, C-7″, -2, -6″, -5″, -3, -4″, -3″, -2″, -1″, -1′, -4′) and 14.3 (q, C-5″). The (*E*)-isomer (3.8 mg) was also isolated.

The pure (*Z*)-isomer **59**; R = Me (20 mg) was oxidised with PDC (95 mg) in dry dichloromethane (5 cm^3) under the conditions described above. Work-up and purification by PLC, diethyl ether–hexane (1:4), gave OPC-8:0 (**10**; *n* = 7), as its

methyl ester (11.3 mg, 56%) (Found: M^+, 308.2359. $C_{19}H_{32}O_3$ requires M, 308.2351). OPC-8:0 Methyl ester had *m/z* 308 (2.2%, M^+), 277 (6.1, $M^+ - OMe$), 240 (9.7, $M^+ - C_5H_8$), 151 (36.6, $M^+ - [CH_2]_7CO_2Me$) and 83 {100, $M^+ - (C_5H_8 + [CH_2]_7CO_2Me)$} [lit.,[8] (corrected for C=^{18}O), *m/z*: 308 (0.5%), 277 (2), 240 (6), 151 (27) and 83 (100)]; ν_{max}(film)/cm^{-1} 1730; δ_C 220,2, 174.3 (s, C-1, -8″), 133.0, 126.2 (d, C-2′, -3′), 53.7 (d, C-5), 51.5 (q, OMe), 38.7 (d, C-4), 35.3, 34.1, 29.6, 29.2, 29.1, 28.1, 27.6, 24.9, 24.8, 22.6, 20.7 (t, C-7″, -2, -6″, -5″, -4″, -3″, -2″, -3, -1″, -1′, -4′) and 14.2 (q, C-5′); δ_H 0.92–0.99 (3 H, t, *J* 7.5), 1.01–1.13 (1 H, m), 1.15–1.45 (10 H, m), 1.54–1.70 (3 H, m), 1.79–1.97 (2 H, m), 2.00–2.15 (3 H, m), 2.15–2.20 (2 H, m), 2.20–2.40 (3 H, m), 3.67 (3 H, s, OMe) and 5.40 (2 H, m, 2′- and 3′-H).

Seleno Lactone **34**; R = Me.—Benzeneselenenyl chloride (716 mg) was added in one portion to a stirred solution of dicarboxylic acid **22** (525 mg) in dry THF (20 cm^3) at −78 °C under nitrogen. The reaction mixture was allowed to warm to room temperature and was then evaporated. The residue was taken up in ethyl acetate and chromatographed on dry column silica, with diethyl ether–chloroform (1:4, then 3:2) as eluent. The resulting oil **34**; R = H solidified on storage and was crystallised from diethyl ether, m.p. 130–131 °C (710 mg, 75%) (Found: C, 52.95; H, 5.05%. M^+, 340.0193. $C_{15}H_{16}O_4Se$ requires C, 53.1; H, 4.75%; M, 340.0212); ν_{max}(KBr)/cm^{-1} 1710 and 1790; δ_C 177.5 , 176.5 (s, C-1, -2′), 133.8 129.5 (d, Ph), 128.5 (s, Ph), 128.3 (d, Ph), 90.1 45.0, 39.5, 36.9 (d, C-7, -6, -4, -3) and 35.3, 34.9, 29.1 (t, C-1′, -2, -5).

The lactonic acid (510 mg) was esterified with diazomethane in the usual way to give the *methyl ester* **34**; R = Me (530 mg, near theoretical), m.p. 68–69 °C (Found: C, 54.5; H, 5.3. $C_{16}H_{18}O_4Se$ requires C, 54.4; H, 5.1%); δ_C 51.6 (q, OMe).

