Intramolecular Cyclization of Allylsilanes in the Synthesis of Guaian-8,12-olide. Stereoselective Formation of *trans*- and *cis*-Fused Methylenelactones

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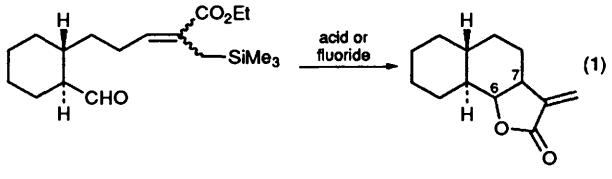
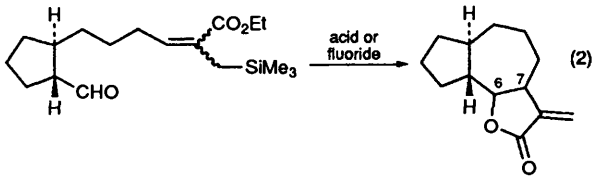
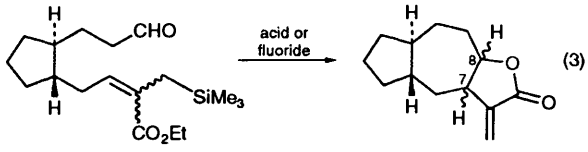
One-step formation of guaian-8,12-olide derivatives, α-methylene-γ-lactones fused to a perhydroazulene carbon framework with various stereochemistries, were performed from monocyclic compounds *via* intramolecular cyclization of ω-formyl-α-trimethylsilylmethyl-α,β-unsaturated esters. Stereochemical features of both Lewis acid- and fluoride-promoted cyclizations are discussed.

We have reported that intramolecular cyclization of ω-formyl-α-trimethylsilylmethyl-α,β-unsaturated esters is a powerful method for the synthesis of α-methylene-γ-lactones fused to bicyclic terpenoid carbon skeletons, and eudesman-6,12-olide[1]† and guaian-6,12-olide[2]† derivatives were synthesized by this method [eqns. (1) and (2), respectively]. By using this method, carbocyclization, lactonization, and α-methylenation could be achieved in one short step, and it was shown that the stereochemistry of the cyclized lactones or the corresponding hydroxy esters depended on the cyclization reagent used (acid or fluoride). The stereochemistry of acid-promoted cyclization was explained by the interaction between two oxygen functionalities.[1] However, stereochemical features of fluoride-promoted cyclization were not clear, because simple protiodesilylation occurred in some cases.[2] Nishitani and Yamakawa reported a similar methodology using acyclic systems.[3]





Guaian- or pseudoguaian-8,12-olide† forms another major class of sesquiterpene lactones with biological activities, such as antitumour activity.[4,5] A number of syntheses have been reported for these types of compound, most of which involve formation of the carbon skeleton and the α-methylene-γ-lactone in independent steps.[6] Recently, some new methodologies towards guaian- or pseudoguaian-8,12-olide have been developed, such as Diels–Alder (retro-Diels–Alder),[7] cycloaddition of aryl diazoketones,[8] photocycloaddition–palladium-catalysed ring expansion,[9] or boron annulation.[10] We planned to utilize our method in the synthesis of these types of compound, and here we report a synthesis of model compounds **3**–**6** from monocyclic precursors *via* acid- or fluoride-promoted intramolecular cyclization of allylsilane derivatives **1** and **2** [eqn. (3)]. Furthermore, we discuss the stereochemistry of both Lewis acid- and fluoride-promoted carbocyclization, since, in contrast to the case of the 6,12-olides,[2] acid- or base-catalysed epimerization at the α-carbon does not occur for either cyclization substrate **1** or **2**.

