The Synthesis of Trisubstituted Tetrahydrofurans *via* the Use of an Organoselenium-mediated Cyclisation Reaction

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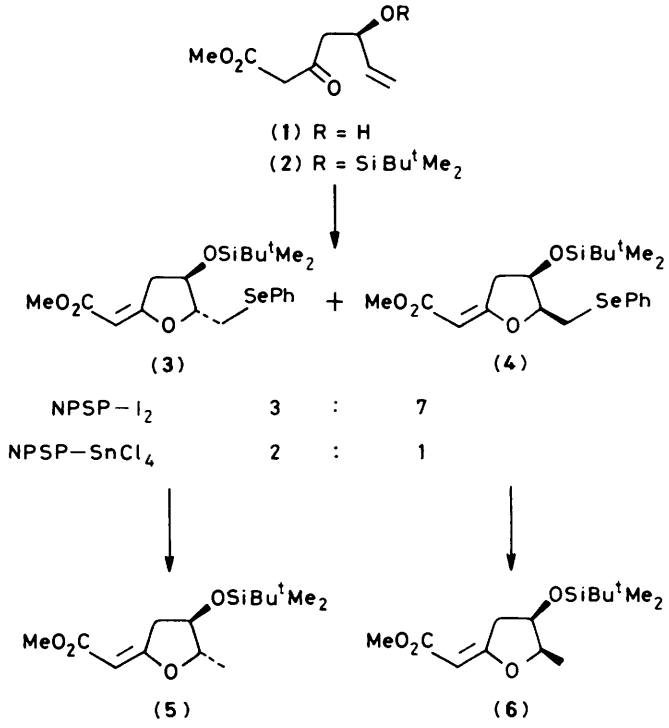
The dianion derived from methyl acetoacetate may be alkylated selectively on the γ-carbon atom to form a 1,2-addition product (**1**) with acrolein. This material after protection as its dimethyl-t-butylsilyl derivative (**2**) can be cyclised with *N*-phenylselenophthalimide (NPSP) in the presence of various catalysts to afford dihydrofuran derivatives which are useful precursors for hydroxy-containing trisubstituted tetrahydrofurans. The *X*-ray crystal structure of methyl *cis*-4-dimethyl-t-butylsilyloxy-5-phenylselenomethyltetrahydrofuran-2-ylideneacetate, compound (**4**), have also been determined.

Polysubstituted tetrahydrofuran rings, especially those containing hydroxy substituents, are common structural features of numerous natural products. Typical recent examples which have attracted synthetic attention are aplasmomycin,[1] boromycin,[2] muscarine,[3] and palytoxin.[4] Organoselenium-mediated cyclisation reactions are now well established for natural product synthesis[5] and have recently been applied to the formation of trisubstituted tetrahydrofurans.[6] Here we show how selenium-based methodology developed in our laboratories[7] can be usefully employed in the construction of 2,4,5-trisubstituted tetrahydrofurans with some degree of stereochemical control.

Results and Discussion

Quenching of the dianion[8] from methyl acetoacetate with acrolein leads exclusively to the 1,2-addition product (**1**) in 84% yield. Attempts to cyclise this material directly *via* the enolic oxygen atom to form a hydrofuran derivative using a variety of *N*-phenylselenophthalimide (NPSP)–Lewis acid catalyst combinations were unsuccessful. However, the offending hydroxy group in these reactions could be protected as the di-methyl-t-butyl silyl ether (**2**) (80%) using standard reaction conditions. Similar attempted protection with either benzyl or acetyl groups was not possible owing to competitive reaction at the enolic oxygen centre. Treatment of the silyl ether (**2**) with NPSP in either dichloromethane or tetrahydrofuran in the presence of catalytic amounts of iodine, rapidly afforded a 3:7 ratio of cyclised products (**3**) and (**4**) in 60% combined yield. The *cis* arrangement of functional groups and the *E*-geometry of the double bond in compound (**4**) was consistent with n.O.e. experiments and was confirmed by *X*-ray crystallographic determination (Figure). Similar reaction with NPSP in the presence of an equivalent of tin(IV) chloride gave (**3**) and (**4**) in a 2:1 ratio (74%) (Scheme 1). Although products (**3**) and (**4**) were separated by careful chromatography it was found to be much more convenient on a large scale to separate the resulting silyl ethers (**5**) and (**6**) after deselenation with Raney nickel or tributyltin hydride. Hydrogenation of the *trans*-furan (**5**) under more vigorous conditions using Raney nickel as the catalyst gave complex reaction mixtures. However, if the silyl protecting group was first removed from compound (**5**) using tetrabutylammonium fluoride the resulting free alcohol (**7**) reacted more rapidly under the hydrogenation conditions [Ni(R)–H_2(80 p.s.i.)–MeOH] to give the trisubstituted tetrahydrofurans (**8**) and (**9**) in a 2:1 ratio. Apparently in this example the free hydroxy group does not influence the direction of the hydrogenation process. Hydrogenation of the *cis*-furan (**6**)



Scheme 1.

using the Raney nickel system [Ni(R)–H_2(80 p.s.i.)–MeOH] proceeded more smoothly to give the all *cis*-compound (**10**) in 71% yield.

Once again this could be deprotected to afford the free alcohol (**11**) using tetrabutylammonium fluoride. In order to confirm that there had been no epimerisation during this deprotection step, by a fluoride-catalysed ring opening–ring closure sequence, it was reprotected to compound (**10**) using dimethyl-t-butylsilyl trifluoromethanesulphonate. Alternatively, the unsaturated furan derivative (**6**) was deprotected with Bu_4NF to give a 60% yield of the alcohol (**12**) which in turn underwent highly stereoselective hydrogenation to provide (**11**) in 65% yield. The conversion of (**11**) into (**10**) also confirms that the stereochemical courses of the hydrogenations of (**6**) and (**12**) are identical.