The Methyl Ester of Unsaturated Lactonic Acid **32**.—A solution of hydrogen peroxide (0.4 cm^3, 3.35 mmol) in THF (2 cm^3) was added dropwise to a stirred solution of the seleno lactonic ester **34**: R = Me (530 mg, 1.5 mmol) in THF (20 cm^3) at 0 °C, and the mixture was allowed to warm up to room temperature overnight. Concentration, dilution with water, and extraction with chloroform, followed by washing (water) and evaporation of the extract, gave an oil, which was chromatographed on silica and eluted with ethyl acetate–hexane (2:3). The resulting oil, the *methyl ester of acid* **32** (282 mg, 96%) [Found: *m/z*, 178.0635. (M − H_2O), $C_{10}H_{10}O_3$ requires, *m/z* 178.0630], had ν_{max}($CHCl_3$)/cm^{-1} 1730 and 1770; δ_C 176.6, 172.1 (s, C-1, -2′), 138.6, 129.4 (d, C-5, -6), 88.7 (d, C-8), 51.9 (q, OMe), 42.5, 39.6 (d, C-4, -3) and 35.2, 29.5 (t, C-2, -1′); δ_H 2.30–2.60 (4 H, m), 3.30–3.41 (2 H, m), 3.70 (3 H, s,), 51.51 (1 H, d, *J* 7.2), 5.90 (1 H, dt, *J* 5.7, 1.8) and 5.96 (1 H, d, *J* 5.7).

Unsaturated Lactonic Acid **32**.—The methyl ester (255 mg) was refluxed with potassium hydroxide (160 mg) in methanol for 3 h. Work-up gave the *lactonic acid* **32**, m.p. 68–69 °C (from diethyl ether) (Found: C, 59.4; H, 5.65. $C_9H_{10}O_4$ requires C, 59.35; H, 5.35%) [Found: *m/z*, 164.0486. (M − H_2O), $C_9H_8O_3$, requires *m/z* 164.0473); ν_{max}(KBr)/cm^{-1} 1750 and 1700; δ_C([$^2H_6$]acetone) 176.4, 172.9 (s, C-1, -2′), 139.4, 129.1 (d, C-5, -6), 88.6 (d, C-7), 42.8, 39.7 (d, C-3, -4) and 34.9, 29.2 (t, C-2, -1′).

HPLC Separation of the Diastereoisomers Formed on Esterification of the Unsaturated Lactonic Acid **32** *and the Saturated Lactonic Acid* **31** *with* (+)-*Borneol* (*Experiments by Dr. W. M. L. Crombie*).—A solution of the unsaturated lactonic acid **32** (520 mg) in ice-cold dichloromethane was stirred with (+)-borneol (560 mg) and dimethylaminopyridine (DMAP) (3 mg), and a solution of dicyclohexylcarbodiimide (DCC) (950 mg) in dichloromethane was added dropwise. The mixture was stirred at room temperature for 24 h. The product was filtered, the filtrate was evaporated and the mixed diastereoisomers were isolated by preparative plate chromatography (two 20 × 20 cm plates of 2 mm thickness) with diethyl ether–hexane (1:1) as developer (640 mg, 70%). The diastereoisomers were separated by HPLC on S15 silica, eluted with 17.5% ethyl acetate in n-hexane at 9 cm^3 min^{-1}, with RI detection. Separation, which was not complete, gave liquid diastereoisomer A (58 mg) and crystalline diastereoisomer B [m.p. 66–69 °C (from ethyl acetate–hexane)] (175 mg), together with a mixed fraction (160 mg). The ^{1}H spectra of the two compounds were almost identical but the ^{13}C spectra differed in that a singlet resonated at δ_C 47.86 in A and at δ_C 48.74 in B, and a triplet resonated at δ_C 36.83 in A and at δ_C 36.86 in B. Although the latter chemical shifts are very similar, they are seen separately in admixture. Hence the mixture before HPLC separation shows 21 carbons instead of 19 for each individual diastereoisomer, including approximately equal amounts of the four peaks mentioned. The singlet is presumably that in the bornyl part adjacent to the ester, the triplet that of the CH_2 adjacent to the ester.

