gassed with nitrogen for 0.5 hr, irradiated with RPR 254-nm lamps, and analyzed directly by VPC using an internal standard. The results are recorded in Table I.

Quenching Experiments. *trans*-Piperylene was purified before use. The chloro ketone (0.3 mmol) was dissolved in 10 ml of ether divided into two 4-ml samples and placed in Pyrex tubes. After addition of 2 ml of methanol and 2 ml of ether to the first and 2 ml of methanol and 2 ml of *trans*-piperylene to the second sample, these were degassed with nitrogen and irradiated together to about 40% conversion with RPR 300-nm lamps in a merry-go-round apparatus. The irradiated samples were analyzed directly by VPC using an internal standard. The results are given in Table I.

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(19) The products from **4** were not fully characterized. For the other ketones, no cyclobutanones were observed.
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A New Stereocontrolled Approach to Spirosesquiterpenes. Synthesis of Acorenone B

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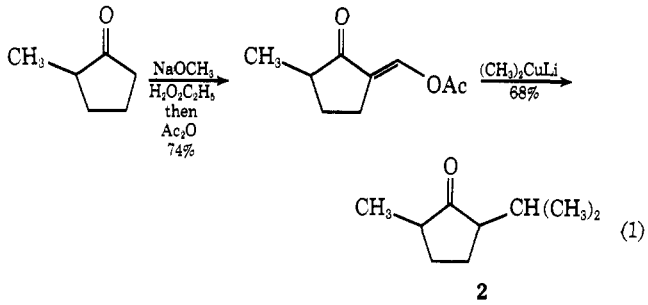
Abstract: The total synthesis of acorenone B illustrates a new approach to secoalkylation and 1,2-alkylative carbonyl transposition. Spiroannelation of 2-isopropyl-5-methylcyclopentanone with cyclopropyldiphenylsulfonium fluoroborate, followed by rearrangement of the oxaspiropentane, gives stereohomogeneous (*Z,Z*)-5-isopropyl-8-methylspiro[3.4]octan-1-one. Formylation followed by acidic treatment effects cyclobutyl ring cleavage to an enol lactone which constitutes a net stereocontrolled geminal alkylation with introduction of a one-carbon and a three-carbon chain differentially functionalized. Standard methods converted the enol lactone to 1-isopropyl-4-methylspiro[4.5]dec-6-en-8-one. Sulfenylation α to the ketone, addition of methyllithium to the carbonyl group, dehydration to the enol thioether, and hydrolysis to the enone complete the synthesis.

The development of synthetic approaches for the generation of a quaternary carbon atom, especially a spiro center, in a stereochemically defined fashion continues to be a major challenge. Among spiro compounds, the spiro[4.5]decane system has attracted the most attention because sesquiterpenes of this ring type are important as biosynthetic intermediates in terpene biogenesis, constituents of essential oils, antifungal agents, and stress metabolites.[1,2] The acoranes form one subset of this class of spirosesquiterpenes for which completely stereocontrolled syntheses are lacking.[3,4] Our recent developments in spiroannelations offer a potential solution to this stereochemical question.[5] In this paper, we report the first stereocontrolled approach to an acorane, acorenone B (**1**).[4,6] The scheme illustrates a new approach to secoalkylation[5] and 1,2-alkylative carbonyl transposition[7] under development in our laboratories.

The starting material for our synthesis is 2-methyl-5-isopropylcyclopentanone (**2**).[8] We have found this compound to be conveniently available by the route outlined in eq. 1.



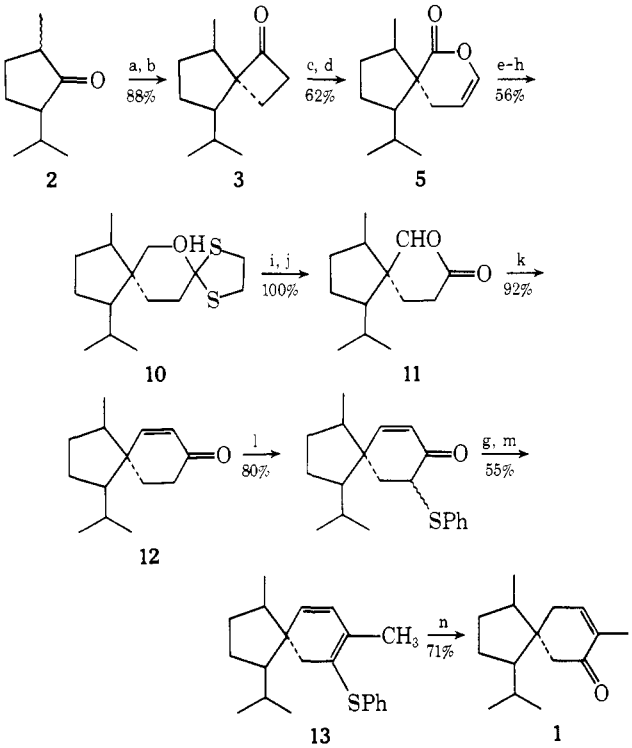
(1)

