Synthetic Studies on Spirovetivane Phytoalexins. IV.[1] A Stereoselective Synthesis of (±)-3-Hydroxysolavetivone[2]

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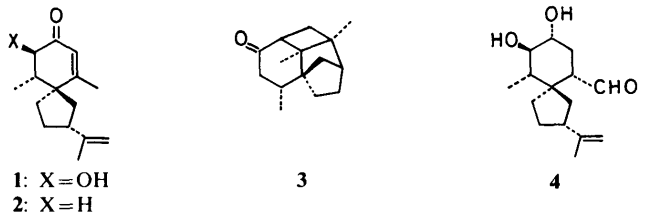
Oxidation of the silyl enol ether of (2*RS*,5*RS*,10*RS*)-6,10-dimethyl-2-pivaloyloxyspiro[4.5]dec-6-en-8-one (5) with triphenyl phosphite ozonide (TPPO) gave stereoselectively the C_9-hydroxylated derivative (6a), which was transformed into a spirovetivane phytoalexin, (±)-3-hydroxysolavetivone (1), by a several-step sequence.

Keywords spiro[4.5]decane; spirovetivane phytoalexin; total synthesis; TPPO oxidation; hydroxylation; α,β-unsaturated ketone; enol silyl ether; deacetoxylation; isopropenyl group

3-Hydroxysolavetivone (**1**) was first isolated as an aglycone of tobacco aroma sesquiterpene glucosides from flue-cured Virginia tobacco leaves in 1977.[3] More recently, it was also identified as one of the stress compounds (phytoalexins), such as solavetivone (**2**) and solanascone (**3**), in the leaves of *Nicotiana tabacum* cv *Samsun NN* or *N. tabacum* × *N. glutinosa* both infected with tobacco mosaic virus.[4] In addition to its significant antibacterial activity,[4b] this natural product is a representative member of the spirovetivane metabolites possessing the hydroxy group at the C_9 position, like oxylubimin (**4**), which is produced by potato tubers infected with fungi.[5] As a part of our continuing synthetic studies on spirovetivane phytoalexins,[1,6] we wish to present herein full details of the total synthesis of (±)-3-hydroxysolavetivone (**1**).

The synthetic plan consisted of two parts (Chart 2): i) a stereoselective preparation of a key intermediate (**6a**) by a crucial hydroxylation of the spirocyclic enone (**5**) and ii) total synthesis of (±)-3-hydroxysolavetivone (**1**), involving the introduction of a three-carbon unit.

At the beginning of the study, the C_9-hydroxylation of the enone (**5**) was investigated. For α′-hydroxylation of α,β-unsaturated ketones, several methods have been developed to date.[7] In the cases of compounds similar to **5**, α′-hydroxylation was shown to occur in low yield and/or low stereoselectivity.[3,8] In fact, oxidation of the spirocyclic enone (**5**) with reagents such as *m*-chloroperbenzoic acid (MCPBA),[7a] MoOPH,[7b] and $Mn(OAc)_3$[7c] gave the α′-hydroxylated products (**6** and **7**) in moderate yields, but the stereoselectivity turned out to be unsatisfactory (Table I). Recently, we demonstrated that triphenyl phosphite ozonide (TPPO) oxidation of 2-trimethylsilyloxy-1,3-dienes served as a useful tool for regio- and stereoselective α′-hydroxylation of the α,β-unsaturated ketones.[9] According to this method, the enone (**5**) was converted into the silyl enol ether, which was treated with TPPO in dichloromethane at −50 °C, followed by addition of triphenyl phosphine to give the desired product (**6a**) and its diastereoisomer (**7a**) in 71% total yield in a ratio of 8:1. This moderately high stereoselectivity should be attributable to the reaction intermediate. Namely, in the TPPO oxidation, the oxidant is considered to react simultaneously at two carbon centers, C_6 and C_9, in the silyl enol ether and form

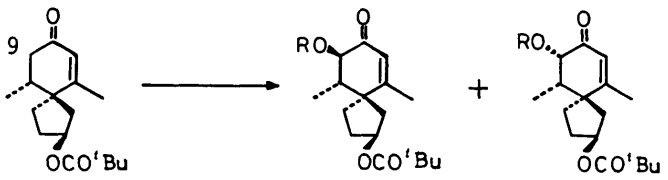


1: X=OH
2: X=H

3 **4**

Chart 1

TABLE I. α′-Hydroxylation of the Enone (**5**)

