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Synthesis of Optically Active α-Methylene γ-Butyrolactones and (+)-Mintlactone

Geoffrey T. Crisp* and Adam G. Meyer

Department of Chemistry, University of Adelaide, Adelaide, South Australia, Australia 5005

Abstract: The combination of baker's yeast reductions of β-keto carbonyls, vinyl triflate formation and a palladium-catalysed, intramolecular, carbonylative coupling affords optically active α-methylene γ-butyrolactones. The synthesis of the unnatural (+)-mintlactone using this methodology is also described.

INTRODUCTION

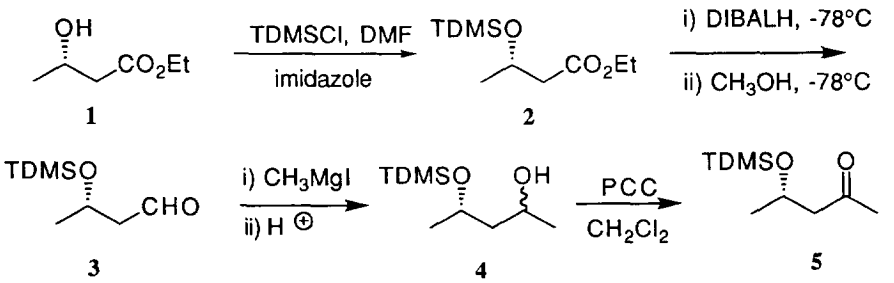
The butenolide substructure appears in many natural products and biologically active compounds such as flavour components and insect pheromones.[1] Many of the naturally occurring γ-butenolides are optically active and so methods for their synthesis must target the introduction of the chiral centre(s). In addition, optically active γ-butenolides are useful synthons for a wide variety of natural products syntheses.[1] There have been numerous routes to the construction of 5-membered lactone ring and several excellent review article are available.[2, 3a,b.]

Recently palladium-catalysed formation of γ-butyrolactones has received increasing attention because of the mild conditions under which the reactions can be performed and the ready availability of the starting materials. Some recent reports include the carbonylation of 3-buten-1-ols and 3-butyn-1-ols to γ-butyrolactones[4], substituted butenolides through hydroarylation/cyclization[5], the general use of palladium(II) catalysts for the formation of oxygen heterocycles[6], as well as the intramolecular carbonylation of halo alcohols[7] and of vinyl halides[8]. Our previous efforts in this area have involved the intramolecular palladium-catalysed carbonylative coupling of hydroxy vinyl triflates to afford substituted α,β-unsaturated butenolides.[9]

We now report on the synthesis of optically active γ-butyrolactones using a combination of baker's yeast reductions of β-keto esters to provide the chiral alcohol, trapping of a kinetic enolate by *N*-phenyltriflimide to provide a vinyl triflate and a palladium-catalysed carbonylation to assemble the γ-butyrolactone.

RESULTS AND DISCUSSION

Ethyl acetoacetate was reduced with baker's yeast to afford ethyl (3*S*)-(+)-3-hydroxybutenoate **1** with ≥95% ee.[10] The elaboration of this starting material is outlined in Scheme 1. The necessary protection of the alcohol function was achieved by reaction with thexyldimethylsilyl chloride to furnish ethyl (3*S*)-3-[(thexyldimethylsilyl)oxy]butanoate **2** in good yield (85%). Reduction of the ester directly to the corresponding aldehyde **3** was accomplished with DIBALH in 83%. The most appropriate means of introducing further functionality to the aldehyde is with organomagnesium reagents. Thus, aldehyde **3** was reacted with methylmagnesium iodide to give an approximate 1:1 mixture of diastereomeric alcohols, (4*S*)-4-[(thexyldimethylsilyl)oxy]pentan-2-ol **4**, in excellent yield (95%). Mild oxidation of **4** with pyridinium chlorochromate (PCC) gave the corresponding methyl ketone **5** in 80% yield.



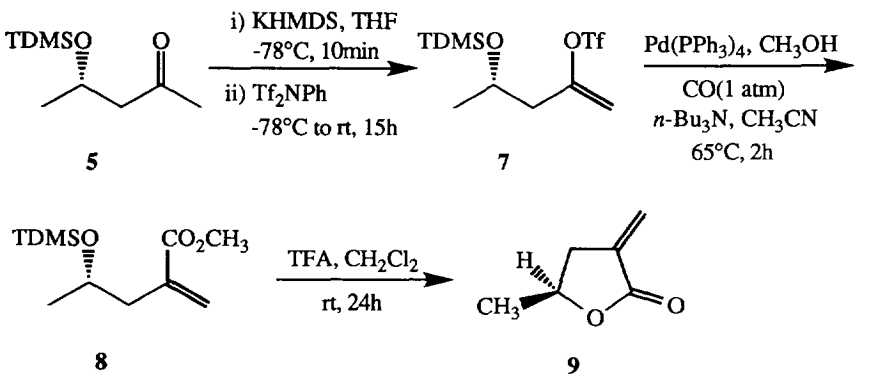
1 **2** **3** **4** **5**

TDMS = $Si(CH_3)_2C(CH_3)_2CH(CH_3)_2$

Scheme 1

Protected keto alcohol **5** was also prepared in low yield via baker's yeast reduction of acetylacetone[11] to afford (4*S*)-(+)-4-hydroxypentan-2-one **6** followed by protection with thexyldimethylsilyl chloride (as described above) to yield the desired methyl ketone **5**.

The ability to regioselectively prepare α-substituted vinyl triflates derived from methyl ketones through a kinetically generated enolate has been reported previously.[12] Thus, methyl ketone **5** was treated with KHMDS as the base to generated the kinetic enolate which was subsequently trapped by N-phenyltriflimide at low temperature (Scheme 2). As a consequence the corresponding (*S*)-vinyl triflate **7** was obtained as one regioisomer in excellent yield (97%). This vinyl triflate was then subjected to a one-carbon homologation *via* a palladium-catalysed carbomethoxylation reaction in the presence of excess methanol. Utilizing the standard conditions[9] of one atmosphere of carbon monoxide, base and methanol the corresponding acrylate, methyl (4*S*)-(+)-2-methylene-4-[(thexyldimethylsilyl)oxy]pentanoate **8**, was obtained in good yield (73%)(Scheme 2). Treatment of **8** with three equivalents of trifluoroacetic acid (TFA) for 24 hours gave the volatile α-methylene γ-butyrolactone, (5*S*)-(-)-dihydro-5-methyl-3-methylene-2(3*H*)-furanone, **9** in 46% isolated yield. The optimal lactonization conditions were predetermined from ^1H NMR experiments in deuterochloroform. Prior attempts at an *in situ* carbonylation by removing the silyl protecting group with tetrabutylammonium fluoride in the presence of palladium(0) were not successful. In all cases starting material was returned despite often long reaction times (>3days) and the application of both heat and sonication to the reaction mixtures.

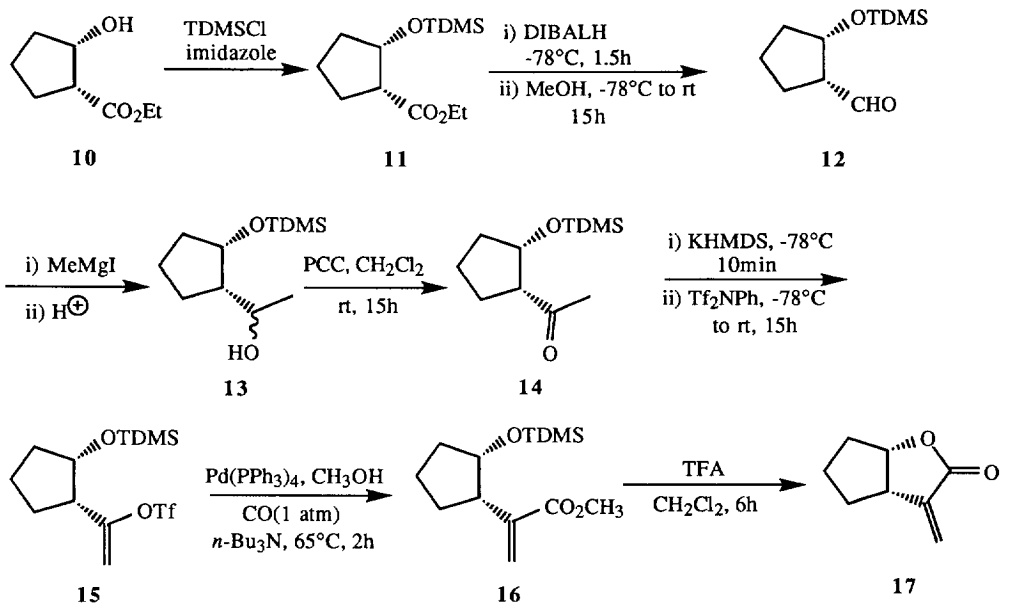


Scheme 2

The determination of enantiomeric composition and absolute configuration of chiral γ-lactones by ^1H NMR studies in the presence of the chiral solvating agents (*R*)-(-)-2,2,2-trifluoro-1-(9-anthryl)ethanol has been reported and is based on a solvation model proposed by Pirkle.[13] Thus, the ^1H NMR spectrum of racemic **9** in the presence of (*R*)-(-)-2,2,2-trifluoro-1-(9-anthryl)ethanol showed the methyl doublet split into a pair of partially resolved overlapping doublets whilst the ^1H NMR spectrum of (*S*)-**9** under the same conditions resulted only in the appearance of one doublet thus indicating the presence of predominantly one enantiomer. This doublet corresponds to the upfield portion of the pair of doublets in the spectrum of the racemate. Applying the model of Pirkle[13] to lactone (*S*)-**9** suggests that the *S*-configuration should be assigned to **9**. Furthermore, the fact that the *R*-enantiomer of **9** was prepared previously and a similar ^1H NMR experiment using (*R*)-(-)-2,2,2-trifluoro-1-(9-anthryl)ethanol showed the methyl doublet corresponded to the downfield portion of the pair of doublets in the racemate and that for (*R*)-**9** the specific rotation was $[\alpha]_D$ +33.8° (*c*=5.82, CH_2Cl_2)[8] confirms the stereochemical assignment for (*S*)-**9** which has a specific rotation of $[\alpha]_D$ -32.4° (*c*=5.8, CH_2Cl_2).