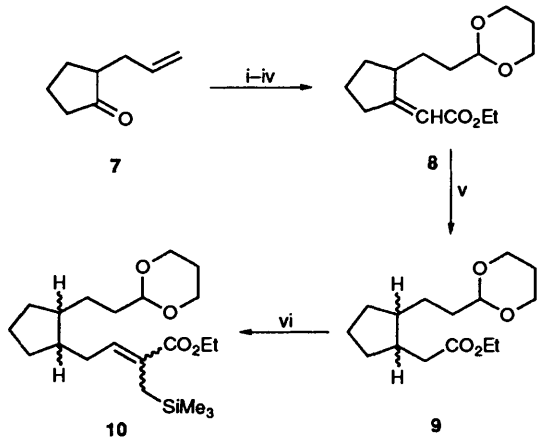


1 *Z*-form
2 *E*-form

3 7α-H, 8α-H
4 7α-H, 8β-H
5 7β-H, 8α-H
6 7β-H, 8β-H

Results and Discussion

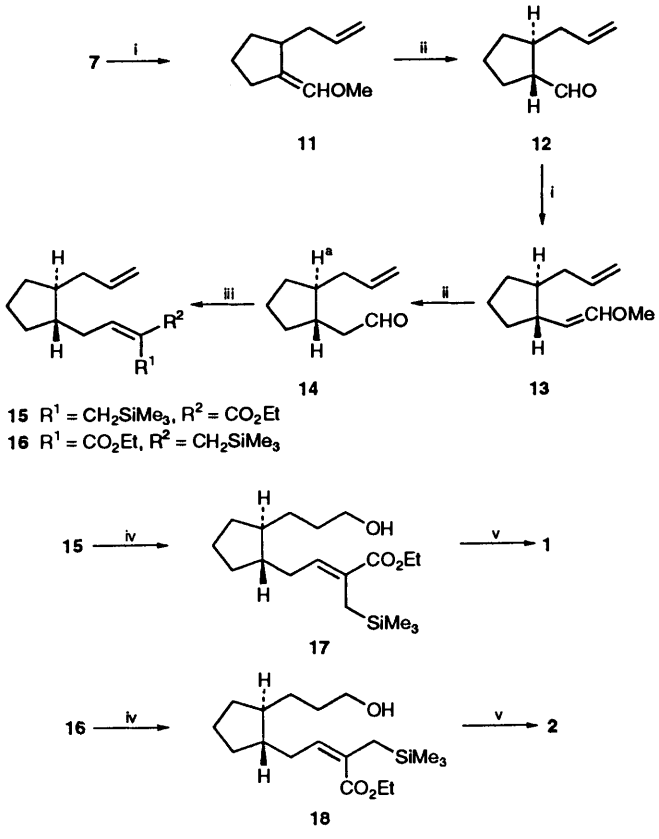
We first intended to obtain cyclization precursors **1** and **2** from 2-allylcyclopentanone **7** by the route outlined in Scheme 1. However, this route was ultimately abandoned since a mixture of *cis*- and *trans*-disubstituted cyclopentanes **9**, obtained by hydrogenation of unsaturated ester **8**, could not be separated at this stage or later. Separation was also troublesome for the geometrical mixture of β-(ethoxycarbonyl)allylsilanes **10** or their corresponding aldehydes.



Scheme 1 *Reagents and conditions:* i, $(EtO)_2P(O)CH_2CO_2Et$, NaH, DME, room temp.; ii (a) $(Pr^iMeCH)_2BH$, diglyme, room temp., (b) aq. NaOH, H_2O_2, 40 °C; iii, PDC, CH_2Cl_2, room temp.; iv, $HO[CH_2]_3OH$, pyridinium toluene-*p*-sulfonate, benzene, reflux; v, H_2, Pd–C, EtOH, room temp.; vi, $(EtO)_2P(O)CH(CO_2Et)CH_2SiMe_3$, NaH, DME, room temp.

† For the numbering of natural sesquiterpenes, see ref. 5.

We therefore changed to another route, as depicted in Scheme 2. This route also starts from 2-allylcyclopentanone **7**, which was subjected to treatment with $Ph_2P(O)CH_2OMe$ to yield, after acid hydrolysis, *trans*-substituted aldehyde **12**. The same reactions were repeated to afford the homologous aldehyde **14**. The *trans*-substitution pattern on the cyclopentane ring was established at this stage by nuclear Overhauser enhancement (NOE) spectroscopy, the NOE effect being observed between H^a and the α-protons of the aldehyde. Introduction of a β-(ethoxycarbonyl)allylsilane moiety was carried out by utilizing Hoffmann's Wittig[11] reaction to furnish esters **15** and **16** in 43 and 18% yield, respectively, after chromatographic separation. Hydroboration of *Z*-ester **15** with $(Pr^iMeCH)_2BH$ gave alcohol **17**, which was oxidized with pyridinium dichromate (PDC) to afford aldehydo ester **1**. Similarly, *E*-ester **16** was converted into aldehydo ester **2** *via* a parallel route.



Scheme 2 *Reagents and conditions:* i, $Ph_2P(O)CH_2OMe$, LDA, THF, room temp.; ii, 5% HCl, THF, reflux; iii, $(EtO)_2P(O)CH(CO_2Et)CH_2SiMe_3$, NaH, DME, room temp., iv (a) $(Pr^iMeCH)_2BH$, diglyme, room temp., (b) aq. NaOH, H_2O_2, 40 °C; vi, PDC, CH_2Cl_2, room temp.

The cyclizations were carried out using $SnCl_4$ and $BF_3{\cdot}OEt_2$, as Lewis acids, and tetrabutylammonium fluoride (TBAF) as the fluoride ion source. The results are summarized in Table 1. Even though the yields were not very good, the desired methylenelactones with the appropriate carbon framework were obtained in one step in all cases. In contrast to the formation of 6,12-olides,[2] the corresponding hydroxy esters or protiodesilylated products were not detected. The stereostructures of the four lactones thus obtained were determined from *J*-values of the ^1H NMR spectral data, shown in Table 2. Two of these lactones, compounds **3** and **6**, were found to be *cis*-lactones, deduced from the NOE effect between 7-H and 8-H.