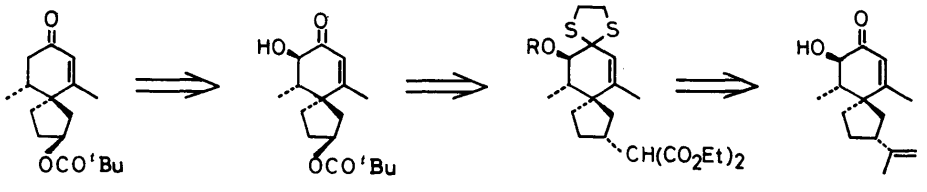


5 **6a—d** **7a—d**

a: R=H, **b**: R=$SiMe_3$, **c**: R=$SiMe_2{}^tBu$, *d*: R=Ac

Entry	Reaction conditions	R	Yield (%)	Ratio (6:7)
1	LDA, DME, −18 °C; TMSCl; TPPO, CH_2Cl_2, −50 °C; Ph_3P, Et_2O, r.t.	H	71	8:1
2	LDA, DME, −18 °C; TMSCl; MCPBA, hexane, −15 °C	TMS	63	1:1
3	LDA, THF, −78 °C; MoOPH, −22 °C; TBDMSCl, imidazole, DMF	TBDMS	52 (83)[a]	2:1
4	$Mn(OAc)_3$, C_6H_6, reflux	Ac	62	2:1

a) The yield based on the consumed starting material. r.t.=room temperature.



5 **6a** **1**

Chart 2

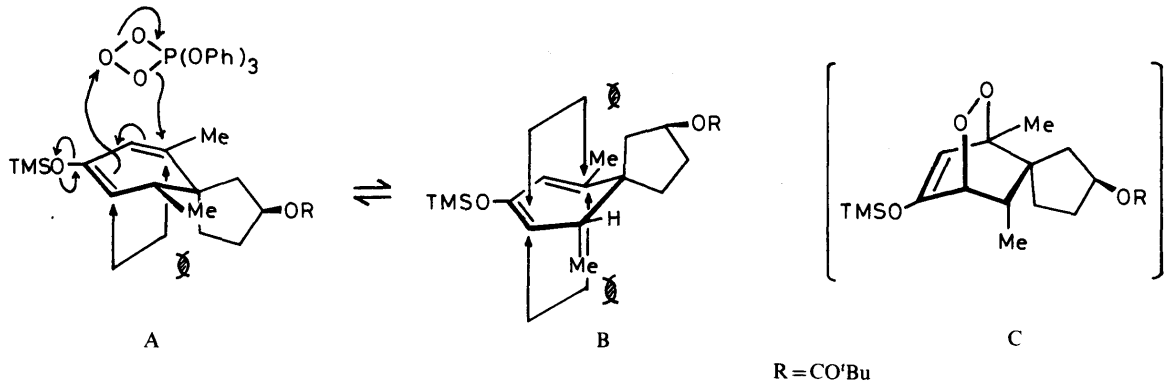


Fig. 1

an endoperoxide (C) (Fig. 1). Because of severe 1,3-diaxial interaction between TPPO and the methylene units at C_1 and C_4, or the methyl unit of C_{10}, the silyl enol ether was attacked from the top side of conformation A by the oxidant, resulting in a predominant formation of **6a**.[9] The stereochemistry of **6a** and **7a** was determined from their proton nuclear magnetic resonance (^{1}H-NMR) spectra. From the fact that the C-9 hydrogen of **6a** has larger coupling constant ($J=12$ Hz) than that of **7a** ($J=5$ Hz), the relative configuration of the C-9 and C-10 hydrogens in **6a** was proved to be *trans*.

Next, introduction of the isopropenyl group at C_2 in **6a** was achieved through the following sequence of reactions. Conversion of **6a** into the *tert*-butyldiphenylsilyl ether (**8**) followed by thioacetalization gave compound **9** in 65% yield. Mesylation of the alcohol (**10**), obtained from **9** by reaction with methyllithium in 79% yield, in the usual manner provided **11**. To introduce a three-carbon unit at C_2, the mesylate (**11**) was treated with the enolate anion of diethyl malonate to afford the diester (**12**) in 62% yield from **10**. Although it was previously reported that a bis-(ethoxycarbonyl)methyl group was easily transformed into an allylic alcohol by Red-Al reduction of its sodium salt,[1] its application to the diester (**12**) resulted in the formation of only a complex mixture, probably owing to the labile nature of the thioacetal moiety. Therefore, a circuitous route was examined as follows. Successive treatment of **12** with sodium hydroxide in ethanol, diethylamine and formalin, and then sodium acetate in refluxing acetic acid provided the unsaturated ester (**14**) in 74% yield *via* the half ester (**13**). Reduction of **14** with diisobutylaluminum hydride in toluene at -70 °C afforded the allylic alcohol (**15**) in 89% yield. In a previous paper on a total synthesis of (±)-solavetivone (**1**),[6a] a similar allylic alcohol was converted into the isopropenyl derivative *via* the unstable allylic chloride in 67% overall yield. In order to achieve this transformation more effectively, acetylation of **15** into **16** and subsequent removal of the acetoxy group [$Pd(OAc)_2$, Ph_3P, and $HCOONH_4$ in dioxane][10] gave the desired compound (**17**) in 86% yield. Finally, deprotection of the *tert*-butyldiphenylsilyl group and thioacetal group was accomplished as follows. By treatment with tetra-*n*-butylammonium fluoride in tetrahydrofuran (THF), **17** was converted into the alcohol (**18**), which was hydrolyzed with silver nitrate in aqueous ethanol to furnish (±)-3-hydroxysolavetivone (**1**) in 54% yield.