Having demonstrated a convenient synthetic pathway to optically active α-methylene γ-butyrolactones *via* vinyl triflate carbomethoxylation its expansion to bicyclic systems was investigated (Scheme 3). Again the starting point for this synthesis took advantage of the ready availability of chirally pure starting materials utilising the baker's yeast reduction of a cyclic β-keto ester. The ester chosen was ethyl 2-oxocyclopentanecarboxylate which, following a literature procedure[14], was reduced to ethyl (1*R*,2*S*)-(+)-2-hydroxycyclopentanecarboxylate **10** in moderate yield (65%). It is known that the *cis* and *trans* configuration of cyclohexane substituents may be determined by measurement of the widths at half height ($W_{0.5h}$) of the relevant ^1H NMR signals.[15] The ^1H NMR spectrum of **10** was consistent with the *cis* diastereomer. The absolute configuration may be assigned as written since the specific rotation of **10**, $[\alpha]_D$ +15.2° (*c*=1.57, $CHCl_3$), was virtually identical to that obtained previously $[\alpha]_D$ +15.1° (*c*=1.57, $CHCl_3$).[14]

Again protection of the hydroxyl moiety as the thexyldimethylsilyl ether **11** (73%) was followed by reduction of the ester group to the corresponding, unstable, aldehyde **12** in moderate yield (68%). Methylation with methylmagnesium iodide afforded alcohol **13** as an approximate 1:1.5 diastereomeric mixture (75%). Subsequent oxidation with PCC afforded the methyl ketone, (1*R*,2*S*)-(+)-2-[(thexyldimethylsilyl)oxy]-1-cyclopentane methyl ketone **14** also in good yield (77%).



TDMS = $Si(CH_3)_2C(CH_3)_2CH(CH_3)_2$

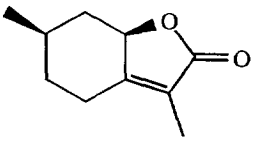
Scheme 3

Subsequent generation of the kinetic enolate, with KHMDS at low temperature, and trapping by N-phenyltriflimide afforded vinyl triflate **15** regiospecifically and in good yield (71%). Carbomethoxylation in the presence of one atmosphere of carbon monoxide, $Pd(PPh_3)_4$ (10 mol%), base and methanol gave the desired acylate **16** in 89%. This provided the necessary precursor to form the corresponding optically active carbocyclic ring fused α-methylene γ-butyrolactone. The protected cyclopentanol derivative thus underwent lactonization readily when treated with trifluoroacetic acid to form (3a*R*,6a*S*)-(-)-hexahydro-3-methylene-2*H*-cyclopenta[b]furan-2-one **17** in good yield (86%) (Scheme 3).

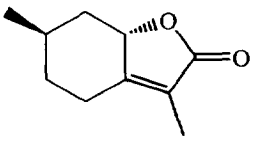
A *cis*-α-methylene lactone **17** has been synthesized previously *via* an intramolecular Hosomi reaction with varying degrees of enantiomeric excess (75-84%).[16] The enantiomeric excess was estimated from the intensity of the vinylic proton signals in the presence of the chiral shift reagent (+)-Eu(hfc)$_3$. A similar ^{1}H NMR experiment performed on lactone **17** revealed no such splitting, or indeed broadening, of the vinylic resonances [δ5.65 (*d*) and δ6.25 (*d*)]. It appears, therefore, that **17** has been produced as predominantly one enantiomer and the absolute stereochemistry confirmed by the specific rotation for **17** of $[\alpha]_D$ -161.3° (*c*=0.53, $CHCl_3$) whereas the literature value for the opposite enantiomer has a specific rotation of $[\alpha]_D$ +125.6° ($CHCl_3$)[16].

Synthesis of (+)-Mintlactone

The essential oil of *Mentha piperita* L. (peppermint oil) is of commercial importance worldwide as a flavouring agent and is produced in many countries. Amongst the minor trace components the menthane derivatives, (-)-mintlactone **18** and its C-3 epimer (+)-*iso*mintlactone **19**, were isolated from a sample of American peppermint oil.[17] These two compounds have also been used as synthetic intermediates in several synthetic procedures.[18]



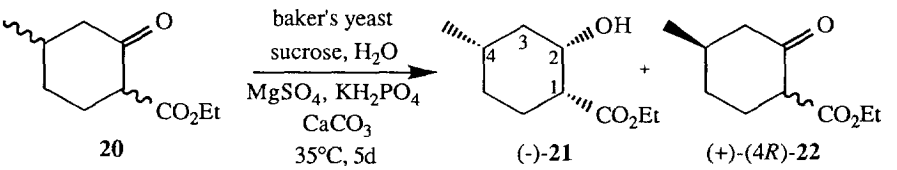
(-)-**18**



(+)-**19**

Initial synthetic methods toward the butenolide monoterpenes **18** and **19** yielded these compounds in racemic form.[18,19] Recently, however, both have been synthesized in their natural, optically pure form by various approaches.[20, 21, 22] It is of interest to note that (+)-mintlactone does not appear to have been synthetically generated or isolated from a natural source. This absence prompted investigation toward its total synthesis by utilizing the methodology described above.

A suitable starting point for the total synthesis of (+)-mintlactone was the fermenting baker's yeast reduction of the β-keto ester (±)-4-methyl-2-cyclohexanone-1-carboxylate **20**, a reaction which had been reported previously[23,24], and afforded β-hydroxy ester, ethyl (1*R*,2*S*,4*S*)-(-)-2-hydroxy-4-methyl-1-cyclohexanecarboxylate, (-)-**21** in 44% yield. Also recovered was unreacted ester (50%) that had been partially resolved to include an excess of (+)-(4*R*)-**22** (Scheme 4).

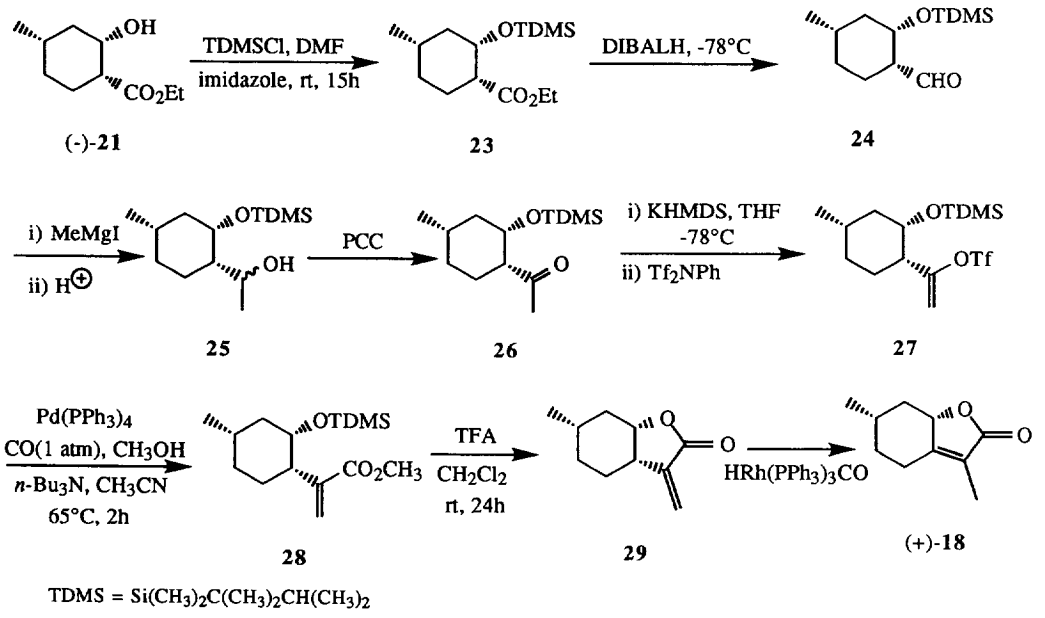


20 (-)-**21** (+)-(4*R*)-**22**

Scheme 4

The enantiomeric purity of **21** was determined by ^1H NMR analysis in the presence of (+)-Eu(hfc)$_3$. In the literature report the resolution of the ester methyl triplet was sufficient for the determination of ee.[23] A similar ^1H NMR experiment conducted on **21** realized no such defined splitting of the methyl triplet with only the diastereotopic ester methylene protons being resolved. Unfortunately the spectrum was insufficiently resolved to enable an accurate confirmation of the ee of (-)-**21**. However, the specific rotation of **21**, $[\alpha]_D$ -24.5° (*c*=0.52, $CHCl_3$), is somewhat higher than that reported previously[23], $[\alpha]_D$ -18.3° (*c*=1.0, $CHCl_3$). Moreover, the relative configuration at C-1 and C-2 of (-)-**21** may be deduced from the ^1H NMR spectrum since $J(1,2)\approx4$Hz and $J(2,3_{ax})\approx11$Hz which is indicative for the axial position of the ester and the equatorial position of the hydroxyl group. Also the signal widths at half height ($W_{0.5h}$) are consistent with these assignments [δ2.89 (*ddd*), $W_{0.5h}$11.83Hz, H_{eq}-C(1) and δ3.66 (*dt*, after D_2O exchange), $W_{0.5h}$20.29Hz, H_{ax}-C(2)].

Utilizing the analogous methodology presented in Scheme 3, β-hydroxy ester (-)-**21** was initially protected as the thexyldimethylsilyl ether to afford **23** (61%)(Scheme 5). Reduction to the corresponding aldehyde **24** was not clean and some ester remained which could not be separated from the desired aldehyde. Consequently, the aldehyde/ester mixture was methylated to form alcohols **25** (83% based on recovered ester) as a diastereomeric mixture with the recovery of unreacted ester during purification. Subsequent oxidation of the alcohol unit yielded methyl ketone **26** (74%) .



Scheme 5

Regioselective triflation produced vinyl triflate **27** in near quantitative yield (98%) and an ensuing palladium-mediated carbomethoxylation afforded acrylate **28** (57%). Quantitative lactonization to **29** was followed by a rhodium-catalyzed double bond isomerization to yield (+)-mintlactone **18**, possessing a pleasant sweet aroma (28% overall yield from **21**).

The spectral data for (+)-mintlactone was found to be identical in all repects to the data reported in the literature for (-)-mintlactone **18**.[21,22] The specific rotation, $[\alpha]_D$ +59.9° (*c*=0.75, EtOH), is in good agreement to that reported for the natural enantiomer, $[\alpha]_D$ -51.8° (*c*=10, EtOH)[17] and -56.6° (*c*=2.2, EtOH),[22] indicating that little loss of stereochemical integrity has occurred during the synthesis. The successful completion of this synthesis also constitutes confirmation of the enantiomeric purity and absolute configuration of the chiral β-hydroxy ester (-)-**21**.