Finally we have briefly examined a hydroxy group epimerisation sequence as a means of access to other hydroxytetrahydrofuran species. For example, a 95% yield of the 3,5-dinitrobenzoyl derivative (**13**) was obtained by treatment of

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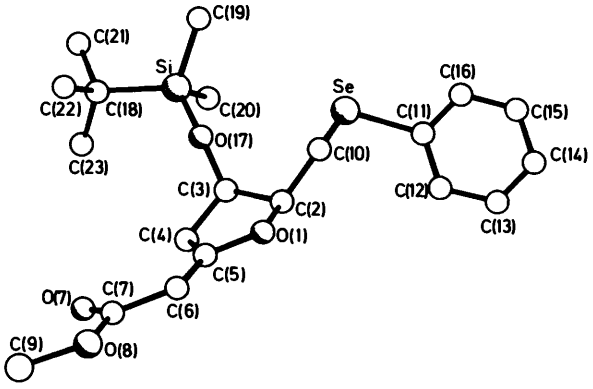
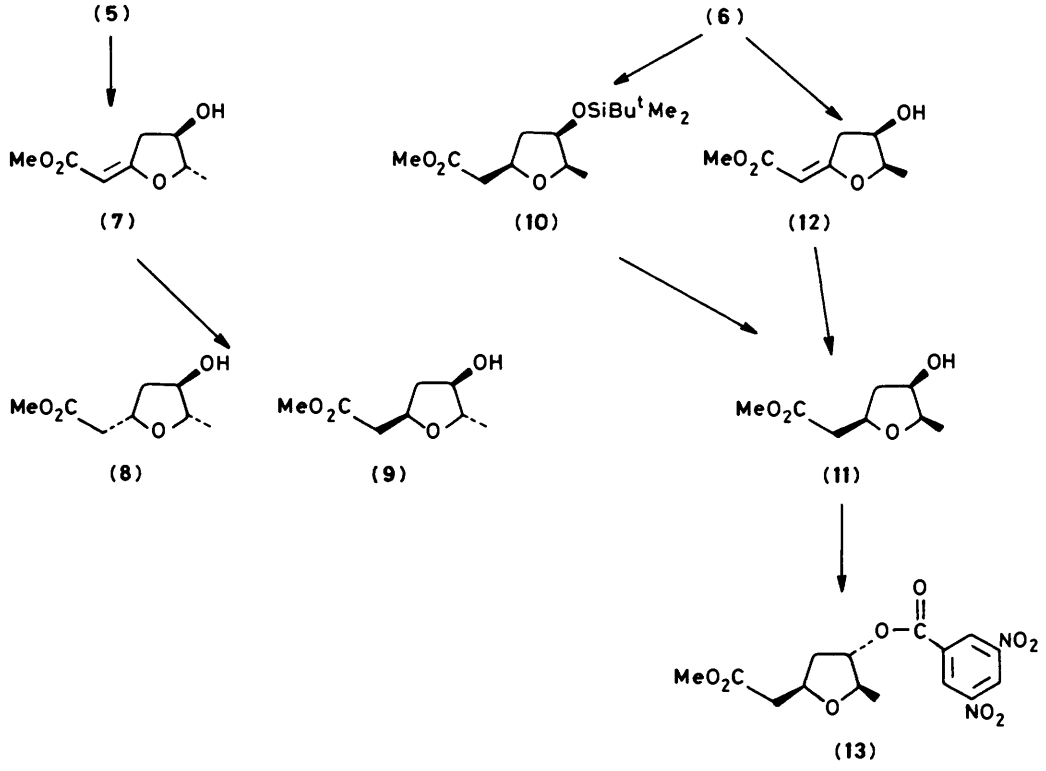


Figure.

mesh, under pressure. Light petroleum refers to the fraction boiling in the range 40—60 °C and ether to diethyl ether. Solutions were dried over sodium sulphate, and solvents by standard methods.

Preparation of Methyl 5-Hydroxy-3-oxohept-6-enoate (**1**).—Methyl acetoacetate (1 g, 0.93 ml, 8.61 mmol) in dry THF (4 ml) was slowly added to a suspension of sodium hydride [50% dispersion in oil; 0.46 g, 9.47 mmol; prewashed with light petroleum (2 × 30 ml) and then dry THF (30 ml)] in THF (20 ml) under argon at −5 °C. The mixture was stirred for 10 min at −5 °C and then butyl-lithium 1.56M solution in hexane; 5.8 ml, 9.04 mmol) added dropwise at −10 °C and a pale yellow solution formed. The mixture was stirred for 20 min at −10 °C after which freshly distilled acrolein (0.53 g, 0.63 ml, 9.47 mmol)



Scheme 2.

(**11**) with 3,5-dinitrobenzoic acid in the presence of triphenylphosphine and diethyl azodicarboxylate.[9]

The above reactions further extend the usefulness of the selenium-mediated cyclisation reactions of alkenyl substituted β-keto esters.

