# General Method for the Preparation of α-Methylene-γ-butyrolactones from (*R*)- and (*S*)-1,2-Isopropylideneglyceraldehydes

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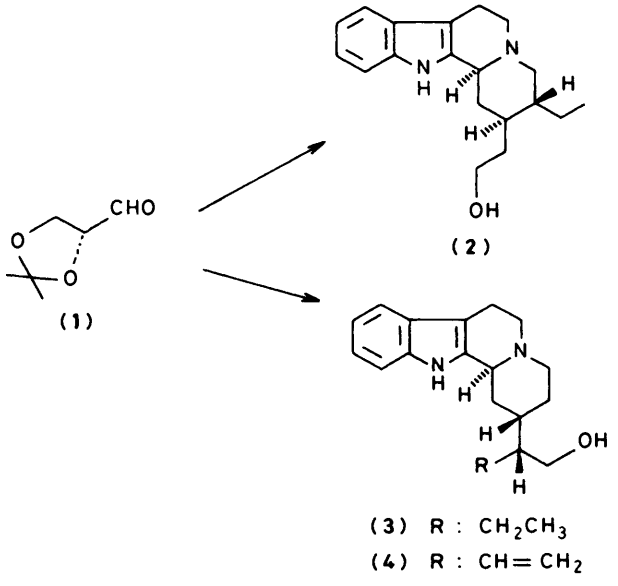
Both (*R*)- and (*S*)-1,2-isopropylideneglyceraldehydes (**1**) and (**18**) are shown to be useful, inexpensive chiral starting materials for syntheses of α-methylene-γ-butyrolactones (**15**) and (**28**) which are potential intermediates for biologically important sesquiterpene lactones.

The α-methylene-γ-butyrolactone unit is a familiar structural feature of the germacrolide, elemanolide, and eudesmanol sesquiterpenes. It has been suggested[1] that their cytotoxic activity arises from the ability of the unsaturated lactone to alkylate a cysteine residue *via* a Michael reaction and as a result of this hypothesis a great deal of effort has been devoted to the development of methods for the construction of α-methylene-γ-butyrolactones and the total synthesis of sesquiterpene lactones.[2]

In a recent development concerned with the total synthesis of optically active natural products, (*R*)-1,2-*O*-isopropylideneglyceraldehyde (**1**) has been used as a chiral synthon for a number of biologically active compounds such as prostaglandins,[3] brefeldin A,[4] ipsdienol,[5] pestalotin,[6] and leukotriene $A_4$.[7]

Our own efforts during the past few years have concentrated on the synthesis of indole alkaloids and led to success of the total syntheses of (−)-dihydrocorynantheol (**2**),[8] (+)-dihydroantirhine (**3**),[9] and (−)-antirhine (**4**).[10]



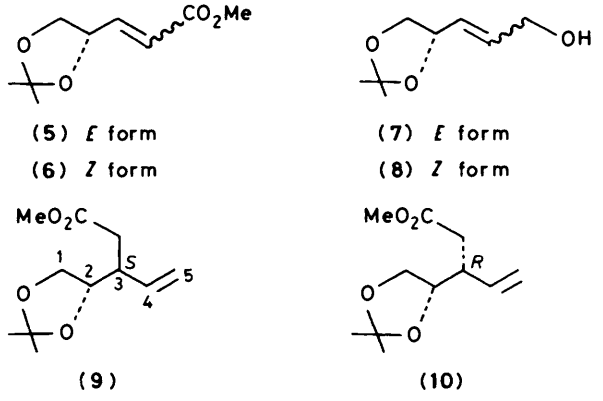

**Scheme 1.**

In our continuing efforts to develop a synthetic route to biologically important sesquiterpene lactones, we required an α-methylene-γ-butyrolactone possessing functional groups at C-2 and C-3.

Here we report an efficient synthesis of 2,3-disubstituted α-methylene-γ-butyrolactones in optically active form from (*R*)- and (*S*)-1,2-isopropylideneglyceraldehydes,[11a,b] respectively.

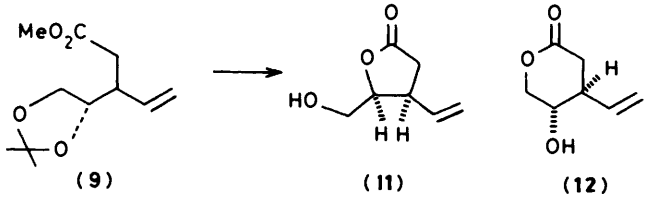
The aldehyde (**1**)[11a] was treated with methoxycarbonylmethylenetriphenylphosphorane to give compounds (**5**) and (**6**) as a mixture (70:30) in 64.1% yield. Di-isobutylaluminium hydride reduction of the (*E*)-olefinic ester (**5**), followed by ortho ester Claisen rearrangement[12] of the resultant allyl alcohol (**7**) provided a separable mixture of compounds (**9**) and (**10**) in 65.8 and 21.5% overall yield, respectively. Similarly, the (*Z*)-olefinic ester (**6**) was converted into (**9**) and (**10**) in 67.7 and 22.2% overall yield, respectively, *via* the (*Z*)-allyl alcohol (**8**).