2

This approach exploits the recent findings of Casey[9] regarding the use of enol acetates of 1,3-dicarbonyl systems as acceptors in conjugate additions with organocuprates. The antistereochemistry of the enol acetate is assigned because of the low field position (δ 7.93) of the vinyl proton.[10] In agreement with other workers,[8] VPC analysis[11] indicated a 70:30 mixture of the *E*:*Z* isomers.

Spiroannelation of **2** as an isomeric mixture with the ylide derived from cyclopropyldiphenylsulfonium fluoroborate under reversible ylide generation conditions[12] followed by rearrangement of the intermediate oxaspiropentane with lithium fluoroborate[5c] in refluxing benzene gave a chromatographically (TLC, VPC, LLC) pure cyclobutanone assigned structure **3** (see Scheme I). This stereochemistry

Scheme I. Synthetic Path

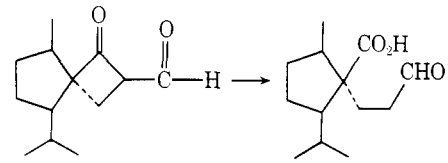


[a] c-PrS$^+$Ph$_2$BF$_4^-$, Me$_2$SO, KOH, 25°. [b] LiBF$_4$, PhH, reflux. [c] HCO$_2$C$_2$H$_5$, NaH, PhH, CH$_3$OH, 25°. [d] TsOH, PhH, H$_2$O, reflux. [e] [(CH$_3$)$_2$CHCH$_2$]$_2$AlH, PhCH$_3$, −25°. [f] CrO$_3$, H$_2$O, H$_2$SO$_4$, acetone, 0°. [g] CH$_3$Li, ether and/or THF, −78°. [h] HSCH$_2$CH$_2$SH, BF$_3$·ether, PhCH$_3$, 0°. [i] Pyridine–SO$_3$, Me$_2$SO, (C$_2$H$_5$)$_3$N, 25°. [j] HgCl$_2$, CH$_3$CN, H$_2$O, reflux. [k] KOH, CH$_3$OH, 25°. [l] LiN(*i*-C$_3$H$_7$) (*c*-C$_6$H$_{11}$), THF, HMPA, PhSSPh, 25°. [m] TsOH, PhH, reflux. [n] HgCl$_2$, dioxane, H$_2$O, reflux.

rests on analogy to other spiroannelation reactions[5c,12] and to the ultimate completion of the synthesis. Furthermore, Eu(thd)$_3$ induced shifts of the methyl groups show three doublets at δ 1.00, 0.97, and 0.87 shift to δ 1.42, 1.27, and 1.13, respectively. The comparability of the shifts implies the isopropyl and methyl groups bear the same geometric relationship with respect to the carbonyl group. The magnitude of these shifts (0.26–0.42 ppm) compared with that of the methylene group α to the carbonyl group of 0.60 ppm implies that relationship is syn.

This step creates three contiguous asymmetric centers with a single relative configuration. Three conclusions seem justified on the basis of this observation. Interconversion of the *E* and *Z* isomers of **2** is faster than ylide addition to the carbonyl group. Of the two isomers, the *Z* isomer, which can present a sterically unhindered face to the bulky ylide, reacts selectively. Finally, the rearrangement of the oxaspiropentane to the cyclobutanone is stereospecific. Similar results were encountered in our earlier work.[13]