The stereochemistry observed for the cyclization can be classified as follows. (1) Only *cis*-lactones were afforded when compound **1** was treated with Lewis acids, although the ratio

Table 1 Cyclization of compounds **1** and **2**

Substrate	Reagent	Yield (%)	Products (proportions) 3	4	5	6
1	$SnCl_4$	12	7			93
1	$BF_3{\cdot}OEt_2$	13	29			71
1	TBAF	11		68	32	
2	$SnCl_4$	27		24	52	24
2	$BF_3{\cdot}OEt_2$	27		26	60	14
2	TBAF	24		48	52	

Table 2 ^1H NMR data of lactones **3–6** in $CDCl_3$[a]

	7-H	8-H	13*E*-H	13*Z*-H
3	3.31 m	4.90 ddd (1.5, 6, 9)	5.55 d (2.5)	6.35 d (2.9)
4	2.86 tq (3.5, 9)	4.18 ddd (3, 9, 12)	5.42 d (3.2)	6.14 d (3.6)
5	2.70 ddq (9, 11, 3.5)	4.23 ddd (6, 9, 11)	5.48 d (3.1)	6.19 d (3.5)
6	3.29 dddt (6, 9, 12, 3.5)	4.67 ddd (3, 9, 12)	5.50 d (3.1)	6.23 d (3.4)

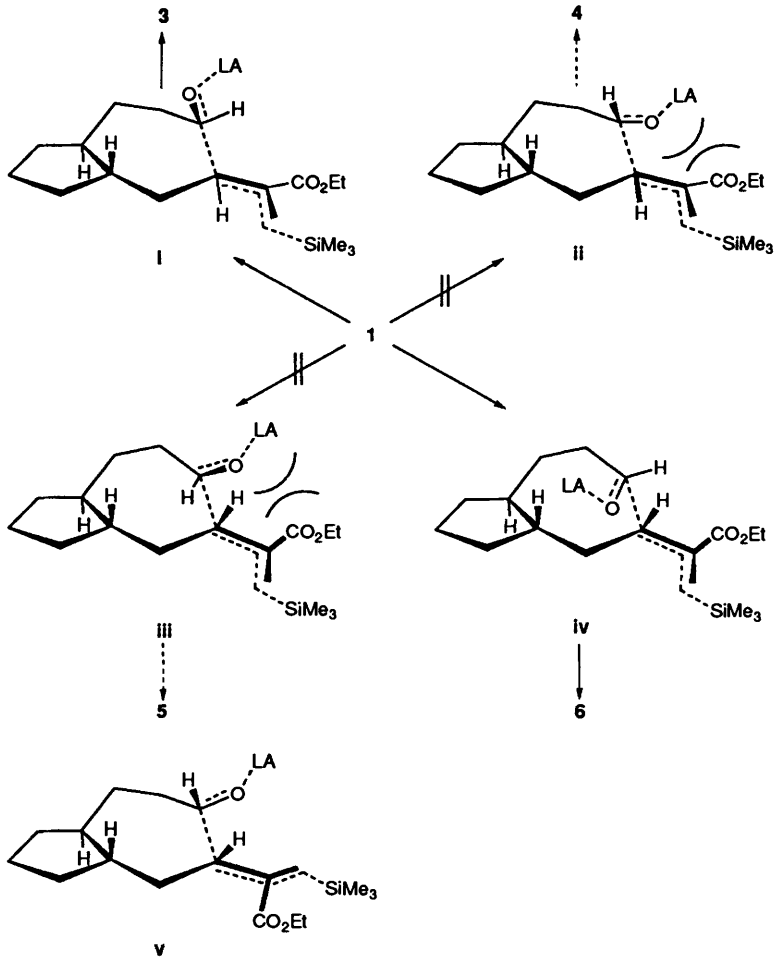
[a] *J*-Values (in Hz) are given in parentheses.

was dependent on the nature of the Lewis acid; (2) in contrast, compound **2** gave three lactones, **4**, **5** and **6**, by treatment with Lewis acids; (3) treatment with TBAF gave only *trans*-lactones, irrespective of the geometry of the precursor.

