A versatile kinetic alkylation-ozonolysis route for the synthesis of lactones: chiral γ-lactones and racemic δ-lactones

Niall W.A. Geraghty* and Declan P. Costello

Chemistry Department, National University of Ireland, Galway, Ireland
E-mail: niall.geraghty@nuigalway.ie

Dedicated to Professor M. Anthony McKervey on the occasion of his 65th birthday

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Abstract

A robust and versatile kinetic alkylation-ozonolysis procedure, previously used for the synthesis of 2-alkyl-2-cyclopenten-1-ones and racemic γ-substituted-γ-lactones, has now been applied to the synthesis of chiral γ-substituted-γ-lactones and δ-substituted-δ-lactones. In addition to the synthesis of lactones with simple alkyl substituents, the method allows terminal ester and halogen groups, and an alkyne bond to be incorporated into the side chain.

Keywords: Kinetic alkylation, ozonolysis, synthesis, chiral γ-substituted-γ-lactones, δ-substituted-δ-lactones

Introduction

Lactones are ubiquitous. They are commonly encountered as subunits in natural products and many simple lactones are of importance as they function as insect pheromones, antibacterial and anti-fungal agents, or flavour and aroma components, and can be found in the essential oils of many plants[1]. The largest sub-group by far consists of γ-lactones with a side-chain in the γ-position which varies both in its length and functionalization. As would be expected, the precise biological activity of these lactones is often crucially dependent on the stereochemistry of the chiral γ-carbon. Reflecting their importance, a wide range of methods has been developed for their synthesis[2], but many of these are not generally applicable being specific to particular γ-substituted γ-lactones, and others are not amenable to scale-up because of the nature of the starting materials or reagents used. Although less common, δ-substituted δ-lactones are also found as structural subunits in a variety of natural products, and simple members of the group function as pheromones for a variety of insects. All of the issues raised above in relation to γ-lactones and their synthesis[2] apply to δ-lactones as well. The structural motif of an alkyl chain,

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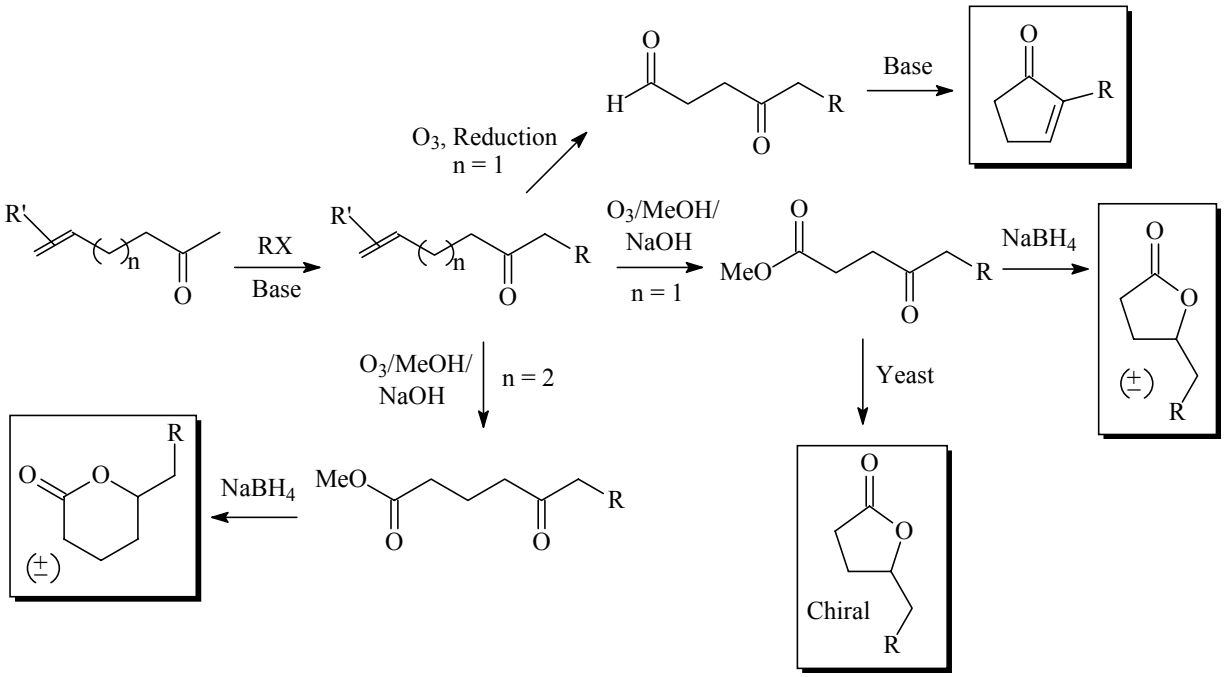
often functionalised, attached to a five-membered ring is repeated in 2-alkyl-2-cyclopenten-1-ones. Although a number of these compounds are naturally occurring and are of importance as perfumery materials, it is their potential as starting materials for the synthesis of more complex materials such as prostaglandins which has resulted in the development of a large number of methods for their preparation[3]. Many of these methods suffer from the disadvantages discussed above in relation to the synthesis of lactones. We have developed a versatile procedure (Scheme 1) which can be adapted to the synthesis of all these materials and have previously reported on its application to the synthesis of 2-alkyl-2-cyclopenten-1-ones[4] and racemic γ-substituted γ-lactones[5]. We now report on its use for the synthesis of chiral γ-substituted γ-lactones and racemic δ-substituted δ-lactones.



Scheme 1

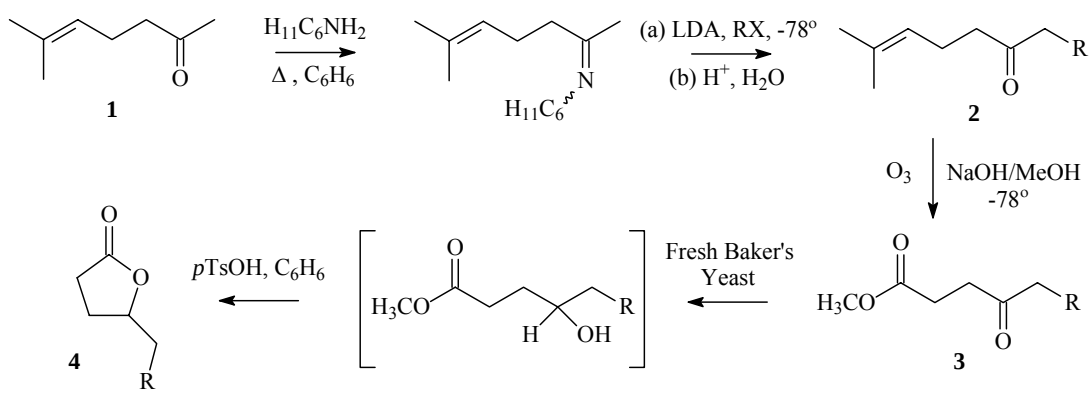
The previously reported work demonstrates that the method possesses a number of attractive features for the synthesis of 2-cyclopenten-1-ones and γ-lactones. In the context of the key kinetic alkylation-ozonolysis sequence, the cheap and readily available starting material, 6-methyl-5-hepten-2-one **1**, behaves as a half-protected 1,4-dicarbonyl compound. Once the required alkyl group has been introduced by regiospecific alkylation of the imine or hydrazone derivative of 6-methyl-5-hepten-2-one, ozonolysis of the alkene, followed by cleavage of the ozonide in the appropriate way, produces either a 1,4-ketoaldehyde or 1,4-ketoester which can be cyclized to a cyclopentenone and a γ-lactone, respectively. If the alkylation step involves the hydrazone and the introduction of a simple alkyl group, then the ketone can be regenerated and the alkene simultaneously cleaved to the aldehyde using ozone and subsequent reductive cleavage of the ozonide using dimethyl sulfide, or hydrogen and Lindlar catalyst. Although it did not prove possible to selectively ozonize a hydrazone in the presence of an alkyne, it was

possible to combine reduction of the ozonide from **2f** (Scheme 2) with selective hydrogenation of the triple bond to the corresponding *Z*-alkene. A further advantage of the approach derives from the fact that the purification of the products does not in general require chromatography as kugelrohr distillation alone gives purities in excess of 95% (GC). These considerations suggested that we consider the possibility of applying the method to the synthesis of chiral γ-substituted-γ-lactones and δ-substituted-δ-lactones.