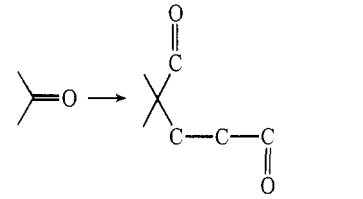
The next stage required conversion of the cyclobutanone to a cyclohexanone with maintenance of stereochemistry. We previously developed ring cleavage methods by introducing halogen and sulfur as anion stabilizing groups.[5] In this case, we developed an alternative approach to secoalkylation by the introduction of a formyl group as the anion stabilizing group. Unlike most formylcycloalkanones which are normally totally enolic, the α-formylcyclobutanone **4** showed no tendency toward enolization [ir 1770 and 1710 cm^{-1}; NMR δ 9.63 (CHO)]. The increased strain associated with putting a second sp^2 center in the small ring as well as the decreased stabilization of the enolized form by steric inhibition of intramolecular hydrogen bonding may account for this phenomenon. In principle, deacylation can occur by attack of nucleophiles at either carbonyl group of **4**. Most α-formylcycloalkanones undergo deformylation



(2)

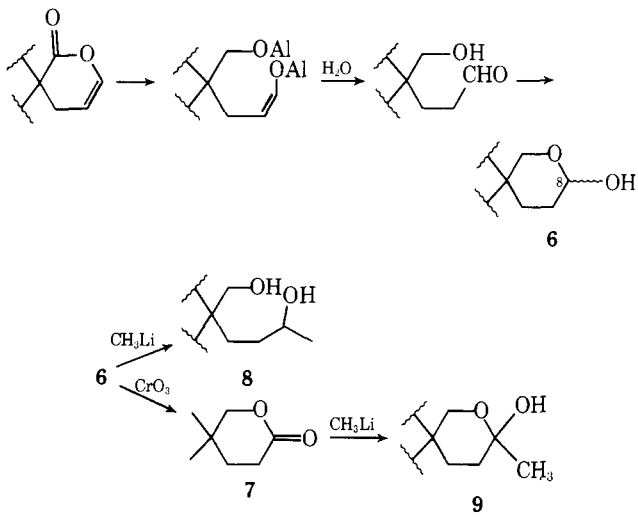
4

upon treatment with nucleophilic bases.[14] In contrast to this trend, the formylcyclobutanone undergoes ring cleavage—presumably the result of the release of strain energy. Both base and acid initiate fragmentation, although the latter gives a cleaner product. The initial product, an aldehyde carboxylic acid (see eq 2), cyclizes under the reaction conditions to form the enol lactone **5**: ir 1745, 1678, 1633 cm^{-1}; NMR δ 6.32 and 5.08 (CH=CH), 2.66 and 2.12 (allylic methylene). The net result of this secoalkylation procedure is the stereoselective replacement of the carbon–oxygen bonds of a carbonyl group by a one-carbon and a three-carbon chain differentially functionalized (eq 3).



(3)

Reduction of **5** produced a lactol **6** which, normally without purification, was oxidized[15] to a δ-lactone **7** [ir 1745 cm^{-1}; NMR δ 4.12 (s, CH$_2$OCO)]. The reduction stops at the stage of the hydroxy aldehyde since the aldehyde unit is protected as its enolate until quenching of the reaction. Integration of the signals for OCHO at δ 4.80 and 5.12 indicates **6** to be a 1:1 mixture of isomers at C-8. Methyllithium adds slowly to the lactol **6** to give the diol **8**. However, attempts to oxidize the diol **8** to the keto aldehyde **11** led to



complex mixtures. Addition of methyllithium to lactone **7** proceeded readily, but direct oxidation of the lactol **9** was thwarted by the stability of the lactol form. To overcome this problem, the hydroxy ketone was "fixed" in the open form by thioketalization to **10,** which was easily and quantitatively oxidized[16] and hydrolyzed[17] to the desired keto aldehyde **11** [ir 1713 cm^{-1}; NMR δ 2.08 (s, CH_3CO), 9.72 (s, CHO)]. Standard aldol cyclization completed the creation of the spiro[4.5]decane skeleton **12** [ir 1670 cm^{-1}; NMR δ 6.58 (d, J = 10.5 Hz) and 5.90 (d, J = 10.5 Hz, CH=CHCO)].