EXPERIMENTAL

General: General experimental procedures and instrument details as described previously.[9]

Ethyl (3*S*)-(+)-3-[(thexyldimethylsilyl)oxy]butanoate (2)

To a solution of imidazole (11.3g, 166mmol) and alcohol **1** (10.0g, 76mmol) in DMF (40ml) was added thexyldimethylsilyl chloride (16.4ml, 83mmol) via a syringe and stirred at room temperature for 12h. The solvent was evaporated *in vacuo*, the residue diluted with water (40ml) and the yellow suspension extracted with ethyl acetate (2x80ml). The organic extracts were dried and the solvent evaporated at room temperature to give an oil which was distilled (80-81°C/0.01mm) to yield the title compound as a colourless oil (17.4g, 84%). ^{1}H NMR: δ0.07 (*s*, 6H, $SiCH_3$), 0.78 (s, 6H, $C(CH_3)_2$), 0.84 (*d*, *J*6.9Hz, 6H, $CH(C\underline{H}_3)_2$), 1.17 (*d*, *J*6.0Hz, 3H, $C\underline{H}_3CH$), 1.22 (*t*, *J*7.2, 3H, $OCH_2C\underline{H}_3$), 1.57 (*m*, 1H, $C\underline{H}(CH_3)_2$), 2.28-2.47 (*m*, 2H, CH_2CO), 4.1 (*q*, *J*7.2, 2H, $OC\underline{H}_2CH_3$), 4.27 (*m*, 1H, $CH_3C\underline{H}CH_2$); IR (neat):

ν_{max}2970 *s*, 1735 *s* (C=O), 1470 *m*, 1380 *s*, 1250 *s*, 1180 *m*, 1140 *s*, 1090 *s*, 1030 *s*, 1000 *m*, 875 *m*cm^{-1}; MS, m/z: 274 (M^+, 6%), 259 (50), 189 (100), 155 (72), 141 (33); HRMS calc. for $C_{14}H_{30}O_3Si$; 274.1964; Found: 274.1971; $[\alpha]_D$ +26.1° (*c*=0.5, CH_2Cl_2).

(*S*)-(+)-3-[(Thexyldimethylsilyl)oxy]butanal (3)

To a hexane (200ml) solution of ester **2** (5.5g, 22mmol) at -78°C was added DIBALH (4.4ml, 24mmol) dropwise *via* syringe over 90 min. The reaction was quenched with a slow addition of methanol (20ml) and allowed to warm to ambient temperature over 15h after which time saturated aqueous ammonium chloride (40ml) and CH_2Cl_2 (40ml) was added. The organic extracts were washed with 10% aqueous citric acid (2x100ml), brine (100ml) and dried. The solvent was evaporated under reduced pressure and the residue purified by flash chromatography (hexanes:ethyl acetate; 4:1) to yield the title product as a colourless oil (4.3g, 83%). ^{1}H NMR: δ0.10 (*s*, 6H, $SiCH_3$), 0.81 (*s*, 6H, $C(CH_3)_2$), 0.87 (*d*, *J*8.3Hz, 6H, $CH(C\underline{H}_3)_2$), 1.24 (*d*, *J*6.3Hz, 3H, CH_3), 1.61 (*m*, 1H, $C\underline{H}(CH_3)_2$), 2.44-2.58 (*m*, 2H, CH_2), 4.34 (*m*, 1H, $CH_3C\underline{H}OSi$), 9.8 (*t*, *J*2.75Hz, 1H, CHO); IR (neat): ν_{max}2950 *s*, 2720 *w* (H-CO), 1720 *s* (C=O), 1460 *m*, 1370 *m*, 1250 *s*, 1110 *m*, 1090 *m*, 1010 *s*, 810 m, 760 *s* cm^{-1}; MS, m/z: 230 (M^+, 2%), 217 (3), 189 (67), 161 (64), 145 (100); HRMS calc. for $C_{12}H_{26}O_2Si$ (M^+): 230.1702; Found: 230.1713; $[\alpha]_D$+8.06° (*c*=0.5, CH_2Cl_2).

(4*S*)-4-[(Thexyldimethylsilyl)oxy]pentan-2-ol (4)

To an ether (200ml) solution of aldehyde **3** (4.7g, 20mmol) at 0°C was added dropwise *via* syringe a solution of methylmagnesium iodide (2.4M in ether) (40mmol, 17ml) over 30min. The clear solution was then allowed to warm over 12h upon being quenched by aqueous 10% NH_4Cl (100ml) at 0°C. The two phases were partitioned and the aqueous layer was extracted with ether (3x100ml). The combined organic extracts were washed with brine (200ml), dried and the solvent evaporated under reduced pressure. The residue was purified by flash chromatography (hexanes:ethyl acetate; 4:1) to yield the title compound as a colourless oil (4.8g, 95%). A small sample was distilled by kugelrohr (75°C/0.005mm). ^{1}H NMR (1:1 mixture of diastereomers): δ0.10 and 0.13 (*s*, 6H, $Si(CH_3)_2$), 0.81 and 0.83 (*s*, 6H, $C(CH_3)_2$), 0.84 and 0.86 (*d*, *J*7.2Hz, 6H, $CH(C\underline{H}_3)_2$), 1.13 and 1.15 (*d*, *J*6.5Hz, 3H, $CHOHC\underline{H}_3$), 1.20 and 1.21 (*d*, *J*7.0Hz, 3H, $C\underline{H}_3COSi$), 1.48-1.63 (*m*, 1H, $C\underline{H}(CH_3)_2$), 2.20-2.29 (*m*, 2H, $C\underline{H}_2$), 3.42-4.18 (*m*, 2H, $CH_3C\underline{H}CH_2$ and $C\underline{H}OH$); IR (neat): ν_{max}3400 *m* (O-H), 2960 *s*, 1470 *m*, 1380 *m*, 1250 *s*, 1120 *m*, 1060 *s*, 830 *s*, 720 *m* cm^{-1}; MS, m/z: 247 ($[M+1]^+$, 100%), 229 (16), 187 (10), 161 (11); Anal. calc. for $C_{13}H_{30}O_2Si$: C, 63.35%; H, 12.27%; Found: C, 63.16%; H, 12.47%.

(4*S*)-(+)-4-[(Thexyldimethylsilyl)oxy]pentan-2-one (5)

To a solution of PCC (0.40g, 2.05mmol) in dichloromethane (30ml) was added a dichloromethane (15ml) solution of **4** (0.25g, 1.02mmol) dropwise *via* syringe. The solution was then stirred at room temperature for 15h upon which it was filtered through a bed of kenite with extensive washing of the residues with dichloromethane. The organic extracts were washed with 5% aqueous $NaHCO_3$ (40ml), dried and the solvent removed under reduced pressure. The brown-black residue was purified by flash chromatography (hexanes:ethyl acetate; 19:1) to yield the title compound as a colourless oil (0.2g, 80%). A small sample was distilled by kugelrohr (75-80°C/0.05mm). ^{1}H NMR: δ0.07 (*s*, 3H, $SiCH_3$), 0.10 (*s*, 3H, $SiCH_3$), 0.81 (s, 6H, $C(CH_3)_2$), 0.87 (*d*, *J*6.84Hz, 6H, $CH(C\underline{H}_3)_2$), 1.16 (*d*, *J*6.24Hz, 3H, $C\underline{H}_3CH$), 1.60 (*m*, 1H, $C\underline{H}(CH_3)_2$), 2.16 (*s*, 3H, CH_3CO), 2.42 [*dd*, *J*5.37, 5.37Hz, 1H, H-C(3)], 2.64 (*dd*, *J*6.99, 6.99Hz, 1H, H-C(3)], 4.27 (*sextet*, *J*5.58Hz, 1H, CHOSi); ^{13}C NMR: δ-3.1, -2.5, 18.4, 18.5, 20.1, 20.2, 23.9, 24.6, 31.5, 34.0, 53.1, 65.4, 208.0; IR (neat): ν_{max}2960 *s*, 1720 *s* (C=O), 1470 *m*, 1380 *s*,

1250 *s*, 1180 *m*, 1130 *s*, 1090 *s*, 1020 *s*, 900 *m*, 875 *m*, 830 *s*, 775 *s* cm^{-1}; MS, m/z: 245 ($[M+1]^+$, 10%), 229 ($[M-CH_3]^+$, 13), 201 ($[M-CH_3CO]^+$, 3), 187 (14), 160 (47), 159 (100), 145 (16), 115 (94), 103 (37); HRMS calc. for $C_7H_{15}O_2Si$ ($[M-C_6H_{13}]^+$); 159.08413; Found: 159.0840; $[\alpha]_D$ +22.35° (*c*=0.5, CH_2Cl_2).

(4*S*)-(+)-4-Hydroxypentan-2-one (6)[11]

A suspension of baker's yeast (200g, Mauripan dried) and sugar (30g) in deionized H_2O (4l) was mechanically stirred at 35°C for 30min. Acetylacetone (5.0g, 49.9mmol) was then added and the mixture allowed to stir at 35°C for 24h. Analysis by GLC and TLC prompted the further addition of yeast (10g) and sugar (50g) after 3,4 and 5 days. After 6 days GLC analysis indicated that the reaction had gone to completion and the mixture was filtered by gravity through a sintered glass funnel. The solution was saturated with $(NH_4)_2SO_4$ and extracted with ether (4x500ml) with methanol being used to break up an emulsion. The extracts were then washed with brine (1l) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue purified by kugelrohr distillation (*ca.* 100°C/20mm, lit.[11] 75-76°C/21mm) and flash chromatography (hexanes:ethyl acetate; 7:3) to yield the title compound as a colourless liquid (1.01g, 20%). ^1H NMR: δ1.19 (*d*, *J*6.33Hz, 3H, $C\underline{H}_3CH$), 2.18 (*s*, 1H, CH_3CO), 2.55 [*dd*, *J*8.49, 8.62Hz, 1H, H-C(3)], 2.65 [*dd*, *J*3.38, 3.37Hz, 1H, H-C(3)], 4.23 (*m*, 1H, $C\underline{H}OH$); ^{13}C NMR: δ22.1, 30.3, 51.3, 63.6, 209.6; IR (neat): ν_{max}3450 *s* (O-H), 2960 *s*, 1710 *s* (C=O), 1455 *s*, 1380 *m*, 1250 *m*, 1110 *s*, 1030 *s*, 920 *m*, 735 *s* cm^{-1}; MS, m/z: 103 ($[M+1]^+$, 23%), 102 (M^+, 5), 87 ($[M-CH_3]^+$, 8), 59 ($[M-CH_3CO]^+$, 100), 58 (65), 45 (50); $[\alpha]_D$ +78.5° (*c*=2.0, $CHCl_3$), $[\alpha]_J$ +90° (*c*=0.04, $CHCl_3$), lit.[11] $[\alpha]_D$ +64° (*c*=2.0, $CHCl_3$) and $[\alpha]_J$ +40° (*c*=0.04, $CHCl_3$).

