Acyl Radical Cyclizations in Synthesis. Part 3. Synthesis of (±)-*trans*-3,5-Bis-(t-butyldimethylsiloxy)-2-Methylenecyclohexanone, an 'A' Ring Model for 1α, 25-Dihydroxyvitamin D_3

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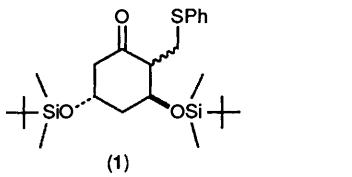
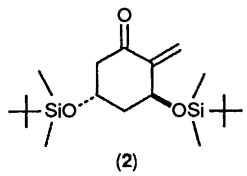
A concise synthesis of (±)-*trans*-3,5-bis(t-butyldimethylsiloxy)-2-methylenecyclohexanone has been developed. The synthesis proceeds in seven steps from ethyl acetoacetate and involves a highly efficient acyl radical cyclization to construct the six-membered ring.

In parts 1[1] and 2[2] of this series we established that hept-6-enoyl radicals bearing ether-type functionality at the 5-(allylic) position undergo cyclization relatively inefficiently giving *ultimately* the *endo*-mode ring-closed radical.

Transposition of the ether function to the 3-position led, on the other hand, predominantly to the *exo*-mode ring-closed radical in good yield.[1,2] Substitution of both the 3- and 5-position resulted in highly efficient cyclization giving a *ca.* 3:1 mixture of *exo*- and *endo*-mode ring-closure products, respectively.[1,2] Furthermore we noted that incorporation of a phenylthio residue at the terminal olefinic (7-) position overrode the effect of a 5-alkoxy residue in the form of an ethylene acetal, and directed cyclization efficiently to the *exo*-mode.[2] We report here, in full,[3] a synthesis of (±)-2-phenylthiomethyl-3,5-bis(t-butyldimethylsiloxy)cyclohexanone (**1**) and thence 'by controlled oxidation and *syn*-elimination' of enone (**2**), an 'A' ring model for 1α,25-dihydroxyvitamin D_3 (**3**),[4] in which the pivotal acyl radical cyclization takes place exclusively *exo*- and in excellent yield owing to a judicious combination of the factors outlined above.



(1)



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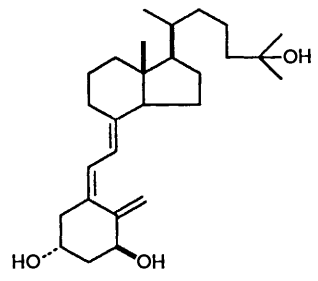

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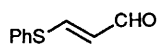

(4)

The entire carbon backbone of the crucial acyl radical precursor (**11**) was assembled in a single step by reaction of the mixed lithium sodium salt[5] of the ethyl acetoacetate dianion with (*E*)-3-(phenylthio)acrolein (**4**) to give the aldol product (**5**) in 70% isolated yield (Scheme 1). In this manner, and with the obvious exception of the key cyclization, the remainder of the synthesis was reduced to a sequence of functional-group manipulation and protection steps. The aldehyde (**4**) was prepared by conjugate addition of thiophenol to acrolein followed by chlorination with *N*-chlorosuccinimide (NCS) and finally dehydrochlorination according to a procedure described[6] by Bakuzis for the preparation of 3-phenylthioacrylonitrile from acrylonitrile. The overall yield for this 2-pot, 3-step procedure, operable on a multigram scale, was 38%. Reduction of ester (**5**) to a mixture of the racemic *anti*- and *syn*-diols (**6**) and (**7**) was achieved with tetramethylammonium triacetoxyborohydride in a mixture of acetonitrile and acetic acid at −30 °C according to the method of Evans[7] (Scheme 1). The ratio of products (**6**) to (**7**) and the combined yield of this reduction was found to vary with the hydride source (commercial,‡ prepared and isolated, or prepared *in situ* from tetramethylammonium borohydride[8] and acetic acid) in the ranges 4:1 to 10:1 and 53–83%, respectively. Eventually a procedure employing *in situ* preparation of the triacetoxyborohydride and leading to an 83% yield of a 4:1 mixture of compounds (**6**) and (**7**) was found to be the most convenient. It proved possible, albeit inefficient, to isolate the pure *anti*-diol from this mixture by crystallization, hence the mixture was usually carried forward to the next step. The configuration of the major isomer was initially assigned to be *anti*, in accordance with the mechanistic rationale of Evans.[7] This assignment was subsequently verified by analysis of the ^1H NMR spectra of the cyclohexanones (**2**), (**13**), and (**14**). Attempts at the stereoselective reduction of the aldol compound (**5**) to the *anti*-diol (**6**) by means of dimethyl- or diisopropyl-silyl chloride according[9] to Davis' method were unsuccessful due to the incompatibility of the thioenol function with the reaction conditions. Reduction with sodium borohydride in ethanol gave a 2:3 mixture of diols (**6**) and (**7**). Protection of the 4:1 mixture of diols with t-butyldimethylsilyl chloride and imidazole in *N*,*N*-dimethylformamide (DMF) gave the *anti*- and *syn*-bis(t-butyldimethylsilyl) ethers (**8**) and (**9**) in 70 and 16% yield, respectively, after separation by chromatography on silica gel (Scheme 1). Silylation of the pure crystalline diol (**6**) in the same manner provided compound (**8**) in 81% yield.