Experimental

^{1}H N.m.r. spectra were obtained on Bruker WH-250, Jeol FX90Q and Varian EM-360A spectrometers in deuteriochloroform solutions with tetramethylsilane as the internal standard and ^{13}C n.m.r. spectra on a Jeol FX90Q spectrometer in deuteriochloroform solutions with $CDCl_3$ 77.0 p.p.m. as the internal standard. I.r. spectra were recorded on a Perkin-Elmer 983 G spectrophotometer as liquid films or chloroform solutions. Mass spectra were obtained on a VG Micromass 7070B instrument. Melting points were determined using a Kofler hot-stage apparatus and are uncorrected. Column chromatography was performed on MN-silica gel 60 230—400 was added and the whole stirred at −5 °C for a further 30 min. The mixture was poured into a mixture of HCl (36%; 2 ml), water (5 ml), and ether (15 ml). The organic phase was separated, the aqueous phase extracted with ether (3 × 20 ml), and the organic extracts combined, dried, and evaporated to leave a yellow oil. The oil was distilled at 180 °C/0.3 mmHg (Kugelrohr) to give *methyl 5-hydroxy-3-oxohept-6-enoate* (**1**) (1.24 g, 84%) as a colourless oil; $\nu_{max.}$(film) 3 480, 1 745, 1 712, and 1 650 cm^{-1}; δ_H (250 MHz) 5.88 (1 H, ddd, *J* 16.3, 10.0, 6.0 Hz, 6-H), 5.07—5.35 (2 H, m, 7-H), 4.61 (1 H, dt, *J* 6.0, 6.3 Hz, 5-H), 3.75 (3 H, s, OMe), 3.53 (2 H, s, 2-H), 3.09 (1 H, br s, OH), and 2.78 (2 H, d, *J* 6.3 Hz, 4-H); *m/z* (no M^+), 116, 101, and 85 (Found: C, 56.03; H, 7.02. $C_8H_{12}O_4$ requires C, 55.81; H, 7.02%).

Methyl 5-Dimethyl-t-butylsilyloxy-3-oxohept-6-enoate (**2**).—The alcohol (**1**) (16.6 g, 96.4 mmol) was stirred at room temperature in dry DMF (40 ml) and imidazole (recrystallised from benzene, 16.41 g, 0.24 mmol, 2.5 equiv.) then dimethyl-t-butylsilyl chloride (14.53 g, 96.4 mmol, 1.0 equiv.) added. The

mixture was stirred overnight at room temperature under argon and water (250 ml) and light petroleum (250 ml) were added. The organic phase was separated and the aqueous phase extracted with light petroleum (3 × 200 ml). The organic phases were then combined, washed with brine (250 ml), dried, filtered through silica gel, and evaporated to afford a pale yellow clear oil. The oil was distilled at 120 °C/10^{-3} mmHg (Kugelrohr) to give *methyl 5-dimethyl-t-butylsilyloxy-3-oxohept-6-enoate* (**2**) (21.95 g, 80%) as a nearly colourless cloudy oil; $\nu_{max.}$(film) 1 730 cm^{-1}; δ_H (250 MHz) 5.84 (1 H, ddd, *J* 17.2, 10.4, 5.9 Hz, 6-H), 5.22 (1 H, ddd, *J* 17.1, 1.4, 1.4 Hz, 7-H), 5.05 (1 H, ddd, *J* 10.3, 1.3, 1.3 Hz, 7-H), 4.59 (1 H, m, 5-H), 3.71 (3 H, s, MeO), 3.47 (2 H, s, CH_2), 2.77 (1 H, dd, *J* 15.2, 7.6 Hz, 4-H), 2.58 (1 H, dd, *J* 15.1, 4.9 Hz, 4-H), 0.86 (9 H, s, Bu^t), 0.03 (3 H, s, SiMe), and 0.02 (3 H, s, SiMe); *m/z* (no M^+), 271, 255, and 229 (Found: C, 58.75, H, 9.1. $C_{14}H_{26}O_4Si$ requires C, 58.70; H, 9.15%).

Cyclisation of Compound (**2**) *using* N-*Phenylselenophthalimide* (*NPSP*) *with Iodine Catalyst*.—The β-keto ester (**2**) (1.24 g, 4.33 mmol) and NPSP (1.44 g, 4.78 mmol, 1.1 equiv.) were stirred in dry THF (25 ml) under argon at room temperature and a weak solution of iodine in THF was added dropwise to the reaction mixture until a brown colouration remained. The mixture was stirred for 90 min after which light petroleum (25 ml) was added and the whole filtered, washed with brine (25 ml), dried, filtered, and evaporated to leave a yellow oily solid. This was purified by chromatography on silica gel (100 g) eluting with 10% ether in light petroleum to give *methyl* (E)-trans-4-*dimethyl-t-butylsilyloxy-5-phenylselenomethyltetrahydrofuran-2-ylideneacetate* (**3**) (364 mg, 18%) as a colourless oil; $\nu_{max.}$(film) 1 700 and 1 650 cm^{-1}; δ_H (250 MHz) 7.48—7.55 (2 H, m, ArH), 7.22—7.30 (3 H, m, ArH), 5.30 (1 H, t, *J* 1.8 Hz, vinylic), 4.42 (1 H, ddd, *J* 6.9, 5.6, 3.1 Hz, 5-H), 4.34 (1 H, ddd, *J* 6.2, 3.7, 3.1 Hz, 4-H), 3.64 (3 H, s, OMe), 3.22 (1 H, dd, *J* 18.7, 6.2 Hz, 3-H), 3.14 (1 H, dd, *J* 18.7, 3.7 Hz, 3-H), 3.01 (1 H, dd, *J* 13.1, 6.9 Hz, C*H*$_2$SePh), 2.96 (1 H, dd, *J* 13.1, 5.6 Hz, C*H*$_2$SePh), 0.83 (9 H, s, Bu^t), 0.07 (3 H, s, SiMe), and 0.05 (3 H, s, SiMe); δ_C (22.51 MHz) 174.2 (s, C-2), 168.7 (s, *C*O$_2$Me), 132.9 (d, ArC), 129.3 (d, ArC), 127.5 (d, ArC), 90.8 (d, C-2′), 89.1 (d, C-5), 73.3 (d, C-4), 50.7 (q, CO$_2$*Me*), 39.6 (t, *C*H$_2$SePh), 29.0 (t, C-3), 25.7 (q, SiMe and SiC*Me*$_3$), and 17.9 (s, Si-C*Me*$_3$); *m/z* 442 (M^+), 385, 255, and 173 (Found: C, 54.15; H, 7.0. $C_{20}H_{30}O_4SeSi$ requires C, 54.41; H, 6.85%) and *methyl* (E)-cis-4-*dimethyl-t-butylsilyloxy-5-phenylselenomethyltetrahydrofuran-2-ylideneacetate* (**4**) (810 mg, 43%) as white crystals, m.p. 85—87 °C (from ether); $\nu_{max.}$($CHCl_3$) 1 700 and 1 640 cm^{-1}; δ_H (250 MHz) 7.40—7.50 (2 H, m, ArH), 7.20—7.30 (3 H, m, ArH), 5.30 (1 H, t, *J* 1.0 Hz, vinylic), 4.56 (1 H, t, *J* 4.2 Hz, 4-H), 4.36 (1 H, dt, *J* 7.1, 3.5 Hz, 5-H), 3.65 (3 H, s, OMe), 3.47 (1 H, d, *J* 18.2 Hz, 3-H), 3.18 (2 H, d, *J* 7.1 Hz, C*H*$_2$SePh), 2.95 (1 H, ddd, *J* 18.2, 5.1, 2.8 Hz, 3-H), 0.88 (9 H, s, Bu^t), 0.13 (3 H, s, SiMe), and 0.12 (3 H, s, SiMe); *m/z* 442 (M^+) and 285 (Found: C, 54.55; H, 6.7. $C_{20}H_{30}O_4SeSi$ requires C, 54.41; H, 6.85%).