The (+)-bornyl ester of the saturated lactonic acid **31** (260 mg) was similarly prepared and isolated (250 mg, 55%). Separation by HPLC as above gave stereoisomer C as a solid and isomer D as a liquid. The ^{13}C spectra of the two differ in respect of two triplets, one resonating at 28.85 in C and at δ_C 28.90 in D. In the case of the other signal, one resonates at δ_C 36.84 in C and δ_C 36.98 in D. In the original mixture of diastereoisomers a total of 21 carbons can be counted, including the four mentioned.

Homologated Unsaturated Lactonic Acid **38**.—The unsaturated lactonic acid **32** (100 mg) was treated with oxalyl dichloride (0.3 cm^3) in dry benzene (7 cm^3) under reflux (2 h). The solid acid chloride formed was dissolved in dry diethyl ether–benzene (3:2) and was added to excess of ethereal diazomethane and kept overnight. The crude diazo ketone was isolated, dissolved in dry methanol (5 cm^3), treated with a mixture of silver benzoate (14 mg) in dry triethylamine (0.3 cm^3) and stirred for 2 h. Work-up and chromatography on silica, with ethyl acetate–hexane (1:1) as eluent, gave the methyl ester of the homologated acid **38** (100 mg, 87%); ν_{max}($CHCl_3$)/cm^{-1} 1740 and 1780.

The ester (91 mg) was hydrolysed with potassium hydroxide (90 mg) in methanol (4 cm^3) at room temperature. Work-up gave the *acid* **38** (73 mg, 81%) after crystallisation from chloroform, m.p. 104–106 °C (Found: C, 61.3; H, 6.35. $C_{10}H_{12}O_4$ requires C, 61.2; H, 6.15%) [Found: *m/z*, 178.0626. (M − H_2O) $C_{10}H_{10}O_3$, requires *m/z*, 178.0630].

Electrolytic Chain Extension of Intermediates Intended for 12-*oxoPDA Synthesis*.—The unsaturated lactone **32** (31.4 mg, 0.17 mmol) was electrolysed with methyl hydrogen suberate (80 mg, 0.43 mmol) and sodium methoxide (0.038 mmol) in methanol according to the usual procedure (above). Work-up by chromatography gave the desired lactonic ester **35**; R = Me (7.7 mg, 17%) [Found: *m/z*, 262.1567. (M − H_2O), $C_{16}H_{22}O_3$, requires *m/z* 262.1587].

A similar reaction between the homologated lactone **38** (52 mg) and methyl hydrogen pimelate (130 mg) gave the same lactonic ester **35**; R = Me (18%).

Electrolysis of the phenylseleno lactone **34**; R = H (90 mg) with methyl hydrogen suberate (150 mg) and work-up by HPLC also gave the lactonic ester **35**; R = Me (13 mg, 17%).

The Cyclopentenol Ester **40**.—DIBAL in toluene (2.2 cm^3, 2.2 mmol) was added to a solution of the unsaturated lactone **32** (109 mg, 0.6 mmol) in dry THF at −40 °C under nitrogen.

Work-up gave crude unsaturated lactol **39**, used without further purification.

A Wittig reagent prepared from sodium hydride (41 mg, 1.72 mmol), dry DMSO (2 cm^3) and triphenyl(propyl)phosphonium bromide (740 mg, 1.92 mmol) was added to the crude unsaturated lactol acid **39** and the mixture was heated for 24 h at 75 °C. Work-up as described earlier, together with esterification, gave, after TLC on silica and development with ethyl acetate–hexane (1:3), the *cyclopentenol ester* **40** as a mixture of (*Z*) and (*E*) isomers (66 mg, 49%); ν_{max}(film)/cm^{-1} 1740; δ_C[signals picked out for (*Z*) isomer]: 173.7 (s, C-2″), 138.8, 133.4, 132.6, 127.3, 75.7 (d, C-2, -3, -2′, -3′, -1), 51.3 (q, OMe), 45.3, 42.5 (d, C-4, -5), 36.4, 23.0, 20.6 (t, C-1″, -1′, -4′) and 14.0 (q, C-5′); δ_C[(*E*) isomer]: 173.7 (s, C-2″), 139.0, 133.1, 131.1, 127.5, 76.0 (d, C-2, -3, -2′, -3′, -1), 51.3 (q, OMe), 44.9, 42.5 (d, C-4, -5), 35.6, 28.3, 25.5 (t, C-1″, -1′, -4′) and 13.7 (q, C-5′).