Results and Discussion

Chiral γ-substituted-γ-lactones

The kinetic alkylation of the cyclohexylimine of commercially available 6-methyl-5-hepten-2-one **1** (Scheme 2) using alkyl halides under standard conditions proceeds regiospecifically giving, after acid hydrolysis, the γ,δ-unsaturated ketones **2a-e** in high yield (Table 1). As before simple kugelrohr distillation gives the products in purities which are in excess of 90%. Many naturally occurring γ-lactones possess unsaturated side-chains and so with a view to their synthesis 2-methyldodec-2-en-9-yn-6-one **2f** was prepared in good yield using 1-bromopent-2-yne. The dienone **2g** was prepared in 91% yield and through ozonolysis in NaOH/MeOH can be used to prepare compounds with a terminal ester group in the side-chain. The more direct route to compounds of this type involves alkylation with ω-haloalkanoates a reaction which proceeds in only modest yield as indicated by the preparation of methyl 13-methyl-9-oxotetradec-12-enoate **2h**.



2-4	R	2-4	R	2-4	R
a	$CH_3(CH_2)_3$	**e**	$CH_3(CH_2)_7$	**i**	$(CH_2)_4Br$
b	$CH_3(CH_2)_4$	**f**	$CH_3CH_2{\equiv}CCH_2$	**j**	$(CH_2)_4CO_2CH_3$
c	$CH_3(CH_2)_5$	**g**	$(CH_2)_4CH{=}CH_2$		
d	$CH_3(CH_2)_6$	**h**	$(CH_2)_6CO_2CH_3$		

Scheme 2

The precursors to γ-lactones with a terminal bromine in the side-chain can be obtained by alkylation of 6-methyl-5-hepten-2-one *N*,*N*-dimethylhydrazone with α,ω-dibromoalkanes. Such an alkylation with 1,4-dibromobutane, followed by periodate cleavage of the hydrazone, gives **2i** in good yield (Table 1). It had previously been shown[6] that alkylation of the corresponding imine produces a complex mixture in which the product resulting from substitution of both bromine atoms predominates. The compound **2i,** together with the compound **3i** derived from it, and the analogous materials **6h**, **7h** and **9h** prepared as part of the δ-lactone work described below, were found to be thermally unstable.

Table 1. Preparation of unsaturated ketones **2** and γ-ketoesters **3**

Product	Ketone **2**			γ-Ketoester **3**		
	Yield (%)[a]	GC Purity (%)[a]	Mol. Formula or reference	Yield (%)[a]	GC Purity (%)[a]	Mol. Formula or reference
a	97	98	(4)	85	90	(5)
b	95	90	(4)	95	92	(5)
c	95	95	(4)	92	90	(7)
d	91	91	(5)	78	94	(5)
e	90	93	$C_{16}H_{30}O$	84	91	(8)
f	86	93	(4)	73	96	(5)
g	91	95	$C_{14}H_{24}O$	-	-	-
h	56	89	(4)	86	90	(5)
i	79[b]	97	$C_{12}H_{21}OBr$	92	85	$C_{10}H_{17}O_3Br$
j	-		-	77	94	$C_{12}H_{20}O_5$

[a]Yield and purity of product after kugelrohr distillation. Analytically pure samples were obtained where required by chromatography or further distillation. [b]Prepared from 6-methyl-5-hepten-2-one *N*,*N*-dimethylhydrazone.

The ozonolytic cleavage in methanolic sodium hydroxide[9] of the alkene bond in **2a-f**, **2h** and **2i** leads to the direct formation of the γ-ketoesters **3a-f**, **3h** and **3i**, respectively**.** The ozonolyis of the dienone **2g** under the same conditions gives the diester **3j**. Once again the products are obtained in good to excellent yields, with kugelrohr distillation alone giving a level of purity which was adequate for further reaction. The ozonolyis of 2-methyldodec-2-en-9-yne-6-one **2f** was particularly carefully monitored by GC to ensure that the alkyne bond remained intact. In general terms this particular combination of kinetic alkylation and ozonolyis constitutes an attractive method of preparing γ-ketoesters which are useful starting materials for the synthesis of a variety of carbocyclic and heterocyclic systems[7].

The completion of the synthesis of γ-substituted γ-lactones involves the asymmetric reduction of the 4-oxo group in the ketoesters **3**. There is an obvious structural relationship between these γ-ketoesters and β-ketoesters which have been selectively and efficiently reduced

using baker's yeast, *Saccharomyces cerevisiae*[10]. Indeed this method has also been applied to a range of γ-ketoacids giving, after acid catalysed lactonization, the corresponding γ-substituted γ-lactones in 13-79% yield (R = *n*-alkyl: C_1-C_5, C_8, C_{11} and C_{13}) and with enantiomeric excesses which were consistently greater than 98%[11]. Immobilized baker's yeast on κ-carrageenan beads has also been used to carry out this asymmetric reduction[12]. A recent study[13] of a series of yeasts has shown that baker's yeast is the most versatile and selective for the microbial bioreduction of γ- and δ-ketoacids and their ethyl esters. The reduction of the γ-ketoesters **3** was carried out using fresh baker's yeast and following the removal of the yeast residues, etc., the crude product was heated in refluxing benzene containing *p*-toluenesulfonic acid. Standard workup and chromatography gave the required γ-lactones (2(3*H*)-furanones) **4** (Table 2).

Table 2. Preparation of γ-substituted γ-lactones **4**

Product	Isolated Yield (%)[a]	Purity (%)[a]	e.e. (%)[b]	α_D	Reference
a	21	93	97	+28º (c = 0.026, CH_2Cl_2)	(13)
a[c]	19	92	96	+26º (c = 0.024, CH_2Cl_2)	(13)
a[d]	11	93	96	+32º (c = 0.021, CH_2Cl_2)	(13)
a[e]	14	93	80	+5º (c = 0.020, CH_2Cl_2)	(13)
a[f]	No Reaction				-
a[g]	No Reaction				-
a[h]	No Reaction				-
b	24	95	93	+25º (c = 0.027, CH_2Cl_2)	(16)
b	24	94	74	+3º (c = 0.018, CH_2Cl_2)	(16)
c	24	92	95	+25º (c = 0.026, CH_2Cl_2)	(17)
d	21	95	97	+26º (c = 0.037, CH_2Cl_2)	(16)
e	22	94	97	+16º (c = 0.013, CH_2Cl_2)	(18)
e[c]	10	92	97	+17º (c = 0.026, CH_2Cl_2)	(18)
f	26	95	86	-49º (c = 0.015, CH_2Cl_2)	(19)
h	No Reaction				-
i	No Reaction				-
j	No Reaction				-