Cyclisation of Compound (**2**) *using NPSP with Tin*^{IV} *Chloride Catalyst*.—The β-keto ester (**2**) (2.02 g, 7.04 mmol) and NPSP (2.55 g, 8.44 mmol, 1.2 equiv.) were stirred in dry THF (60 ml) under argon at room temperature and tin(IV) chloride (0.824 µl, 7.04 mmol, 1.0 equiv.) added dropwise. After the reaction had been stirred for 90 min at room temperature, light petroleum (100 ml) was added and the mixture filtered into a separating funnel. The organic phase was washed with saturated aqueous sodium hydrogen carbonate (50 ml) and brine (50 ml), dried, filtered through silica gel and the filtrate evaporated to a yellow oil. This oil was purified by chromatography on silica gel (100 g) eluting with 10% ether in light petroleum to give a 2;1 mixture of methyl (*E*)-*trans*-4-dimethyl-t-butylsilyloxy-5-phenylselenomethyltetrahydrofuran-2-ylideneacetate (**3**) and methyl (*E*)-*cis*-4-dimethyl-t-butylsilyloxy-5-phenylselenomethyltetrahydrofuran-2-ylideneacetate (**4**) (2.29 g, 74%) identical in all respects with (**3**) and (**4**) prepared above.

Deselenation of Compounds (**3**) *and* (**4**) *with Tributyltin Hydride*.—A mixture of the selenides (**3**) and (**4**) (0.3343 g, 0.76 mmol) was heated in dry toluene (30 ml) to reflux and a suspension of azoisobutyronitrile (AIBN) in tributyltin hydride (100 mg in 1.266 ml; 306 µl, 1.14 mmol, 1.5 equiv.) added in portions to the mixture. The mixture was heated to reflux for 1 h and the solvents evaporated to leave a yellow oil. The oil was purified by chromatography on silica gel (25 g) eluting with 15% ether in light petroleum to give *methyl* (E)-trans-4-*dimethyl-t-butylsilyloxy-5-methyltetrahydrofuran-2-ylideneacetate* (**5**) (105.6 mg, 49%) as a colourless oil; $\nu_{max.}$(film) 1 708, 1 647, 1 123, and 1 081 cm^{-1}; δ_H (250 MHz) 5.30 (1 H, t, *J* 1.8 Hz, vinylic), 4.27 (1 H, dq, *J* 6.5, 4.0 Hz, 5-H), 4.04 (1 H, ddd, *J* 6.5, 4.6, 4.0 Hz, 4-H), 3.63 (3 H, s, OMe), 3.35 (1 H, ddd, *J* 18.3, 6.5, 1.8 Hz, 3-H), 3.05 (1 H, ddd, *J* 18.3, 4.6, 1.8 Hz, 3-H), 1.26 (3 H, d, *J* 6.5 Hz, Me), 0.88 (9 H, s, Bu^t), and 0.09 (6 H, s, SiMe); *m/z* 285 (M^+ − H), 271, 255, 229, 197, and 75 (Found: C, 58.9; H, 9.4. $C_{14}H_{26}O_4Si$ requires C, 58.70; H, 9.15%) and *methyl* (E)-cis-4-*dimethyl-t-silyloxy-5-methyltetrahydrofuran-2-ylidenacetate* (**6**) (63.07 mg, 29%) as white crystals; m.p. 50—52 °C (from ether); $\nu_{max.}$(film) 1 708 and 1 640 cm^{-1}; δ_H (250 MHz) 5.30 (1 H, t, *J* 2.2 Hz, vinylic), 4.36 (1 H, dq, *J* 6.1, 3.5 Hz, 5-H), 4.33 (1 H, dd, *J* 5.1, 3.5 Hz, 4-H), 3.66 (3 H, s, MeO), 3.38 (1 H, d, *J* 18.3 Hz, 3-H), 3.03 (1 H, ddd, *J* 18.3, 5.1, 2.2 Hz, 3-H), 1.33 (3 H, d, *J* 6.1 Hz, Me), 0.89 (9 H, s, Bu^t), 0.09 (3 H, s, SiMe), and 0.08 (3 H, s, SiMe); δ_C (22.51 MHz) 174.8 (s, C-2), 168.9 (s, *C*O$_2$Me), 89.6 (d, C-2′), 83.3 (d, C-5), 71.1 (d, C-4), 50.4 (q, CO$_2$*Me*), 41.0 (t, C-3), 25.6 (q, SiMe and C*Me*$_3$), 18.0 (s, *C*Me$_3$), and 13.8 (q, Me); *m/z* (no M^+), 271, 255, and 229 (Found: C, 58.59; H, 8.94. $C_{14}H_{26}O_4Si$ requires C, 58.70; H, 9.15%).