Saponification of compound (**8**) with potassium hydroxide in aq. tetrahydrofuran (THF) overnight at room temperature provided the acid (**10**) in 88% yield (Scheme 2). The so-formed acid was converted into the corresponding acyl radical precursor—the acyl selenide (**11**)—by reaction with *N*-(phenylseleneno)phthalimide (NPSP) and tributylphosphine according to the method of Grieco[10] in 77% isolated yield. Alternatively, compound (**11**) was prepared from acid (**10**) by

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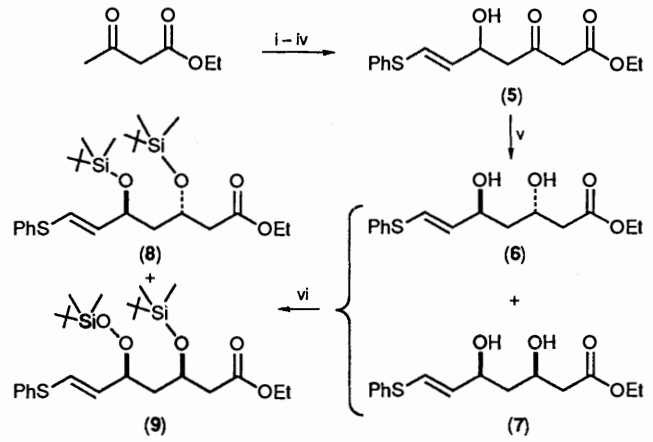
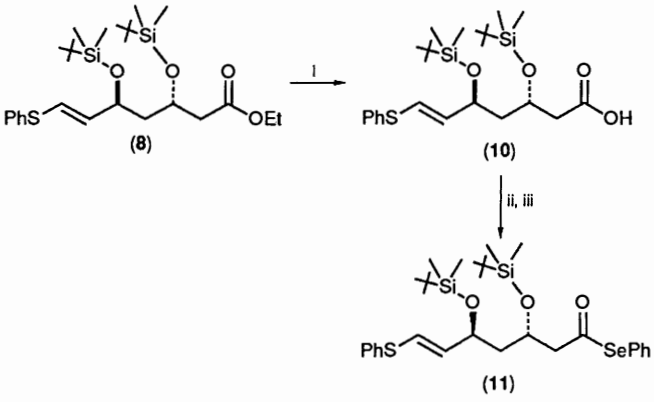
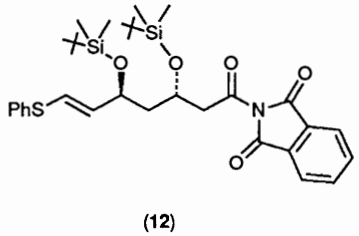


Scheme 1. *Reagents:* i, NaH; ii, BuLi; iii, (**4**); iv, H_3O^+; v, $Me_4N^+ {}^-B(OAc)_3H$; vi, Bu^{t}MeSiCl, imidazole.

reaction first with triethylamine and then with the combination of benzeneselenenyl chloride and tributylphosphine in 73% yield (Scheme 2). In general we prefer and recommend the latter procedure, which we have elaborated into a general method[11] compatible with various functional groups and demanding steric environments, owing to the significantly lower cost* and/or shorter laboratory preparation of benzeneselenenyl chloride over that of NPSP.[12] Furthermore we found that in order to obtain high yields from the Grieco procedure it was necessary to use highly purified NPSP otherwise the formation of significant amounts of the *N*-acyl phthalimide (**12**) was observed.

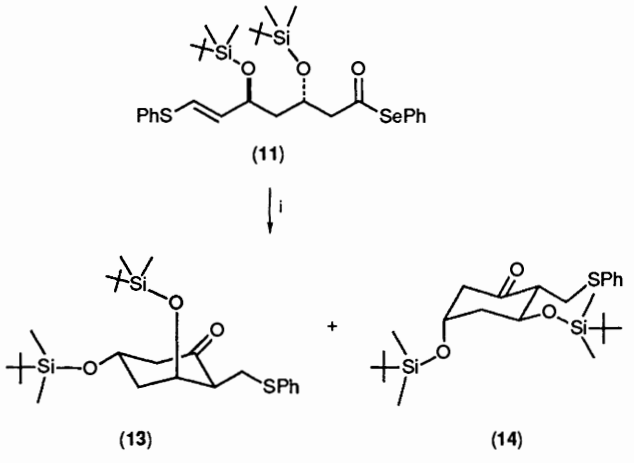


Scheme 2. *Reagents and conditions:* i, KOH, aq. THF; ii, Et_3N; iii, PhSeCl, PBu_3.