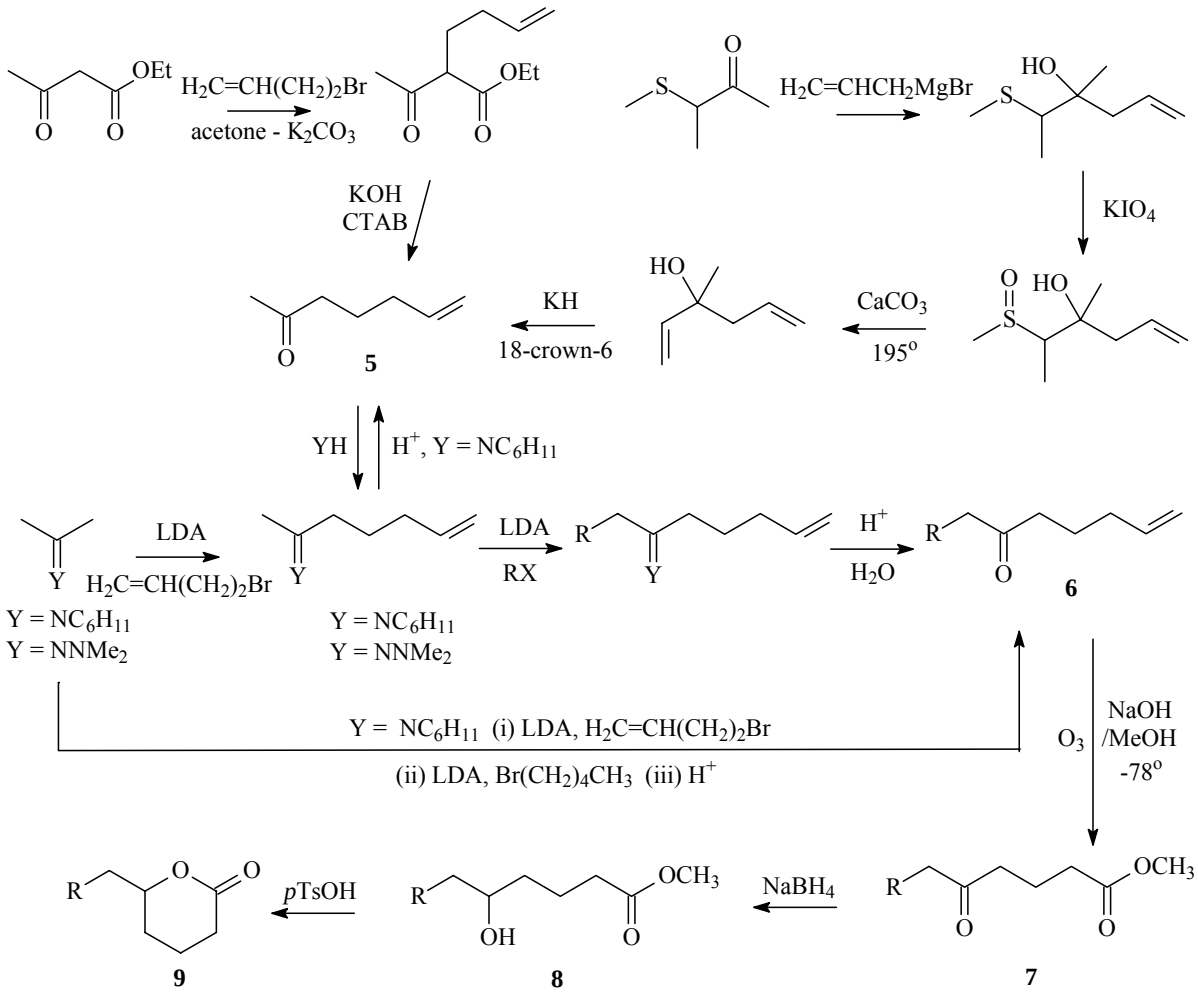
[a]Yield and purity of product after chromatography. [b]Determined by chiral GC using a Restek Rt-βDEXcst (30m, 0.32mm, 0.25μm) column. [c]Double the standard amount of fresh baker's yeast. [d]Additional yeast added during the reaction. [e]Dried baker's yeast. [f]Fresh baker's yeast in petroleum spirit. [g]Alginate immobilized baker's yeast. [h]Immobilized baker's yeast in petroleum spirit.

Although the enantiomeric excesses and the purity of the lactones were in general good, the chemical yields obtained were disappointingly low. It is possible that hydrolysis of the ester group, and loss of the acid thus formed during work-up, may be responsible for the modest yields of lactone obtained. The use of larger amounts of yeast, the addition of extra yeast in the course of the reaction, or the use of dried yeast failed to improve the yield, and no reaction occurred when fresh or dried yeast in petroleum spirit[14], or alginate immobilized yeast[15] were used. The γ-ketoesters **3h** and **3i**, which have terminal ester groups on the alkyl chains, were recovered unchanged after treatment with baker's yeast under the standard conditions, and **3j**, which has a terminal bromine atom, gave a mixture containing some unreacted starting material but none of the expected lactone. Although the absolute configuration of the lactone **4f** is unknown, its α_D suggests that the stereochemistry of the yeast reduction of **3f** may be significantly different to that of the other γ-ketoesters considered.

δ-Substituted-δ-lactones

The commercial availability and low cost of the starting material 6-methyl-5-hepten-2-one **1** is a key element in the attractiveness of the kinetic alkylation-ozonolysis route for the synthesis of γ-substituted-γ-lactones[5] and 2-alkylcyclopent-2-enones[4]. The availability of a suitable δ,ε-unsaturated ketone such as 6-hepten-2-one **5** is a prerequisite in the extension of this kinetic alkylation-ozonolysis approach to the synthesis of δ-substituted-δ-lactones. Two methods for the synthesis of **5** were developed in the course of this work (Scheme 3).

3-(Methylthio)-2-butanone was reacted with allyl magnesium bromide to give 3-methyl-2-(methylsulfanyl)-5-hexen-3-ol as a 76:24 mixture of diastereomers. Periodate oxidation followed by thermolysis in the presence of calcium carbonate gave 3-methyl-1,5-hexadien-3-ol, which on treatment with potassium hydride and 18-crown-6 gave the unsaturated ketone **5** in an overall yield of 60%. The ketone was also prepared using a modification of a previously published method[20] which involved the selective C-alkylation of ethyl acetoacetate with 4-iodobut-1-ene followed by dealkoxycarbonylation. The overall yield in this case was 44%. 6-Hepten-2-one cyclohexylimine was prepared in the standard way and alkylated with a range of alkyl halides to give the unsaturated ketones **6a-h** (Scheme 3) (Table 3). The ketone **6b** was also prepared from acetone cyclohexylimine in a one-pot double alkylation procedure involving 4-bromobut-1-ene and 1-bromopentane. The overall yield (from acetone) in this case was 50% which, when compared with the overall yield of 44% obtained using the route which begins with 3-(methylthio)-2-butanone, suggests that the former is the method of choice for the preparation of the unsaturated ketones **6**. The ω-bromoenone **6h** was prepared *via* the *N*,*N*-dimethylhydrazone of 6-hepten-2-one which had been prepared from the parent ketone or acetone *N*,*N*-dimethylhydrazone. The conversion of the unsaturated ketones **6** to the δ-ketoesters **7** (Table 3) was accomplished in the usual way by ozonolyis at -78º in methanolic sodium hydroxide. The purification of **6** and **7** involved only kugelrohr distillation and again resulted in purities which were generally in excess of 90%.