Deprotection of Compound (**5**) *with Tetrabutylammonium Fluoride* (*TBAF*).—The silyl ether (**5**) (927 mg, 3.24 mmol) was stirred at 0 °C and TBAF (1M in THF; 8 ml, 8.00 mmol, 2.5 equiv.) added in one portion. The mixture was stirred at 0 °C for 30 min and water (25 ml) and ether (25 ml) were added. The organic phase was separated, the aqueous phase extracted with ether (3 × 25 ml), and the combined organic phases were washed with brine (50 ml), dried, filtered and the filtrate evaporated to leave a white solid. This was purified by column chromatography on silica gel (50 g) eluting with ether to give *methyl* (E)-trans-4-*hydroxy-5-methyltetrahydrofuran-2-ylideneacetate* (**7**) (462 mg, 83%) as a white solid, m.p. 61—63 °C; $\nu_{max.}$($CHCl_3$) 3 594br, 1 695, 1 640, and 1 127 cm^{-1}; δ_H (250 MHz) 5.34 (1 H, t, *J* 1.8 Hz, vinylic), 4.48 (1 H, dq, *J* 6.6, 2.3 Hz, 5-H), 4.20 (1 H, br dt, *J* 4.4, 2.3 Hz, 4-H), 3.66 (3 H, s, *Me*O$_2$C), 3.28 (2 H, dd, *J* 4.4, 1.8 Hz, 3-H), 2.68 (1 H, br s, OH), and 1.27 (3 H, d, *J* 6.6 Hz, Me); δ_C (22.51 MHz) 174.8 (s, C-2), 169.3 (s, *C*O$_2$Me), 90.2 (d, *C*HCO$_2$Me), 86.3 (d, C-5), 74.1 (d, C-4), 50.7 (q, CO$_2$*Me*), 39.1 (t, C-3), and 18.1 (q, Me); *m/z* 172 (M^+), 155, and 141 (Found: C, 56.06; H, 6.96. $C_8H_{12}O_4$ requires C, 55.81; H, 7.02%).

Hydrogenation of the Ester (**7**) *to Compounds* (**8**) *and* (**9**).—The unsaturated ester (**7**) (90.59 mg, 0.53 mmol) was stirred in methanol with Raney nickel (W4; *ca.* 50 mg) under 80 p.s.i. hydrogen at room temperature for 2 days. The reaction mixture was filtered and evaporated to a colourless oil which was purified by column chromatography on silica gel (6 g) eluting with 50% ether in light petroleum to give a 2:1 inseparable mixture (67.32 mg, 73%) as a colourless oil of (±) methyl (2*R*,4*S*,5*S*)-4-hydroxy-5-methyltetrahydrofuran-2-ylacetate (**8**); $\nu_{max.}$(film) 3 430 and 1 737 cm^{-1}; δ_H (250 MHz) 4.43—4.51 (1 H, m, 2-H), 3.99—4.05 (1 H, m, 4-H), 3.87 (1 H, dq, *J* 6.4, 3.4 Hz, 5-

H), 3.70 (3 H, s, OMe), 2.66 (1 H, dd, *J* 15.5, 6.9 Hz, 2'-H), 2.52 (1 H, dd, *J* 15.4, 6.1 Hz, 2'-H), 2.03 (1 H, ddd, *J* 13.2, 6.0, 2.7 Hz, 3-H), 2.00 (1 H, br s, OH), 1.86 (1 H, ddd, *J* 13.2, 9.3, 6.3 Hz, 3-H), and 1.22 (3 H, d, *J* 6.5 Hz, Me); *m/z* 175 (M^+ + H), 156, 130, 117, 101, 98, 57, and 43; and (±) methyl (2*R*,4*R*,5*R*)-4-hydroxy-5-methyltetrahydrofuran-2-ylacetate (**9**) as a colourless oil; $\nu_{max.}$(film) 3 430 and 1 737 cm^{-1}; δ_H (250 MHz) 4.43—4.51 (1 H, m, 2-H), 3.99—4.05 (2 H, m, 4-H and 5-H), 3.70 (3 H, s, OMe), 2.75 (1 H, dd, *J* 15.9, 6.4 Hz, 2'-H) 2.64 (1 H, dd, *J* 15.8, 6.0 Hz, 2'-H), 2.47 (1 H, ddd, *J* 13.8, 8.0, 6.2 Hz, 3-H), 2.00 (1 H, br s, OH), 1.75 (1 H, ddd, *J* 13.6, 5.9, 4.6 Hz, 3-H), and 1.17 (3 H, d, *J* 6.4 Hz, Me); *m/z* 175 (M^+ + H), 156, 130, 117, 101, 98, 57, and 43.