(4*S*)-(+)-2-[(Trifluoromethanesulfonyl)oxy]-4-[(thexyldimethylsilyl)oxy]pent-1-ene (7)

A solution of ketone **5** (0.3g, 1.23mmol) in THF (5ml) was added dropwise *via* syringe to a solution of KHMDS (0.5M in toluene) (2.95ml, 1.48mmol) that had been precooled to -78°C. The mixture was allowed to stir for 10 minutes upon which a solution of N-phenyltriflimide (0.53g, 1.48mmol) in THF (5ml) was added dropwise and the solution allowed to warm to room temperature over 15h. The solvent was evaporated under reduced pressure and the residue dissolved in dichloromethane (20ml), washed with water (20ml) and the solvent evaporated under reduced pressure. The yellow residue was purified by flash chromatography (hexanes) to yield the title compound as a colourless oil (0.45g, 97%). ^1H NMR: δ0.07 (*s*, 3H, $SiCH_3$), 0.10 (*s*, 3H, $SiCH_3$), 0.82 (*s*, 6H, $C(CH_3)_2$), 0.83 (*d*, *J*3.99Hz, 6H, $CH(C\underline{H}_3)_2$), 1.19 (*d*, *J*5.97Hz, 3H, $C\underline{H}_3CH$), 1.59 (*m*, 1H, $C\underline{H}(CH_3)_2$), 2.40 [*dd*, *J*5.61, 5.62Hz, 1H, H-C(3)], 2.47 [*dd*, *J*6.96, 6.96Hz, 1H, H-C(3)], 4.05 (*sextet*, *J*5.93Hz, 1H, CHOSi), 4.99 (*d*, J_{gem}3.36Hz, 1H, vinylic), 5.13 (*d*, J_{gem}3.33Hz, 1H, vinylic); ^{13}C NMR: δ-2.5, -3.0, 18.4, 18.5, 20.1, 20.2, 23.4, 24.8, 34.1, 44.5, 65.1, 106.6, 118.6 (*q*, J_{CF}319.8Hz), 154.3; IR (neat): ν_{max}2950 *s*, 1675 *m* (C=C), 1470 *m*, 1425 *s* (asymS=O), 1380 *m*, 1255 *s* (asymC-OSO_2), 1210 *s* (C-F), 1140 *s* (symS=O), 1100 *m* (S-O), 1000 *m*, 950 *m*, 910 *m*, 830 *m*, 780 *m*, 705 *m* cm^{-1}; MS, m/z: 377 ($[M+1]^+$, 36%), 361 ($[M-CH_3]^+$, 4), 291 ($[M-C_6H_{13}]^+$, 54), 251 (65), 227 ($[M-OTf]^+$, 42), 207 (17), 187 (100); HRMS calc. for $C_{14}H_{27}F_3O_4SSi$: 376.1353; Found: 376.1371; Anal. calc. for $C_{14}H_{27}F_3O_4SSi$: C, 44.66%; H, 7.23%; Found: C, 44.83%; H, 7.11%; $[\alpha]_D$ 0° (*c*=0.5, CH_2Cl_2).

Methyl (4*S*)-(+)-2-methylene-4-[(thexyldimethylsilyl)oxy]pentanoate (8)

To an acetonitrile (50ml) solution that had been saturated with carbon monoxide for 20 minutes was added vinyl triflate **7** (0.49g, 1.30mmol), $Pd(PPh_3)_4$ (0.15g, 0.13mmol), *n*-Bu_3N (0.62ml, 2.60mmol), methanol (5.27ml, 130mmol) and lithium chloride (0.06g, 1.30mmol). The reaction was then heated at

65°C for 2h. Upon cooling to ambient temperature, ether (50ml) was added and the solution filtered through a bed of kenite with extensive ether washing of the residues. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (hexanes:ethyl acetate; 49:1) to yield the title compound as a colourless oil (0.33g, 90%). ^{1}H NMR: δ0.01 (*s*, 3H, $SiCH_3$), 0.06 (*s*, 3H, $SiCH_3$), 0.81 (*s*, 6H, $C(CH_3)_2$), 0.86 (*d*, *J*6.85Hz, 6H, $CH(CH_3)_2$), 1.25 (*d*, *J*4.81Hz, 3H, $C\underline{H}_3CH$), 1.61 (*m*, 1H, $C\underline{H}(CH_3)_2$), 2.40 (*d*, *J*6.33Hz, 2H, $CHC\underline{H}_2$), 3.75 (*s*, 3H, OCH_3), 3.98 (*sext*, 1H, CHOSi), 5.59 (*d*, J_{gem}1.26Hz, 1H, vinylic), 6.20 (*d*, J_{gem}1.75Hz, 1H, vinylic); ^{13}C NMR: δ-2.5, -3.1, 18.5, 18.6, 20.2, 20.3, 23.6, 24.7, 34.0, 42.7, 51.7, 67.0, 127.9, 137.5, 167.6; IR (neat): ν_{max}2950 *s*, 1720 *s* (C=O), 1630 *m* (C=C), 1440 *m*, 1380 *m*, 1330 *m*, 1280 *s*, 1250 *m*, 1195 *s*, 1160 *s*, 1095 *s*, 1005 *s*, 950 *m*, 890 *m*, 830 *s*, 775 *s*, 680 *m* cm^{-1}; MS, m/z: 271 ([M-CH_3]$^+$, 2%), 255 ([M-OCH_3]$^+$, 5), 201 ([M-C_6H_{13}]$^+$, 100), 169 (75), 157 (29), 127 ([M-$OSiC_8H_{19}$]$^+$, 7), 103 (64); HRMS calc. for $C_{15}H_{30}O_3Si$ ([M-OCH_3]$^+$): 255.17803; Found: 255.17885; $[\alpha]_D$ +10.96° (*c*=0.52, $CHCl_3$).

(5*S*)-(-)-Dihydro-5-methyl-3-methylene-2(5*H*)-furanone (9)

To a solution of ester **8** (0.33g, 1.15mmol) in dichloromethane (20ml) was added trifluoroacetic acid (0.27ml, 3.46mmol) dropwise *via* syringe. The solution was stirred at room temperature for 24h upon which it was washed with 5% aqueous $NaHCO_3$, dried and the solvent removed by a stream of nitrogen over the solution. The residue was purified by kugelrohr distillation (100-105°C/15mm) to yield the title compound as a colourless oil (0.06g, 46%). ^{1}H NMR: δ1.43 (*d*, *J*6.17Hz, 3H, CH_3), 4.69 (*sextet*, *J*6.20Hz, 1H, $C\underline{H}CH_3$), 2.55 [*d of m*, J_d17.02Hz, 1H, H-C(4)], 3.10 [*d of m*, J_d17.0Hz, 1H, H-C(4)], 5.64 (*t*, *J*2.47Hz, 1H, vinylic), 6.24 (*t*, *J*2.82Hz, 1H, vinylic); ^{13}C NMR: δ22.0, 35.1, 74.0, 122.1, 134.8, 144.9; IR (neat): ν_{max}2980 *s*, 1760 *br s* (C=O), 1665 *s* (C=C), 1440 *m*, 1390 *s*, 1340 *s*, 1260 *s*, 1205 *m*, 1165 *s*, 1085 *s*, 1040 *s*, 955 *m*, 870 *m*, 815 *m*, 755 *m* cm^{-1}; MS, m/z: 112 (M$^+$, 7%), 73 (65), 67 ([M-HCO_2]$^+$, 77), 43 (CH_3CO^+, 100); $[\alpha]_D$ -32.8° (*c*=5.8, CH_2Cl_2), lit.[8] for (+)-**9** $[\alpha]_D$ +33.8 (*c*=5.82, $CHCl_3$).

Ethyl (1*R*,2*S*)-(+)-2-hydroxy-1-cyclopentanecarboxylate (10)[14]

A suspension of baker's yeast (Mauripan dried, 12.0g), sugar (152.0g), $MgSO_4$ (1.0g), KH_2PO_4 (4.0g) and $CaCO_3$ (5.0g) in deionized water (1l) was stirred gently at 36°C for 45 min. Ethyl 2-oxocyclopentane carboxylate (10.2g, 65.3mmol) was added dropwise and the mechanically stirred solution was kept at 36°C for 2 days. At this point GLC analysis indicated the absence of starting material. The mixture was filtered through a sintered glass funnel by gravity and the solution extracted with ether (5x250ml), washed with brine (500ml) and dried with $MgSO_4$. Evaporation of the solvent under reduced pressure gave a yellow oil that was purified by fractional distillation (46-47°C/0.04mm, lit.[14] 59-61°C/0.4mm) to yield the title product as a colourless liquid (6.72g, 65%). ^{1}H NMR: δ1.29 (*t*, *J*7.18Hz, 3H, CH_3), 1.64 (*m*, 1H, cyclopentane CH), 1.78 (*m*, 2H, cyclopentane CH), 1.96 (*m*, 3H, cyclopentane CH), 2.68 [*ddd*, *J*4.32, 4.26, 4.34Hz, 1H, H-C(1)], 3.16 (*br s*, 1H, OH), 4.19 (*q*, *J*7.21Hz, 2H, $C\underline{H}_2CH_3$), 4.44 [*ddd*, *J*3.70, 3.55, 3.61Hz, 1H, H-C(2)]; ^{13}C NMR: δ14.0, 21.8, 26.0, 33.8, 49.4, 60.4, 73.6, 174.6; IR (neat): ν_{max}3480 *s* (O-H), 2970 *s*, 1735 *s* (C=O), 1450 *m*, 1375 *m*, 1350 *m*, 1305 *m*, 1195 *s*, 1100 *m*, 1035 *s*, 860 *w*, 735 *w* cm^{-1}; MS, m/z: 129 ([M-C_2H_5]$^+$, 27%), 112 ([M-C_2H_5OH]$^+$, 18), 100 (100), 72 (88); $[\alpha]_D$ +15.2° (*c*=1.57, $CHCl_3$), lit.[14] $[\alpha]_D$ +15.1° (*c*=1.57, $CHCl_3$).