6-9	R	6-9	R	6-9	R
a	$CH_3(CH_2)_3$	**d**	$CH_3(CH_2)_6$	**g**	$H_2C{=}CH(CH_2)_4$
b	$CH_3(CH_2)_4$	**e**	$CH_3(CH_2)_9$	**h**	$Br(CH_2)_6$
c	$CH_3(CH_2)_5$	**f**	$CH_3CH_2C{\equiv}CCH_2$	**i**	$(CH_2)_4CO_2CH_3$

Scheme 3

Although the reduction of γ-ketoesters using sodium borohydride in methanol containing sodium hydrogenphosphate gives the corresponding γ-lactones directly[5], the δ-ketoesters **7** under the same conditions give the corresponding δ-hydroxyesters **8**, or at best a mixture of the hydroxyesters and the corresponding δ-lactones **9** (Table 4). Treatment of this mixture, or the pure δ-hydroxyester, with *p*-toluenesulfonic acid in refluxing benzene gives the δ-lactone **9** (Table 4). Despite the fact that the conversion of the δ-ketoesters **7** to the δ-lactones **9** proceeds in some cases in modest yields, this kinetic alkylation-ozonolysis based approach to the synthesis of δ-substituted-δ-lactones is competitive with most of those currently available in the literature, and the fact the method can also be applied to the preparation of chiral and racemic γ-substituted γ-lactones[5] and 2-substituted 2-cyclopenten-2-ones[4], emphasizes the synthetic utility of this combination of reactions.

Table 3. Preparation of δ,ε-unsaturated ketones **6** and δ-ketoester **7**

Product	Ketone **6**			δ-Ketoester **7**		
	Yield (%)[a]	GC Purity (%)[a]	Mol. Formula or reference	Yield (%)[a]	GC Purity (%)[a]	Mol. Formula or reference
a	97	94	(21)	94	93	(24)
b	98	93	(22)	96	91	(25)
b[b]	67	98	(22)	-	-	-
c	80	97	(21)	90	91	(26)
d	87	94	(23)	83	93	(27)
e	84	94	$C_{17}H_{32}O$	87	91	(24)
f	51	93	$C_{12}H_{18}O$	85	89	$C_{12}H_{18}O_3$
g	90	90	$C_{13}H_{22}O$	-	-	-
h[c]	73	-[d]	$C_{13}H_{23}OBr$	80	-[d]	$C_{13}H_{23}O_3Br$
i	-		-	82	93	(28)

[a]Yield and purity of the product after kugelrohr distillation. Analytically pure samples were obtained where required by chromatography or further distillation. [b]Prepared in a one-pot procedure from acetone cyclohexylimine; product purification involved chromatography on silica. [c]Prepared from 6-hepten-2-one *N*,*N*-dimethylhydrazone. [d]Unstable on GC.

Table 4. Preparation of δ-hydroxyesters **8** and δ-lactones **9**

Product	δ-Hydroxyester **8**		δ-Lactone **9**		
	Yield (%)[a]	Mol. Formula or reference	Yield (%)[b]	GC Purity (%)[b]	Mol. Formula or reference
a	44	(29)	89	94	(31)
b	-[c]	-	82	90	(32)
c	50	(30)	61	92	(31)
d	-[c]	-	61	95	(32)
e	78	(29)	79	92	(31)
f	-[c]	-	47	96	$C_{11}H_{16}O_2$
h	-[c]	-	31	-[d]	$C_{12}H_{21}O_2Br$
i	79	$C_{13}H_{24}O_5$	73	90	$C_{12}H_{20}O_4$

[a]Yield of product after kugelrohr distillation. Analytically pure samples were obtained where required by chromatography or further distillation. [b]Yield and purity of product after chromatography. [c]The reaction gives a mixture of δ-hydroxyester 8 and δ-lactone 9; conversion to the lactone was completed by treatment with *p*TsOH. [d]Unstable on GC.

Experimental Section

Alkylated ketones 2a-i. General procedure for 6-methyl-5-hepten-2-one cyclohexylimine alkylation

n-BuLi (5.6ml, 0.014mol) was added dropwise under a nitrogen atmosphere to a stirred solution of diisopropylamine (1.32g, 0.013mol) in dry THF (10ml) in an ice-salt bath. The resulting solution was stirred at 0º for 20min before being cooled to -78º. 6-Methyl-5-hepten-2-one cyclohexylimine[4] (2.00g, 0.010mol) in dry THF (15ml) was added over 15min to this solution. The solution was maintained at -78º during the addition and the solution was stirred at this temperature for a further 1.5h. A solution of the alkylating agent (0.012mol) and HMPA (2ml) in THF (5ml) was added over 30min. The reaction mixture was then stirred at -78º for a further 30min before being allowed to rise to room temperature overnight. 10% HCl (100ml) was added and the mixture was refluxed and vigorously stirred for approximately 12h, during which time the progress of the hydrolysis was monitored by IR and GC. After cooling, the mixture was extracted with ether (3 x 50ml) and the combined organic extracts were washed with 5% $NaHCO_3$ before being dried over $MgSO_4$. Removal of the solvent gave the products **2a-i** as yellow oils which were purified by kugelrohr distillation.

2-Methylpentadec-2-en-6-one 2e. ν_{max}/cm^{-1} 1716 (C=O), 1619 (C=C). $\delta_H(CDCl_3)$ 5.06 (H-3, ^3J = 7.1 Hz), 2.38 and 2.42 (CH_2-5 and CH_2-7, ^3J = 7.3 Hz), 2.25 (CH_2-4), 1.67 and 1.61 (CH_3-1 and CH_3-16), 1.56 (CH_2-8), 1.26 (CH_2-9 – CH_2-14), 0.88 (CH_3-15, ^3J = 6.8 Hz). $\delta_C(CDCl_3)$ 211.2 (CO), 132.5 (C-2), 122.8 (C-3), 42.8 and 42.7 (C-5 and C-7), 31.8 (C-4), 29.4, 29.2, 29.1, 29.0, 25.6 and 23.8 (CH_2), 22.6 and 22.5 (C-1 and C-16), 17.6 (C-14), 14.0 (C-15). Anal. Calcd. for $C_{16}H_{30}O$ (238.41): C, 80.61; H, 12.68. Found: C, 80.21; H, 12.92.

2-Methyltrideca-2,12-dien-6-one 2g. ν_{max}/cm^{-1} 1716 (C=O), 1641 (C=C). $\delta_H(CDCl_3)$ 5.78(H-12), 5.06 (H-3, ^3J = 7.1 Hz), 4.97 (CH_2-13), 2.43 - 2.37 (CH_2-5 and CH_2-7), 2.25 (CH_2-4), 2.05 (CH_2-11), 1.67 and 1.61 (CH_3-1 and CH_3-14), 1.57 (CH_2-8), 1.41 - 1.27 (CH_2-9 and CH_2-10). $\delta_C(CDCl_3)$ 210.9 (CO), 138.7 (C-12), 132.5 (C-2), 122.8 (C-3), 114.3 (C-13), 42.7 and 42.6 (C-5 and C-7), 33.5 (C-4), 28.6 (C-11), 25.6 (CH_2), 23.5 and 23.2 (C-1 and C-14), 17.6 and 14.0 (CH_2). Anal. Calcd. for $C_{14}H_{20}O$ (208.34): C, 80.71; H, 11.61. Found: C, 80.40; H, 11.59.