t-Butyldimethylsilyl Ether **41**.—The (*Z*)/(*E*) unsaturated alcohol **40** (66 mg, 0.29 mmol), TBDMS chloride (91 mg, 0.2 mmol) and imidazole (82 mg, 1.2 mmol) were stirred in dry DMF (1.5 cm^5) for 20 h under nitrogen at room temperature. Water (10 cm^3) was added and the mixture was extracted with chloroform. The extracts were dried ($MgSO_4$) evaporated and chromatographed on silica eluted with ethyl acetate–hexane (1:4) to give the TBDMS derivative **41** in mixed (*Z*)/(*E*) form (98 mg, 99%). Separation of the stereoisomers using TLC on silica containing 15% silver nitrate [developer ethyl acetate–benzene (1:10)] gave the polar (*Z*)-**41** (77 mg, 85%); δ_C 173.8 (s, C-2″), 139.4, 133.8, 132.5, 126.6 (d, C-2, -3, -2′, -3′), 76.3 (d, C-1), 51.3 (q, OMe), 46.9, 42.5 (d, C-4, -5), 37.1 (t, C-1″), 23.3, 20.9 (t, C-1′, -4′), 14.2 (q, C-5′) and 25.9, 18.1, −3.9, −4.9 (signals of TBDMS group).

The less polar (*E*)-**41** (15 mg, 15%) had δ_C 174.0 (s, C-2″), 139.5, 133.8, 133.0, 127.3 (d, C-2, -3, -2′, -3′), 76.2 (d, C-1), 51.4 (q, OMe), 46.6, 42.5 (d, C-4, -5), 37.0 (t, C-1″), 28.5, 25.7 (t, C-1′, -4′), 13.9 (q, C-5′) and 26.0, 18.1, −3.8, −4.9 (signals of TBDMS group).

The TBDMS-Protected Aldehyde **46**.—DIBAL in toluene (1.8 cm^3, 1.8 mmol) was added dropwise under nitrogen to a stirred solution of the ester **41**; R = Me (185 mg, 0.55 mmol) in dry THF (4 cm^3) at −75 °C. After 1 h the reaction mixture was quenched with water, acidified with hydrochloric acid, saturated with salt and extracted with ethyl acetate. The organic layers were dried ($MgSO_4$) and evaporated and the residue was chromatographed on silica and eluted with ethyl acetate–hexane (1:4) to give the *alcohol* **42**; R = H (169 mg, almost theoretical); δ_C 139.5, 133.0, 132.1, 128.2, 76.7 (d, C-2, -3, -2′, -3′, -1), 61.2 (t, C-2″), 47.0, 43.2 (d, C-4, -5), 34.6 (t, C-1″), 23.5, 20.8 (t, C-1′, -4′), 14.2 (q, C-5′) and 25.9, 18.1, −3.9, −4.9 (signals of TBDMS group).

The tosyl ester **42**; R = toluene-*p*-sulphonyl was prepared from the alcohol (175 mg, 0.55 mmol) and tosyl chloride (270 mg, 1.42 mmol) in dry pyridine at 0 °C as an oil (230 mg, 82%).

The alcohol **42**; R = H (260 mg, 0.84 mmol) and PDC (475 mg, 1.36 mmol) in dry dichloromethane were stirred under nitrogen for 18 h. The reaction mixture was diluted with ether and filtered through a pad of flash silica. Evaporation of the filtrate and chromatography on silica, with ethyl acetate–hexane (1:10) as eluent, gave the aldehyde **46** (202 mg, 78%) as an oil; ν_{max}(film)/cm^{-1} 1720; δ_H 9.82 (1 H, t, *J* 1.7), (C-2″ aldehyde proton); δ_C 202.4 (d, C-2″), 138.8, 133.8, 132.7, 127.5, 76.2, 46.9 (d, C-2, -3, -2′, -3′, -1, -5), 46.8 (t, C-1″), 23.6, 20.9 (t, C-1′, -4′), 14.2 (q, C-5′) and 25.9, 18.1, −3.9, −4.8 (signals of TBDMS group).