This synthetic product was proved to be identical with natural 3-hydroxysolavetivone by comparison of spectral data. Although a successful transformation of natural solavetivone into natural 3-hydroxysolavetivone has been reported,[3] the present synthesis is the first total synthesis of (±)-3-hydroxysolavetivone.

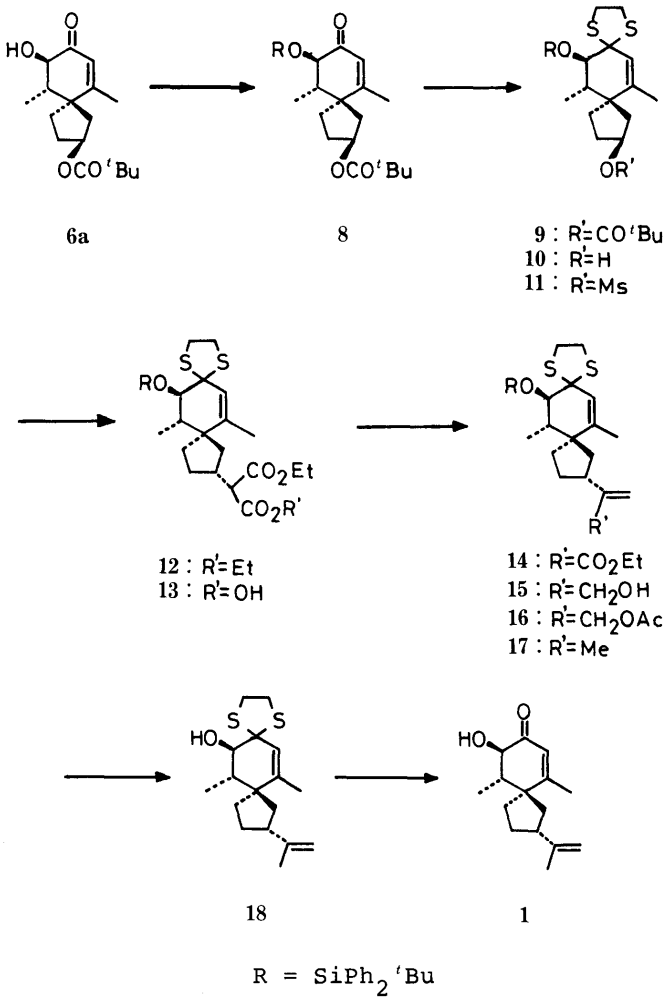


Chart 3

Experimental

Melting points are uncorrected. Infrared (IR) spectra were recorded on a Hitachi 260-10 spectrophotometer. Ultraviolet (UV) spectra were recorded on a Hitachi 124 spectrophotometer. ^{1}H-NMR spectra were recorded on a Hitachi R-22 (90 MHz) or JEOL FX-90Q (90 MHz) with tetramethylsilane as an internal standard. The following abbreviations for the signal

patterns are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad. Mass spectra (MS) and high resolution mass spectra (HRMS) were obtained with a JEOL JMS-D300 mass spectrometer. For column chromatography, Merck Kieselgel 60 (70—230 mesh) was used, and for preparative thin layer chromatography (TLC), Merck Kieselgel 60 PF_{254} was used. Extracts were dried over $MgSO_4$.