11-Bromo-2-methyl-2-undecen-6-one (2i). The ketone **2i** was prepared from 6-methyl-5-hepten-2-one dimethylhydrazone[33] using a modified version of the procedure outlined above. A solution of the hydrazone in THF was added to the LDA at 0ºand the resulting solution was stirred at this temperature for 15h. After cooling to -70º, 1,4-dibromobutane is added and the solution is stirred for 1h, warmed to 0º and stirred for a further hour. The usual workup gives the alkylated hydrazone which is added to phosphate buffer (15ml, prepared by the addition of 1M sodium dihydrogen phosphate to 1M sodium hydrogen phosphate to give a pH of 7) and methanol (75ml). Sodium periodate (2.35g, 0.011mol) in water (25ml) was then added dropwise. A faint pink precipitate, which quickly became yellow in colour, was observed after about 2min. The mixture was stirred overnight, and the precipitate was removed by filtration

and washed with dichloromethane (2 x 50ml). Water (300ml) was added to the filtrate, producing further precipitate which was again removed by filtration. The filtrate was extracted with dichloromethane (3 x 75ml), the combined extracts were dried over $MgSO_4$ and the solvent was removed. Kugelrohr distillation (115-122º, 0.1mmHg) gave 11-bromo-2-methyl-2-undecen-6-one **2i** as a pale yellow oil (1.04g, 79%, 97% pure by GC). ν_{max}/cm^{-1} 1713 (C=O), 1659 (C=C). $\delta_H(CDCl_3)$ 5.06 (H-3, ^3J = 6.8 Hz), 3.41 (CH_2-Br, ^3J = 6.8 Hz), 2.38 - 2.42 (CH_2-5 and CH_2-7), 2.26 (CH_2-4), 1.87 (CH_2-10), 1.67 and 1.61 (CH_3-1 and CH_3-12), 1.60 (CH_2-9), 1.37 (CH_2-8). $\delta_C(CDCl_3)$ 210.7 (CO), 132.7 (C-2), 122.6 (C-3), 42.7 and 42.4 (C-5 and C-7), 33.6 (C-11), 32.5 (C-4), 27.6 and 25.6 (CH_2), 22.7 and 22.4 (C-1 and C-12), 17.6 (CH_2).

γ-Ketoesters 3a-f and 3h-j. General ozonolysis procedure

The unsaturated ketone **2** (0.011mol) was dissolved in dry dichloromethane (100ml), methanolic NaOH (2.5M, 21.5ml, 0.054mol) was added, and the solution was cooled to -78º. Ozone was passed into the solution using a gas dispersion tube, initially turning it yellow. At the end of the reaction, after approximately 1h, the solution becomes clear or, in some cases, turns blue. In the case of the alkyne **2f** the ozonolysis was monitored by GC. The reaction flask was then placed in an ice-water bath and water (75ml) and ether (75ml) were added. The mixture was stirred for 1h at 0º, the layers were separated and the aqueous layer was extracted with ether (3 x 50ml). The combined ether extracts were dried over $MgSO_4$ and after the removal of the solvent kugelrohr distillation gave the ester **3** as a clear, fruity smelling, oil.

Methyl 9-bromo-4-oxononanoate 3i. ν_{max}/cm^{-1} 1736 (ester C=O), 1715 (C=O). $\delta_H(CDCl_3)$ 3.68 (CH_3O), 3.41 (Br-CH_2, ^3J = 6.8 Hz), 2.73 (CH_2-3, ^3J = 6.6 Hz), 2.59 (CH_2-2, ^3J = 6.3 Hz), 2.49 (CH_2-5, ^3J = 7.3 Hz), 1.87 (CH_2-8), 1.62 (CH_2-6), 1.45 (CH_2-7). $\delta_C(CDCl_3)$ 208.6 (CO), 173.2 (CO_2), 51.7 (CH_3O), 42.5 (C-3), 37.0 (C-5), 33.5 (C-9), 32.4 (C-8), 27.6 (C-2), 27.4 (C-6), 22.7 (C-7).

Dimethyl 4-oxodecanedioate 3j. ν_{max}/cm^{-1} 1738 and 1732 (ester C=O), 1716 (ketone C=O). $\delta_H(CDCl_3)$ 3.66 and 3.65 (2 x CH_3O), 2.73 (CH_2-3, ^3J = 6.6 Hz), 2.58 (CH_2-2, ^3J = 6.6 Hz), 2.46 (CH_2-5, ^3J = 7.4 Hz), 2.32 (CH_2-9, ^3J = 6.5 Hz), 1.55-1.67 (CH_2-6 and CH_2-8), 1.31 (CH_2-7). $\delta_C(CDCl_3)$ 208.7 (CO), 174.0 and 173.2 (2 x CO_2), 51.6 and 51.4 (2 x CH_3O), 42.3 (C-3), 36.9 (C-2), 33.7 (C-5), 28.5 (C-9), 27.6 (C-6), 24.5 and 23.5 (CH_2). Anal. Calcd. for $C_{12}H_{20}O_5$ (244.28): C, 59.00; H, 8.25. Found: C, 58.8; H, 8.15.

γ-Lactones (4a-f). General procedure for yeast reduction and lactonization

α-Glucose (31g, 0.17mol) potassium dihydrogen phosphate (0.07g, 0.5mmol) and magnesium phosphate (0.04g, 0.3mmol) were dissolved in boiled water. The flask was equilibrated at 32º and fresh baker's yeast (*Saccharomyces cerevisiae*) (28g) was added. Once the mixture was fermenting vigorously, the γ-ketoester **3** (5.4mmol) and 1M KOH (10ml) were added followed by boiled water (90ml). After adjusting the solution's pH to 6-7 using more 1M KOH, it was stirred at 32º for approximately 60h, the pH being maintained at 6-7 by the addition of further portions of 1M KOH. Glucose test paper was used during this period to indicate when further α-

glucose (10g) was required and the reaction was terminated when uptake of α-glucose ceased. The mixture was then cooled to 0º and celite (40g) was added. After stirring for 4h at this temperature, the celite was removed by filtration and washed with ether (200ml), and the filtrate was continuously extracted with ether (500ml) for 24h. The combined organic extracts were dried over magnesium sulfate. After removal of the solvent the residue was dissolved in dry benzene (20ml) containing *p*-toluenesulfonic acid (0.1g) and the solution was refluxed for 24h. Ether (50ml) was added, the solution was washed with brine (30ml) and 10% $NaHCO_3$ (30ml), and was dried over $MgSO_4$. Following removal of the solvent the crude product was chromatographed on silica (petroleum ether/ether, 95:5) to give the γ-lactones (dihydro-5-alkyl-2(3*H*)-furanones) **4** as colourless liquids whose spectroscopic data were in agreement with literature data. The enantiomeric excesses of the products were obtained by chiral GC on a Restek Rt-βDEXcst (30m, 0.32mm, 0.25μm) column.