Hydrogenation of Compound (**6**) *to* (**10**).—Compound (**6**) (3.1032 g, 10.8 mmol) was stirred in methanol (50 ml) with Raney nickel (W4; *ca.* 1 g) under hydrogen (80 p.s.i.) for 8 h at room temperature. The catalyst was then filtered off and the filtrate evaporated to a cloudy colourless oil. This was purified by chromatography on silica gel (100 g) eluting with 10% ether in light petroleum to give *methyl* cis-4-*dimethyl-t-butylsilyloxy*-5-*methyltetrahydrofuran*-2-*ylacetate* (**10**) (2.2137 g, 71%) as a colourless oil; $\nu_{max.}$(film) 1 733 cm^{-1}; δ_H (250 MHz) 4.23 (1 H, dddd, *J* 8.0, 6.9, 6.9, 5.2 Hz, 2-H), 4.11 (1 H, ddd, *J* 6.0, 3.9, 2.4 Hz, 4-H), 3.80 (1 H, dq, *J* 6.3, 3.8 Hz, 5-H), 3.63 (3 H, s, OMe), 2.74 (1 H, dd, *J* 15.6, 6.9 Hz, 2'-H), 2.53 (1 H, dd, *J* 15.6, 6.9 Hz, 2'-H), 2.30 (1 H, ddd, *J* 13.5, 8.0, 5.7 Hz, 3-H), 1.60 (1 H, ddd, *J* 13.3, 5.2, 2.5 Hz, 3-H), 1.15 (3 H, d, *J* 6.3 Hz, Me), 0.85 (9 H, s, Bu^t), and 0.01 (6 H, s, SiMe); δ_C (22.51 MHz) 170.7 (s, MeO_2C), 78.5 (d, C-4), 73.1 (d, C-2 or -5), 72.9 (d, C-2 or -5), 50.5 (q, MeO_2C), 40.9 (t, C-2' or -3), 40.7, (t, C-2' or -3), 25.1 (q, SiMe and CMe_3), 17.4 (s, CMe_3), and 14.5 (q, Me); *m/z* (no M^+), 273, 231, 131, and 83 (Found: C, 58.13; H, 10.03. $C_{14}H_{28}O_4Si$ requires C, 58.29; H, 9.78%).

Deprotection of Compound (**10**) *to* (**11**) *with TBAF*.—The silyl ether (**10**) (1.01 g, 3.51 mmol) was stirred in dry THF (30 ml) at room temperature and 1M-TBAF in THF (10 ml, 10 mmol, *ca.* 3 equiv.) added. The mixture was stirred for 3 h at room temperature prior to the addition of water (20 ml) and ether (30 ml). The organic phase was separated, the aqueous phase extracted with ether (3 × 30 ml) and the combined organic extracts washed with brine (50 ml), dried, and filtered. The filtrate was evaporated to give a yellow oil (689.05 mg) which was purified by chromatography on silica gel (50 g) eluting with ether to give *methyl* cis-4-*hydroxy*-5-*methyltetrahydrofuran*-2-*ylacetate* (**11**) (79.09 mg, 13%) as a colourless oil; $\nu_{max.}$ (film) 3 600—3 100br and 1 730 cm^{-1}; δ_H (250 MHz) 4.19 (1 H, dddd, *J* 9.1, 5.9, 5.4, 5.2 Hz, 2-H), 4.11 (1 H, br m, 4-H), 3.75 (1 H, dq, *J* 6.3, 3.2 Hz, 5-H), 3.70 (3 H, s, OMe), 2.80 (1 H, br s, OH), 2.77 (1 H, dd, *J* 16.6, 5.4 Hz, $CH_AH_BCO_2Me$), 2.69 (1 H, dd, *J* 16.6, 5.2 Hz, $CH_AH_BCO_2Me$), 2.47 (1 H, ddd, *J* 14.1, 9.1, 6.3 Hz, 3-H), 1.81 (1 H, ddd, *J* 14.2, 5.9, 1.4 Hz, 3-H), and 1.29 (3 H, d, *J* 6.3 Hz, Me); *m/z* (no M^+), 156, and 143 (Found: C, 55.25; H, 8.3. $C_8H_{14}O_4$ requires C, 55.15; H, 8.10%).

Protection of Compound (**11**) *with Dimethyl-t-butylsilyl Trifluoromethanesulphonate to Compound* (**10**).—The alcohol (**11**) (289 mg, 1.66 mmol), 2,6-dimethylpyridine (386 µl, 3.31 mmol, 2.0 equiv.) and dimethyl-t-butylsilyl trifluoromethanesulphonate (658 µl, 2.87 mmol, 1.7 equiv.) were stirred in dry CH_2Cl_2 (15 ml) under argon at room temperature. After 2 h, saturated aqueous sodium hydrogen carbonate (50 ml) was added, the organic phase separated, and the aqueous phase extracted with CH_2Cl_2 (3 × 20 ml). The organic phases were combined, dried, filtered through silica gel and the filtrate evaporated to leave a pale yellow oil. The oil was purified by chromatography on silica gel (25 g) eluting with 20% ether in light petroleum to yield *methyl* cis-5-*methyl*-4-*dimethyl-t-butylsilyloxytetrahydrofuran*-2-*ylacetate* (**10**) (472 mg, 98%) as a nearly colourless oil identical in all respects with prepared previously.