The completion of the synthesis entails a 1,2-carbonyl transposition and introduction of a methyl group at the former carbonyl carbon atom. We recently developed a new approach for 1,2-alkylative carbonyl transpositions which seemed suitable although no case of an enone had been examined.[7] Sulfenylation[18] required employment of a THF–HMPA mixture (4:1 v/v) as solvent to give a 2.3:1 isomeric mixture with respect to the phenylthio substituent. The isomeric ratio was determined by the ratio of the doublets for the C=CHC(=O) at δ 6.00 and 5.97. Without separating the isomers, methyllithium was added to the carbonyl group. Delightfully, this reaction did not suffer complications from enolization. Direct dehydration of the reactive tertiary alcohol produced the dienol thioether **13.** Assignment of structure **12** rather than double bond isomers was indicated by the vinyl methyl group (δ 2.00, t, J = 2 Hz), an AB pattern for the disubstituted double bond (δ 5.35 and 5.89, J = 10 Hz), and a broadened AB pattern for the allylic methylene (δ 2.51 and 2.15, J = 20 Hz).

The predominant difficulty in the alkylative carbonyl transposition was the hydrolysis of the enol thioether which was only 50% complete after refluxing for 48 hr in aqueous dioxane containing mercuric chloride. This procedure is to be preferred over the titanium tetrachloride method[19] which caused extensive decomposition. The conjugated isomer **1** was the direct product of hydrolysis. Comparison of the infrared, ultraviolet, and NMR spectra of the synthetic racemic acorenone B with those of an authentic sample indicated their identity. It may be noted that acorenone[20] and acorenone B simply are related by a 1,3-carbonyl transposition. Thus, this approach may be utilized as a stereoselective route to this isomer.

The methods outlined in this paper have allowed extension of the stereoselective annelation of a four-membered ring to that of a six-membered ring. Methods to allow modification of the four-membered ring to other ring sizes as well as acyclic units of interest in natural products are under investigation. While our methods have focused on the cyclobutanones as a way to elaborate carbonyl groups,[21] taken in conjunction with the work of Seebach,[22] Ghosez,[23] Brady,[24] among others, these methods also allow elaboration of olefins.

Experimental Section

Infrared spectra were determined on a Perkin-Elmer 267 spectrometer and calibrated at 1601 cm^{-1}. Nuclear magnetic resonance spectra were recorded on a Joelco MH-100. Chemical shifts are given in δ units relative to internal Me_4Si and multiplicities are expressed as m = multiplet, s = singlet, d = doublet, t = triplet, b = broad. Mass spectra were run on a AEI MS-902 high resolution mass spectrometer at an ionizing current of 98 mA and voltage of 70 eV.

All reactions were performed under nitrogen. THF and ethyl ether were dried by distillation from sodium benzophenone ketyl. Me_2SO, DMF, HMPA, and benzene were dried by distillation from calcium hydride. Methanol was dried by distillation from magnesium methoxide. Preparative layer chromatography was performed on 200 × 200 × 1.5 or 200 × 400 × 1.5 mm layers of Merck silica gel PF 254.

Preparation of 2-Isopropyl-5-methylcyclopentanone (2). A mechanically stirred slurry of 25.7 g (46.5 mmol) of commercial sodium methoxide in 1 l. of anhydrous diethyl ether was cooled in an ice–salt bath to −10°.[25] A solution of 46.6 g (46.5 mmol) of 2-methylcyclopentanone and 47.5 g (64.2 mmol) of distilled ethyl formate was added over a 0.5-hr period. The white slurry changed to a yellow slush within 20 min after completion of the addition. The mixture was stirred 40 hr at room temperature and then added to 650 ml of dry DMF. Acetic anhydride (50 ml, 53 mmol) was added and a white precipitate formed immediately. After 15 min, 300 ml of ice–water was added, and the mixture neutralized with solid ammonium chloride and extracted with 3 × 400 ml of diethyl ether. The combined ether extracts were washed with 3 × 70 ml of saturated aqueous sodium chloride, dried over sodium sulfate, and evaporated to yield 70 g of crude product. Distillation at 110–115° (0.5–1.0 mm) resulted in 57.5 g (74%) of 2-(*anti*-acetoxymethylene)-5-methylcyclopentanone: ir (CCl_4) 1775, 1722, 1652, 1608 cm^{-1}; NMR (CCl_4) δ 7.93 (1 H, t, J = 2.5 Hz), 2.17 (3 H), s superimposed on δ 2.0–2.8 (3 H, m), 1.2–1.7 (2 H, m), 1.08 (3 H, d, J = 6.5 Hz).