The Protected Triol **47**; R = *Mesyl*.—A Grignard reagent was prepared from the tetrahydropyranyloxy bromide **43** (359 mg, 1.35 mmol) and activated magnesium turnings (70 mg, 2.88 mmol) in dry THF (4 cm^3) refluxed for 1 h under nitrogen. The Grignard reagent (4 cm^3, 1.35 mmol) was added to a solution of the aldehyde **46** (194 mg, 0.63 mmol) in dry THF and gently refluxed (2 h), when the reaction mixture was quenched by the addition of saturated aq. ammonium chloride (10 cm^3). Work-up by extraction with ethyl acetate and chromatography on silica, and elution with ethyl acetate–hexane (1:5), gave the alcohol **47**; R = OH (285 mg, 92%) as a pair of racemic diastereoisomers. The latter were separated by TLC, with ethyl acetate–hexane (1:8) as developer. The less polar *compound A* (124 mg, 46%) had δ_C 140.1, 132.5, 132.1, 128.3 (d, C-2, -3, -2′, -3′), 98.8, 76.9, 70.1 (d, C-1, -3″ + pyranyloxy methine), 67.6, 62.2 (t, C-8″ + pyranyl CH_2O), 47.3, 43.8 (d, C-4, -5), 39.5, 37.6, 30.8, 29.8, 29.6, 26.3, 25.6, 23.5, 20.9, 19.7 (t, methylenes) and 14.2 (q, C-5′), 25.9, 18.1, −4.1, −4.9 (signals of TBDMS group). The more polar *component B* (146 mg, 54%) had δ_C 140.3, 133.0, 131.9, 128.2 (d, C-2, -3, -2′, -3′), 98.7, 76.3, 70.0 (d, C-1, -3″ + pyranyloxy methine), 67.6, 62.1 (t, C-8″ + pyranyl CH_2O), 47.2, 42.3 (d, C-4, -5), 39.9, 38.8, 30.8, 29.7, 29.5, 26.3, 25.6, 23.4, 20.8, 19.6 (t, methylenes), 14.2 (q, C-5′) and 25.9, 17.9, −4.00, −4.92 (signals of TBDMS group).

Methanesulphonyl chloride (5 drops) was stirred overnight with the alcohol **47**; R = H (diastereoisomer B) (29 mg) in dry pyridine (1 cm^3) at 20 °C. Extraction with chloroform and chromatography [silica; ethyl acetate–hexane (1:3)] gave the mesyl ester in almost theoretical yield (33 mg). The mesyl ester of diastereoisomer A was prepared similarly.

Reductive Removal of the Mesyloxy Group from Diastereoisomers A and B of Compound **47**; R = *Mesyl*.—Lithium aluminium hydride (47 mg) was refluxed under nitrogen in dry diethyl ether (6 cm^3) for 2 h. A portion of this solution (2 cm^3) was added to a solution of diastereoisomer B (75 mg) in dry diethyl ether (4 cm^3) and the mixture was gently refluxed (3 h) and stirred overnight at room temperature. The reaction was quenched with ethyl acetate, then with saturated aq. ammonium chloride and extracted with ethyl acetate. The extracts were dried ($MgSo^4$) evaporated and chromatographed on silica with ethyl acetate–hexane (1:10, then 1:6) as eluent to give the mesate-free product, deoxygenated at C-2″ (58 mg, 92%); δ_C 140.3, 132.6, 131.7, 128.7 (d, C-2, -3, -2′, -3′), 98.8, 76.3 (d, C-1 + pyranyloxy methine), 67.6, 62.2 (t, C-8″ + pyranyl CH_2O), 47.5, 46.1 (d, C-4, -5), 32.3, 30.8, 30.0, 29.9, 29.5, 28.0, 26.3, 25.6, 23.4, 20.8, 19.7 (t, methylenes), 14.2 (C-5′) and 25.9, 18.1, −3.9, −4.9 (signals of TBDMS group).