(**12**)

The scene was now set for the all-important radical cyclization. Dropwise addition, during 5 min, of freshly distilled tributylstannane in benzene containing a catalytic quantity of azoisobutyronitrile (AIBN) to a solution of *anti*-compound (**11**) in benzene at reflux under nitrogen provided the diastereoisomeric cyclohexanones (**13**) and (**14**) in virtually quantitative combined yield in the ratio 1:1.2 (Scheme 3). For the purposes of this synthesis the separation of compounds (**13**) and (**14**) is strictly not necessary as both in principle are precursors to the target molecule (**2**); however, separation was carried out for the purpose of characterization and to rule out conclusively the possibility that the mixture was one of *exo*- and *endo*-mode ring-closure products. Several points relating to this cyclization are worthy of emphasis. The yield was reproducibly excellent, varying between 91–98%, on both the 1- and 3.6-mmol scale. Impractical, slow addition (or the use of syringe-pump techniques) for the addition of the stannane were not necessary—indeed in our opinion and experience such methods in the limit can often prove detrimental to overall yield owing to the breakdown of radical chain-propagation. The high yield is almost certainly due to a combination of the Thorpe–Ingold effect (restricted conformational mobility) and the ability of the phenylthio group to stabilize the ring-closed radical and so prevent ring opening and/or expansion.[2] To the best of our knowledge all efficient 6-*exo*-mode radical cyclizations, be they of the acyl, alkyl, aryl or vinyl type, benefit from some form of restricted conformational mobility.[13] Finally the products (**13**) and (**14**) were isolated virtually free of contamination by stannyl residues by simple evaporation of the solvent and chromatography on silica gel, so reflecting the practical superiority of selenium reagents over the corresponding bromides and iodides in tin hydride reactions, where purification is frequently a problem.



Scheme 3. *Reagents and conditions:* i, Bu_3SnH, AIBN, 80 °C.

The crystalline cyclohexanone (**13**) was carefully oxidized according to Heaney's method[14] with 1 molar equivalent of magnesium monoperoxyphthalate in ethanol at room temperature to give the corresponding sulphoxides which, after extractive work-up, were pyrolysed in benzene at reflux in the presence of 2,3-dihydropyran as a scavenger for benzenesulphenic acid to yield the crystalline target molecule (**2**) in 60% isolated yield for the two steps. Controlled oxidation and pyrolytic *syn*-elimination of the phenylthio moiety of compound (**14**) provided target compound (**2**) in a similar manner.

In a further demonstration of the efficiency of cyclization of appropriately substituted hept-6-enoyl radicals the *syn*-bis-silyl ether (**9**) was converted, *via* the acid (**15**) to the selenol ester (**16**) which on treatment with tributylstannane and AIBN in benzene at reflux provided the cyclohexanones (**17**) and (**18**) in 81% isolated yield as a 1.1:1 mixture of stereoisomers in which the all *cis*-isomer predominated (Scheme 4).

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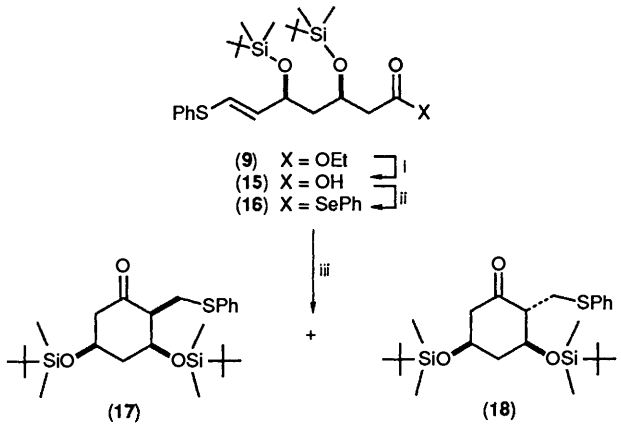

Scheme 4. *Reagents:* i, KOH; ii, Et_3N, PhSeCl, PBu_3; iii, Bu_3SnH, AIBN.

In conclusion we have developed a concise, practical entry into the stable, crystalline α-methylenecyclohexanone (**2**) which proceeds in seven steps and 17% yield from ethyl acetoacetate. Efforts, currently underway, to establish a practical asymmetric entry into (5*S*)-(**5**) and hence into (3*S*,5*S*)-(**2**) and to develop a method for the construction of an appropriate two-carbon unit onto the ketone group of compound (**2**) will be reported in due course.