Since the (3*S*)- and (3*R*)-methyl esters (**9**) and (**10**) were available, lactonisation was examined under a variety of conditions and the results are summarised in the Table.




**Scheme 2.**

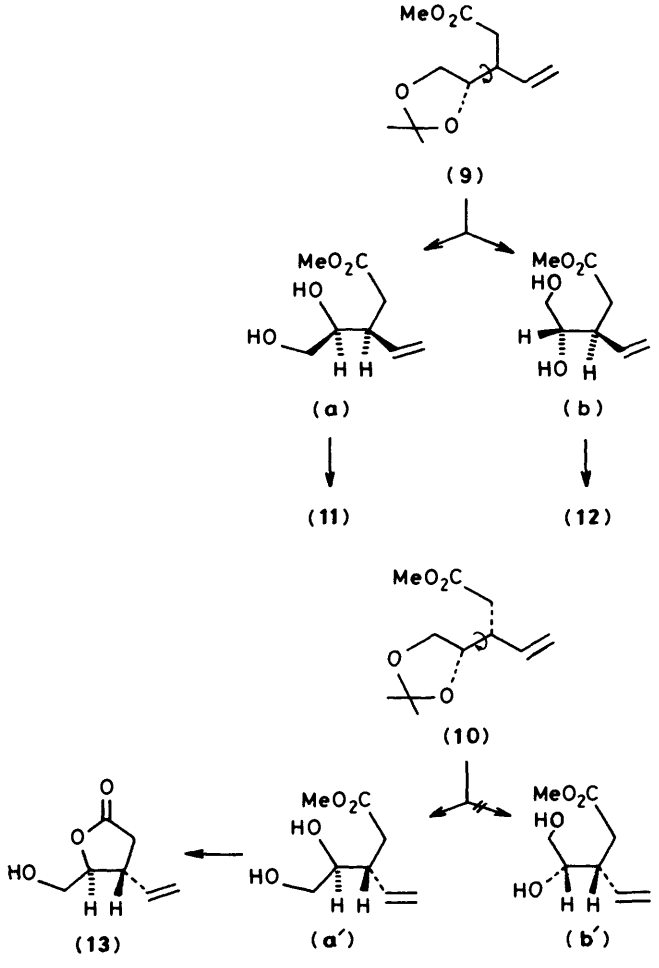
**Table.** Lactonisation of the (3*R*)-methyl ester (**9**) under acidic conditions




| Entry no. | Reaction conditions: Solvent | Acid | Temp. (°C) | Time (h) | Products (**11**):(**12**) | Yield (%) |
|---|---|---|---|---|---|---|
| 1 | MeOH | 30% $H_2SO_4$ | 60 | 2 | 100:0 | 85.3 |
| 2 | MeOH | 10% $H_2SO_4$ | R.t. | 2 | 77:23 | 81.3 |
| 3 | MeOH | 10% $H_2SO_4$ | 0 | 3 | 57:43 | 60.1 |
| 4 | MeOH | *p*-TsOH | R.t | 2 | 83:17 | 80.0 |
| 5 | MeOH | *p*-TsOH | 0 | 2 | 84:16 | 48.3 |
| 6 | THF | 10% $H_2SO_4$ | R.t. | 2 | 89:11 | 35.3 |
| 7 | THF | 10% $H_2SO_4$ | 0 | 2 | 55:45 | 20.7 |

As can be seen from the Table, treatment of compound (**9**) under less acidic conditions (entries 2—7) always produced a mixture of γ- and δ-lactones (**11**) and (**12**) whose i.r. spectra showed characteristic absorptions due to ketone groups at 1 770 $cm^{-1}$ for (**11**) and 1 720 $cm^{-1}$ for (**12**), respectively. Treatment of compound (**9**) under more acidic conditions however (entry 1) afforded exclusively the γ-butyrolactone (**11**) in 85.3% yield; under these conditions, none of the δ-lactone (**12**) was detected. Interestingly, the anti-type γ-butyrolactone (**13**) was easily obtained in 88.4% yield by treatment of compound (**10**) with 10% aqueous sulphuric acid in methanol at room temperature.

These facts may be explained as follows; the kinetic preference for the formation of the γ-lactone (**11**) from (**9**) rather than the δ-lactone (**12**), reflects the difference in energy of the transition states for cyclisation. This energy difference is less for the substrate (**9**) than for (**10**) because: (i) the transition state for the cyclization of (a) ⟶ the γ-lactone (**11**) is destabilised by torsional strain between the hydroxymethyl and vinyl groups; (ii) the transition state for the cyclisation of (b′) ⟶ the δ-lactone is destabilised by the enforced axial orientation of an hydroxy (or vinyl) substituent.