Deprotection of Compound (**6**) *with Tetrabutylammonium Fluoride* (*TBAF*).—Deprotection of the silyl ether (**6**) (1.5482 g, 5.41 mmol) under the same conditions as used for compound (**5**) above gave *methyl* (E)-cis-4-*hydroxy*-5-*methyltetrahydrofuran*-2-*ylideneacetate* (**12**) (563 mg, 60%) as a white solid; $\nu_{max.}$($CHCl_3$) 3 597br, 1 699, 1 643, and 1 125 cm^{-1}; δ_H (250 MHz) 5.35 (1 H, br t, *J* 1.5 Hz, $CHCO_2Me$), 4.34—4.42 (2 H (2 H, m, 4-H and 5-H), 3.66 (3 H, s, OMe), 3.52 (1 H, br d, *J* 18.6 Hz, 3-H), 3.08 (1 H, ddd, *J* 18.7, 5.1, 2.4 Hz, 3-H), 2.12 (1 H, br s, OH), and 1.42 (3 H, d, *J* 6.2 Hz, Me); δ_C (22.51 MHz) 174.8 (s, C-2), 169.3 (s, CO_2Me), 90.1 (d, $CHCO_2Me$), 83.3 (d, C-5), 70.5 (d, C-4), 50.8 (q, CO_2Me), 41.1 (t, C-3), and 13.3 (q, Me); *m/z* 173 and 172 (M^+) (Found: C, 55.62; H, 7.05. $C_8H_{12}O_4$ requires C, 55.81; H, 7.02%).

Hydrogenation of Compound (**12**) *to* (**11**) *using Raney Nickel Catalyst*.—Compound (**12**) (312.3 mg, 1.81 mmol) was stirred in methanol (5 ml) with Ni(R) (W4; *ca.* 100 mg) under hydrogen (100 p.s.i.) for 16 h. The mixture was then filtered through silica gel and the filtrate evaporated and purified by chromatography through silica gel (12 g) eluting with ether to give *methyl* cis-4-*hydroxy*-5-*methyltetrahydrofuran*-2-*ylacetate* (**11**) (205 mg, 65%) as a colourless oil, identical in all respects with (**11**) obtained previously.

Esterification of Compound (**11**) *to* (**13**).—The alcohol (**11**) (54.22 mg, 0.31 mmol) was stirred at room temperature with triphenylphosphine (163.4 mg, 0.62 mmol, 2.0 equiv.) and 3,5-dinitrobenzoic acid (139.7 mg, 0.66 mmol, 2.1 equiv.) under argon in dry THF (10 ml) and diethyl azadicarboxylate (100 µl, 0.62 mmol, 2.0 equiv.) was added. The mixture was stirred overnight, treated with water (20 ml) and then extracted with CH_2Cl_2 (3 × 20 ml). The organic phase was dried, filtered and the filtrate evaporated to give a yellow solid (352.5 mg). Purification of this by chromatography on silica gel (30 g) eluting with 60% ether in light petroleum gave *methyl* 4-(3,5-*dinitrobenzoyloxy*)-5-*methyltetrahydrofuran*-2-*ylacetate* (**13**) (108.5 mg, 95%) as a white solid, m.p. 90—91 °C; $\nu_{max.}$ 1 731, 1 547, 1 344, 1 276, and 1 163 cm^{-1}; δ_H (250 MHz) 9.25 (1 H, t, *J* 2.2 Hz, aryl 4-H), 9.15 (2 H, d, *J* 2.2 Hz, aryl 2-H and 6-H), 5.22 (1 H, dt, *J* 6.9, 1.6 Hz, 4-H), 4.56 (1 H, m, 2-H), 4.21 (1 H, dq, *J* 6.5, 2.6 Hz, 5-H), 3.73 (3 H, s, OMe), 2.75 (1 H, dd, *J* 15.8, 6.9 Hz, $CH_AH_BCO_2Me$), 2.63 (1 H, dd, *J* 15.8, 6.0 Hz, $CH_AH_BCO_2Me$), 2.36 (1 H, ddd, *J* 14.0, 5.2, 1.4 Hz, 3-H), 2.10 (1 H, ddd, *J* 14.1, 10.4, 6.4, Hz, 3-H), and 1.38 (3 H, d, *J* 6.5 Hz, Me); *m/z* (no M^+), 353, 337, 195, and 157 (Found: C, 48.85; H, 4.25; N, 7.45. $C_{15}H_{16}N_2O_9$ requires C, 48.91; H, 4.39; N, 7.61%).

Crystallographic Analysis of Compound (**4**).—Crystals of $C_{20}H_{30}O_4SeSi$ are triclinic with a = 10.112(3), b = 10.179(3), c = 12.791(4) Å, α = 68.68(2), β = 74.23(3), γ = 64.93(2) Å, U = 1 100 $Å^3$, space group $P\bar{1}$, Z = 2, M = 441.5, D_c = 1.34 g cm^{-3} μ(Cu-K_α) = 30 cm^{-1}. Refined unit cell parameters were obtained by centering 15 reflections on a Nicolet R3m diffractometer. 2 254 Independent reflections were measured (θ < 50°) with Cu-K_α radiation (graphite monochromator) and using the ω-scan technique. Of these 2 037 had $|F_o| > 3\,\sigma(|F_o|)$ and were considered to be observed. The data were corrected for Lorentz and polarisation factors. No absorption correction was applied.