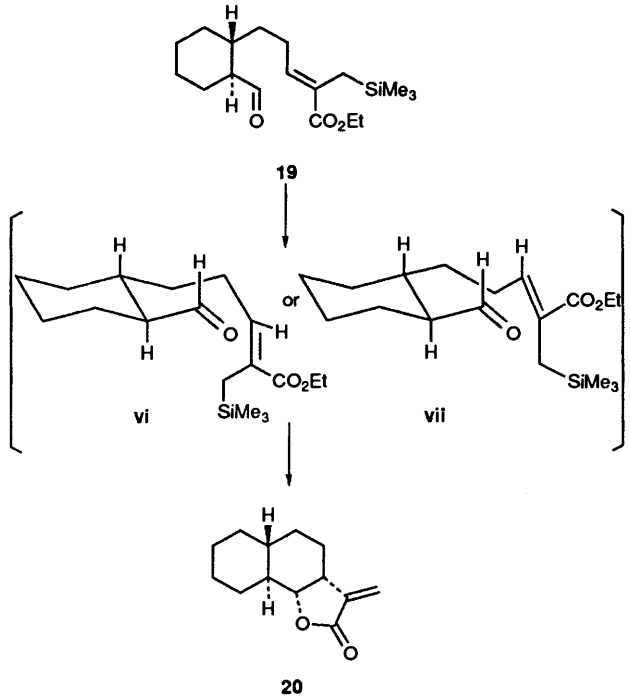
We earlier reported[1] that the stereoselectivity of protonic or Lewis acid-promoted cyclization can be explained by an interaction between two oxygen functionalities in the intermediate.[1,2] The results obtained here give further support for this explanation as follows (Scheme 3). Since two double bonds are expected to take a synclinal position in the precyclization transition state,[12,13] intermediates **ii** and **iii**, which are expected to give rise to products **4** and **5**, respectively, from substrate **1**, are unfavourable because of an interaction between two oxygen functionalities, while the corresponding intermediates **i** and **iv** have no such interactions, and therefore compounds **3** and **6** were produced. Scheme 3 is also applicable for Lewis acid-promoted cyclization of compound **2**, in which the trimethylsilylmethyl and ethoxycarbonyl groups are reversed, and opposite to those shown in the scheme. The formation of compound **6** from substrate **2** can be explained by the intermediacy of conformation **v**.

As for fluoride-promoted cyclizations, we previously attempted to rationalize the stereoselective cyclization of aldehydo ester **19** to γ-lactone **20** in terms of two conformations **vi** and **vii**; however, we could not decide through which of these conformations compound **20** was attained (Scheme 4).[1] The conformation **vi** has a chair–chair decalin system with 'crossed' double bonds (C=C and C=O), while conformation **vii** has a chair–boat decalin with the two double bonds 'parallel'. The results obtained here reveal that the 'parallel' approach is more likely to explain the stereoselectivity (Scheme 5). Thus, the *trans*-disubstituted five-membered ring prevents *cis*-lactone-directed parallel approach of two double bonds (intermediates **viii** and **xi**), which explains why *cis*-lactones (**3** and **6**) were not obtained from both substrates **1** and **2**, while *trans*-lactones (**4** and **5**) were obtained from conformations **ix** and **x**, respectively.* In contrast, the 'crossed' double-bond approach does

* Fluoride-promoted cyclization proceeds under kinetic control with a pentacoordinate silicon atom as intermediate: see ref. 14.



Scheme 3 LA = Lewis acid



Scheme 4

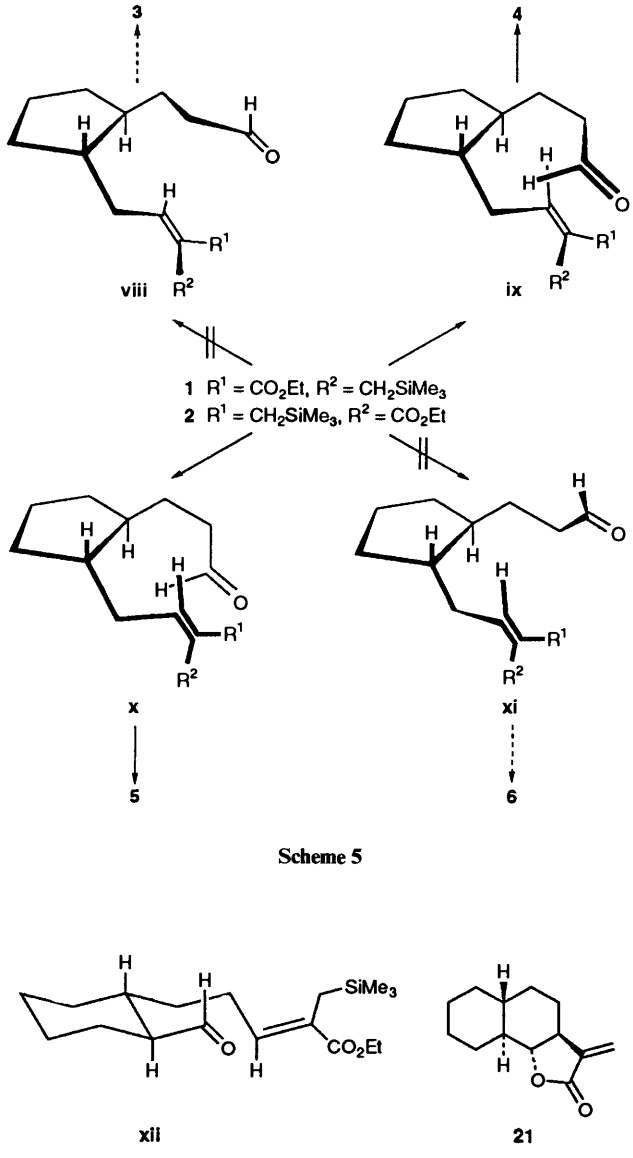
not rationalize the results, since both *trans*- and *cis*-lactone-directed conformations are plausible. The 'crossed' approach also does not explain why *trans*-lactone **21** was not the major product from aldehydo ester **19** through intermediate **xii**, where the side chain on the decalin has an equatorial orientation while the corresponding rotamer **vi** has the more congested axial side chain (Scheme 4).