(2*RS*,5*RS*,9*SR*,10*RS*)-9-Hydroxy-6,10-dimethyl-2-pivaloyloxyspiro-[4.5]dec-6-en-8-one (6a) a) With TPPO: A solution of the enone (**5**) (389 mg, 1.40 mmol) in dimethoxyethane (DME) (6 ml) was added dropwise to a solution of lithium diisopropylamide (LDA), prepared from diisopropylamine (0.24 ml, 1.71 mmol) and *n*-butyllithium (1.5 M in hexane, 1.17 ml, 1.71 mmol) in DME (1.5 ml), at −18 °C. The reaction mixture was stirred for 1 h at this temperature, then trimethylsilyl chloride (0.36 ml, 2.84 mmol) was added in one portion. The resulting mixture was stirred for 2 h at room temperature, concentrated *in vacuo*, and diluted with hexane. The precipitate was filtered off and the filtrate was evaporated under reduced pressure to give the crude silyl enol ether of **5**, which was used in the next step without further purification. A solution of the silyl enol ether in dry CH_2Cl_2 (7 ml) was added at −50 °C to the TPPO solution which was prepared from triphenyl phosphite (0.74 ml, 2.80 mmol) and an excess of ozone in dry CH_2Cl_2 (14 ml) according to the literature.[11] The mixture was stirred for 8 h at this temperature. After successive addition of triethylamine (a few drops) and a solution of triphenyl phosphine (562.2 mg, 2.14 mmol) in ether (10 ml), the reaction mixture was stirred for 5 h at room temperature. Removal of the solvent and purification of the residue by column chromatography with benzene–AcOEt (9 : 1) afforded a mixture of **6a** and **7a** (291.8 mg, 71%). The ratio of **6a** and **7a** was determined from the ^{1}H-NMR spectra. The mixture was separated by recrystallization from hexane or by medium-pressure column chromatography (benzene : AcOEt = 9 : 1).

6a: Colorless needles, mp 97—98 °C (hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3480, 1720, 1675, 1615. UV λ_{max}^{EtOH} nm (ε): 238 (10500). ^{1}H-NMR (CCl_4) δ: 1.15 (9H, s, *tert*-Bu), 1.28 (3H, d, J = 7 Hz, C_{10}-Me), 2.03 (3H, d, J = 1 Hz, C_6-Me), 3.72 (1H, d, J = 12 Hz, C_9-H), 5.07 (1H, m, C_2-H), 5.69 (1H, d, J = 1 Hz, C_7-H). MS *m/z* (%): 294 (M^+, 1.7), 134 (100). *Anal.* Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 69.38; H, 8.99.

7a: A colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590, 3490, 1720, 1680, 1615. UV λ_{max}^{EtOH} nm (ε): 239 (10800). ^{1}H-NMR (CCl_4) δ: 0.78 (3H, d, J = 7 Hz, C_{10}-Me), 1.17 (9H, s, *tert*-Bu), 1.89 (3H, d, J = 1 Hz, C_6-Me), 3.30 (1H, br s, OH), 4.27 (1H, d, J = 5 Hz, C_9-H), 5.16 (1H, m, C_2-H), 5.70 (1H, d, J = 1 Hz, C_7-H). MS *m/z* (%): 294 (M^+, 0.6), 134 (100). HRMS Calcd for $C_{17}H_{26}O_4$: 294.1828. Found: 294.1820.

b) With MCPBA: A solution of the silyl enol ether [prepared from **5** (94.3 mg, 0.34 ml), LDA (0.41 mmol), and trimethylsilyl chloride (0.086 ml, 0.68 mmol) as described above] in dry hexane (1 ml) was added to a suspension of MCPBA (80.4 mg, 0.37 mmol) in dry hexane (4 ml) at −15 °C and the reaction mixture was stirred for 30 min at room temperature. The precipitate was filtered off and the filtrate was evaporated under reduced pressure. The residue was purified by preparative TLC to give **6b** and **7b** in 33 (41.1 mg) and 30% (37.3 mg) yields, respectively. These silyl ethers were converted into **6a** and **7a** by the action of K_2CO_3 in dry MeOH.

c) With MoOPH: A solution of the enone (**5**) (55.4 mg, 0.20 mmol) in dry THF (0.8 ml) was added dropwise to a solution of LDA (0.22 mmol) in dry THF (0.2 ml) at −78 °C, and the resulting mixture was stirred for 30 min. This mixture was added to a solution of MoOPH (129.7 mg, 0.03 mmol) in dry THF (2.5 ml) at −22 °C. After being stirred for 2 h at this temperature, the mixture was diluted with saturated Na_2SO_3 solution and allowed to warm to room temperature. The mixture was extracted with ether, and the extract was washed with 1.5 N HCl solution and brine, and then dried. The solvent was removed to give a residue. *tert*-Butyldimethylsilyl chloride (34.3 mg, 0.23 mmol) and imidazole (30.9 mg, 0.45 mmol) were added to a solution of the crude products in dry DMF (0.5 ml) at room temperature, and the resulting mixture was stirred for 6 h at this temperature. The mixture was diluted with brine and extracted with ether. The extract was dried and evaporated. The residue was purified by preparative TLC with benzene–AcOEt (10 : 1) to give **6c** and **7c** in 32 (26.3 mg) and 17% (14.7 mg) yields, respectively, together with **5** (19.4 mg).