To 165 g (0.87 mol) of anhydrous cuprous iodide (Fisher) in 1 l. of anhydrous diethyl ether cooled in a Dry Ice–isopropanol bath was added 985 ml of 1.7 *M* (1.68 mol) methyllithium in ether. After stirring 20 min, 53.45 g (0.318 mol) of 2-(*anti*-acetoxymethylene)-5-methylcyclopentanone was added dropwise. The suspension was stirred 0.5 hr at −70° and the temperature then allowed to rise to −20°. Ether saturated with dry hydrogen chloride was added and followed by addition of 1 l. of water. After separation of layers and extracting the aqueous layer with additional ether, the combined ether layers were washed with 3 × 30 ml of water, dried over magnesium sulfate, and distilled to yield 38.82 g (86%) of 2-isopropyl-5-methylcyclopentanone, bp 134–138° [lit.[8] 84° (31 mm)]. Spectral properties were identical with those reported in the literature.[8]

Preparation of 5-Isopropyl-8-methylspiro[3.4]octan-1-one (3). A solution of 23.00 g (0.165 mol) of 2-isopropyl-5-methylcyclopentanone in 800 ml of degassed Me_2SO was prepared at room temperature. Initially 30.0 g of cyclopropyldiphenylsulfonium fluoroborate and 8.7 g of powdered potassium hydroxide were added. After 15 hr, an additional 50.0 g of sulfonium salt and 14.0 g of base were added. The total amount of salt and base was 80.0 (0.259 mol) and 22.7 g (0.406 mol), respectively. After a total of 63 hr, the mixture was extracted with 3 × 200 ml of pentane, and the combined pentane extracts were washed with 3 × 100 ml of saturated aqueous sodium bicarbonate. After drying over sodium sulfate, the pentane was removed by distillation through a 300-mm Widmer column. In one run, the oxaspiropentane was distilled at 40–60° (0.5–0.8 mm). Normally, the crude product was added to 500 ml of dry benzene containing a spatula tip of lithium fluoroborate and refluxed 1 hr. The benzene was removed by distillation through a Widmer column and the residue distilled at 50–58° (0.4 mm) to give 26.80 g (89%) of the desired cyclobutanone. If desired, further purification could be achieved by eluting through 800 g of silica gel (MCB, grade 62, 60–200 mesh) and eluting with 2% ether in hexane: ir (CCl_4) 1760 cm^{-1}; NMR (CCl_4) δ 2.75 (2 H, m), 1.4–

2.4 (9 H, m), 1.00 (3 H, d, J = 7 Hz), 0.95 (3 H, d, J = 7 Hz), 0.86 (3 H, d, J = 7 Hz); MS *m/e* (rel %) 180 (9), 138 (9), 137 (22), 123 (13), 110 (10), 109 (100), 95 (55), 81 (65), 67 (26), 55 (16), and 41 (34); mol wt (calcd for $C_{12}H_{20}O$, 180.1514) 180.1520.

2-Formyl-5-isopropyl-8-methylspiro[3.4]octan-1-one (4). To a suspension of 510 mg (12 mmol) of sodium hydride (57% mineral oil suspension, washed with benzene before use) and **3** (1.80 g, 10 mmol) in 25 ml of dry benzene were added 5 ml of ethyl formate and 15 mg of methanol. The reaction mixture was allowed to stir at room temperature for 48 hr and then quenched with 20 ml of water. The organic layer was separated and washed with 10% aqueous potassium carbonate solution. The aqueous layers were combined and acidified carefully with concentrated hydrochloric acid under ice cooling, and the separated oil was extracted with ethyl acetate. The organic layer was washed with brine, dried over magnesium sulfate, and evaporated in vacuo to produce 1.915 g (92%) of **4** as a pale yellow oil which is homogeneous by TLC (5% ethyl acetate in hexane): ir ($CHCl_3$) 2730 (CHO), 1770 (cyclobutanone), 1710 (CHO); NMR (CCl_4) δ 0.7–1.2 (9 H, $3CH_3$), 1.2–2.9 (9 H), 4.04–4.52 (m, 1 H, C(=O)CH—CHO), 9.63 (d, J = 6 Hz, 1 H, CHO); MS *m/e* (rel %) 53 (100), 55 (17), 57 (19), 67 (50), 69 (48), 70 (100), 79 (15), 81 (58), 95 (27), 109 (100), 110 (50), 123 (18), 137 (27), 152 (15), 165 (5), 180 (5), 208 (5), mol wt (calcd for $C_{13}H_{20}O_2$, 208.1462) 208.1464.