Recently, Nishitani *et al.* reported that seven-membered-ring-directed carbocyclization of an ω-formyl-β-(ethoxycarbonyl)-allylsilane does not proceed in acyclic systems.[3b] The difference between their system and our compounds **1** and **2** is the absence of a 1,2-disubstituted five-membered ring. We presume that this five-membered ring is essential for the folded conformation to take precedence over the extended one.

In conclusion, the utility and limitations of intramolecular cyclization of ω-formyl-β-(ethoxycarbonyl)allylsilanes in the synthesis of guaianolides and pseudoguaianolides are revealed. In addition to the Lewis acid-promoted cyclization, the stereochemistry of fluoride-promoted cyclization was proposed. Since regioselective synthesis of the *Z*-precursor is established,[3] it would be possible to synthesize a *trans*-lactone or a *cis*-lactone selectively by this method.

Experimental

General Procedures.—UV spectra were taken on a Hitachi 220A UV spectrophotometer. IR spectra were determined on a Hitachi 270-30 spectrophotometer. Both ^1H and ^{13}C NMR spectra were measured on a JEOL GSX-400 (400 MHz) spectrometer. Chemical shifts are reported downfield from tetramethylsilane on the δ-scale (ppm), while chloroform was used as the internal standard [$\delta_H(CHCl_3) = 7.25$] for all



Scheme 5

compounds having a trimethylsilyl group and for all ^{13}C NMR spectra. *J*-Values are given in Hz. Both low-resolution and high-resolution mass spectra were obtained on a Hitachi M-80 mass spectrometer. Analytical TLC was performed on pre-coated TLC plates (Kieselgel 60 F254, layer thickness 0.2 mm). Wakogel C-200 and C-300, Florisil (100–200 mesh), or ICN Alumina N Act 1 were used for column chromatography. Anhydrous Na_2SO_4 or $MgSO_4$ were used for drying of extracted organic layers. For reactions which required dry solvents, tetrahydrofuran (THF) and 1,2-dimethoxyethane (DME) were distilled from $LiAlH_4$; diglyme, CH_2Cl_2, and hexane were distilled from CaH_2.

3-[2-(*Methoxymethylene*)*cyclopentyl*]*prop*-1-*ene* **11**.—To a stirred solution of lithium diisopropylamide (LDA), prepared from BuLi (6.8 cm^3, 17 mmol; 2.5 mol dm^{-3} in hexane) and diisopropylamine (4.3 cm^3) in THF (20 cm^3) under Ar, was added a solution of $Ph_2P(O)CH_2OMe$ (3.54 g) in THF (95 cm^3) at 0 °C. After this mixture had been stirred for 20 min, a solution of ketone **7** (1.46 g, 11.8 mmol) in THF (10 cm^3) was added, with cooling to −60 °C. The reaction mixture was stirred at room temperature for 1 day, aq. NH_4Cl was added, and the mixture was extracted with Et_2O. Purification of the product by silica gel (30 g) column chromatography using hexane–AcOEt (19:1) as eluent afforded the *vinyl ether* **11** (1.32 g, 74%) as an oil (Found: M^+, 152.1177. $C_{10}H_{16}O$ requires M, 152.1202); ν_{max}(neat)/cm^{-1} 1690 (C=C), 1645 (C=C) and 1125 (C–O); δ_H($CDCl_3$; assigned for the major isomer) 3.56 (3 H, s, OMe), 4.92–5.10 (2 H, m, CH=CH_2) and 5.68–5.91 (2 H, m, =C*H*OMe and C*H*=CH_2); δ_C($CDCl_3$; assigned for the major isomer) 25.16, 29.51, 31.75, 38.00, 39.08, 59.33, 115.00, 124.10, 138.04 and 139.30; *m*/*z* 152 (M^+, 5%), 111 (100), 89 (21) and 45 (14).

trans-2-(*Prop*-2-*enyl*)*cyclopentanecarbaldehyde* **12**.—Compound **11** (1.226 g, 8.05 mmol) was dissolved in 5% aq. HCl–THF (150 cm^3; 1:4 ratio) and the mixture was refluxed for 40 min. After the mixture had cooled to room temperature, aq. $NaHCO_3$ was added and the resulting solution was extracted with Et_2O. The extract was chromatographed on Florisil (40 g) with hexane–AcOEt (99:1) as eluent to obtain *aldehyde* **12** (884.5 mg, 79%) as an oil (Found: M^+, 138.1041. $C_9H_{14}O$ requires M, 138.1045); ν_{max}(neat)/cm^{-1} 2715 (CHO), 1725 (C=O) and 1645 (C=C); δ_H($CDCl_3$) 4.98–5.09 (2 H, m, CH=CH_2), 5.77 (1 H, m, C*H*=CH_2) and 9.60 (1 H, d, *J* 2.5, CHO); δ_C($CDCl_3$) 24.74, 26.42, 32.21, 39.07, 40.44, 58.17, 116.15, 136.68 and 203.65; *m*/*z* 138 (M^+, 1%), 120 (12), 109 (12), 95 (57), 79 (46), 67 (100) and 41 (88).