Experimental

The general Experimental conditions are as in Part 1.[1]

(E)-3-(*Phenylthio*)*propenal* (**4**).—To a stirred solution of thiophenol (10 ml, 98 mmol) in chloroform (75 ml) under nitrogen at 0 °C was added triethylamine (0.7 ml, 5.1 mmol) dropwise during 10 min. Acrolylaldehyde (6.6 ml, 99 mmol) was then added dropwise during 15 min such that the temperature of the reaction mixture did not exceed 5 °C. After being stirred for a further 1 h at 0 °C the reaction mixture was allowed to warm to room temperature, then was poured into diethyl ether (250 ml) and washed successively with aq. sodium hydroxide (2M; 2 × 100 ml), water (2 × 100 ml), and brine (100 ml). After being dried over magnesium sulphate, filtered and evaporated under reduced pressure, the product mixture provided crude 3-(phenylthio)propanal as a pale green oil (13.31 g, 82%) with δ (200 MHz) 2.75 (2 H, t), 3.16 (2 H, t), 7.18–7.37 (5 H, m), and 9.74 (1 H, br s), which was used without further purification.

The thus prepared saturated aldehyde (13.00 g, 78.2 mmol), as a solution in benzene (75 ml), was added dropwise during 20 min to an ice-cooled, stirred solution of NCS (15.67 g, 117.3 mmol) under nitrogen in benzene (100 ml) such that the reaction temperature did not rise above 1 °C. The reaction mixture was stirred for a further 2.5 h at 0 °C before a solution of triethylamine (3.96 g, 39 mmol) in benzene (20 ml) was added dropwise during 15 min, during which time the reaction temperature did not exceed 5 °C. The reaction mixture was then allowed to warm to room temperature and was then poured into diethyl ether (500 ml) and washed successively with dil. hydrochloric acid (2M; 3 × 150 ml), water (2 × 200 ml), and brine (100 ml). The mixture was dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give a golden brown oil (12.06 g) which, after purification by chromatography on silica gel [eluant light petroleum (40–60 °C)–diethyl ether (3:1)], gave the title αβ-unsaturated aldehyde (**4**) as a pale yellow oil (5.98 g, 47%), δ (200 MHz) 5.96 (1 H, dd, *J* 18.0, 8.4 Hz), 7.53 (5 H, br s), 7.63 (1 H, d, *J* 18.0 Hz), and 9.40 (1 H, d, *J* 8.4 Hz) [lit.,[15] δ 5.90 (1 H, dd, *J* 16.0, 7 Hz), 7.40 (5 H, s), 7.54 (1 H, d, *J* 16.0 Hz), and 9.33 (1 H, d, *J* 7.0 Hz)].

(±)-*Ethyl* (E)-5-*Hydroxy*-3-*oxo*-7-(*phenylthio*)*hept*-6-*enoate* (**5**).—Ethyl acetoacetate (1.57 g, 12 mmol) was added dropwise during 20 min to a stirred suspension of sodium hydride (80% dispersion; 0.40 g, 13 mmol) in THF (25 ml) at 0 °C under nitrogen. The mixture was stirred for a further 10 min at 0 °C, and when effervescence had ceased a solution of butyl-lithium in hexane (2.1M; 6.3 ml, 13 mmol) was added during 20 min and the reaction mixture was then stirred at 0 °C for 50 min. To the stirred, resultant orange-yellow solution under nitrogen at 0 °C was added a solution of aldehyde (**4**) (1.80 g, 11.0 mmol) in THF (10 ml) during 30 min. The reaction mixture was stirred for a further 30 min at 0 °C and was then poured into cold diethyl ether (50 ml)–hydrochloric acid (2M; 50 ml). The organic phase was further diluted with diethyl ether (50 ml) and was then washed successively with hydrochloric acid (2M; 2 × 50 ml), water (2 × 50 ml), and brine (50 ml) and dried ($MgSO_4$). Filtration, concentration under reduced pressure, and chromatography on silica gel [eluant diethyl ether–light petroleum (40–60 °C) (3:2)] of the crude reaction mixture afforded the *title ester* (**5**) as an orange oil (2.07 g, 64%), δ(200 MHz) 1.24 (3 H, t), 2.75 (2 H, d, *J* 5.8 Hz, 4-H_2), 3.07 (1 H, br s, OH), 3.45 (2 H, s, 2-H_2), 4.12 (2 H, q), 4.65 (1 H, m, 5-H), 5.76 (1 H, dd, *J* 15.0, 6.0 Hz, 6-H), 6.48 (1 H, dd, *J* 15.2, 1.25 Hz, 7-H), and 7.30 (5 H, m); ν_{max}($CHCl_3$) 3 472, 2 978, 1 738, 1 708, 1 581, 1 317, 1 024, and 943 cm^{-1}; *m/z* 294.0942 ($M^{+\cdot}$ $C_{15}H_{18}O_4S$ requires *M*, 294.0926), 276, 248, 230, 189, 167 (100%), 139, 128, 121, 110, 109, 95, 94, 65, and 51.