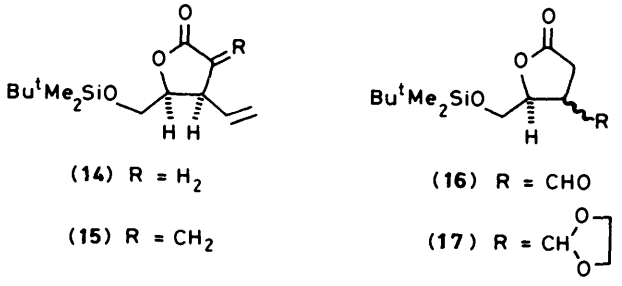



Scheme 3.

Protection of the primary alcohol in compound (**11**) as a dimethyl-t-butylsilyl ether and subsequent cleavage of the double bond in (**14**) provided the aldehyde (**16**) as a diastereoisomeric mixture at C-3 in the ratio 1:1. These labile aldehydes were protected as acetals without purification to give an inseparable mixture of the lactone (**17**) (*ca.* 1:1) in 40.8% overall yield from (**14**). Similarly, the anti-type γ-butyrolactone (**13**) was also converted into (**17**) in 40% overall yield as a diastereoisomeric mixture at C-3 (1:1).

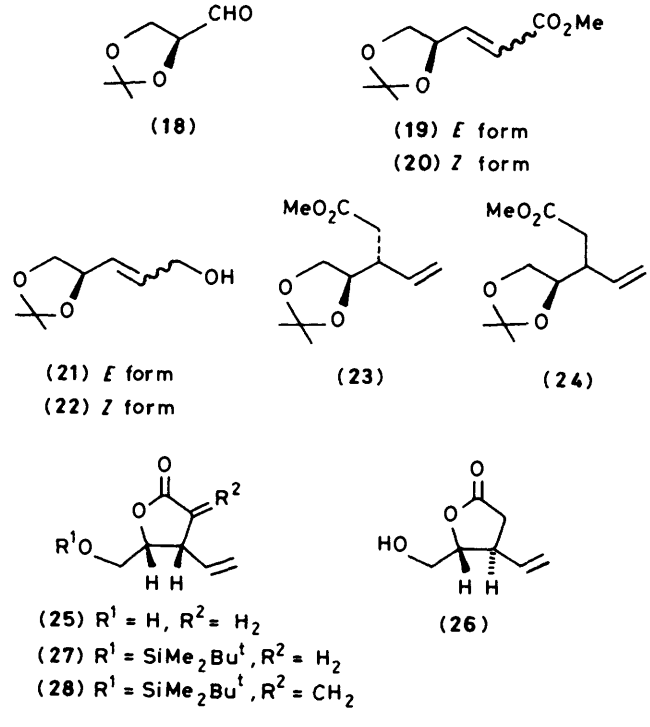
Next we examined the introduction of an α-methylene unit into a γ-butyrolactone. After extensive examination, we found that the best result was obtained by modifying the procedure recently developed by Murray.[13]

Thus, formylation of the parent lactone (**14**) using lithium hexamethyldisilazane and ethyl formate in dimethoxyethane, followed by heating of the mixture under reflux (without isolation of the lithium salt) with paraformaldehyde, gave the α-methylene-γ-butyrolactone (**15**) in 44.8% yield (83% yield based on recovered starting material).




Scheme 4.

Application of this synthetic route to (*S*)-glyceraldehyde (**18**)[11b] derived from (−)-ascorbic acid gave the *syn*-type γ-butyrolactone (**25**) in 26.2% overall yield *via* (**19**), (**21**), and (**23**); 10.6% overall yield *via* (**20**), (**22**), and (**23**), respectively. The *anti*-type γ-butyrolactone (**26**) was also obtained by a treatment of (**24**) with acid. Protection of the primary alcohol in (**25**), followed by introduction of a methylene unit into (**27**) provided the α-methylene-γ-butyrolactone (**28**) in 38.4% overall yield.




Scheme 5.

Thus, we have achieved the enantioselective synthesis of four possible γ-butyrolactone and two α-methylene-γ-butyrolactone derivatives in optically active form which can be potential intermediates leading to a variety of natural products having an α-methylene-γ-butyrolactone moiety. By this strategy, enantioselective syntheses of secologanin sesquiterpene lactone and avenaciolide are also possible.