trans-3-[2-(2-*Methoxyvinyl*)*cyclopentyl*]*prop*-1-*ene* **13**.—By the same procedure described for the preparation of compound **11**, compound **12** (608.6 mg, 4.40 mmol), along with $Ph_2P(O)CH_2OMe$ (1.53 g) in the presence of LDA, produced *title compound* **13** (563.7 mg, 77%) as an oil (Found: M^+, 166.1314. $C_{11}H_{18}O$ requires M, 166.1358); ν_{max}(neat)/cm^{-1} 1655 (C=C); δ_H($CDCl_3$; assigned for the major isomer) 3.51 (3 H, s, OMe), 4.60 (1 H, dd, *J* 12 and 8, C*H*=CHOMe), 4.90–5.03 (2 H, m, CH=CH_2), 5.80 (1 H, m, C*H*=CH_2) and 6.26 (1 H, d, *J* 12, CH=C*H*OMe); δ_C($CDCl_3$; assigned for the major isomer) 23.32, 31.24, 34.16, 38.01, 45.25, 46.35, 55.95, 107.08, 114.87, 138.16 and 146.73; *m*/*z* 166 (M^+, 10%), 137 (8), 124 (100), 97 (42), 93 (39), 84 (42) and 41 (43).

trans-2-(*Prop*-2-*enyl*)*cyclopropaneethanal* **14**.—Compound **13** (319.5 mg, 1.92 mmol) was hydrolysed by the same procedure described for compound **11** to yield the *aldehyde* **14** (292.0 mg, 100%) as an oil [Found: *m*/*z* 134.1070 (M − H_2O). $C_{10}H_{14}$ (M − H_2O) requires *m*/*z* 134.1096]; ν_{max}(neat)/cm^{-1} 2730 (CHO), 1730 (C=O) and 1645 (C=C); δ_H($CDCl_3$) 1.54 (1 H, d quint, *J* 5 and 8, C*H*CH_2CH=CH_2), 1.93 (1 H, m, C*H*CH_2CHO), 1.96 (1 H, m, C*H*HCH=CH_2), 2.23 (1 H, ddq, *J* 7, 14 and 1.5, CH*H*CH=CH_2), 2.29 (1 H, ddd, *J* 2.5, 9 and 16, C*H*HCHO), 2.60 (1 H, ddd, *J* 2, 4.5 and 16, CH*H*CHO), 4.96–5.09 (2 H, m, CH=CH_2), 5.77 (1 H, m, C*H*=CH_2) and 9.76 (1 H, t, *J* 2, CHO); δ_C($CDCl_3$) 23.62, 31.37, 32.34, 38.73, 39.37, 45.16, 49.23, 115.58, 137.40 and 202.80; *m*/*z* 152 (M^+, 0.4%), 134 (2), 119 (7), 108 (52), 97 (32) and 67 (100).

Ethyl (Z)- *and* (E)-4-[trans-2-(*Prop*-2-*enyl*)*cyclopentyl*]-2-(*trimethylsilylmethyl*)*but*-2-*enoate* **15** *and* **16**.—To a stirred suspension of NaH (278 mg, 11.6 mmol; 60% in mineral oil, which was removed by washing with hexane) in DME (6.2 cm^3) under Ar was added a solution of $(EtO)_2P(O)CH_2CO_2Et$ (1 cm^3) in DME (2.1 cm^3) at 0 °C. After being stirred at room temp. for 40 min, a solution of ICH_2SiMe_3 (0.9 cm^3) in DME (2.1 cm^3) was added at once. The reaction mixture was heated to 70 °C for 4 h, cooled to 0 °C, and a second portion of NaH (190 mg) was added. After being stirred for 1.5 h at room temperature the mixture was treated with a solution of aldehyde **14** (376.6 mg, 2.47 mmol) in DME (7.6 cm^3), and the mixture was stirred for another 18 h. The reaction was quenched by the addition of aq. NH_4Cl, and the resulting solution was extracted with Et_2O. Silica gel (10 g) column chromatography using

hexane–AcOEt (49:1) as eluent was repeated several times until isomers **15** (327.1 mg, 43%) and **16** (136.4 mg, 18%) were obtained. *Compound* **15** was an oil (Found: C, 70.2; H, 10.15. $C_{18}H_{32}O_2Si$ requires C, 70.07; H, 10.45%); λ_{max}(EtOH)/nm 233 (ε/dm^3 mol^{-1} cm^{-1} 6000); ν_{max}(neat)/cm^{-1} 1715 (C=O), 1640 (C=C) and 1250 (C–O); δ_H($CDCl_3$) 0.00 (9 H, s, $SiMe_3$), 1.29 (3 H, t, *J* 7, OCH_2*Me*), 1.80 (2 H, s, CH_2SiMe_3), 4.17 (2 H, q, *J* 7, OCH_2Me), 4.93–5.04 (2 H, m, CH=CH_2), 5.80 (1 H, m, CH=CH_2) and 6.64 (1 H, t, *J* 7, CH=CCO_2Et); δ_C($CDCl_3$) −0.99 (3 C), 14.29, 17.34, 23.72, 31.80, 32.20, 34.13, 39.24, 44.77, 45.02, 60.37, 115.20, 130.32, 137.64, 137.94 and 168.43; *m/z* 308 (M^+, 8%), 293 (17), 263 (4), 200 (20), 185 (24) and 73 (100).