(±)-*Ethyl* (E)-3,5-anti-*Dihydroxy*-7-(*phenylthio*)*hept*-6-*enoate* (**6**).—To a stirred solution of tetramethylammonium borohydride (1.48, 16.6 mmol) in dry acetonitrile (20 ml) at 10 °C under nitrogen was added glacial acetic acid (4.0 ml) during 20 min. When effervescence had ceased, the reaction mixture was cooled to 0 °C, further glacial acetic acid (15.0 ml) was added, and the temperature was lowered to −30 °C. To this stirred solution was added a solution of the hydroxy ketone (**5**) (0.77 g, 2.6 mmol) in acetonitrile (5 ml) during 15 min. After completion (TLC control, 90 min) the cold reaction mixture was poured into a mixture of diethyl ether (250 ml) and aq. sodium potassium tartrate (0.5M; 100 ml). The organic layer was washed successively with further aq. sodium potassium tartrate (100 ml), water (2 × 100 ml), and brine (100 ml), then dried ($MgSO_4$). Filtration, and concentration of the ethereal solution under reduced pressure, afforded a yellow oil which, after chromatography on silica gel [eluant light petroleum–diethyl ether (4:1)], yielded a pale yellow oil (0.65 g, 83%) which consisted of a 4:1 mixture of the racemic *anti*- and *syn*-diols (**6**) and (**7**). By crystallization from light petroleum–diethyl ether a sample of the anti-*diol* (**6**) was obtained as needles, m.p. 48–50 °C; δ(200 MHz) 1.27 (3 H, t), 1.54–1.86 (2 H, m, 4-H_2), 2.49 (2 H, d, *J* 4.9 Hz, 2-H_2), 3.29 (2 H, br s, OH), 4.18 (2 H, q), 4.27–4.43 (1 H, m, 3-H), 4.44–4.59 (1 H, m, 5-H), 5.77 (1 H, dd, *J* 16.8, 6.0 Hz, 6-H), 6.51 (1 H, d, *J* 16.4 Hz, 7-H), and 7.23–7.39 (5 H, m); ν_{max}($CHCl_3$) 3 486, 2 985, 1 715, 1 611, 1 581, 1 475, 1 374, 1 307, 1 190, 1 090, 1 067, 1 020, and 947 cm^{-1} (Found: C, 61.0; H, 6.8. $C_{15}H_{20}O_4S$ requires C, 60.79; H, 6.80%).

(±)-*Ethyl* (E)-3,5-anti-*Bis*(*t-butyldimethylsiloxy*)-7-(*phenylthio*)*hept*-6-*enoate* (**8**) *and* (±)-*Ethyl* (E)-3,5-syn-*Bis*(*t-butyldimethylsiloxy*)-7-(*phenylthio*)*hept*-6-*enoate* (**9**).—To a stirred solution of t-butyldimethylsilyl chloride (3.00 g, 20.0 mmol) and imidazole (3.0 g, 44.1 mmol) in dry DMF (15 ml) at room temperature under nitrogen was added a 4:1 mixture of the diols (**6**) and (**7**) (3.00 g, 10.1 mmol). The resulting solution was stirred at room temperature for 18 h, then poured into water (250 ml) and extracted with diethyl ether (3 × 100 ml). The extracts were washed successively with hydrochloric acid (2M; 3 × 100 ml), water (3 × 100 ml), and brine (100 ml), then dried

($MgSO_4$), filtered, and concentrated under reduced pressure to give a golden oil (4.66 g), chromatography of which on silica gel [eluant light petroleum–diethyl ether (20:1)] afforded first the *anti*-bis-silyl ether (**8**) as an oil (3.71 g, 70%), δ(400 MHz) −0.06 (6 H, s), −0.07 (6 H, s), 0.87 (9 H, s), 0.89 (9 H, s), 1.24 (3 H, t), 1.82–1.67 (2 H, m, 4-H_2), 2.49 (2 H, m, 2-H_2), 4.12 (2 H, q), 4.22–4.31 (2 H, m, 3- and 5-H), 5.78 (1 H, dd, *J* 15.2, 7.3 Hz, 6-H), 6.32 (1 H, d, *J* 15.2 Hz, 7-H), and 7.23–7.38 (5 H, m); ν_{max}(film) 3 058, 2 945, 2 885, 2 851, 1 735, 1 608, 1 581, 1 471, 1 254, 1 160, 1 307, 1 084, and 940 cm^{-1}. Further elution with the same solvent gave the *syn*-isomer (**9**), also an oil (0.83 g, 16%), δ(400 MHz) −0.08 (6 H, s), 0.01 (6 H, s), 0.87 (9 H, s), 0.90 (9 H, s), 1.25 (3 H, t), 1.60–1.85 (2 H, m), 2.50 (2 H, m), 4.13 (2 H, q), 4.21–4.34 (2 H, m), 5.84 (1 H, dd, *J* 14.6, 6.7 Hz), 6.36 (1 H, d, *J* 14.6 Hz), and 7.20–7.40 (5 H, m); ν_{max}(film) 1 735 cm^{-1}.