Synthesis of 6-hepten-2-one (5). Method A. (i) Preparation of 3-methyl-2-(methylsulfanyl)-5-hexen-3-ol. A solution of allyl bromide (15.72g, 0.13mol) in dry ether (20ml) was added over 1h to a mixture of magnesium (8.86g, 0.86mol) and dry ether (80ml**)** containing a few crystals of iodine. The resulting mixture was stirred vigorously for 7h and then heated to reflux for a brief period. After cooling in ice-water, the excess magnesium was removed by filtration and 3-(methylthio)-2-butanone (10.64g, 0.09mol) in dry ether (40ml) was added at 0-4º over 1h to the solution of allylmagnesium bromide which was then refluxed for 20h. Chilled 10% HCl (50ml) was them added, the aqueous layer was extracted with ether and having been washed with washed with 5% $NaHCO_3$ (2 x 50ml), the combined ether extracts were dried over $MgSO_4$. Removal of the solvent and kugelrohr distillation (110-116º, 0.75mmHg) gave 3-methyl-2-(methylsulfanyl)-5-hexen-3-ol as a clear malodorous liquid (13.85g, 96%, 99% pure by GC, 76:24 mixture of diastereomers). ν_{max}/cm^{-1} 3464 (OH), 1639 (C=C). $\delta_H(CDCl_3)$ 5.92 (H-5), 5.16 – 5.10 (CH_2-6), 2.69 (CH-S, ^3J = 7.0 Hz), 2.43 (OH), 2.41 - 2.22 (CH_2-4), 2.16 (CH_3-S), 1.26 (CH_3-1, ^3J = 6.6 Hz), 1.22 (CH_3-COH). $\delta_C(CDCl_3)$ 133.2 (C-5), 118.0 (C-6), 73.9 (C-OH), 53.5 (CH-S), 42.5 (C-4), 23.6 (**C**H_3-COH), 16.1 (C-1), 15.4 (CH_3-S). Anal. Calcd. for $C_8H_{16}OS$ (160.28): C, 59.95; H, 10.06. Found: C, 59.60; H, 10.26.

(ii) Preparation of 3-methyl-2-(methylsulfinyl)-5-hexen-3-ol. 3-Methyl-2-(methylsulfanyl)-5-hexen-3-ol (6.40g, 0.04mol) was dissolved in dry methanol (125ml) and the solution was cooled in an ice-bath prior to the dropwise addition of sodium periodate (8.56g, 0.04mol) dissolved in the minimum volume of water. The reaction mixture was then stirred at room temperature until GC analysis indicated that the reaction was complete (36 – 48h). Any solid remaining was removed by filtration and washed with methanol (200ml), and the combined filtrate and washings were added to water (50ml). The addition of acetone (200ml) resulted in the precipitation of further solid which was again removed by filtration and washed with methanol (100ml). After the combined organic phases were dried over $MgSO_4$, removal of the solvent gave 3-methyl-2-(methylsulfanyl)-5-hexen-3-ol as a yellow malodorous liquid (6.35g, 90%, 90% pure by GC) which was used without further purification. ν_{max}/cm^{-1} 3382 (OH), 1640 (C=C),

1012 (S=O). δ_H($CDCl_3$) 5.72 (H-5), 5.02 – 4.95 (CH_2-6), 2.52 – 2.39 (CH_2-4), 2.37 (CH_3SO), 2.25 (CH-S), 1.18 (C**H**$_3$-COH), 1.15 (CH_3-1, ^3J = 5.1 Hz). δ_C($CDCl_3$) 132.9 (C-5), 119.0 (C-6), 74.2 (C-OH), 63.8 (CH-2), 43.7 (C-4), 37.1 (**C**H_3-SO), 25.3 (**C**H_3-COH).

(iii) Preparation of 3-methyl-1,5-hexadien-3-ol. 3-Methyl-2-(methylsulfanyl)-5-hexen-3-ol (5.33g, 0.03mol) and calcium carbonate[34] (10.00g, 0.10mol) were placed in a micro-distillation apparatus and heated to 195º. The 3-methyl-1,5-hexadien-3-ol (2.98g, 88%, 95% pure by GC) which distilled over 30min was collected in an ice/water cooled receiver. The spectroscopic data obtained for the product were consistent with published data[35].

(iv) Preparation of 6-hepten-2-one (5).[16] Potassium hydride (2.00g, 35% dispersion in oil, 17mmol) was washed with petroleum ether under a nitrogen atmosphere, and dry THF (20ml) and 18-crown-6 (0.75g, 2.8mmol) were added. 3-Methyl-1,5-hexadien-3-ol (1.50g, 13.3mmol) was added dropwise to the stirred mixture which was then refluxed for 3.5h (or until the reaction was complete (GC)). Water (20ml) was added and the mixture was extracted with ether (3x50ml). The combined ether layers were dried over $MgSO_4$ and, after removal of the solvent, the residue was kugelrohr distilled to give 6-hepten-2-one **5** (1.19g, 79%, 93% pure by GC) as a colourless liquid with a fruity smell whose spectroscopic data were in agreement with published data[37].

Method B. (i) Preparation of ethyl 2-acetyl-5-hexenoate. 4-Iodobutene (7.11g, 0.04mol) in dry acetone (10ml) was added to a stirred mixture of ethyl acetoacetate (3.9g, 0.03mol) and K_2CO_3 (10.38g, 0.075g) in dry acetone (50ml). The reaction was monitored by GC and was complete in 96h. The solids were removed by filtration through celite and washed with acetone (250ml). The combined organic layers were dried over $MgSO_4$. Removal of solvent and kugelrohr distillation (110-114º/0.5mmHg) gave ethyl 2-acetyl-5-hexenoate[38] (4.26g, 77%, 97% pure by GC) as a pale yellow liquid. When the reaction was carried out using 4-bromobutene a 1.7:1 mixture of ethyl 2-acetyl-5-hexenoate and ethyl 3-(3-butenyloxy)-2-butenoate was obtained from which the latter was separated by chromatography on silica gel: ν_{max}/cm^{-1} 1712 (C=O), 1623 (C=C). δ_H($CDCl_3$) 5.76 (CH_2=C**H**), 5.02 – 5.10 (C**H$_2$**=CH), 4.95 (CH=C-O), 4.07 (COOCH_2, ^3J = 7.1 Hz), 3.75 (C=COCH_2, ^3J = 6.7 Hz), 2.41 (CH_2=CHC**H**$_2$, ^3J = 4.9 Hz), 2.24 (CH_3-4), 1.21 (C**H**$_3CH_2$, ^3J = 7.1 Hz). δ_C($CDCl_3$) 170.0 (C-1), 168.1 (C-3), 133.8 (CH_2=**C**H), 117.2 (**C**H_2=CH), 91.2 (C-2), 67.2 (C=CO**C**H_2), 59.2 (COO**C**H_2), 32.9 (CH_2=CH**C**H_2), 18.9 (C-4), 14.3 (C**H**$_3CH_2$). Anal. Calcd. for $C_{10}H_{16}O_3$ (184.23): C, 65.19; H, 8.75. Found: C, 65.20; H, 8.86.

(ii) Preparation of 6-hepten-2-one[39]**.** Ethyl 2-acetyl-5-hexenoate (5.00g, 0.03mol) in toluene (20ml) was added to a 0.1% solution of cetyltrimethylammonium bromide in 5% potassium hydroxide (200ml). The mixture was stirred vigorously for 5min, sonicated for 30min and then heated at 80º until GC analysis indicated that none of the ketoester remained (15 min). After the addition of ice (50ml) and acidification with 1M H_2SO_4, the mixture was extracted with ether (3 x 200ml) and the combined extracts were dried over $MgSO_4$. Fractional distillation using a Vigreux column gave the solvent, toluene, followed by 6-hepten-2-one (b.p. 118º, 1.92g, 57%, 90% pure by GC).

Alkylated ketones (6a-g). General procedure for 6-hepten-2-one cyclohexylimine alkylation
The ketones **6a-g** were prepared by the alkylation procedure described above for 6-methyl-5-hepten-2-one cyclohexylimine.