d) With $Mn(OAc)_3$: $Mn(OAc)_3$ (137.4 mg, 0.59 mmol) was added to a solution of the enone (**5**) (51.0 mg, 0.18 mmol) in dry benzene (2 ml), and the mixture was refluxed for 2 h. 91.6 mg and 45.8 mg of $Mn(OAc)_3$ were added at 2-h intervals. The cooled mixture was extracted with AcOEt, and the extract was washed with 1 N HCl, saturated $NaHCO_3$ solution, and brine, and then dried. Removal of the organic solvent *in vacuo* provided an oily residue, which was purified by preparative TLC with hexane–AcOEt (5 : 1) to give **6d** and **7d** in 42 (25.6 mg) and 20% (12.8 mg) yields, respectively. These acetates were converted into **6a** and **7a** by the action of K_2CO_3 in dry MeOH.

(2*RS*,5*RS*,9*SR*,10*RS*)-9-*tert*-Butyldiphenylsilyloxy-6,10-dimethyl-2-pivaloyloxyspiro[4.5]dec-6-en-8-one (8) *tert*-Butyldiphenylsilyl chloride (0.055 ml, 0.23 mmol) and imidazole (32.0 mg, 0.47 mmol) were added to a solution of **6a** (22.8 mg, 0.078 mmol) in DMF (0.5 ml), and the mixture was stirred for 12 h at 50 °C. After addition of brine under cooling, the resulting mixture was extracted with ether and the ethereal phase was washed with H_2O and brine, and then dried. Evaporation of the solvent gave a residue, which was purified by preparative TLC with hexane–AcOEt (5 : 1) to afford 8 (38.0 mg, 98%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720, 1690, 1625. UV λ_{max}^{EtOH} nm (ε): 206 (13000), 218 (11600), 240 (5800). ^{1}H-NMR ($CDCl_3$) δ: 0.98 (3H, d, J = 6 Hz, C_{10}-Me), 1.08 and 1.15 (each 9H, s, *tert*-Bu), 1.84 (3H, br s, C_6-Me), 4.04 (1H, d, J = 8 Hz, C_9-H), 5.10 (1H, m, C_2-H), 5.55 (1H, br s, C_7-H), 7.1—7.8 (10H, m, Ph × 2). MS *m/z* (%): 475 (M^+ − 57, 100). HRMS Calcd for $C_{29}H_{35}O_4Si$: 475.2302. Found: 475.2299.

(2*RS*, 5*RS*, 9*SR*, 10*RS*)-9-*tert*-Butyldiphenylsilyloxy-6,10-dimethyl-2-pivaloyloxyspiro[4.5]dec-6-en-8-one Ethylene Dithioacetal (9) Ethanedithiol (0.005 ml, 0.064 mmol) and $BF_3 \cdot Et_2O$ (1 drop) were added to a solution of the enone (**8**) in dry CH_2Cl_2 (0.5 ml) at 0 °C. The mixture was stirred for 1.5 h at room temperature, quenched with 5% NaOH solution, and extracted with CH_2Cl_2. The organic phase was washed with 5% NaOH solution, H_2O, and brine, dried, and then evaporated. The residue was purified by preparative TLC with hexane–AcOEt (5 : 1) to afford **9** (17.3 mg, 66%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735, 1618. ^{1}H-NMR ($CDCl_3$) δ: 0.75 (3H, d, J = 6 Hz, C_{10}-Me), 1.02 and 1.05 (each 9H, s, *tert*-Bu), 1.58 (3H, d, J = 1.6 Hz, C_6-Me), 2.7—3.4 (4H, m, $SCH_2 \times 2$), 4.09 (1H, d, J = 10 Hz, C_9-H), 4.7—5.1 (1H, m, C_2-H), 5.34 (1H, d, J = 1.6 Hz, C_7-H), 7.1—7.9 (10H, m). MS *m/z* (%): 608 (M^+, 4), 251 (100). HRMS Calcd for $C_{35}H_{48}O_3S_2Si$: 608.2811. Found: 608.2803.