(±)-(E)-3,5-anti-*Bis*(*t-butyldimethylsiloxy*)-7-(*phenylthio*)-*hept*-6-*enoic Acid* (**10**).—To a solution of the ester (**8**) (0.91 g, 1.7 mmol) in a mixture of methanol (10 ml) and THF (10 ml) was added, at room temperature during 20 min, a solution of potassium hydroxide (0.55 g, 9.8 mmol) in water (3.5 ml). The reaction mixture was stirred overnight at room temperature, then poured into a mixture of diethyl ether (30 ml) and water (70 ml). After acidification to pH 4–5 with hydrochloric acid (2M; 10 ml) the organic phase was decanted off and the aq. phase was further extracted with diethyl ether (2 × 30 ml). The combined organic phases were then washed successively with water (30 ml) and brine (30 ml), dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give the crude product. Filtration on silica gel [eluant light petroleum–diethyl ether (5:1)] then gave the title acid (**10**) as an oil (0.75 g, 88%), δ(200 MHz) 0.06–0.09 (12 H, m), 0.88 (18 H, 2 s), 1.57–1.75 (2 H, m, 4-H_2), 2.36–2.58 (2 H, m, 2-H_2), 4.12–4.29 (2 H, m, 3- and 5-H), 5.63 (1 H, dd, *J* 15.7, 7.3 Hz, 6-H), 6.27 (1 H, d, *J* 15.7, Hz, 7-H), 7.17–7.34 (5 H, m), and 10.90 (1 H, br s); ν_{max}($CHCl_3$) 3 065, 2 952, 2 918, 2 858, 1 708, 1 611, 1 581, 1 471, 1 357, 1 254, 1 084, and 940 cm^{-1}.

(±)-Se-*Phenyl* (E)-3,5-anti-*Bis*(*t-butyldimethylsiloxy*)-7-(*phenylthio*)*hept*-6-*eneselenoate* (**11**).—A solution of triethylamine (0.51 g, 5.0 mmol) in dichloromethane (10 ml) was added during 3 min to a stirred solution of the acid (**10**) (2.50 g, 5.0 mmol) in dichloromethane (30 ml) under nitrogen at room temperature. After a further 10 min at room temperature the volatiles were removed under reduced pressure to yield the crude triethylammonium salt of acid (**10**). This salt was taken up in dry THF (40 ml) and added slowly during 5 min at room temperature to a stirred solution of benzeneselenenyl chloride (1.06 g, 5.5 mmol) and tributylphosphine (1.12 g, 5.5 mmol) in dry THF (50 ml) under nitrogen. After being stirred for a further 75 min at room temperature the reaction mixture was poured into a mixture of diethyl ether (300 ml) and aq. sodium hydroxide (2M; 500 ml). The aq. layer was separated and further extracted with diethyl ether (3 × 50 ml). The combined extracts were then washed successively with water (3 × 100 ml) and brine (100 ml), dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give the crude selenol ester. Chromatography of this yellow oil on silica gel [eluant light petroleum–diethyl ether (3:1)] gave the *title compound* (**11**) as an oil (2.32 g, 73%), δ(200 MHz) 0.06 (6 H, s), 0.09 (6 H, s) 0.88 (18 H, 2 s), 1.62–1.88 (2 H, m, 4-H_2), 2.90 (2 H, d, *J* 5.7 Hz, 2-H_2), 4.28–4.36 (2 H, m, 3- and 5-H), 5.78 (1 H, dd, *J* 16.0, 7.5 Hz, 6-H), 6.32 (1 H, d, *J* 15.4 Hz, 7-H), and 7.25–7.40 (10 H, m); ν_{max}($CHCl_3$) 3 058, 2 939, 2 851, 2 885, 1 721, 1 608, 1 581, 1 471, 1 461, 1 437, 1 361, 1 254, 1 084, and 1 023 (Found: C, 58.4; H, 7.5. $C_{31}H_{48}O_3SSeSi_2$ requires C, 58.55; H, 7.61%).