Ethyl (1*R*,2*S*)-(+)-2-[(thexyldimethylsilyl)oxy]-1-cyclopentanecarboxylate (11)

To a DMF (45ml) solution of thexyldimethylsilyl chloride (10.38mmol, 2.04ml) and imidazole (20.76mmol, 1.41g) was added alcohol **10** (1.5g, 9.43mmol). The mixture was allowed to stir at ambient

temperature for 15h upon which it was extracted with hexane (3x50ml). The organic extracts were washed with H_2O (2x150ml), dried and the solvent evaporated under reduced pressure to give a colourless liquid. Purification by flash chromatography (hexanes: ethyl acetate; 19:1) yielded the title compound as a colourless liquid (2.08g, 73%). A small sample was distilled by kugelrohr (90-100°C/0.03mm). ^1H NMR: δ0.05 (*s*, 3H, $SiCH_3$), 0.08 (*s*, 3H, $SiCH_3$), 0.79 (*s*, 6H, $C(CH_3)_2$), 0.84 (*d*, *J*6.85Hz, 6H, $CH(C\underline{H}_3)_2$), 1.26 (*t*, *J*7.21Hz, 3H, $CH_2C\underline{H}_3$), 1.57 (*m*, 1H, cyclopentane CH), 1.61 (m, 1H, $C\underline{H}(CH_3)_2$), 1.67-1.82 (*m*, 3H, cyclopentane CH), 1.89 (*m*, 1H, cyclopentane CH), 2.16 (*ddtt*, *J*14.65, 7.07, 5.78, 6.80Hz, 1H, cyclopentane CH), 2.71 [*ddd*, *J*4.95, 4.89, 5.00Hz, 1H, H-C(1)], 4.01 (*dq*, *J*7.23, 7.14Hz, 1H, diastereotopic $C\underline{H}_2CH_3$), 4.19 (*dq*, *J*7.24, 7.09Hz, 1H, diastereotopic $C\underline{H}_2CH_3$), 4.47 [*ddd*, *J*3.65, 4.55, 3.60Hz, 1H, H-C(2)]; ^{13}C NMR: δ-3.3, -2.6, 14.1, 18.4, 18.5, 19.9, 20.0, 20.1, 20.5, 21.8, 34.1, 35.2, 51.4, 60.1, 75.4, 172.6; IR (neat): ν_{max}2950 *s*, 1740 *s* (C=O), 1470 *m*, 1370 *m*, 1250 *s*, 1180 *s*, 1110 *m*, 1060 *s*, 930 *m*, 830 *s*, 775 *s* cm^{-1}; MS, m/z: 280 ($[M-H_2O]^+$, 2%), 215 ($[M-C_6H_{13}]^+$, 4), 187 (9), 133 (6), 103 (12), 75 (35), 31 (100); HRMS calc. for $C_{10}H_{19}O_3Si$ ($[M-C_6H_{13}]^+$): 215.11035; Found: 215.11096; $[\alpha]_D$ +21.6° (*c*=0.5, $CHCl_3$).

(1*R*,2*S*)-(+)-2-[(Thexyldimethylsilyl)oxy]-1-cyclopentanecarbaldehyde (12)

To a hexane (60ml) solution of ester **11** (1.54g, 5.12mmol) at -78°C was added DIBALH (1.0ml, 5.64mmol) dropwise *via* syringe over 5 min. The mix was kept at -78°C for 2h upon which TLC analysis prompted further addition of DIBALH (0.18ml, 1.02mmol) with additional stirring for 1h. The reaction was quenched with a slow addition of methanol (8ml) and allowed to warm to ambient temperature over 15h. The organic extracts were washed with 10% aqueous citric acid (2x100ml), brine (100ml) and dried. The solvent was evaporated under reduced pressure and the residue purified by flash chromatography (hexanes:ethyl acetate; 9:1) to yield the title product as an unstable colourless oil (0.89g, 68%). ^1H NMR: δ0.08 (*s*, 3H, $SiCH_3$), 0.10 (*s*, 3H, $SiCH_3$), 0.80 (*s*, 6H, $C(CH_3)_2$), 0.86 (*d*, *J*6.86Hz, 6H, $CH(CH_3)_2$), 1.61 (*m*, 1H, $C\underline{H}(CH_3)_2$), 1.53-1.80 (*m*, 4H, cyclopentane CH), 1.88 (*m*, 1H, cyclopentane CH), 2.16 (*ddtt*, *J*13.84, 4.59, 4.59, 6.95Hz, 1H, cyclopentane CH), 2.65 [*ddt*, *J*5.65, 2.88, 8.36Hz, 1H, H-C(1)], 4.62 [*ddd*, *J*4.82, 3.89, 3.51Hz, 1H, H-C(2)], 9.75 (*d*, *J*2.75Hz, 1H, CHO); ^{13}C NMR: δ-3.0, -2.5, 18.3, 18.4, 20.0, 20.2, 22.3, 23.1, 24.7, 34.1, 35.9, 56.9, 75.7, 204.0; IR (neat): ν_{max}2955 *s*, 2720 *w* (H-CO), 1725 *s* (C=O), 1470 *m*, 1380 *m*, 1250 *s*, 1160 *m*, 1115 *m*, 1050 *s*, 940 m, 830 *s*, 780 *s* cm^{-1}; MS, m/z: 257 ($[M+1]^+$, 2%), 205 (12), 187 (8), 171 ($[M-C_6H_{13}]^+$, 100), 75 (47); HRMS calc. for $C_{14}H_{29}O_2Si$ ($[M+1]^+$): 257.19369; Found: 257.19466; $[\alpha]_D$+15.8° (*c*=0.5, $CHCl_3$).

(1*S*,2*S*)-(+)-2-[(Thexyldimethylsilyl)oxy]cyclopentan-1-yl methanol (13)

To an ether (35ml) solution of aldehyde **12** (0.89g, 3.47mmol) at 0°C was added dropwise *via* syringe a solution of methylmagnesium iodide (2.2M in ether) (6.94mmol, 3.15ml) over 5min. The clear solution was then allowed to warm over 15h upon being quenched by aqueous 10% NH_4Cl (10ml) at 0°C. The two phases were partitioned and the aqueous layer was extracted with ether (3x30ml). The combined organic extracts were washed with brine (100ml), dried and the solvent evaporated under reduced pressure. The residue was purified by flash chromatography (hexanes:ethyl acetate; 19:1) to yield the title compound as a colourless oil (0.71g, 75%). A small sample was distilled by kugelrohr (100-110°C/0.02mm). ^1H NMR: δ0.14 (*s*, 6H, $Si(CH_3)_2$), 0.84 (*d*, *J*3.97Hz, 6H, $C(CH_3)_2$), 0.87 (*d*, *J*3.95Hz, 3H, $CHC\underline{H}_3$), 0.89 (*d*, *J*3.98Hz, 3H, $CHC\underline{H}_3$), 1.15 and 1.19 (*d*, *J*6.45 and 6.32Hz, 3H, $CHC\underline{H}_3$), 1.48-1.80 (*m*, 6H, $C\underline{H}(CH_3)_2$ and cyclopentane CH), 1.94 (*m*, 1H, cyclopentane CH), 3.38 (*br s*, 1H, OH), 3.87 and 4.14 (2x*dq*, *J*7.88, 6.41Hz and 12.58, 6.42Hz, 1H, $C\underline{H}OH$), 4.31 and 4.37 [2x*ddd*, *J*2.64, 2.61, 2.80 and

4.46, 4.58, 4.12Hz, 1H, H-C(2)]; ^{13}C NMR: δ-3.1, -2.3, 18.3, 18.7, 19.9, 20.5, 21.6, 21.8, 22.0, 22.4, 34.1, 36.3, 50.1, 67.1, 77.7; IR (neat): ν_{max}3455 *m* (O-H), 2960 *s*, 1470 *m*, 1370 *m*, 1255 *s*, 1140 *m*, 1045 *s*, 910 *m*, 830 *s*, 775 *s*, 740 *m* cm^{-1}; MS, m/z: 187 ([M-C_6H_{13}]$^+$, 27%), 95 (58), 74 (92), 31 (100); HRMS calc. for $C_{11}H_{19}O_2Si$ ([M-C_6H_{13}]$^+$): 187.11544; Found: 187.11472; Anal. calc. for $C_{15}H_{32}O_2Si$: C, 66.11%; H, 11.84%; Found: C, 65.98%; H, 11.54%.

(1*R*,2*S*)-(+)-2-[(Thexyldimethylsilyl)oxy]-1-cyclopentyl methyl ketone (14)

This compound was prepared from alcohols **13** (0.68g, 2.50mmol) in an analogous manner to that described for **5**. Flash chromatography (hexanes:ethyl acetate; 19:1) gave the title compound as a colourless oil (0.52g, 77%). A small portion was distilled by kugelrohr (120-130°C/0.04mm). ^{1}H NMR: δ0.08 (*s*, 3H, $SiCH_3$), 0.10 (*s*, 3H, $SiCH_3$), 0.78 (*s*, 6H, $C(CH_3)_2$), 1.52-1.75 (*m*, 5H, C<u>H</u>$(CH_3)_2$ and cyclopentane CH), 1.84 (*m*, 1H, cyclopentane CH), 2.17 (*m*, 1H, cyclopentane CH), 2.17 (*s*, 3H, CH_3CO), 2.78 [*ddd*, *J*5.14, 5.29, 5.36Hz, 1H, H-C(1)], 4.58 [*ddd*, *J*4.19, 3.35, 4.54Hz, 1H, H-C(2)]; ^{13}C NMR: δ-3.2, -2.3, 18.3, 18.5, 19.9, 20.2, 22.0, 23.8, 24.7, 30.1, 34.0, 35.5, 58.8, 75.9, 208.1; IR (neat): ν_{max}2950 *s*, 1715 *s* (C=O), 1470 *m*, 1380 *m*, 1250 *s*, 1155 *m*, 1110 *m*, 1060 *s*, 875 *m*, 835 *s*, 775 *s* cm^{-1}; MS, m/z: 185 ([M-C_6H_{13}]$^+$, 37%), 141 (12), 115 (4), 106 (4), 91 (9), 75 (22), 58 ([CH_2=C(OH)CH_3]$^+$, 15), 43 (CH_3CO^+, 100); HRMS calc. for $C_9H_{17}O_2Si$ ([M-C_6H_{13}]$^+$): 185.09979; Found: 185.10045; Anal. calc. for $C_{15}H_{30}O_2Si$: C, 66.61%; H, 11.18%; Found: C, 66.72%; H, 11.18%; $[\alpha]_D$ +14.3° (*c*=0.51, $CHCl_3$).