8,9-Dehydro-1-isopropyl-4-methyl-7-oxaspiro[4.5]decan-6-one (5). The formylcyclobutanone **4** (1.900 g, 9.13 mmol) was refluxed in 300 ml of benzene containing 35 mg of *p*-toluenesulfonic acid monohydrate and 50 mg of water for 24 hr. After cooling, the reaction was washed with saturated aqueous sodium bicarbonate and brine, dried over magnesium sulfate, and evaporated in vacuo. The residue was submitted to preparative TLC (20% ethyl acetate in hexane) to give 1.273 g (67%) of **5**: ir ($CHCl_3$) 1745 (C=O), 1678 (C=C); NMR (CCl_4) 0.90 (d, J = 7.5 Hz, 6 H), 1.02 (d, J = 7.5 Hz, 3 H), 1.2–2.3 (8 H), 2.64 (dm, J = 19 Hz), 5.08 (ddd, J = 11, 10, 7 Hz, 1 H), 6.32 (ddd, J = 11, 6, 3 Hz, 1 H); MS *m/e* (rel %) 70 (14), 8 (32), 109 (100), 110 (10), 121 (10), 122 (11), 123 (10), 137 (27), 152 (13), 208 (8); mol wt (calcd for $C_{13}H_{20}O_2$, 208.1462) 208.1466.

1-Isopropyl-4-methyl-7-oxaspiro[4.5]decan-8-ol (6). Diisobutylaluminum hydride (2.12 ml of 1.40 M solution in toluene, 2.97 mmol) was added dropwise with stirring to a solution of 205 mg (0.99 mmol) of **5** in 5 ml of dry toluene cooled to −25°. The reaction mixture was stirred under nitrogen at −25° for 3 hr and quenched with methanol until gas evolution ceased (~0.2 ml). After warming to room temperature, it was stirred an additional 15 min and diluted with 20 ml of ether and 20 ml of brine. The organic layer was separated, and the aqueous layer was extracted with ether. The organic extracts were combined, dried over magnesium sulfate, and evaporated in vacuo to afford 210 mg (quantitative) of **4** as a colorless oil which is homogeneous by TLC (15% ethyl acetate in hexane): ir ($CHCl_3$) 3605, 3410 cm^{-1}; NMR ($CDCl_3$) δ 0.80–1.2, (9 H), 1.2–2.1 (11 H), 3.36 and 3.56 (two d, J = 12 Hz, 1 H), 3.53 and 3.60 (two s, 1 H), 3.92; 4.04 (two d, J = 12 Hz, 1 H), 4.80 and 5.12 (two m, 1 H); MS *m/e* (rel %) 55 (63), 67 (42), 69 (49) 79 (30), 81 (75), 82 (100), 83 (22), 93 (20), 95 (83), 96 (20), 107 (20), 109 (28), 123 (22), 137 (18), 138 (18), 150 (23), 151 (14), 163 (7), 194 (2), 212 (2); mol wt (calcd for $C_{12}H_{24}O_2$, 212.1775) 212.1775.

1-Isopropyl-4-methyl-7-oxaspiro[4.5]decan-8-one (7). Jones' reagent[15] (0.12 ml of 2.26 M chromic acid solution in 23% aqueous sulfuric acid, 0.27 mmol) was added slowly to an ice-cooled solution of lactol **6** (100 mg, 0.47 mmol) in 3 ml of acetone over a period of 15 min. Then the reaction mixture was quenched with isopropyl alcohol. After evaporation of the solvent, the residue was extracted with ether. The ethereal layer was washed sequentially with brine, saturated aqueous sodium bicarbonate, and brine, dried over magnesium sulfate, and evaporated in vacuo to give 90 mg (91%) of **7** as a colorless oil which was chromatographically homogeneous (20% ethyl acetate in hexane): ir ($CHCl_3$) 1745 cm^{-1}; NMR (CCl_4) 0.92 (d, J = 6 Hz, 3 H), 1.04 (d, J = 6 Hz, 6 H), 1.1–2.3 (m, 9 H), 2.4–2.6 (m, 2 H), 4.12 (s, 2 H); MS *m/e* (rel %) 41 (100), 44 (37), 55 (70), 67 (54), 69 (43), 79 (33), 81 (69), 82 (92), 93 (37), 95 (77), 107 (29), 109 (38), 138 (23), 150 (22), 168 (25), 179 (4), 195 (4), 210 (0.5); mol wt (calcd for $C_{13}H_{22}O_2$, 210.1619) 210.1607.