(2RS,3RS,5RS)-3,5-*Bis*(*t-butyldimethylsiloxy*)-2-(*phenylthiomethyl*)*cyclohexanone* (**13**) *and* (2RS,3SR,5SR)-3,5-*Bis*(*t-butyldimethylsiloxy*)-2-(*phenylthiomethyl*)*cyclohexanone* (**14**).—To a stirred solution of selenol ester (**11**) (2.30 g, 3.6 mmol) in dry benzene (30 ml) at reflux under nitrogen was added, dropwise during 5 min, a solution of tributylstannane[16] (1.21 g, 4.2 mmol) in benzene (8 ml) containing AIBN (*ca.* 10 mg). After a further 60 min at reflux the reaction was complete (TLC control) and, after cooling to room temperature, the solvents were evaporated off under reduced pressure to give an oil. Chromatography of this oil on silica gel [eluant light petroleum–diethyl ether (15:1)] yielded, first, the 2,3-cis-*cyclohexanone* (**13**) as a white, crystalline solid (0.77 g, 45%), m.p. 51–52 °C (from MeOH); δ(400 MHz) 0.016 (3 H, s), 0.019 (3 H, s), 0.05 (3 H, s), 0.08 (3 H, s), 0.82 (9 H, s), 0.84 (9 H, s), 1.73 (1 H, ddd, *J* 13.6, 10.8, 2 Hz, 4-H_{ax}), 2.20 (1 H, m, $w_{\frac{1}{2}}$ 26 Hz, 4-H_{eq}), 2.33 (1 H, ddd, *J* 13.2, 10.4, 0.8 Hz, 6-H_{ax}), 2.45 (1 H, m, $w_{\frac{1}{2}}$ 18 Hz, 2-H_{ax}), 2.67 (1 H, ddd, *J* 13.2, 5.2, 2 Hz, 6-H_{eq}), 2.81 (1 H, dd, *J* 14, 9.6 Hz, C*H*HSPh), 3.41 (1 H, dd, *J* 14, 4 Hz, CH*H*SPh), 4.26 (1 H, dddd, *J* 10.4, 10.4, 5.2, 4.8 Hz, 5-H), 4.52 (1 H, dt, *J* 2, 2 Hz, 3-H), and 7.13–7.29 (5 H, m); δ_C(100 MHz) −5.06, −4.77, −4.72, −4.42, 17.90, 17.92, 25.64, 25.71, 28.91, 42.43, 51.50, 54.01, 67.21, 68.49, 126.08, 129.08, 135.78, and 206.88; ν_{max}($CHCl_3$) 2 952, 2 925, 2 885, 2 851, 1 712, 1 601, 1 465, 1 357, 1 104, 1 057, and 993 cm^{-1} (Found: C, 62.4; H, 9.0. $C_{25}H_{44}O_3SSi_2$ requires C, 62.45; H, 9.22%).

Further elution with the same solvent gave the 2,3-*trans*-cyclohexanone (**14**) as an oil (0.93 g, 55%), δ(400 MHz) 0.023 (6 H, s), 0.34 (3 H, s), 0.067 (3 H, s), 0.84 (9 H, s), 0.89 (9 H, s), 1.84 (1 H, ddd, *J* 13.2, 9.6, 2.4 Hz, 4-H_{ax}), 2.12 (1 H, dddd, *J* 13.2, 4, 2, 2 Hz, 4-H_{eq}), 2.41 (1 H, ddd, *J* 14, 4, 2 Hz, 6-H_{eq}), 2.48 (1 H, dd, *J* 14, 3.2 Hz, 6-H_{ax}), 2.70 (1 H, ddd, *J* 8.8, 8.8, 4 Hz, 2-H_{ax}), 3.14 (1 H, dd, *J* 13.6, 8.8 Hz, C*H*HSPh), 3.21 (1 H, dd, *J* 13.6, 4 Hz, CH*H*SPh), 4.07 (1 H, ddd, *J* 9.6, 8.8, 4 Hz, 3-H_{ax}), 4.30 (1 H, m, $w_{\frac{1}{2}}$ 10 Hz, 5-H_{eq}), and 7.07–7.32 (5 H, m); δ_C(100 MHz) −5.11, −4.96, −4.73, −4.48, 17.91, 17.92, 25.61, 25.76, 28.73, 41.95, 49.04, 59.85, 66.62, 70.59, 125.23, 127.74, 128.79, 137.53, and 206.27; ν_{max}($CHCl_3$) 2 952, 2 945, 2 885, 2 858, 1 718, 1 581, 1 464, 1 254, 1 100, 1 084, 1 047, and 1 007 cm^{-1}.

(±)-trans-3,5-*Bis*(*t-butyldimethylsiloxy*)-2-*methylenecyclohexanone* (**2**).—A solution of magnesium monoperoxyphthalate[14] hexahydrate (115 mg, 0.23 mmol) in water (2 ml) was added to a stirred solution of the cyclohexanone (**13**) (200 mg, 0.42 mmol) in ethanol (3 ml) at room temperature under nitrogen. After completion of the reaction (30 min, TLC control) the mixture was poured into a mixture of chloroform (25 ml) and water (2 ml). After filtration to remove solid residues the aq. phase was further extracted with chloroform (2 × 5 ml). The combined organic phases were washed successively with aq. sodium hydrogen carbonate (5%; 15 ml) and water (15 ml) and dried ($MgSO_4$). Filtration, and evaporation of the volatiles under reduced pressure, gave the crude sulphoxides as an oil (207 mg, 99%) that solidified on storage. The sulphoxides were taken up in a mixture of benzene (7.5 ml) and 2,3-dihydropyran (2.5 ml) and brought to reflux under nitrogen for 6 h. Removal of the volatiles under reduced pressure gave a green oil, which after chromatography on silica gel [eluant light petroleum (40–60 °C)–diethyl ether (10:1)] yielded the α-*methylenecyclohexanone* (**2**) as a white, crystalline solid (92 mg, 62%), m.p. 40–44 °C; δ(200 MHz) 0.05–0.08 (12 H, m), 0.85 (9 H, s), 0.90 (9 H, s), 1.80–1.96 (1 H, m, 4-H), 2.02–2.16 (1 H, m, 4-H), 2.50–2.66 (2 H, m, 6-H_2), 4.32–4.44 (1 H, m, 3-H), 4.86–4.74 (1 H, m, 5-H), 5.43 (1 H, br s, =C*H*H), and 5.84 (1 H, br s, =CH*H*); δ_C(100 MHz) −4.99, −4.91, −4.85, −4.81, 17.97, 18.15, 25.69, 25.78, 42.05, 49.07, 65.34, 68.93, 118.73, 149.77, and 200.48; ν_{max}($CHCl_3$) 2 930, 2 884, 2 852, 1 691, 1 622, 1 461, 1 107, 1 092, 1 066, and 839 cm^{-1} (Found: C, 61.3; H, 10.6. $C_{19}H_{38}O_3Si_2$ requires C, 61.56; H, 10.33%).