## Experimental

I.r. spectra were recorded with Shimadzu IR-400 and JASCO IR-810 spectrophotometers. Mass spectra were obtained with a JEOL-JMS-OISG-2 spectrometer. N.m.r. spectra were taken for solutions in deuteriochloroform (tetramethylsilane as internal standard) with a JEOL JNM-PMX-60 instrument. Optical rotation was measured with a JASCO-DIP-4 automatic polarimeter. All products described in the Experimental section were homogeneous by t.l.c. and h.p.l.c.

*Methyl* (4S,2E)-4,5-*Isopropylidenedioxypent*-2-*enoate* (**5**) *and Methyl* (4S,2Z)-4,5-*Isopropylidenedioxypent*-2-*enoate* (**6**).—To a stirred suspension of 50% sodium hydride dispersion (338 mg, 8.08 mmol) (prewashed with dry pentane) in dry dimethoxyethane (20 ml) was added in small portions methoxycarbonylmethyltriphenylphosphonium bromide (3.35 g, 8.08 mmol) at 0 °C. After the solution had been stirred at room temperature for 1 h under nitrogen, it was treated with the aldehyde (**1**) (1.05 g, 8.08 mmol) in dry dimethoxyethane (2 ml). After 2 h at room temperature, the reaction was quenched by the addition of acetic acid (485 mg, 8.08 mmol), and then diluted with water. The mixture was extracted with ethyl acetate, and the extract washed with brine, dried ($MgSO_4$), filtered and evaporated to give a residue which was chromatographed on silica gel (50 g). Elution with hexane–ethyl acetate (9:1 v/v) gave the (*E*)-olefinic methyl ester (**5**)* (675 mg, 44.9%) as a syrup; $[\alpha]_D$ +37.7° (*c* 0.29 in $CHCl_3$); $\nu_{max.}$($CHCl_3$) 1 700 and 1 650 $cm^{-1}$; δ($CDCl_3$) 1.42 (3 H, s, Me), 1.45 (3 H, s, Me), 3.63 (1 H, dd, *J* 12 and 8 Hz, OCH*H*CHO), 3.75 (3 H, s, OMe), 4.1 (1 H, dd, *J* 12 and 8 Hz, OC*H*CHCHO), 4.65 (1 H, ddd, *J* 8,8, and 6 Hz, $CH_2CHO$), 6.04 (1 H, dd, *J* 15 and 1.5 Hz, CH=C*H*–CO), and 6.87 (1 H, dd, *J* 15 and 6 Hz); *m/z* 171 ($M^+$ − 15), and the (*Z*)-olefinic methyl ester (**6**)* (288 mg, 19.2%) as a syrup; $[\alpha]_D$ +101.4° (*c* 0.29 in $CHCl_3$); $\nu_{max.}$($CHCl_3$) 1 715 and 1 840 $cm^{-1}$; δ($CDCl_3$) 1.37 (3 H, s, Me), 1.43 (3 H, s, Me), 3.5 (1 H, dd, *J* 15 and 8 Hz), 3.68 (3 H, s, OMe), 4.35 (1 H, dd, *J* 15 and 8 Hz), 5.45 (1 H, ddd, *J* 8,8, and 6 Hz, $CH_2CHO$), 5.78 (1 H, dd, *J* 11 and 1.5 Hz, CH=C*H*CO), and 6.33 (1 H, dd, *J* 11 and 6 Hz, C*H*=CHCO); *m/z* 171 ($M^+$ − 15).

*Methyl* (4R,2E)-4,5-*Isopropylidenedioxypent*-2-*enoate* (**19**) *and Methyl* (4R,2Z)-4,5-*Isopropylidenedioxypent*-2-*enoate* (**20**).—The same treatment of (*S*)-1,2-isopropylideneglyceraldehyde (**18**) (8.0 g, 46.2 mmol; prepared from (−)-ascorbic acid according to the procedure developed by Takano[11b] with the phosphorane provided the (*E*)-olefinic methyl ester (**19**)* (2.44 g, 28.4%) as a syrup; $[\alpha]_D$ −35.7° (*c* 0.31 in $CHCl_3$); *m/z* 171 ($M^+$ − 15), and the (*Z*)-olefinic methyl ester (**20**)* (1.41 g, 16.4%) as a syrup; $[\alpha]_D$ −99.8° (*c* 0.15 in $CHCl_3$); *m/z* 171 ($M^+$ − 15). Both i.r. and n.m.r. spectra of (**19**) and (**20**) were identical with those of (**5**) and (**6**), respectively.