Compound **16** was an oil (Found: C, 70.3; H, 10.3%); λ_{max}(EtOH)/nm 236 (ε/dm^3 mol^{-1} cm^{-1} 7000); ν_{max}(neat)/cm^{-1} 1720 (C=O), 1645 (C=C) and 1250 (C–O); δ_H($CDCl_3$) −0.02 (9 H, s, $SiMe_3$), 1.29 (3 H, t, *J* 7, OCH_2*Me*), 1.73 (2 H, s, CH_2SiMe_3), 4.17 (2 H, q, *J* 7, OCH_2Me), 4.91–5.02 (2 H, m, CH=CH_2), 5.66 (1 H, t, *J* 7.5, CH=CCO_2Et) and 5.79 (1 H, m, CH=CH_2); δ_C($CDCl_3$) −1.63 (3 C), 14.28, 23.68, 24.17, 31.71, 31.80, 34.54, 39.20, 44.90, 45.51, 59.98, 114.95, 129.54, 137.98, 138.13 and 168.51; *m/z* 308 (M^+, 9%), 293 (14), 263 (6), 200 (20), 185 (25) and 73 (100).

Ethyl (Z)- *and* (E)-4-[trans-2-(3-*Hydroxypropyl*)*cyclopentyl*]-2-(*trimethylsilylmethyl*)*but*-2-*enoate* **17** *and* **18**.—To a stirred solution of $NaBH_4$ (128 mg) in diglyme (3.5 cm^3) was added 2-methylbut-2-ene (1.2 cm^3) at room temperature under Ar. After being cooled to 0 °C, the mixture was treated with BF_3·OEt_2 (0.26 cm^3) and was stirred for 6 h. To this was added a solution of compound **15** (59.2 mg, 0.19 mmol) in DME (3.5 cm^3). After the mixture had been stirred at room temperature for 18 h, water (2 cm^3), aq. NaOH (2 cm^3; 3 mol dm^{-3}) and 30% H_2O_2 (2.8 cm^3) were added successively and dropwise at 0 °C. The resulting aqueous solution was stirred at 0 °C for 1 h, and at room temp. for 30 min. Addition of aq. NaCl, followed by extraction with Et_2O, afforded compound **17** (55.4 mg, 88%), which was used in the next step without purification. *Compound* **17** was an oil (Found: M^+, 326.2250. $C_{18}H_{34}O_3Si$ requires M, 326.2278); ν_{max}(neat)/cm^{-1} 3420 (OH), 1715 (C=O), 1640 (C=C) and 1250 (C–O); δ_H($CDCl_3$) −0.01 (9 H, s, $SiMe_3$), 1.29 (3 H, t, *J* 7, OCH_2*Me*), 1.80 (2 H, s, CH_2SiMe_3), 3.64 (2 H, t, *J* 6, CH_2OH), 4.17 (2 H, q, *J* 7, OCH_2Me) and 6.63 (1 H, t, *J* 7.5, CH=CCO_2Et); δ_C($CDCl_3$) −0.99 (3 C), 14.27, 17.33, 23.74, 31.09, 31.64, 32.18, 32.21, 34.16, 45.32, 45.42, 60.39, 63.23, 130.29, 137.67 and 168.46; *m/z* 326 (M^+, 2%), 311 (10), 281 (5), 200 (38), 185 (56) and 73 (100).

By the same procedure, compound **16** (64.4 mg) was converted into *hydroxy ester* **18** (65.9 mg, 97%) as an oil (Found: M^+, 326.2176); ν_{max}(neat)/cm^{-1} 3400 (OH), 1720 (C=O), 1635 (C=C) and 1250 (C–O); δ_H($CDCl_3$) −0.02 (9 H, s, $SiMe_3$), 1.29 (3 H, t, *J* 7, OCH_2*Me*), 1.72 (2 H, s, CH_2SiMe_3), 3.62 (2 H, t, *J* 6, CH_2OH), 4.16 (2 H, q, *J* 7, OCH_2Me) and 5.66 (1 H, t, *J* 7.5, CH=CCO_2Et); *m/z* 326 (M^+, 2%), 311 (3), 281 (4), 200 (33), 185 (48) and 73 (100).