(2*RS*,5*RS*,9*SR*,10*RS*)-9-*tert*-Butyldiphenylsilyloxy-2-hydroxy-6,10-dimethylspiro[4.5]dec-6-en-8-one Ethylene Dithioacetal (10) An ethereal solution of methyllithium (0.4 M, 4.1 ml) was added dropwise to a solution of the ester (**9**) (500 mg, 0.82 mmol) in dry ether (5 ml) at 0 °C with stirring. After additional stirring for 20 min at this temperature, 5% aqueous AcOH solution was added, and the resulting mixture was extracted with ether. The ethereal extract was washed with saturated $NaHCO_3$, H_2O, and brine, dried, and then evaporated. The residue was purified by preparative TLC with hexane–AcOEt (5 : 1) to afford the alcohol (**10**) (341 mg, 79%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 3400. ^{1}H-NMR ($CDCl_3$) δ: 0.82 (3H, d, J = 6 Hz, C_{10}-Me), 1.08 (9H, s, *tert*-Bu), 1.57 (3H, d, J = 1 Hz, C_6-Me), 2.8—3.5 (4H, m, $SCH_2 \times 2$), 4.15 (1H, m, C_2-H), 4.16 (1H, d, J = 10 Hz, C_9-H), 5.38 (1H, d, J = 1 Hz, C_7-H), 7.1—8.0 (10H, m, Ph × 2). MS *m/z* (%): 524 (M^+, 7), 199 (100). HRMS Calcd for $C_{30}H_{40}O_2S_2Si$: 524.2232. Found: 524.2322.

(2*RS*,5*SR*,9*RS*,10*SR*)-9-tert-Butyldiphenylsilyloxy-2-bis(ethoxycarbonyl)methyl-6,10-dimethylspiro[4.5]dec-6-en-8-one Ethylene Dithioacetal (12) A solution of **10** (125 mg, 0.24 mmol) and mesyl chloride (0.02 ml, 0.29 mmol) in dry pyridine (1 ml) was stirred for 4 h at 0 °C. Saturated $NaHCO_3$ solution was added, and the resulting mixture was extracted with ether. The usual work-up gave a crude methylate (**11**). A solution of the product in dry DME (4 ml) was added to a solution of the enolate anion of diethyl malonate [prepared from NaH (60% mineral oil, 47.6 mg, 1.20 mmol) and diethyl malonate (0.18 ml, 1.20 mmol) in dry DME (3 ml)] at room temperature and the resulting mixture was refluxed for 7 h. After the addition of saturated NH_4Cl solution under ice-water cooling, the mixture was extracted with AcOEt. The extract was washed with brine, dried, and then evaporated. The residue was chromatographed on a column with hexane–AcOEt (5 : 1) to provide the diester (**12**) (98.9 mg, 62%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750, 1730. ^{1}H-NMR ($CDCl_3$) δ: 0.75 (3H, d, J = 6 Hz, C_{10}-Me), 1.09 (9H, s, *tert*-Bu), 1.20 and 1.23 (each 3H, t, J = 8 Hz, $COCH_2CH_3$), 1.62 (3H, d, J = 1 Hz, C_6-Me), 2.9—4.0 (5H, m, $SCH_2 \times 2$ and C_2-CH), 4.11 and 4.17 (each 2H, q, J = 8 Hz, $COCH_2CH_3$), 4.19 (1H, d, J = 8 Hz, C_9-H), 5.14 (1H, d, J = 1 Hz, C_7-H). MS *m/z* (%): 666 (M^+, 0.9), 175 (100). HRMS Calcd for $C_{37}H_{50}O_5S_2Si$: 666.2868. Found: 666.2968.

(2*RS*,5*SR*,9*RS*,10*SR*)-9-*tert*-Butyldiphenylsilyloxy-2-(1-ethoxycarbonylvinyl)-6,10-dimethylspiro[4.5]dec-6-en-8-one (14) A solution of **12** (13.1 mg, 0.020 mmol) and KOH (6.5 mg, 0.093 mmol) in EtOH (0.5 ml) was stirred for 12 h at room temperature. The solution was diluted with saturated NH_4Cl solution and cold 5% HCl, and extracted with AcOEt. The extract was washed with H_2O and brine, dried, and then evaporated to give a residue, which was purified by preparative TLC with benzene–

AcOEt (2:1) to afford the half ester (**13**) (9.8 mg, 80%). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3000, 1730, 1610. ^{1}H-NMR ($CDCl_3$) δ: 0.72 (3H, d, J=7 Hz, C_{10}-Me), 1.07 (9H, s, *tert*-Bu), 1.22 (3H, t, J=8 Hz, $COCH_2CH_3$), 1.64 (3H, br s, C_6-Me), 2.9—3.4 (4H, m, $SCH_2 \times 2$), 4.12 (2H, q, J=8 Hz, $COCH_2CH_3$), 5.40 (1H, br s, C_7-H).