*Claisen Rearrangement of* (4S,2E)-4,5-*Isopropylidenedioxypent*-2-*en*-1-*ol* (**7**) and (4S,2Z)-4,5-*Isopropylidenedioxypent*-2-*en*-1-*ol* (**8**).—A mixture of the allyl alcohol (**7**) (1.48 g, 9.37 mmol), trimethyl orthoacetate (11.3 g, 94.0 mmol), and propionic acid (69 mg, 0.937 mmol) was stirred and heated at 140—145 °C for 30 min with removal of methanol. Excess of trimethyl orthoacetate and propionic acid were distilled off and the resultant residue chromatographed on silica gel (50 g). Elution with hexane–ethyl acetate (95:5, v/v) provided the methyl ester (**9**)* (1.32 g, 65.8%); $[\alpha]_D$ +24.0° (*c* 0.20 in $CHCl_3$); $\nu_{max.}$($CHCl_3$) 1 720 $cm^{-1}$; δ($CDCl_3$) 1.31 (3 H, s, Me), 1.38 (3 H, s, Me), 2.22—2.93 (3 H, m, C$H_2$CO and C*H*–CH=$CH_2$), 3.60 (3 H, s, OMe), 3.73—4.23 (3 H, m, $OCH_2CHO$), 4.86 (1 H, dd, *J* 16 and 2 Hz, CH=C*H*H), 4.95 (1 H, dd, *J* 9 and 2 Hz, CH=CH*H*), and 5.6 (1 H, ddd, *J* 16,9, and 7 Hz, C*H*=$CH_2$); *m/z* 199 ($M^+$ − 15), and (**10**)* (431 mg, 21.5%); $[\alpha]_D$ +13.5° (*c* 0.22 in $CHCl_3$); $\nu_{max.}$($CHCl_3$) 1 720 $cm^{-1}$; δ($CDCl_3$) 1.35 (3 H, s, Me), 1.41 (3 H, s, Me), 2.20—2.70 (3 H, m, C$H_2$CO and C*H*CH=$CH_2$), 3.68 (3 H, s, OMe), 3.83—4.1 (3 H, m, $OCH_2CHO$), 5.03 (1 H, dd, *J* 17 and 2 Hz, CH=C*H*H), 5.05 (1 H, dd, *J* 9 and 2 Hz, CH=CH*H*) 5.36 (1 H, ddd, *J* 17,9, and 7 Hz, C*H*=$CH_2$); *m/z* 199 ($M^+$ − 15).

The methyl esters (**9**) (1.1 g, 67.7%) and (**10**) (361 mg, 22.2%) were also obtained from the (*Z*)-allyl alcohol (**8**) (1.2 g) by the same procedure as that described above.

*Claisen Rearrangement of* (4R,2E)-4,5-*Isopropylidenedioxypent*-2-*en*-1-*ol* (**21**).—A mixture of the allyl alcohol (**21**) (21 mg, 0.133 mmol), trimethyl orthoacetate (80.4 mg, 0.669 mmol), and propionic acid (1 mg, 0.0133 mmol) was stirred and heated at 150 °C for 1.5 h with removal of methanol by distillation. After work-up, the residue was chromatographed on silica gel (3 g) with chloroform as eluant to give the methyl ester (**23**)* (20.7 mg, 72.8%); $[\alpha]_D$ −24.0° (*c* 0.12 in $CHCl_3$); *m/z* 199 ($M^+$ − 15), and (**24**)* (6.3 mg, 22.1%); $[\alpha]_D$ −13.6° (*c* 0.06 in $CHCl_3$); *m/z* 199 ($M^+$ − 15). Both i.r. and n.m.r. spectra of (**23**) and (**24**) were identical with those of (**9**) and (**10**), respectively.

(2S,3S)-2-*Hydroxymethyl*-3-*vinyl*-γ-*butyrolactone* (**11**).—A mixture of the methyl ester (**9**) (720 mg, 336 mmol) and 30% aqueous sulphuric acid (1.5 ml) in methanol (5 ml) was heated at 60 °C for 2 h. After cooling to room temperature the mixture was extracted with ethyl acetate. The extract was washed with brine, dried ($MgSO_4$), and then evaporated to leave a residue which was chromatographed on silica gel (15 g). Elution with chloroform gave the γ-butyrolactone (**11**) (407.2 mg, 85.3%) as a syrup; $[\alpha]_D$ +43.5° (*c* 0.31 in $CHCl_3$); $\nu_{max.}$($CHCl_3$) 3 600—3 200 and 1 770 $cm^{-1}$; δ($CDCl_3$) 2.28—2.87 (2 H, m, $CH_2CO$), 2.78—3.20 (1 H, m, C*H*CH=$CH_2$), 3.52—3.85 (2 H, m, $CH_2OH$), 4.53 (1 H, ddd, *J* 8,4, and 4 Hz, $CH_2CHOH$), 5.03 (1 H, dd, *J* 18 and 2 Hz, CH=C*H*H), 5.05 (1 H, dd, *J* 9 and 2 Hz, CH=CH*H*), and 5.80 (1 H, ddd, *J* 16,9, and 8 Hz, C*H*=$CH_2$) [Found: *m/z* 142.0642 ($M^+$). $C_7H_{10}O_3$ requires 142.0828 ($M^+$)].