(1*R*,2*S*)-(+)-2-[(Thexyldimethylsilyl)oxy]-1-{1-methylene-1-[(trifluoromethanesulfonyl) oxy]}cyclopentane (15)

This compound was prepared from methyl ketone **14** (0.42g, 1.55mmol) in an analogous manner to that described for **7**. Flash chromatography (hexanes) gave the title compound as a colourless oil (0.36g, 71%). A small portion was distilled by kugelrohr (110-120°C/0.03mm). ^{1}H NMR: δ0.06 (*s*, 3H, $SiCH_3$), 0.08 (*s*, 3H, $SiCH_3$), 0.79 (*s*, 6H, $C(CH_3)_2$), 0.85 (*d*, *J*5.99Hz, 6H, $CH(C\underline{H}_3)_2$), 1.53-1.93 (*m*, 7H, C<u>H</u>$(CH_3)_2$ and cyclopentane CH), 2.59 [*br dt*, *J*3.62, 7.62Hz, 1H, H-C(1)], 4.35 [*ddd*, *J*2.45, 1.16, 3.89Hz, 1H, H-C(2)], 4.99 (*dd*, *J*1.49, 1.48Hz, 1H, vinylic), 5.16 (*d*, J_{gem}3.55Hz, 1H, vinylic); ^{13}C NMR: δ-3.5, -2.6, 18.5, 18.6, 20.1, 20.3, 21.5, 24.8, 26.3, 34.2, 34.9, 50.9, 73.4, 105.3, 118.5 (*q*, J_{CF}320.0Hz), 156.8; IR (neat): ν_{max}2955 *s*, 1670 *m* (C=C), 1420 *s* (asymS=O), 1250 *s* (asymC-OSO_2), 1210 *s* (C-F), 1140 *s* (symS=O), 1100 *m*, 1060 *m* (S-O), 925 *s*, 830 *m*, 780 *m*, 735 *s* cm^{-1}; MS, m/z: 317 ([M-C_6H_{13}]$^+$, 14%), 227 (9), 167 (24), 103 (100); HRMS calc. for $C_{10}H_{16}F_3O_4SSi$ ([M-C_6H_{13}]$^+$): 317.04907; Found: 317.04992; Anal. calc. for $C_{16}H_{29}F_3O_4SSi$: C, 47.74%; H, 7.26%; Found: C, 47.76%; H, 7.29%; $[\alpha]_D$ +10.0° (*c*=0.5, $CHCl_3$).

Methyl (1*R*,2*S*)-(+)-2-[2-(thexyldimethylsilyl)oxycyclopent-1-yl]propenoate (16)

This compound was prepared from vinyl triflate **15** (0.27g, 0.67mmol) in an analogous manner to that described for **8**. Flash chromatography (hexanes:ethyl acetate; 99:1) gave the title compound as a pale yellow viscous oil (0.22g, 89%). A small sample was distilled by kugelrohr (130-140°C/0.01mm) to give a colourless oil. ^{1}H NMR: δ0.06 (*s*, 3H, $SiCH_3$), 0.08 (*s*, 3H, $SiCH_3$), 0.79 (*s*, 6H, $C(CH_3)_2$), 0.85 (*d*, *J*6.77Hz, 6H, $CH(C\underline{H}_3)_2$), 1.46-1.67 (*m*, 4H, C<u>H</u>$(CH_3)_2$ and cyclopentane CH), 1.74-1.93 (*m*, 3H, cyclopentane CH), 2.75 [*br m*, 1H, H-C(1)], 3.73 (*s*, 3H, OCH_3), 4.32 [*m*, 1H, H-C(2)], 5.58 (*t*, *J*1.31Hz, 1H, vinylic), 6.26 (*s*, 1H, vinylic); ^{13}C NMR: δ-3.3, -2.8, 18.5, 18.6, 20.2, 20.4, 21.5, 24.7, 26.5, 34.3, 35.4, 47.5, 51.6, 74.1, 125.5, 139.2, 168.0; IR (neat): ν_{max}2950 *s*, 1720 *s* (C=O), 1630 *m* (C=C), 1440 *m*, 1380 *m*, 1250 *s*, 1150 *s*, 1055 *s*, 985 *m*, 930 *s*, 815 *s*, 775 *s*, 735 *m* cm^{-1}; MS,

m/z: 297 ([M-CH_3]$^+$, 1%), 281 (4), 227 ([M-C_6H_{13}]$^+$, 100), 195 (82), 185 (70); HRMS calc. for $C_{16}H_{29}O_3Si$ ([M-CH_3]$^+$): 297.18732; Found: 297.18937; Anal. calc. for $C_{17}H_{32}O_3Si$: C, 65.33%; H, 10.32%; Found: C, 64.98%; H, 10.19%; $[\alpha]_D$ +40.4° (*c*=0.52, $CHCl_3$).

(3a*S*,6a*S*)-(-)-Hexahydro-3-methylene-cyclopenta[b]furan-2-one (17)

This compound was prepared from propenoate **16** (50mg, 0.16mmol) in an analogous manner to that described for **9** save that the reaction was conducted over 6h. Flash chromatography (hexanes:ethyl acetate; 9:1) gave the title compound as a pale yellow liquid (42mg, 86%). ^{1}H NMR: δ1.57 (*dt*, *J*5.89, 11.75Hz, 1H, cyclopentane CH), 1.65-1.78 (*m*, 3H, cyclopentane CH), 1.95 (*ddt*, *J*2.87, 8.81, 6.08Hz, 1H, cyclopentane CH), 2.07 (*m*, 1H, cyclopentane CH), 3.43 [*m*, 1H, H-C(3a)], 5.00 [*t*, *J*5.18Hz, 1H, H-C(6a)], 5.65 (*d*, J_{gem}2.26Hz, 1H, vinylic), 6.25 (*d*, J_{gem}2.61Hz, 1H, vinylic); ^{13}C NMR: δ23.0, 33.8, 35.6, 42.9, 83.2, 122.8, 140.4, 171.2; IR (neat): ν_{max}2960 *s*, 1750 *s* (C=O), 1660 *m* (C=C), 1455 *m*, 1405 *s*, 1320 *s*, 1265 *s*, 1200 *m*, 1150 *m*, 1110 *s*, 1040 *m*, 980 *s*, 950 *m*, 810 *m*, 735 *w* cm^{-1}; MS, m/z: 138 (M$^+$, 23%), 109 ([M-CHO]$^+$, 64), 85 (100), 83 (68), 81 (50); HRMS calc. for $C_8H_{10}O_2$: 138.06808: Found: 138.06749; $[\alpha]_D$ -161.32° (*c*=0.53, $CHCl_3$), lit.[16] for **17** of unknown absolute stereochemistry at C(3a and 6a) $[\alpha]_D$ +125.6 ($CHCl_3$).

Ethyl (1*R*,2*S*,4*S*)-(-)-2-hydroxy-4-methyl-1-cyclohexanecarboxylate (21)[24]

A suspension of baker's yeast (6.0g, Mauripan dried), sugar (76g), $MgSO_4$ (0.5g), KH_2PO_4 (1.0g) and $CaCO_3$ (2.5g) in deionized H_2O (500ml) was allowed to gently stir at 35°C for 45 min. Ethyl 4-methyl-2-cyclohexanone-1-carboxylate (5.0g, 27.14mmol) was then added and the mix allowed to stir at 35°C for 5 days. During this period TLC analysis prompted the addition of further portions of yeast (4.0g) and sugar (20g) at 15, 24, 40, 48, 72 and 96 hours. The mixture was filtered by gravity through a sintered glass funnel and the residues washed with H_2O (100ml) and ethyl acetate (100ml). The combined aqueous solution was saturated with NaCl and extracted with ethyl acetate (4x250ml). The combined organic extracts were dried over $MgSO_4$ and the solvent removed under reduced pressure. Gradient flash chromatography (hexanes:ethyl acetate; 19 to 9:1) yielded the title compound as a colourless liquid (1.1g, 44% based on recovered starting material). A small sample was distilled by kugelrohr (80-90°C/0.02mm). ^{1}H NMR: δ0.85 (*m*, 1H, cyclohexane CH), 0.93 (*d*, *J*6.11Hz, 3H, CH_3), 1.29 (*t*, *J*7.12Hz, $CH_2C\underline{H}_3$), 1.33 (*m*, 1H, cyclohexane CH), 1.40-1.64 (*m*, 3H, cyclohexane CH), 1.88 (*d of m*, J_d12.84Hz, 1H, cyclohexane CH), 2.14 (*dq*, *J*13.94, 3.25Hz, 1H, cyclohexane CH), 2.82 [*ddd*, *J*4.21, 3.99, 3.63Hz, H_{eq}-C(1)], 3.50 (*d*, *J*10.43Hz, 1H, OH, exchangeable with D_2O), 3.58 [*m* (*dt* after D_2O exchange, *J*11.34, 4.42Hz), 1H, H_{ax}-C(2)], 4.20 (*ddq*, *J*21.02, 3.83, 6.72Hz, 2H, $C\underline{H}_2CH_3$); ^{13}C NMR: δ14.0, 21.8, 26.5, 30.3, 31.3, 40.2, 44.9, 60.2, 70.5, 174.4; IR (neat): ν_{max}3460 *s* (O-H), 2925 *s*, 1730 *s* (C=O), 1455 *m*, 1380 *m*, 1335 *m*, 1305 *m*, 1255 *m*, 1180 *s*, 1130 *m*, 1095 *m*, 1060 *m*, 1030 *s*, 970 *w*, 950 *w*, 920 *w*, 860 *w*, 835 *w*, 735 *m* cm^{-1}; MS, m/z: 187 ([M+1]$^+$, 3%), 186 (M$^+$, 6), 185 ([M-1]$^+$, 3), 168 ([M-H_2O]$^+$, 15), 158 ([M-CO]$^+$, 35), 141 ([M-OC_2H_5]$^+$, 120), 115 (47), 101 (82), 96 (94), 73 ($CO_2C_2H_5^+$, 71), 46 (100); HRMS calc. for $C_{10}H_{18}O_3$: 186.12559; Found: 186.12489; $[\alpha]_D$ -24.52° (*c*=0.52, $CHCl_3$), lit.[24] -18.3° (*c*=1.0, $CHCl_3$).