Heptadec-1-en-6-one **6e**: ν_{max}/cm^{-1} 1719 (C=O), 1641 (C=C). δ_H($CDCl_3$) 5.76 (H-2), 4.96 –5.04 (CH_2-1), 2.38 and 2.40 (CH_2-5 and CH_2-7, ^3J = 7.1 Hz), 2.06 (CH_2-3, ^3J = 7.3 Hz, ^3J = 6.8 Hz), 1.64 (CH_2-4), 1.56 (CH_2-8), 1.26 (CH_2-9 – CH_2-16), 0.88 (CH_3-17, ^3J = 6.9 Hz). δ_C($CDCl_3$) 211.5 (CO), 138.1 (C-2), 115.2 (C-1), 43.0 and 41.9 (C-5 and C-7), 33.2 (C-3), 31.9 (C-4), 29.6 - 29.3 (6 x CH_2), 23.9, 22.8, and 22.7 (CH_2), 14.1 (C-17). Anal. Calcd. for $C_{17}H_{32}O$ (252.44): C, 80.88; H, 12.78. Found: C, 80.57; H, 12.67.

Dodeca-1-en-9-yn-6-one **6f**: ν_{max}/cm^{-1} 2354 (C≡C), 1715 (C=O), 1640 (C=C). δ_H($CDCl_3$) 5.56 (H-2), 5.04 – 4.97 (CH_2-1), 2.60 (CH_2-8, ^3J = 7.3 Hz), 2.44 and 2.42 (CH_2-5 and CH_2-7, ^3J = 7.5 Hz), 2.13 (CH_2-11, ^3J = 7.6 Hz), 2.06 (CH_2-3, ^3J = 7.1 Hz), 1.69 (CH_2-4), 1.09 (CH_2-12, ^3J = 7.4 Hz). δ_C($CDCl_3$) 209.2 (CO), 137.8 (C-2), 115.2 (C-1), 82.3 (C-10), 79.4 (C-9), 42.0 and 41.9 (C-5 and C-7), 33.0 (C-3), 22.6 (C-4), 14.1 (C-8), 13.4 (C-12), 12.2 (C-11). Anal. Calcd. for $C_{12}H_{18}O$ (178.27): C, 80.85; H, 10.18. Found: C, 80.45; H, 9.87.

Trideca-1,12-dien-6-one **6g**: ν_{max}/cm^{-1} 1713 (C=O), 1640 (C=C). δ_H($CDCl_3$) 5.79 (H-2 and H-12), 5.03 – 4.92 (CH_2-1 and CH_2-13), 2.39 and 2.40 (CH_2-5 and CH_2-7, ^3J = 7.3 Hz), 2.03 (CH_2-3 and CH_2-11), 1.67 (CH_2-4), 1.57 (CH_2-8), 1.40 (CH_2-10), 1.29 (CH_2-9). δ_C($CDCl_3$) 211.0 (CO), 138.8 and 137.9 (C-12 and C-2), 115.1 and 114.3 (C-1 and C-13), 42.7 and 41.8 (C-5 and C-7), 33.5 (C-3), 33.0 (C-4), 28.6 (C-11), 28.5 (C-10), 23.6 (C-8), 22.7 (C-9). Anal. Calcd. for $C_{13}H_{22}O$ (194.31): C, 80.35; H, 11.41. Found: C, 80.14; H, 11.62.

13-Bromotridec-1-en-6-one (6h). 6-Hepten-2-one *N*,*N*-dimethylhydrazone was prepared from acetone *N*,*N*-dimethylhydrazone using the method of Heathcock[40], or from 6-hepten-2-one[33], and was alkylated with 1,6-dibromohexane (as described above for 6-methyl-5-hepten-2-one *N*,*N*-dimethylhydrazone) giving 13-bromotridec-1-en-6-one *N*,*N*-dimethylhydrazone (81%, b.p. 210-212º, 1.0mmHg). ν_{max}/cm^{-1} 1640 (C=N), 911 (olefinic C-H). δ_H($CDCl_3$) 5.77 (H-2), 5.01 – 4.89 (CH_2-1), 3.33 (CH_2-Br, ^3J = 6.7 Hz), 2.37 (CH_2-5), 2.33 (2 x CH_3-N), 2.14 (CH_2-3), 2.03 (CH_3-7, ^3J = 6.9 Hz), 1.80 (CH_2-12), 1.53 (CH_2-4), 1.40 (CH_2-8), 1.30 - 1.19 (CH_2-11, CH_2-10, CH_2-9). δ_C($CDCl_3$) 172.2 (C=N), 138.1 (C-2), 115.0 (C-1), 47.5 ($(CH_3)_2$-N), 35.9 (C-5), 33.8 (C-3), 32.6 (CH_2), 29.5 (7-CH_2), 29.2 (C-13), 28.4, 27.9, 26.4, 25.8 and 14.0 (CH_2). Treatment of this compound with sodium periodate as described previously gave 13-bromotridec-1-en-6-one **6h** as a thermally unstable, pale yellow, liquid (73%, b.p. 172-176º, 0.8mmHg). ν_{max}/cm^{-1} 1714 (C=O), 1638 (C=C). δ_H($CDCl_3$) 5.76 (H-2), 5.03 – 4.96 (CH_2-1), 3.40 (CH_2-Br, ^3J = 6.7 Hz), 2.40 and 2.39 (CH_2-5 and CH_2-7, ^3J = 7.4 Hz), 2.05 (CH_2-3, ^3J = 7.3 Hz, ^3J = 6.9 Hz), 1.85 (CH_3-12, ^3J = 7.1 Hz), 1.67 (CH_2-4, ^3J = 7.3 Hz), 1.57 (CH_2-8), 1.45 (CH_2-9), 1.37 - 1.23 (CH_2-11, CH_2-10). δ_C($CDCl_3$) 211.1 (C=O), 138.0 (C-2), 115.1 (C-1), 42.7 and 41.8 (CH_2-5 and CH_2-7), 33.9 (C-3), 32.6 (C-4), 28.9 (C-13), 28.5, 27.9, 23.6, 22.0 and 14.0 (CH_2).

δ-Ketoesters 7a-f, 7h and 7i. Ozonolysis of the unsaturated ketones **6a-h** in methanolic sodium hydroxide as described above gave the δ-ketoesters **7a-f**, **7h** and **7i**.

Methyl 5-oxoundec-8-ynoate **7f**: ν_{max}/cm^{-1} 1736 (ester C=O), 1719 (ketone C=O). $\delta_H(CDCl_3)$ 3.67 (CH_3O), 2.60 (CH_2-6, ^3J = 7.2 Hz), 2.51 (CH_2-2, ^3J = 7.1 Hz), 2.42 (CH_2-7), 2.35 (CH_2-4, ^3J = 7.3 Hz), 2.14 (CH_2-10), 1.91 (CH_2-3, ^3J = 7.2 Hz), 1.09 (CH_3-1, ^3J = 7.5 Hz). $\delta_C(CDCl_3)$ 208.5 (CO), 173.5 (CO_2), 82.2 (C-9), 76.7 (C-8), 51.5 (CH_3O), 41.9 and 41.5 (C-4 and C-6), 32.9 (C-2), 18.7 (C-3), 14.1 (C-7), 13.4 (C-11), 12.2 (C-10). Anal. Calcd. for $C_{12}H_{18}O_3$ (210.27): C, 68.54; H, 8.63. Found: C, 68.74; H, 8.41.