The structure was solved by direct methods and the non-hydrogen atoms refined anisotropically. The position of all hydrogen atoms were idealised (C–H = 0.96 Å), assigned isotropic thermal parameters, U(H) = 1.2U_{eq}(C), and allowed

Table 1. Atomic co-ordinates ($\times 10^4$)

Atom	*x*	*y*	*z*
Se	−3 064(1)	2 545(1)	4 259(1)
Si	758(1)	2 277(1)	2 191(1)
O(1)	−3 670(2)	3 369(3)	965(2)
C(2)	−3 141(3)	2 489(4)	2 050(3)
C(3)	−1 479(3)	1 725(4)	1 755(3)
C(4)	−1 381(4)	1 580(4)	596(3)
C(5)	−2 683(3)	2 858(4)	119(3)
C(6)	−2 987(4)	3 523(4)	−941(3)
C(7)	−1 966(4)	3 112(4)	−1 906(3)
O(7)	−781(3)	2 096(3)	−1 896(2)
O(8)	−2 506(3)	4 055(3)	−2 876(2)
C(9)	−1 558(5)	3 863(5)	−3 913(3)
C(10)	−3 668(4)	3 554(4)	2 762(3)
C(11)	−4 875(4)	2 414(4)	5 168(3)
C(12)	−5 762(5)	1 939(5)	4 873(4)
C(13)	−7 034(5)	1 800(6)	5 605(5)
C(14)	−7 367(5)	2 090(5)	6 609(4)
C(15)	−6 482(5)	2 559(6)	6 898(4)
C(16)	−5 226(5)	2 726(5)	6 175(4)
O(17)	−749(2)	2 688(2)	1 679(2)
C(18)	2 404(4)	2 034(4)	1 063(3)
C(19)	377(5)	3 918(5)	2 685(4)
C(20)	1 085(4)	524(5)	3 384(4)
C(21)	3 752(5)	1 834(6)	1 536(5)
C(22)	2 113(6)	3 424(6)	30(4)
C(23)	2 769(5)	639(6)	709(5)

Table 2. Bond lengths (Å)

Se–C(10)	1.940(3)	Se–C(11)	1.913(4)
Si–O(17)	1.652(3)	Si–C(18)	1.876(3)
Si–C(19)	1.850(6)	Si–C(20)	1.848(4)
O(1)–C(2)	1.452(4)	O(1)–C(5)	1.349(4)
C(2)–C(3)	1.528(4)	C(2)–C(10)	1.501(6)
C(3)–C(4)	1.515(6)	C(3)–O(17)	1.422(5)
C(4)–C(5)	1.485(4)	C(5)–C(6)	1.331(5)
C(6)–C(7)	1.443(5)	C(7)–O(7)	1.206(4)
C(7)–O(8)	1.348(4)	O(8)–C(9)	1.433(4)
C(11)–C(12)	1.365(8)	C(11)–C(16)	1.357(7)
C(12)–C(13)	1.398(7)	C(13)–C(14)	1.344(8)
C(14)–C(15)	1.355(10)	C(15)–C(16)	1.388(7)
C(18)–C(21)	1.545(8)	C(18)–C(22)	1.527(5)
C(18)–C(23)	1.513(8)		

to ride on their parent atoms. A ΔF map revealed the orientation of all the methyl groups. These groups were refined as rigid bodies. Refinement was by block-cascade full-matrix least-squares to $R = 0.034$, $R_w = 0.037$, [$w^{-1} = \sigma^2(F) + 0.000\,36F^2$]. Computations were carried out on an Eclipse SI40 computer using the SHELXTL program system.[10]

The atomic co-ordinates, bond lengths, and bond angles are listed in Tables 1, 2, and 3 respectively. The fractional co-ordinates of the hydrogen atoms and isotropic thermal parameters and the anisotropic thermal parameters for the non-hydrogen atoms have been deposited as Supplementary Data. [SUP No. 56407 (3 pp.)]* and the tables of structure factors are available from the Editorial Office on request.

Table 3. Bond angles (°)

C(10)–Se–C(11)	101.2(2)	O(17)–Si–C(18)	110.8(2)
O(17)–Si–C(19)	104.6(2)	C(18)–Si–C(19)	111.0(2)
O(17)–Si–C(20)	110.5(2)	C(18)–Si–C(20)	109.2(2)
C(19)–Si–C(20)	110.7(2)	C(2)–O(1)–C(5)	110.6(2)
O(1)–C(2)–C(3)	104.8(2)	O(1)–C(2)–C(10)	107.0(2)
C(3)–C(2)–C(10)	117.9(4)	C(2)–C(3)–C(4)	101.4(3)
C(2)–C(3)–O(17)	110.0(3)	C(4)–C(3)–O(17)	110.5(3)
C(3)–C(4)–C(5)	104.5(3)	O(1)–C(5)–C(4)	109.4(3)
O(1)–C(5)–C(6)	119.1(2)	C(4)–C(5)–C(6)	131.5(3)
C(5)–C(6)–C(7)	123.1(3)	C(6)–C(7)–O(7)	127.2(3)
C(6)–C(7)–O(8)	110.4(3)	O(7)–C(7)–O(8)	122.4(3)
C(7)–O(8)–C(9)	116.7(3)	Se–C(10)–C(2)	112.3(2)
Se–C(11)–C(12)	122.7(3)	Se–C(11)–C(16)	117.5(4)
C(12)–C(11)–C(16)	119.7(4)	C(11)–C(12)–C(13)	119.7(5)
C(12)–C(13)–C(14)	120.5(6)	C(13)–C(14)–C(15)	119.6(5)
C(14)–C(15)–C(16)	120.8(5)	C(11)–C(16)–C(15)	119.8(6)
Si–O(17)–C(3)	129.5(2)	Si–C(18)–C(21)	109.2(3)
Si–C(18)–C(22)	110.2(2)	C(21)–C(18)–C(22)	109.2(4)
Si–C(18)–C(23)	110.9(3)	C(21)–C(18)–C(23)	107.9(3)
C(22)–C(18)–C(23)	109.4(4)		

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