Ethyl (1*R*,2*S*,4*S*)-(-)-2-[(thexyldimethylsilyl)oxy]-4-methyl-1-cyclohexanecarboxylate (23)

This compound was prepared from ester **21** (0.73g, 3.92mmol) in an analogous manner to that described for **11**. Flash chromatography (hexanes:ethyl acetate; 49:1) gave the title compound as a colourless oil (0.79g, 61%). A small sample was distilled by kugelrohr (120-130°C/0.005mm). ^{1}H NMR: δ0.08 (*s*,

6H, $Si(CH_3)_2$), 0.81 (*s*, 6H, $C(CH_3)_2$), 0.86 (*d*, *J*6.86Hz, 6H, $CH(C\underline{H}_3)_2$), 0.97 (*d*, *J*5.71Hz, 3H, $CHC\underline{H}_3$), 1.25 (*t*, *J*7.11Hz, 3H, $CH_2C\underline{H}_3$), 1.36-1.48 (*m*, 4H, cyclohexane CH), 1.50-1.64 (*m*, 3H, cyclohexane CH), 1.76 (*m*, 1H, cyclohexane CH), 1.90 (*dq*, *J*13.62, 3.38Hz, 1H, cyclohexane CH), 2.76 [*ddd*, *J*5.06, 4.29, 4.20Hz, 1H, H_{ax}-C(2)], 3.79 [*dddd*, *J*5.06, 5.25, 5.32, 4.95Hz, 1H, H_{eq}-C(1)], 4.08 (*ddq*, *J*20.56, 3.41, 7.18Hz, 2H, $C\underline{H}_2CH_3$); ^{13}C NMR: δ-3.0, -2.6, 14.2, 18.5, 18.6, 20.1, 20.2, 22.1, 24.7, 25.8, 29.1, 30.7, 34.1, 39.1, 46.1, 59.7, 71.3, 173.7; IR (neat): ν_{max}2950 s, 1735 s (C=O), 1460 m, 1340 m, 1320 m, 1250 s, 1180 s, 1105 s, 1070 s, 1000 m, 955 m, 890 m, 825 s, 775 s, 665 m cm^{-1}; MS, m/z: 313 ($[M-CH_3]^+$, 1%), 283 ($[M-C_2H_5O]^+$, 1), 243 ($[M-C_6H_{13}]^+$, 32), 215 (6), 197 (5), 143 (2), 120 (3), 118 (3), 103 (8), 95 (10), 85 ($C_6H_{13}^+$, 66), 83 (100), 75 (25), 73 (10); HRMS calc. for $C_{17}H_{33}O_3Si$ ($[M-CH_3]^+$): 313.21989; Found: 313.2203; Anal. calc. for $C_{18}H_{36}O_3Si$: C, 65.80%; H, 11.04%; Found: C, 66.10%; H, 11.18%; $[\alpha]_D$ -19.68° (*c*=0.49, $CHCl_3$).

(1*R*,2*S*,4*S*)-(-)-1-[2-(Thexydimethylsilyl)oxy-4-methylcyclohex-1-enyl] ethanol (25)

A 1:1 mixture (as determined by ^1H NMR) of aldehyde **24** and ester **23** (0.25g, 0.88mmol) in ether (50ml) was cooled to -78°C. A solution of methylmagnesium iodide (2.35M in ether) was then added dropwise *via* syringe over 5 min. The solution was slowly warmed to -20°C and allowed to stir at this temperature for 1h. Lowering the temperature to -78°C was followed by quenching of the reaction with aqueous 10% NH_4Cl (10ml). The two phases were partioned and the aqueous layer extracted with ether (3x10ml). The combined organic extracts were washed with brine (100ml), dried and the solvent evaporated under reduced pressure. Flash chromatography (hexanes:ethyl acetate; 19:1) gave recovered **23** and the title compound as a viscous colourless oil (0.22g, 83%, based on aldehyde **24**). ^1H NMR: δ0.13 (*s*, 3H, $SiCH_3$),0.15 (*s*, 3H, $SiCH_3$), 0.89 (*d*, *J*7.00Hz, 6H, $CH(C\underline{H}_3)_2$), 1.04 (*d*, *J*6.87Hz, 3H, $CHC\underline{H}_3$), 1.23 (*d*, *J*6.36Hz, $CH(OH)C\underline{H}_3$), 1.13-1.26 (*m*, 1H, cyclohexane CH), 1.37-1.54 (*m*, 4H, cyclohexane CH), 1.57-1.95 (*m*, 3H, cyclohexane CH and $C\underline{H}(CH_3)_2$), 1.90 (*m*, 1H, cyclohexane CH), 2.43 (*s*, 1H, OH), 3.98 [*m*, 1H, H_{ax}-C(2)], 4.03 (*dq*, *J*4.30, 6.32Hz, 1H, $C\underline{H}OH$); ^{13}C NMR: δ-2.9, -1.8, 18.5, 18.6, 19.7, 20.2, 20.5, 21.7, 22.2, 24.9, 29.2, 30.8, 33.9, 39.6, 46.6, 68.7, 73.5; IR (neat): 3390 s (O-H), 2950 s, 1460 m, 1380 m, 1250 s, 1105 s, 1060 s, 1040 s, 995 m, 970 m, 925 m, 870 s, 830 s, 775 s, 665 m cm^{-1}; MS, m/z: 216 ($[M+1]^+$, 1%), 215 (M^+, 5), 141 (2), 133 (2), 123 (26), 95 (4), 85 (4), 81 (32), 75 (100), 73 (47), 67 (8), 58 (7), 53 (17); HRMS calc. for $C_{11}H_{22}O_2Si$ ($[M-C_6H_{13}]^+$): 215.14674; Found: 215.1464.

(1*R*,2*S*,4*S*)-(-)-2-[(Thexyldimethylsilyl)oxy]-4-methyl-1-cyclohexanyl methyl ketone (26)

This compound was prepared from alcohols **25** (0.23g, 0.77mmol) in an analogous manner to that described for **14**. Flash chromatography (hexanes:ethyl acetate; 24:1) gave the title product as a pale yellow oil (0.17g, 74%). ^1H NMR: δ0.11 (*s*, 6H, $Si(CH_3)_2$), 0.83 (*s*, 6H, $C(CH_3)_2$), 0.87 (*d*, *J*7.64Hz, 6H, $CH(C\underline{H}_3)_2$), 0.95 (*d*, *J*5.20Hz, 3H, $CHC\underline{H}_3$), 1.30-1.49 (*m*, 3H, cyclohexane CH), 1.53-1.69 (*m*, 3H, cyclohexane CH and $C\underline{H}(CH_3)_2$), 1.91 (*dt*, *J*9.52, 3.22Hz, 1H, cyclohexane CH), 2.19 (*s*, 3H, CH_3CO), 2.25 (*m*, 1H, cyclohexane CH), 2.88 [*m*, 1H, H_{eq}-C(1)], 3.85 [*dt*, *J*9.32, 5.34Hz, 1H, H_{ax}-C(2)]; ^{13}C NMR: δ-2.7, -2.3, 18.6, 18.8, 20.3, 20.5, 22.2, 25.0, 25.7, 29.6, 31.2, 33.0, 34.2, 39.9, 52.2, 72.6, 211.5; IR (neat): ν_{max}2950 *s*, 1715 *s* (C=O), 1460 *m*, 1380 *m*, 1350 *m*, 1250 *s*, 1180 *m*, 1160 *m*, 100 *s*, 1065 *s*, 1050 *s*, 945 *w*, 915 *w*, 870 *s*, 825 *s*, 775 *s*, 665 *m* cm^{-1}; MS, m/z: 283 ($[M-CH_3]^+$, 0.4%), 214 (20), 213 ($[M-C_6H_{13}]^+$, 100), 169 (26), 120 (5), 105 (8), 93 (3), 75 (7); HRMS calc. for $C_{16}H_{31}O_2Si$ ($[M-CH_3]^+$): 283.20932; Found: 283.2095; $[\alpha]_D$ -28.0° (*c*=0.5, $CHCl_3$).

(1*R*,2*S*,4*S*)-(-)-2-[(Thexyldimethylsilyl)oxy]-4-methyl-1-{1-methylene-1-[(trifluoro methanesulfonyl)oxy]}cyclohexane (27)

This compound was prepared from methyl ketone **26** (0.12g, 0.39mmol) in an analogous manner to that described for **15**. Flash chromatography (hexanes) gave the title compound as a colourless oil (0.24g, 98%). ^{1}H NMR: δ0.08 (*s*, 3H, $SiCH_3$), 0.10 (*s*, 3H, $SiCH_3$), 0.82 (*s*, 6H, $C(CH_3)_2$), 0.86 (*d*, *J*6.84Hz, 6H, $CH(C\underline{H}_3)_2$), 0.99 (*d*, *J*6.24Hz, 3H, $CHC\underline{H}_3$), 1.13-1.26 (*m*, 2H, cyclohexane CH), 1.37-1.68 (*m*, 4H, cyclohexane CH and $C\underline{H}(CH_3)_2$), 2.00 (*m*, 1H, cyclohexane CH), 2.32 (*m*, 1H, cyclohexane CH), 2.68 [*ddd*, *J*4.86, 4.00, 3.95Hz, 1H, H_{eq}-C(1)], [*dddd*, *J*4.48, 4.60, 4.04, 4.46Hz, 1H, H_{ax}-C(2)], 5.26 (*d*, J_{gem}2.58Hz, 1H, vinylic), 5.33 (*d*, J_{gem}3.52Hz, 1H, vinylic); ^{13}C NMR: δ-3.2, -2.5, 18.6, 20.2, 20.3, 21.8, 24.0, 24.5, 24.9, 29.6, 30.3, 34.1, 38.7, 45.6, 70.3, 107.4, 118.5 (*q*, J_{CF}320.0Hz), 156.5; IR (neat): ν_{max}2950 *s*, 1670 *w* (C=O), 1460 *m*, 1420 *s* (asymS=O), 1250 *s* (asymC-OSO_2), 1210 *s* (C-F), 1150 *s* (symS=O), 1100 *m* (S-O), 1070 *m*, 1050 *m*, 925 *m*, 875 *m*, 830 *m*, 780 *m*, 615 *m* cm^{-1}; MS, m/z: 415 ([M-CH_3]$^+$, 0.25%), 345 ([M-C_6H_{13}]$^+$, 36), 277 (2), 207 (5), 195 (12), 121 (100), 105 (9), 93 (77), 79 (36), 75 (7), 67 (4); HRMS calc. for $C_{12}H_{20}F_3O_4SSi$ ([M-C_6H_{13}]$^+$): 345.08036; Found: 345.0800; $[\alpha]_D$ -7.84° (*c*=0.51, $CHCl_3$).