A mixture of **13** (62.5 mg, 0.098 mmol), diethylamine (0.054 ml, 0.52 mmol), and 35% formalin (0.090 ml, 1.1 mmol) was refluxed for 20 min with stirring, then allowed to cool. NaOAc (9.2 mg, 0.068 mmol) and AcOH (0.01 ml) were added, and the mixture was refluxed for a 15-min period. After addition of water, the resulting mixture was extracted with AcOEt. The organic layer was washed with H_2O, dried, and evaporated. The residue was chromatographed on a column with hexane–AcOEt (5:1) to afford **14** (50.9 mg, 93%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1710, 1630. UV λ_{max}^{EtOH} nm (ε): 208 (21000). ^{1}H-NMR ($CDCl_3$) δ: 0.78 (3H, d, J=7 Hz, C_{10}-Me), 1.08 (9H, s, *tert*-Bu), 1.26 (3H, t, J=7 Hz, $COCH_2CH_3$), 1.65 (3H, s, C_6-Me), 2.9—3.4 (4H, m, $SCH_2 \times 2$), 4.0—4.3 (3H, m, C_9-H and OCH_2CH_3), 5.40 (2H, m, C_7-H and COC=CH), 6.01 (1H, br s, COC=CH), 7.1—7.9 (10H, m, Ph×2). MS *m/z* (%): 606 (M^+, 0.8), 275 (100). HRMS Calcd for $C_{35}H_{46}O_3S_2Si$: 606.2654. Found: 606.2638.

(2*RS*,5*SR*,9*RS*,10*SR*)-9-*tert*-Butyldiphenylsilyloxy-2-(3-hydroxypropen-2-yl)-6,10-dimethylspiro[4.5]dec-6-en-8-one Ethylene Dithioacetal (15) Diisobutylaluminum hydride (1.74 M solution in toluene, 0.39 ml) was added to a solution of the ester (**14**) (93.1 mg, 0.15 mmol) in dry toluene (1.5 ml) at −70 °C. The mixture was stirred for 5 min at this temperature, quenched with saturated NH_4Cl and 5% HCl, and then extracted with AcOEt. The extract was washed with H_2O, dried, and evaporated. The residue was purified by column chromatography with hexane–AcOEt (5:1) to yield **15** (75.0 mg, 89%) as colorless needles. mp 158—159 °C (ether–hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 1649. ^{1}H-NMR ($CDCl_3$) δ: 0.76 (3H, d, J=7 Hz, C_{10}-Me), 1.10 (9H, s, *tert*-Bu), 1.65 (3H, d, J=1 Hz, C_6-Me), 2.9—3.4 (4H, m, $SCH_2 \times 2$), 3.98 (2H, br s, $C=CCH_2OH$), 4.29 (1H, d, J=8 Hz, C_9-H), 4.81 and 4.94 (each 1H, br s, C=CH), 5.41 (1H, br s, C_7-H), 7.1—8.0 (10H, m, Ph×2). MS (CI) *m/z* (%): 565 (M^+ + 1, 0.9), 363 (100). HRMS Calcd for $C_{33}H_{44}O_2S_2Si$: 564.2552. Found: 564.2568.

(2*RS*,5*SR*,9*RS*,10*SR*)-2-(3-Acetoxypropen-2-yl)-9-*tert*-butyldiphenylsilyloxy-6,10-dimethylspiro[4.5]dec-6-en-8-one Ethylene Dithioacetal (16) A mixture of the alcohol (**15**) (20.0 mg, 0.035 mmol), Ac_2O (0.008 ml, 0.089 mmol), and pyridine (0.25 ml) was stirred for 8 h at room temperature. Saturated $NaHCO_3$ solution was added under cooling, and the resulting solution was extracted with ether. The ethereal layer was washed with saturated $CuSO_4$ solution, H_2O, and brine, and then dried. Evaporation of the solvent gave a residue, which was purified by column chromatography with benzene–AcOEt (10:1) to give **16** (19.6 mg, 92%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735, 1653. ^{1}H-NMR ($CDCl_3$) δ: 0.74 (3H, d, J=7 Hz, C_{10}-Me), 1.09 (9H, s, *tert*-Bu), 1.63 (3H, d, J=1 Hz, C_6-Me), 2.06 (3H, s, OAc), 3.0—3.3 (4H, m, $SCH_2 \times 2$), 4.26 (1H, d, J=7 Hz, C_9-H), 4.43 (2H, s, CH_2OAc), 4.87 and 4.95 (each 1H, br s, C=CH), 5.43 (1H, d, J=1 Hz, C_7-H), 7.2—8.0 (10H, m, Ph×2). MS (CI) *m/z* (%): 607 (M^+ + 1, 0.7), 61 (100). HRMS Calcd for $C_{31}H_{37}O_3S_2Si$: 549.1953. Found: 549.1966.