(±)-(E)-3,5-syn-*Bis*(*t-butyldimethylsiloxy*)-7-(*phenylthio*)-*hept-6-enoic Acid* (**15**).—Saponification of the *syn*-ester (**9**) (1.47 g, 2.8 mmol), as described for the preparation the *anti*-acid (**10**), gave the title acid (**15**) as an oil (1.03 g, 74%), δ(200 MHz) 0.06–0.09 (12 H, m), 0.86 (9 H, s), 0.88 (9 H, s), 1.66–1.82 (2 H, m, 4-H_2), 2.38–2.65 (2 H, m, 2-H_2), 4.08–4.24 (2 H, m, 3- and 5-H), 5.68 (1 H, dd, *J* 16.2, 7.6 Hz, 6-H), 6.32 (1 H, d, *J* 16.2 Hz, 7-H), 7.15–7.34 (5 H, m), and 10.68 (1 H, br s).

(±)-Se-*Phenyl* (E)-3,5-syn-*Bis*(*t-butyldimethylsiloxy*)-7-(*phenylthio*)*hept-6-eneselenoate* (**16**).—Reaction of acid (**15**) (0.25 g, 0.5 mmol) with triethylamine and subsequently with benzeneselenenyl chloride and tributylphosphine, as described for the preparation of the *anti*-selenol ester (**11**), gave the *title selenol ester* (**16**) as a pale green oil (0.23 g, 72%), δ(200 MHz) 0.01–0.09 (12 H, m), 0.86 (9 H, s), 0.88 (9 H, s), 1.62–1.88 (2 H, m, 4-H_2), 2.90 (2 H, d, *J* 5.7 Hz, 2-H_2), 4.28–4.36 (2 H, m, 3- and 5-H), 5.78 (1 H, dd, *J* 16.3, 7.5 Hz, 6-H), 6.34 (1 H, d, *J* 16.3 Hz, 7-H), and 7.24–7.52 (10 H, m); $\nu_{max}(CHCl_3)$ 3 053, 2 942, 2 929, 2 922, 2 908, 2 852, 1 709, 1 606, 1 580, 1 462, 1 436, 1 405, 1 375, 1 361, 1 190, 1 107, 1 057, 1 040, 999, 951, 881, 845, and 826 cm^{-1} (Found: C, 58.4; H, 7.5. $C_{31}H_{48}O_3SSeSi_2$ requires C, 58.55; H, 7.61%).

Reaction of Seleno Ester (**16**) *with Tributylstannane*.—The selenol ester (**16**) (0.58 g, 0.91 mmol) was treated in benzene at reflux with tributylstannane and AIBN as described in the preparation of compounds (**13**) and (**14**). After 1 h at reflux the solvent was removed under reduced pressure and the residue was chromatographed on silica gel [eluant light petroleum–diethyl ether (15:1)] to give an inseparable mixture of the *cyclohexanones* (**17**) and (**18**) in the ratio 1.1:1 as an oil (0.36 g, 81%) (Found: C, 62.2; H, 9.6. $C_{25}H_{44}O_3SSi_2$ requires C, 62.17; H, 9.22%). The two isomers were distinguishable by ^1H NMR spectroscopy at 400 MHz, in particular by the resonances of their respective 3-H, 5-H, and CH_2SPh protons. Isomer (**17**) had δ(400 MHz) 3.18 (1 H, dd, *J* 12.8, 6.4 Hz, C*H*HSPh), 3.35 (1 H, dd, *J* 12.8, 7 Hz, CH*H*SPh), 4.00 (1 H, tt, *J* 9.6, 4.8 Hz, 5-H), and 4.21 (1 H, dt, *J* 9.6, 3.2 Hz, 3-H). Isomer (**18**) had δ(400 MHz) 3.10 (1 H, dd J 12.8, 8.6 Hz, C*H*HSPh), 3.27 (1 H, dd, *J* 12.8, 2 Hz, CH*H*SPh), 3.55 (1 H, dt, *J* 11.2, 3.2 Hz, 3-H), and 3.76 (1 H, tt, *J* 10.2, 3.8 Hz, 5-H). The 400 MHz ^1H NMR spectrum also contained a series of poorly resolved multiplets at δ 1.30 (2 × 4-H_{ax}), 1.9 (2 × 4-H_{eq}), and 2.2–2.8 (2 × 2-H and 4 × 6-H).

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