(*Z*)-1-Isopropyl-(*E*)-2-(3′,3′-ethylenedithiobutyl)-(*Z*)-2-hydroxymethyl-(*Z*)-3-methylcyclopentane (10). Methyllithium (0.31 ml of a 1.52 M solution in hexane, 0.47 mmol) was added dropwise with stirring to a solution of 82 mg (0.39 mmol) of **7** in 1 ml of dry ether and 1 ml of dry THF, and the mixture was cooled to −78°. After addition, the reaction mixture was stirred for 30 min at −78° and then quenched with 15 mg of ammonium chloride. After stirring at −78° for an additional 10 min, the reaction mixture was warmed to room temperature and diluted with ether. The solution was washed with brine, dried over magnesium sulfate, and evaporated in vacuo to give 88 mg of **9**: ir ($CHCl_3$) 3400 cm^{-1}; NMR (CCl_4) 0.7–1.2 (12 H), 1.2–2.2 (11 H), 3.0–3.8 (m, 3 H).

To a mixture of 88 mg (0.39 mmol) of this crude product **9** obtained above and 73 mg (0.78 mmol) of ethylenedithiol in 3 ml of dry toluene was added 15 mg of boron trifluoride–etherate with ice cooling. The reaction mixture was allowed to stand in a refrigerator for 16 hr and then diluted with ether. The solution was washed with saturated aqueous sodium bicarbonate and brine, dried over magnesium sulfate, and evaporated under reduced pressure. The residue was purified by preparative TLC (25% ethyl acetate in *n*-hexane) to give 73 mg (62% based on lactone **7**) of **10**: ir ($CHCl_3$) 3640, 3420 cm^{-1}; NMR ($CDCl_3$) 0.90 (d, J = 7 Hz, 3 H), 0.96 (d, J = 7 Hz, 3 H), 1.03 (d, J = 7 Hz, 3 H), 1.2–2.1 (m, 1 H with s, 3 H, at 1.8), 3.22 (s, 1 H), 3.34 (s, 4 H), 3.59 (s, 2 H); MS *m/e* (rel %) 55 (38), 69 (29), 81 (39), 95 (27), 105 (38), 109 (38), 118 (35), 119 (100), 127 (32), 137 (15), 155 (10), 167 (5), 19 (5), 209 (9), 242 (2), 302 (1); mol wt (calcd. for $C_{16}H_{30}OS_2$, 302.1738) 302.1728.

(*Z*)-2-Isopropyl-1-(3′,3′-ethylenedithiobutyl)-(*Z*)-5-methylcyclopentane-1-carboxaldehyde. Pyridine sulfur trioxide, prepared from 288 mg of pyridine and 203 mg of chlorosulfonic acid in 2 ml of carbon tetrachloride at 0°, decanted, washed with *n*-hexane, and used without further purification, was dissolved in 1.5 ml of Me_2SO and added dropwise to a mixture of 105 mg (0.348 mmol) of thioketal **8** and 351 mg (3.48 mmol) of triethylamine in 1.0 ml of dry Me_2SO at room temperature. The reaction mixture was stirred at room temperature for 15 hr, diluted with ether, washed successively with aqueous solutions of hydrochloric acid (10%), sodium bicarbonate (saturated), and sodium chloride. Drying over magnesium sulfate followed by evaporation gave 110 mg (quantitative) of **9** as a colorless oil which was chromatographically homogeneous. Further purification was achieved by preparative TLC (20% ethyl acetate in *n*-hexane, R_f 0.60) to allow recovery of 76 mg (73% recovery): ir ($CHCl_3$) 2734, 1712 cm^{-1}; NMR ($CDCl_3$) δ 0.7–1.0 (m, 9 H), 1.1–2.2 (m, 11 H with singlet, 3 H, superimposed at 1.79), 3.32 (s, 4 H), 9.72 (s, 1 H); MS *m/e* (rel %) 55 (18), 59 (13), 61 (11), 81 (17), 93 (22), 95 (14), 119 (100), 121 (12), 133 (15), 151 (9), 177 (5), 195 (5), 227 (5), 270 (4), 286 (1), 288 (1), 300 (2); mol wt (calcd for $C_{16}H_{28}OS_2$, 300.1582) 300.1573.