Methyl (1*R*,2*S*,4*S*)-(-)-2-[2-thexyldimethylsilyl)oxy-4-methylcyclohexan-1-yl] propenoate (28)

This compound was prepared from vinyl triflate **27** (0.24g, 0.56mmol) in an analogous manner to that described for **16**. Flash chromatography (hexanes:ethyl acetate; 99:1) gave the title compound as a pale yellow oil (0.11g, 58%). ^{1}H NMR: δ0.05 (*s*, 3H, $SiCH_3$), 0.18 (*s*, 3H, $SiCH_3$), 0.92 (*s*, 3H, CCH_3), 0.94 (*s*, 3H, CCH_3), 1.01 (*d*, *J*7.30Hz, 6H, $CH(C\underline{H}_3)_2$), 1.21 (*d*, *J*6.95Hz, 3H, $CHC\underline{H}_3$), 1.17-1.54 (*m*, 2H, cyclohexane CH), 1.65-1.91 (*m*, 4H, cyclohexane CH and $C\underline{H}(CH_3)_2$), 2.05 (*m*, 1H, cyclohexane CH), 2.27 (*m*, 1H, cyclohexane CH), 2.92 [*m*, 1H, H_{eq}-C(1)], 3.86 (*s*, 3H, OCH_3), 4.16 [*dddd*, *J*3.38, 2.67, 3.02, 3.48Hz, 1H, H_{ax}-C(2)], 5.82 (*s*, 1H, vinylic), 6.41 (*s*, 1H, vinylic); ^{13}C NMR: δ-3.2, -2.3, 18.6, 18.7, 20.3, 20.4, 21.7, 22.6, 24.8, 28.4, 31.1, 34.0, 38.8, 42.4, 51.6, 70.1, 126.1, 141.4, 168.2; IR (neat): ν_{max}2950 *s*, 1720 *s* (C=O), 1630 *w* (C=C), 1465 *m*, 1440 *m*, 1380 *w*, 1250 *s*, 1210 *m*, 1145 *s*, 1050 *s*, 1000 *m*, 890 *m*, 830 *m*, 775 *m* cm^{-1}; MS, m/z: 325 ([M-CH_3]$^+$, 1%), 309 (1), 255 ([M-C_6H_{13}]$^+$, 100), 223 (23), 195 (9), 149 (4), 129 (4), 120 (23), 105 (50), 89 (20), 73 ($CO_2C_2H_5^+$, 31); HRMS calc. for $C_{18}H_{33}O_3Si$ ([M-CH_3]$^+$): 325.21989; Found: 325.2194; $[\alpha]_D$ -9.52° (*c*=0.42, $CHCl_3$).

(3a*R*,6*S*,7a*S*)-(-)-Hexahydro-6-methyl-3-methylene-2(3*H*)benzofuranone (29)

This compound was prepared from propenoate **28** (86mg, 0.25mmol) in an analogous manner to that described for **17**. Flash chromatography (hexanes:ethyl acetate; 97:3) gave the title compound as a colourless oil (42mg, 100%). ^{1}H NMR: δ0.78-1.01 (*m*, 2H, cyclohexane CH), 0.91 (*d*, *J*6.48Hz, 3H, CH_3), 1.37 (*br m*, 1H, cyclohexane CH), 1.50 (*d of m*, J_d13.75Hz, 1H, cyclohexane CH), 1.76 (*m*, 1H, cyclohexane CH), 2.08 (*m*, 1H, cyclohexane CH), 2.12 (*m*, 1H, cyclohexane CH), 3.12 [*m*, 1H, H-C(3a)], 4.63 [*ddd*, *J*6.80, 3.09, 6.87Hz, 1H, H-C(7a)], 5.50 (*d*, J_{gem}3.31Hz, 1H, vinylic), 6.28 (*d*, J_{gem}3.32Hz, 1H, vinylic); ^{13}C NMR: δ21.9, 23.8, 28.5, 28.9, 38.9, 40.0, 77.5, 119.8, 137.4, 170.8; IR (neat): ν_{max}2925 *s*, 1765 *s* (C=O), 1665 *w* (C=C), 1455 *m*, 1405 *w*, 1315 *m*, 1255 *m*, 1230 *m*, 1220 *m*, 1100 *m*, 990 *m*, 815 *w*, 750 *w* cm^{-1}; $[\alpha]_D$ -19.2° (*c*=0.5, $CHCl_3$).

(+)-Mintlactone (18)

Benzofuranone **29** (27mg, 0.16mmol) and 1,4-dioxane (2ml) were added *via* syringe to $HRh(PPh_3)_3CO$ (0.12g, 0.14mmol). The solution quickly darkened to a brown/orange and was allowed to stir at ambient temperature with hourly monitoring by TLC. After 2 days the solvent was removed under reduced pressure to yield a red oil. Flash chromatography (hexanes:ethyl acetate; 9:1) gave the title compound as as a colourless liquid (16mg, 59%). ^1H NMR: δ0.89-1.09 (*m*, 2H, cyclohexane CH), 1.01 (*d*, *J*6.69Hz, 3H, CH_3), 1.71 (*m*, 1H, cyclohexane CH), 1.81 (*t*, ^5J1.50Hz, 3H, CH_3C=), 1.95 (*d of m*, J_d13.15Hz, 1H, cyclohexane CH), 2.19 (*br ddd*, *J*5.51, 5.33, 5.79Hz, 1H, cyclohexane CH), 2.42 (*m*, 1H, cyclohexane CH), 2.79 (*ddd*, *J*14.24, 2.61, 1.77Hz, 1H, cyclohexane CH), 4.63 [*br dd*, *J*5.53, 6.38Hz, 1H, H-C(7a)]; ^{13}C NMR: δ8.2, 21.2, 25.4, 29.7, 34.5, 41.9, 79.9, 119.5, 162.3, 174.9; IR (neat): ν_{max}2925 *s*, 1750 *s* (C=O), 1690 *m* (C=C), 1455 *m*, 1380 *w*, 1330 *m*, 1300 *m*, 1230 *w*, 1100 *m*, 1070 *m*, 1030 *s*, 1000 *m*, 860 *m*, 765 *m*, 750 *m*, 685 *m* cm^{-1}; MS, m/z: 167 ($[M+1]^+$, 12%), 166 (M^+, 100), 151 ($[M-CH_3]^+$, 3), 138 ($[M-CO]^+$, 45), 137 ($[M-CHO]^+$, 77), 123 (26), 120 (11), 109 (64), 105 (22), 95 (60), 91 (20), 81 (84), 67 (91); HRMS calc. for $C_{10}H_{14}O_2$: 166.09974; Found: 166.0991; $[\alpha]_D$ +59.9° (*c*=0.75, EtOH), lit.[17] $[\alpha]_D$ for (-)-mintlactone -51.8° (*c*=10, EtOH).

REFERENCES

1 Nagao, Y.; Dai, W-M.; Ochiai, M.; Shiro, M. *J. Org. Chem.* **1989**, *54*, 5211-5217.

2. a) Grieco, P.A. *Synthesis* **1975**, 67-82; b) Gammill, R. M.: Wilson, C. A.: Bryson, T. A. *Synth. Commun.*, **1975**, 245-268; c) Hoffmann, H. M. R.: Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 94-110; d) Petragnani, N.: Ferraz, H. M. C.: Silva, G. V. J. *Synthesis* **1986**, 157-183; e) Sarma, J.: Sharma, R. P. *Heterocycles* **1986**, *24*, 441-457.

3. a) Rao, Y. S. *Chem. Rev.* **1964**, *64*, 353-388; **1976**, *76*, 625-675. b) Knight, D. W. *Contemporary Organic Synthesis* **1994**, 287.

4. Tamaru, Y.; Hojo, M.; Yoshida, Z. *J. Org. Chem.* **1991**, *56*, 1099-1105.

5. Arcadi, A.; Bernocchi, E.; Burini, A.; Cacchi, S.; Marinelli, F.; Pietroni, B. *Tetrahedron* **1988**, *44* ,481-490.

6. Hosokawa, T.; Murahashi, S-I. *Heterocycles* **1992**, *33*, 1079-1100.

7. Cowell, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 4193-4198

8. Martin, L. D.; Stille, J. K. *J. Org. Chem.* **1982**, *47*, 3630-3633.

9. Crisp, G. T.; Meyer, A. G. *J. Org. Chem.* **1992**, *57*, 6972-6975.

10. Wipf, B.; Kupfer, E.; Bertazzi, R.; Leuenberger, H. G. N. *Helv. Chim. Acta.* **1983**, *66*, 485-488. Nakamura, K.; Kawai, Y.; Nakajima, N.; Ohno, A. *J. Org. Chem.* **1991**, *56*, 4778-4783.

11. Bolte, J.; Gourcy, J-G.; Veschambre, H. *Tetrahedron Lett.* **1986**, *27*, 565-568.

12. Ritter, K. *Synthesis* **1993**, 735-762 and references therein.

13. a) Pirkle, W. H.; Sikkenga, D. L.; Parlin, M. S. *J. Org. Chem.* **1977**, *42*, 384-387. b) Pirkle, W. H.; Sikkenga, D. L. *J. Org. Chem.* **1977**, *42*, 1370-1374.

14. Wahhab, A.; Tavares, D. F.; Rauk, A. *Can. J. Chem.* **1990**, *68*, 1559-1563.

15. Jackman, L. M.; Sternhell, S. *Applications of NMR Spectroscopy in Organic Chemistry*, Pergamon Press, Oxford, **1969**, p. 288.

16. Yamakawa, K. **1994**, personal communication. The quoted ee in the text is superior to that reported (64%ee) in : Nishitani, K.; Yamakawa, K. *Tetrahedron Lett.* **1991**, *32*, 387-390.

17. Takahashi, K.; Someya, T.; Muraki, T.; Yoshida, T. *Agric. Biol. Chem.* **1980**, *44*, 1535-1543.
18. Tsuboi, S.; Shimozuma, K.; Takeda, A. *J. Org. Chem.* **1980**, *45*, 1517-1520.
19. Chavan, S. P.; Zubaidha, P. K.; Ayyangar, *Tetrahedron Lett.* **1992**, *33*, 4605-4608. Corey, R. M.; Ritchie, B. M.; Shrier, A. M. *Tetrahedron Lett.* **1990**, *31*, 6789-4792. Fujita, T.; Watanabe, S.; Miharu, K.; Itoh, K.; Sugahara, K. *J. Chem. Biotechnol.* **1985**, *35A*, 57-63.
20. Shishido, K.; Irie, O.; Shibuya, M. *Tetrahedron Lett.* **1992**, *33*, 4589-4592.
21. Carda, M.; Marco, J. A. *Tetrahedron* **1992**, *48*, 9789-9800.
22. Chavan, S. P.; Zubaidha, P. K.; Dhondge, V. D. *Tetrahedron* **1993**, *49*, 6429-6436.
23. Frater, G.; Gunther, W.; Muller, U. *Helv. Chim. Acta.* **1989**, *72*, 1846-1851. Herrandon, B.; Seebach, D. *Helv. Chim. Acta.* **1989**, *72*, 690-714.
24. Gilbert, J. C., Selliah, R. D. *J. Org. Chem.* **1993**, *58*, 6255-6265.

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