(2*RS*,5*SR*,9*RS*,10*SR*)-9-*tert*-Butyldiphenylsilyloxy-2-isopropenyl-6,10-dimethylspiro[4.5]dec-6-en-8-one Ethylene Dithioacetal (17) A mixture of **16** (35.4 mg, 0.058 mmol), $Pd(OAc)_2$ (0.13 mg, 1 mol%), PPh_3 (1.5 mg, 10 mol%), $HCOONH_4$ (7.3 mg, 0.12 mmol) and dioxane (0.5 ml) was refluxed for 3 h. After removal of the solvent, the residue was diluted with H_2O and extracted with ether. The organic phase was washed with brine, dried, and evaporated. Purification of the product was carried out by column chromatography with hexane–AcOEt (10:1) to afford **17** (29.6 mg, 93%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1640, 890. ^{1}H-NMR ($CDCl_3$) δ: 0.75 (3H, d, J=7 Hz, C_{10}-Me), 1.09 (9H, s, *tert*-Bu), 1.63 (6H, br s, C_6-Me and C=CMe), 2.9—3.4 (4H, m, $SCH_2 \times 2$), 4.25 (1H, d, J=7 Hz, C_9-H), 4.59 (2H, br s, $C=CH_2$), 5.42 (1H, d, J=1 Hz, C_7-H), 7.2—7.9 (10H, m, Ph×2). MS *m/z* (%): 548 (M^+, 1), 491 (100). HRMS Calcd for $C_{29}H_{35}OS_2Si$: 491.1896. Found: 491.1875.

(2*RS*,5*SR*,9*RS*,10*SR*)-9-Hydroxy-2-isopropenyl-6,10-dimethylspiro[4.5]dec-6-en-8-one Ethylene Dithioacetal (18) A solution of *n*-Bu_4NF (1 M solution in THF, 0.069 ml) was added to a solution of **17** (19.0 mg, 0.035 mmol) in THF (1 ml), and the mixture was stirred for 48 h at room temperature. After addition of brine, the resulting mixture was extracted with ether. The extract was washed with brine, dried, and evaporated. The residue was purified by preparative TLC with hexane–AcOEt (5:1) to give the alcohol (**18**) (6.2 mg, 57%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1640, 890. ^{1}H-NMR ($CDCl_3$) δ: 1.11 (3H, d, J=6.8 Hz, C_{10}-Me), 1.72 (6H, s, C_6-Me and C=CMe), 3.2—3.7 (5H, m, C_9-H and $SCH_2 \times 2$), 4.68 (2H, br s, $C=CH_2$), 5.50 (1H, br s, C_7-H). MS *m/z* (%): 310 (M^+, 100). HRMS Calcd for $C_{17}H_{26}OS_2$: 310.1422. Found: 310.1405.

(±)-3-Hydroxysolavetivone (1) A solution of **18** (3.4 mg, 0.011 mmol) and $AgNO_3$ (3.8 mg, 0.022 mmol) in 95% aqueous EtOH (0.2 ml) was stirred for 30 min at 60 °C. An additonal 1.9 mg (0.011 mmol) of $AgNO_3$ was added, and stirring was continued for a further 30 min at the same temperature. After being cooled to room temperature, the mixture was diluted with AcOEt and filtered. The filtrate was washed with brine, dried, and evaporated. An oily crude product was purified by preparative TLC with benzene–AcOEt (10:1) to yield **1** (2.4 mg, 94%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3480, 1680, 1641, 890. UV λ_{max}^{EtOH} nm (ε): 241 (10100). ^{1}H-NMR ($CDCl_3$) δ: 1.25 (3H, d, J=6 Hz, C_{10}-Me), 1.78 (3H, s, C=CMe), 2.03 (3H, d, J=1 Hz, C_6-Me), 3.84 (1H, d, J=13 Hz, C_9-H), 4.75 (2H, s, $C=CH_2$), 5.84 (1H, d, J=1 Hz, C_7-H). MS *m/z* (%): 234 (M^+, 2), 176 (100). HRMS Calcd for $C_{15}H_{22}O_2$: 234.1617. Found: 234.1615.

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