(2R,3R)-2-*Hydroxymethyl*-3-*vinyl*-γ-*butyrolactone*(**25**).—The γ-butyrolactone (**25**) (2.3 mg, 86.7%), $[\alpha]_D$ −47.0° (*c* 0.023 in $CHCl_3$) was obtained from the methyl ester (**23**) (4.0 mg, 0.0187 mmol) using the same procedure as that described above. Both i.r. and n.m.r. spectra of (**25**) were identical with those of (**11**).

(2S,3R)-2-*Hydroxymethyl*-3-*vinyl*-γ-*butyrolactone* (**13**).—A mixture of the methyl ester (**10**) (69.7 mg, 0.326 mmol) and 10% aqueous sulphuric acid (0.5 ml) in methanol (3.5 ml) was stirred for 2 h at room temperature. After work-up, the residue was chromatographed on silica gel (5 g) with chloroform as eluant to afford the γ-butyrolactone (**13**) (40.9 mg, 88.4%) as a syrup; $[\alpha]_D$ +83.1° (*c* 2.19 in $CHCl_3$); $\nu_{max.}$($CHCl_3$) 3 600—3 200 and 1 770 $cm^{-1}$; δ($CDCl_3$) 2.30—2.87 (2 H, m, $CH_2CO$), 3.12—3.60 (1 H, m, C*H*CH=$CH_2$), 3.60—4.05 (2 H, m, $CH_2OH$), 4.27 (1 H, ddd, *J* 8,5, and 2 Hz, $CH_2CHOCO$), 5.15 (1 H, dd, *J* 16 and

* Analysis for this compound is difficult because of its volatility and $M^+$ − Me in the mass spectra of this compound appears because of stabilisation as an oxonium-cationic radical after demethylation.

2 Hz, CH=C*H*H), 5.17 (1 H, dd, *J* 9 and 2 Hz, CH=CH*H*), and 5.80 (1 H, ddd, *J* 16,9, and 7 Hz, C*H*=$CH_2$) [Found: *m/z* 142.0611 ($M^+$). $C_7H_{10}O_3$ requires 142.0628 ($M^+$)].

(2R,3S)-2-*Hydroxymethyl*-3-*vinyl*-γ-*butyrolactone* (**26**).—The γ-butyrolactone (**26**) (3.2 mg) {$[\alpha]_D$ −80.9° (*c* 0.032 in $CHCl_3$) [Found: *m/z* 142.0615 ($M^+$). $C_7H_{10}O_3$ requires 142.0628 ($M^+$)]} was obtained from the methyl ester (**24**) by the same procedure as that described above. Both i.r. and n.m.r. spectra of (**26**) were identical with those of (**13**).

(4S,2E)-4,5-*Isopropylidenedioxypent*-2-*en*-1-*ol* (**7**) *and* (4R,2E)-4,5-*Isopropylidenedioxypent*-2-*en*-1-*ol* (**21**).—To a stirred solution of the (*E*)-olefinic methyl ester (**5**) (12.2 g, 65.6 mmol) in dry toluene (100 ml) was added dropwise di-isobutylaluminium hydride (1.76M in hexane; 93.2 ml, 164 mmol) over 45 min at −78 °C under nitrogen. The mixture was stirred for 2.5 h at −78 °C, and then quenched with saturated aqueous ammonium chloride; it was then stirred for an additional 30 min. The precipitate was filtered off through a Celite pad and washed with ethyl acetate. The combined filtrate and washings were washed with brine, dried ($MgSO_4$), and then evaporated to leave a residue which was chromatographed on silica gel (300 g). Elution with chloroform–methanol (98:2, v/v) afforded the allyl alcohol (**7**) (8.55 g, 82.5%) as a syrup; $[\alpha]_D$ +26.7° (*c* 0.21 in $CHCl_3$); $\nu_{max.}$($CHCl_3$) 3 600—3 200 $cm^{-1}$; δ($CDCl_3$) 1.41 (6 H, s, $Me_2C$), 3.53 (2 H, t, *J* 8 Hz, $CH_2O$), 4.5 (1 H, ddd, *J* 8, 8, and 6 Hz, $CH_2CHO$), 5.6 (1 H, dd, *J* 15 and 6 Hz, C*H*=CH), and 5.8—6.22 (1 H, m, C*H*$CH_2OH$) (Found: C, 60.3; H, 9.2. $C_8H_{14}O_3$ requires C, 60.7; H, 8.9%).

The allyl alcohol (**21**) (21 mg, 99.3%), $[\alpha]_D$ −27.6° (*c* 0.29 in $CHCl_3$) was obtained from the (*E*)-olefinic methyl ester (**19**) (25 mg, 0.134 mmol) by the same procedure as that described above. Both i.r. and n.m.r. spectra of compound (**21**) were identical with those of (**7**).