Methyl 5-oxo-12-bromododecanoate **7h**: ν_{max}/cm^{-1} 1738 (ester C=O), 1714 (C=O). $\delta_H(CDCl_3)$ 3.67 (CH_3-O), 3.40 (CH_2-Br, ^3J = 6.8 Hz), 2.48 (CH_2-2, ^3J = 7.2 Hz), 2.40 (CH_2-6, ^3J = 7.3 Hz), 2.34 (CH_3-4, ^3J = 7.2 Hz,), 1.89 (CH_2-3), 1.85 (CH_2-11), 1.57 (CH_2-7), 1.45 (CH_2-8), 1.36 - 1.23 (CH_2-10, CH_2-9). $\delta_C(CDCl_3)$ 210.2 (C=O), 173.6 (CO_2), 51.5 (CH_3-O), 42.7 and 41.4 (CH_2-4 and CH_2-6), 33.9 (C-2), 32.9 (C-3), 28.9 (C-12), 28.4, 27.9, 23.5, 18.8 and 14.0 (CH_2).

δ-Hydroxyesters 8a, 8c, 8e and 8i. Sodium borohydride (0.049g, 1.3mmol) and sodium hydrogen phosphate dodecahydrate (0.054g, 0.15mmol) were dissolved in dry methanol (10ml). The solution was cooled to 0º and the ketoester **7a**, **7c**, **7e** or **7i** (1.3mmol) in dry methanol (10ml) was added over 10min. Stirring at 0º was continued for 5min and at room temperature for 24h, or until the reaction was complete (IR). Water (30ml) was added and the mixture was extracted with ether (3 x 30ml). After drying over Na_2SO_4 and the removal of solvent, the residue was kugelrohr distilled to give the hydroxyester **8a**, **8c**, **8e** or **8i** (Table 4), as a clear colourless liquid which gave spectroscopic data in agreement with those in the literature.

Dimethyl 5-hydroxyundecanedioate **8i**: ν_{max}/cm^{-1} 3453 (OH), 1736 (C=O). $\delta_H(CDCl_3)$ 3.67 and 3.68 (CH_3O), 3.50 (CH-5), 2.31 and 2.35 (CH_2-2 and CH_2-10, ^3J = 7.3 Hz), 1.99 (OH), 1.92 – 1.60 (CH_2-4 and CH_2-6), 1.41 (CH_2-3, CH_2-7, CH_2-8, CH_2-9). $\delta_C(CDCl_3)$ 174.2 and 174.1 (C=O), 71.1 (C-5), 51.5 and 51.4 (CH_3O), 37.1 and 36.6 (C-4 and C-6), 33.9 and 33.8 (C-2 and C-10), 29.0, 25.2, 24.8 and 20.9 (CH_2). An analytically pure sample of this material could not be obtained.

δ-Lactones 9a, 9c, 9e and 9i. The hydroxyester **8a**, **8c**, **8e** or **8i** (0 68mmol) and a catalytic amount of *p*-toluenesulfonic acid (0.01g, 0.06mmol) were dissolved in dry benzene (20ml) and the solution was refluxed until the reaction was complete (approximately 24h (IR)). Ether was added (100ml) and the solution was washed with brine (50ml) and 10% $NaHCO_3$ (3x50ml). The organic phase was dried over Na_2SO_4 after the removal of solvent, the residue was chromatographed on silica (petroleum ether/ether) to give the δ-lactone **9a**, **9c**, **9e** or **9i** (Table 4) as a colourless liquid with spectroscopic data in agreement with those in the literature.

Methyl 6-(6-oxotetrahydro-2*H*-pyran-2-yl)hexanoate **9i**: ν_{max}/cm^{-1} 1736 (lactone and ester C=O). $\delta_H(CDCl_3)$ 4.29 (CH-O), 2.52 (C**H**$_2$CO$_2$CH), 2.32 (C**H**$_2$CO$_2$CH$_3$, ^3J = 7.4 Hz), 1.81 – 1.98 ((C**H**$_2$)$_2$CH (ring)), 1.75 – 1.31 ((C**H**$_2$)$_4$CH$_2$ CO$_2$CH$_3$). $\delta_C(CDCl_3)$ 173.9 (ester C=O), 171.8 (lactone C=O), 80.3 (OCH), 51.3 (CH_3O), 35.4 (**C**H$_2$(CH$_2$)$_4$CO$_2$CH$_3$) 33.7 (CH$_2$CO$_2$CH$_3$), 29.2 (CH(CH$_2$)$_2$**C**H$_2$CO$_2$), 28.6, 27.6, 24.5, 24.4 and 18.3 (CH_2). Anal. Calcd. for $C_{13}H_{24}O_5$ (228.29): C, 63.14; H, 8.83. Found: C, 62.74; H, 8.62.

δ-Lactones 9b, 9d, 9f and 9h. Reduction of the hydroxyester **7b**, **7d**, **7f** or **7h** using sodium borohydride as described above gave a mixture of the corresponding hydroxyester **8** and lactone **9**. The crude product was dissolved in dry benzene (20ml) containing *p*-toluenesulfonic acid (0.02g, 0.12mmol) and the solution was refluxed for 24h. The reaction was worked up as before and the product was chromatographed on silica (petroleum ether/ether) to give the δ-lactone **9b**, **9d**, **9f** or **9h** as a colourless liquid with spectroscopic data in agreement with those in the literature.

6-(3-Hexynyl)tetrahydro-2*H*-pyran-2-one 9f. ν_{max}/cm^{-1} 1735 (lactone C=O). δ_H($CDCl_3$) 4.45 (CH-O), 2.53 (C**H**$_2$CO), 2.35 (C≡CC**H**$_2$CH$_2$, ^3J = 6.4 Hz), 2.15 (CH$_3$C**H**$_2$, ^3J = 7.3 Hz, ^5J = 2.0 Hz), 1.97 – 1.83 (COCH$_2$(C**H**$_2$)), 1.56 and 1.74 (C≡CCH$_2$C**H**$_2$), 1.11 (CH$_3$, ^3J = 7.5 Hz). δ_C($CDCl_3$) 171.6 (lactone C=O), 82.4 (CH$_3$CH$_2$**C**≡C), 78.9 (CH$_3$CH$_2$C≡**C**), 76.7 (CHO), 34.9 (**C**H$_2$CH$_2$C≡C), 29.3 (**C**H$_2$CO), 27.5 (CO(CH$_2$)$_2$**C**H$_2$), 18.3(COCH$_2$**C**H$_2$), 14.5(C≡C**C**H$_2$CH$_2$), 14.1 (**C**H$_3$), 12.2 (CH$_3$**C**H$_2$). Anal. Calcd. for $C_{11}H_{16}O_2$ (180.24): C, 73.30; H, 8.95. Found: C, 73.51; H, 9.21.

6-(7-Bromoheptyl)tetrahydro-2*H*-pyran-2-one 9h. ν_{max}/cm^{-1} 1734 (lactone C=O). δ_H($CDCl_3$) 4.28 (CH-O), 3.41 (BrCH$_2$, ^3J = 6.8 Hz), 2.51 (C**H**$_2$CO$_2$), 1.97 – 1.80 (COCH$_2$(C**H**$_2$)$_2$), 1.76 – 1.65 (Br(CH$_2$)$_6$C**H**$_2$), 1.62 – 1.25 (BrCH$_2$(C**H**$_2$)$_5$). δ_C($CDCl_3$) 171.8 (lactone C=O), 80.5 (OCH), 35.7 (Br(CH$_2$)$_6$**C**H$_2$), 33.9 and 32.6 (CH$_2$), 29.4 (**C**H$_2$CO), 29.1 (BrCH$_2$), 28.5 and 28.0 (CH$_2$), 27.8 (CO(CH$_2$)$_2$**C**H$_2$).

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