Ethyl (Z)- *and* (E)-4-[trans-2-(2-*Formylethyl*)*cyclopentyl*]-2-(*trimethylsilylmethyl*)*but*-2-*enoate* **1** *and* **2**.—To a stirred solution of compound **17** (55.4 mg, 0.17 mmol) in CH_2Cl_2 (10 cm^3) was added PDC (161.9 mg) and the mixture was stirred at room temp. for 1 day. Et_2O was added, and the precipitate was filtered off. The filtrate was concentrated to minimum amount of solvent, and the solution was further filtered through a Florisil (5 g) column with Et_2O as eluent to afford *compound* **1** (33.2 mg, 60%) as an oil (Found: M^+, 324.2113. $C_{18}H_{32}O_3Si$ requires M, 324.2122); ν_{max}(neat)/cm^{-1} 2720 (CHO), 1730 (C=O), 1710 (C=O), 1640 (C=C) and 1250 (C–O); δ_H($CDCl_3$) −0.01 (9 H, s, $SiMe_3$), 1.29 (3 H, t, *J* 7, OCH_2*Me*), 1.80 (2 H, s, CH_2SiMe_3), 4.17 (2 H, q, *J* 7, OCH_2Me), 6.61 (1 H, t, *J* 7.5, CH=CCO_2Et) and 9.77 (1 H, t, *J* 2, CHO); δ_C($CDCl_3$) −0.99 (3 C), 14.27, 17.40, 23.63, 27.05, 31.93, 32.11, 33.96, 42.93, 45.00, 45.34, 60.42, 130.60, 137.13, 168.36 and 202.67; *m/z* 324 (M^+, 2%), 309 (18), 296 (7), 279 (5), 200 (35), 185 (60) and 73 (100). Similarly, hydroxy ester **18** (65.9 mg) was oxidized to *aldehydo ester* **2** (34.4 mg, 53%), which was obtained as an oil (Found: M^+, 324.2121); ν_{max}(neat)/cm^{-1} 2750 (CHO), 1730 (C=O) and 1250 (C–O); δ_H($CDCl_3$) −0.02 (9 H, s, $SiMe_3$), 1.30 (3 H, t, *J* 7, OCH_2*Me*), 1.74 (2 H, s, CH_2SiMe_3), 4.17 (2 H, q, *J* 7, OCH_2Me), 5.65 (1 H, t, *J* 7.5, CH=CCO_2Et) and 9.77 (1 H, t, *J* 2, CHO); *m/z* 324 (M^+, 1%), 309 (8), 296 (6), 279 (6), 200 (30), 185 (54) and 73 (100).

Cyclization of Compounds **1** *and* **2** *with* $SnCl_4$.—To a stirred solution of compound **2** (15.7 mg, 0.048 mmol) in CH_2Cl_2 (3 cm^3) was added $SnCl_4$ (0.2 cm^3; 1 mol dm^{-3} solution in CH_2Cl_2) at 0 °C under Ar. The reaction mixture was stirred at room temperature for 1 day, further $SnCl_4$ (0.2 cm^3, total 0.4 mmol) was added, and the mixture was stirred for 1 day. Water was added, and the mixture was extracted with Et_2O. The extract was chromatographed on silica gel (1 g) with hexane–AcOEt (49:1) as eluent to obtain a mixture of lactones (**4**, **5** and **6**; 2.7 mg, 27%) as an oil; ν_{max}(neat)/cm^{-1} 1770 (C=O) and 1270 (C–O); δ_H see Table 2.

Similarly, compound **1** (21.2 mg, 0.065 mmol) afforded a mixture of *cis*-lactones **3** and **6** (1.6 mg, 12%) as an oil; ν_{max}(neat)/cm^{-1} 1770 (C=O) and 1270 (C–O); δ_H see Table 2; *m/z* 206 (M^+, 15%), 178 (39), 134 (56) and 82 (100).

Cyclization of Compounds **1** *and* **2** *with* BF_3·OEt_2.—To a stirred solution of compound **2** (9.8 mg, 0.030 mmol) in CH_2Cl_2 was added BF_3·OEt_2 (0.05 cm^3, 0.41 mmol) under Ar at 0 °C, and the mixture was stirred at room temperature for 1 day. Extraction with CH_2Cl_2, followed by silica gel (1 g) column chromatography using hexane–AcOEt (19:1) as eluent, gave lactones **4**, **5** and **6** (1.7 mg, 27%) as an oil.

Similarly, compound **1** (15.9 mg, 0.049 mmol) afforded a mixture of *cis*-lactones **3** and **6** (1.3 mg, 13%) as an oil.

Cyclization of Compounds **1** *and* **2** *with TBAF*.—To a stirred solution of compound **2** (8.7 mg, 0.027 mmol) in THF (1 cm^3) was added a solution of TBAF (15.9 mg, 0.061 mmol) in THF (1 cm^3) at 0 °C under Ar. After being stirred at 0 °C for 1.5 h, the mixture was treated with aq. NH_4Cl, and was then extracted with Et_2O. Silica gel (1 g) column chromatography using hexane–AcOEt (49:1) gave a mixture of *trans*-lactones (**4** and **5**; 1.3 mg, 24%) as an oil.

The same procedure was applied to compound **1** (11.9 mg, 0.037 mmol) to give the same *trans*-lactones (0.8 mg, 11%).

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