Treated in a similar way, stereoisomer A (59 mg) gave an identical demesyloxy product (38 mg, 78%).

Formation of Diol **48** *by Deprotection*.—The demesyloxy product from compound **47** (101 mg, 0.21 mmol) and t-butylammonium fluoride (0.85 cm^3, 0.85 mmol) were stirred in THF (4 cm^3) and the mixture was heated at 56 °C for 3.5 h. TLC examination indicated that removal of the silyl group was incomplete so further t-butylammonium fluoride (0.4 cm^3, 0.4 mmol) was added, the mixture being heated for a further 1 h. Isolation of the product by chromatography [silica; eluent ethyl acetate–hexane (1:5)] gave the pyranyl-protected, but desilylated, product. It had δ_C 141.4, 132.3, 132.1, 128.1 (d, C-2, -3, -2′, -3′), 98.7, 76.5 (d, C-1 + pyranyloxy methine), 67.6, 62.1 (t, C-8″ and pyranyl CH_2O), 46.2 (d, C-4, -5), 33.4, 30.7, 29.8, 29.4, 28.1, 26.2, 25.5, 23.1, 20.7, 19.6 (t, methylenes) and 14.1 (q, C-5′).

The tetrahydropyranyl protection was removed from the desilylated product (68 mg) by heating it in ethanol at 56 °C with toluene-*p*-sulphonic acid (5 mg) for 4 h. Chromatography [silica; eluent ethyl acetate–hexane (1:2)] gave the *diol* **48** (27 mg, 52%); δ_C 141.6, 132.5, 132.1, 128.1 (d, C-2, -3, -2′, -3′), 76.6

(d, C-1), 63.0 (t, C-8″), 46.2 (d, C-4, -5), 33.5, 32.8, 29.9, 29.6, 29.4, 28.1, 25.8, 23.1, 20.8 (t, methylenes) and 14.3 (q, C-5′).

Attempts to remove both protecting groups in one operation, *e.g.* heating with a mixture of acetic acid, water and THF, gave complex mixtures.

Methyl Ester of 12-*oxophytodienoic Acid* (12-*OxoPDA*) **1**.—A mixture of the diol **48** (31 mg, 0.011 mmol) and PDC (30 mg, 0.087 mmol) in dry DMF was stirred overnight at room temperature. The dark brown reaction mixture was diluted with chloroform and treated with excess of ethereal diazomethane. The mixture was concentrated, adsorbed onto dry silica and chromatographed on this material, with ethyl acetate–hexane (1:2) as eluent, to give the crude product. The latter was purified by TLC (HF_{254} Polygram) with diethyl ether–hexane as developing solvent to give the *methyl ester of* 12-*oxoPDA* (6.5 mg, 20%) (Found: M^+, 306.2189. $C_{19}H_{30}O_3$ requires M, 306.2171). It had (using the fatty acid numbering as in structure **1**): δ_H 0.97 (3 H, t, *J* 7.5, 18-H_3), 1.15 (1 H, m, 8-H), 1.31 (6 H, m, 5-, 6- and 7-H_2), 1.62 (4 H, m, 3- and 4-H_2), 1.72 (1 H, m, 8-H), 2.06 (2 H, quintet, *J* 7.5, 17-H_2), 2.15 (1 H, m, 14-H), 2.31 (2 H, t, *J* 7.5, 2-H_2), 2.40–3.00 (3 H, m, 13-, 14- and 9-H), 3.67 (3 H, s, OMe), 5.40 (2 H, m, 15- and 16-H), 6.19 (1 H, dd, *J* 5.9, 1.8, 11-H) and 7.74 (1 H, dd, *J* 5.9, 2.8, 10-H). The spectrum compared satisfactorily with that of authentic 12-oxoPDA, formed by flax enzyme, and isolated and methylated by Dr. D. O. Morgan in our laboratory.

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