(4S,2Z)-4,5-*Isopropylidenedioxypent*-2-*en*-1-*ol* (**8**) *and* (4R,2Z)-4,5-*Isopropylidenedioxypent*-2-*en*-1-*ol* (**22**).—To a stirred solution of the (*Z*)-olefinic methyl ester (**6**) (3.13 g, 16.8 mmol) in dry toluene (35 ml) was added dropwise di-isobutylaluminium hydride (1.76M in hexane; 33.5 ml, 59.0 mmol) over 40 min at −78 °C under nitrogen; the mixture was then stirred for 2.5 h at −78 °C. After work-up, the residue was chromatographed on silica gel (40 g). Elution with hexane–ethyl acetate (8:2, v/v) gave the allyl alcohol (**8**) (2.38 g, 89.9%) as a syrup; $[\alpha]_D$ +17.1° (*c* 0.34 in $CHCl_3$); $\nu_{max.}$($CHCl_3$) 3 600—3 200 $cm^{-1}$; δ($CDCl_3$) 1.41 (6 H, s, $Me_2C$), 3.47 (2 H, t, *J* 8 Hz), 4.77 (1 H, ddd, *J* 8, 8, and 6 Hz, $CH_2CHO$), 5.46 (1 H, dd, *J* 11 and 6 Hz, C*H*=CH), and 5.63—6.0 (1 H, m, CH=C*H*) (Found: C, 60.8; H, 9.2. $C_8H_{14}O_3$ requires C, 60.7; H, 8.9%).

The allyl alcohol (**22**) (48 mg, 94.1%), $[\alpha]_D$ −16.5° (*c* 0.22 in $CHCl_3$) was obtained from the (*Z*)-olefinic methyl ester (**20**) (60 mg, 0.323 mmol) by the same procedure as that described above. Both i.r. and n.m.r. spectra of (**22**) were identical with those of (**8**).

(2S,3S)-2-*Dimethyl*-t-*butylsilyloxymethyl*-3-*vinyl*-γ-*butyrolactone* (**14**).—A mixture of the γ-butyrolactone (**11**) (160 mg, 113 mmol), imidazole (153 mg, 226 mmol) and dimethyl-t-butylsilyl chloride (255 mg, 169 mmol) in dry dimethylformamide (4 ml) was stirred at room temperature for 3.5 h under nitrogen. Evaporation of the solvent left a residue which was extracted with ether. The extract was washed with brine, dried ($MgSO_4$), and evaporated to give a residue which was chromatographed on silica gel (10 g). Elution with hexane–ethyl acetate (8:2, v/v) gave the protected γ-butyrolactone (269.3 mg, 93.4%) as a syrup; $[\alpha]_D$ +40.5° (*c* 0.26 in $CHCl_3$); $\nu_{max.}$($CHCl_3$) 1 770 $cm^{-1}$; δ($CDCl_3$) 0.08 (6 H, s, $Me_2Si$), 0.86 (9 H, s, Bu$^t$), 2.13—2.73 (2 H, m, $CH_2CO$), 2.87—3.3 (1 H, m, C*H*CH=$CH_2$), 3.63—3.87 (2 H, m, $CH_2OSi$), 4.17 (1 H, ddd, *J* 11, 6, and 3 Hz, $CH_2CHO$), 5.11 (1 H, dd, *J* 8 and 2 Hz, CH=CH*H*), 5.13 (1 H, dd, *J* 16 and 2 Hz, CH=C*H*H), and 5.84 (1 H, ddd, *J* 16, 8, and 7 Hz, C*H*=$CH_2$) [Found: *m/z* 257.1568 ($M^+$ + 1). $C_{13}H_{25}O_3Si$ requires 257.1571 ($M^+$ + 1)].

(2R,3R)-*Dimethyl*-t-*butylsilyloxymethyl*-3-*vinyl*-γ-*butyrolactone* (**27**).—The protected γ-butyrolactone (13.9 mg, 85.7%), $[\alpha]_D$ − 42.0° (*c* 0.12 in $CHCl_3$) [Found: *m/z* 257.1583 ($M^+$ + 1). $C_{13}H_{25}O_3Si$ requires 257.1573 ($M^+$ + 1)], was obtained from the γ-butyrolactone (**25**) (9.0 mg, 0.0584 mmol) using the same procedure as that described above. Both i.r. and n.m.r. spectra were identical with those of (**14**).

(2S,3R/S)-2-*Dimethyl*-t-*butylsilyloxymethyl*-3-*ethylenedioxymethyl*-γ-*butyrolactone* (**17**).—To a stirred solution of the γ-butyrolactone (**14**) (127.8 mg, 0.499 mmol) in dioxane (3 ml) was added dropwise a solution of osmium tetraoxide (0.394M in dioxane; 1.27 ml, 0.499 mmol) and the mixture was stirred for 15 min in the dark at room temperature in order to allow the osmate ester to form. After dilution with water, a solution of sodium periodate (267 mg, 1.248 mmol) in water (1.83 ml) was added over 6 min and the mixture was stirred for an additional 20 min at room temperature. Solid was filtered off and the filtrate was extracted with ether. The extract was washed with brine, dried ($MgSO_4$), and then evaporated to give the practically pure aldehyde (**16**) (110 mg); $\nu_{max.}$($CHCl_3$) 1 770 and 1 730 $cm^{-1}$; δ($CDCl_3$) 9.67 (1 H, s, CHO). This compound was used in the next reaction without further purification.

A mixture of the crude aldehyde (110 mg, 0.426 mmol), ethylene glycol (112 mg, 1.81 mmol), and toluene-*p*-sulphonic acid (15 mg, 0.087 mmol) was refluxed for 2.5 h under nitrogen. The mixture was cooled to room temperature and diluted with ether. The organic layer was washed with saturated aqueous sodium hydrogen carbonate and brine, and dried ($MgSO_4$), and evaporated to leave a residue which was chromatographed on silica gel (5 g). Elution with hexane–ethyl acetate (9:1, v/v) afforded an inseparable 1:1 mixture of the 3*S*/*R*-acetals (**17**) (61 mg, 40.8%) as a syrup; $[\alpha]_D$ +9.64° (*c* 0.083 in $CHCl_3$); $\nu_{max.}$($CHCl_3$) 1 770 $cm^{-1}$; δ($CDCl_3$) 0.07 (6 H, s, $Me_2Si$), 0.90 (9 H, s, Bu$^t$), 2.33—2.87 (3 H, m, $CH_2CO$ and $CHCH<^{O}_{O}$)) 3.60—4.0 (2 H, m, $CH_2OSi$), 3.87 (4 H, br s, $OCH_2CH_2$), 4.33—4.60 (1 H, m, $CH_2CHOCO$), 4.80 (0.5 H, d, *J* 3 Hz, $CH<^{O}_{O}$), and 5.07 (0.5 H, d, *J* 6 Hz, $CH<^{O}_{O}$) [Found: *m/z* 303.1620 ($M^+$ + 1). $C_{14}H_{27}O_5Si$ requires 303.1626 ($M^+$ + 1)].

(2S,3R)-2-*Dimethyl*-t-*butylsilyloxymethyl*-3-*vinyl*-α-*methylene*-γ-*butyrolactone* (**15**).—To a stirred solution of the protected γ-butyrolactone (**14**) (200 mg, 0.78 mmol) in dry dimethoxyethane (0.5 ml) was added dropwise first a solution of lithium hexamethyldisilazane (1M in hexane; 743 μl, 0.743 mmol) and then a solution of ethyl formate (65.5 μl, 0.81 mmol) in dry dimethoxyethane (0.2 ml) at −78 °C; the mixture was then stirred for 19 h at room temperature under nitrogen. Solid paraformaldehyde (51 mg, 1.69 mmol) was added and the mixture was refluxed with stirring for 1 h. After cooling, the mixture was diluted with ether and the ethereal layer was washed with brine, dried ($MgSO_4$), and evaporated to leave a residue which was chromatographed on silica gel (10 g). Elution with hexane–ethyl acetate (95:5, v/v) gave the α-methylene-γ-butyrolactone (**15**) (93.8 mg, 44.8%) as a syrup; $[\alpha]_D$ +35° (*c* 0.2 in $CHCl_3$); $\nu_{max.}$($CHCl_3$) 1 760 $cm^{-1}$; δ($CDCl_3$) 0.07 (6 H, s, $Me_2Si$), 0.83 (9 H, s, Bu$^t$), 3.43—3.93 (3 H, m, $CH_2CO$ and C*H*CH=$CH_2$), 4.35 (1 H, ddd, *J* 9, 2, and 2 Hz, $CH_2CHO$), 4.93—5.33 (3 H, m, olefinic H), and 5.50—6.13 (2 H, m, olefinic H) [Found: *m/z* 269.1584 ($M^+$ + 1). $C_{14}H_{25}O_3Si$ requires 269.1574 ($M^+$ + 1)].

(2R,3S)-2-*Dimethyl-t-butylsilyloxymethyl*-3-*vinyl*-α-*methylene*-γ-*butyrolactone* (**28**).—α-Methylene-γ-butyrolactone (**28**) (6.1 mg, 44.8%) [Found: *m/z* 269.1579 ($M^+ + 1$). $C_{14}H_{25}O_3Si$ requires 269.1574 ($M^+ + 1$)] was obtained from the protected γ-butyrolactone (**27**) (13 mg) using the same procedure as that described above. Both i.r. and n.m.r. spectra were identical with those of compound (**15**).

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