(*Z*)-2-Isopropyl-(*Z*)-5-methyl-1-(3-oxobutyl)-1-cyclopentanecarboxaldehyde (11). A mixture of 37 mg (0.123 mol) of the above thioketal and 100 mg (0.369 mmol) of mercuric chloride in 4 ml of 3:1 acetonitrile:water was refluxed for 15 hr. After cooling, the reaction mixture was diluted with ether, washed with saturated aqueous sodium bicarbonate and brine, dried over magnesium sulfate, and evaporated in vacuo. The residue was triturated with *n*-hexane. The filtrate was evaporated in vacuo to give 28 mg (quantitative) of **11** as a yellow oil which was chromatographically homogeneous. Further purification for characterization was achieved by preparative TLC (20% ethyl acetate in *n*-hexane, R_f 0.35) to give 19 mg (70% recovery) of **11** as a colorless oil: ir ($CHCl_3$) 1713 cm^{-1}; NMR (CCl_4) 0.7–1.1 (m, 9 H), 1.2–2.0 (m, 9 H), 2.08 (s, 3 H), 2.2–2.5 (m, 2 H), 9.72 (s, 1 H); MS *m/e* (rel %) 41 (64), 43 (100), 55 (40), 79 (22), 81 (37), 93 (27), 95 (35), 109 (24), 127 (20), 224 (2); mol wt (calcd for $C_{14}H_{24}O_2$, 224.1776) 224.1771.

6,7-Dehydro-1-isopropyl-4-methylspiro[4.5]decan-8-one (12). A solution of 64 mg (0.286 mmol) of **11** in 4 ml of 10% potassium hydroxide in methanol was stirred at room temperature for 14 hr. After the solvent was evaporated, the residue was diluted with 5 ml of water and 10 ml of ether. The organic layer was separated, and the aqueous layer was washed with ether. The combined organic layers were washed with brine, dried over magnesium sulfate, and evaporated in vacuo to give 54 mg (92%) which was chromatographically homogeneous. Further purification for characterization, achieved by preparative TLC (20% ethyl acetate in *n*-hexane,

R_f 0.55), gave 42 mg (78% recovery) of **12**: ir ($CHCl_3$) 1670 cm^{-1}; NMR (CCl_4) δ 0.86, 0.93, 0.94 (three d, J = 7 Hz, 3 H each), 1.2–2.2 (m, 9 H), 2.32 (m, 2 H), 5.90 (d, J = 10.5 Hz, 1 H), 6.58 (d, J = 10.5 Hz, 1 H); MS *m/e* (rel %) 41 (70), 55 (39), 67 (20), 69 (33), 77 (28), 79 (50), 81 (22), 82 (25), 91 (28), 92 (35), 94 (38), 94 (21), 107 (33), 109 (22), 121 (38), 122 (100), 123 (46), 124 (42), 135 (22), 136 (20), 163 (19), 164 (45), 191 (7), 206 (29); mol wt (calcd for $C_{14}H_{22}O$, 206.1671) 206.1665.

6,7-Dehydro-1-isopropyl-4-methyl-9-phenylthiospiro[4.5]decan-8-one. *n*-Butyllithium (0.85 ml of a 1.45 *M* *n*-hexane solution, 1.23 mmol) was added to a solution of 173 mg (1.23 mmol) of isopropylcyclohexylamine in 3 ml of dry THF cooled to −25°. After 30 min, a mixture of 84 mg (0.41 mmol) of **12** in 1 ml of dry HMPA and 1 ml of dry THF was added dropwise over a period of 5 min. The reaction mixture was stirred at −25° for 30 min, at 0° for 1 hr, and warmed to room temperature (10 min). Diphenyl disulfide (268 mg, 1.23 mmol) in 1.5 ml of dry THF was added at once, and the reaction mixture was stirred at room temperature for 1 hr. After quenching with 10% aqueous hydrochloric acid, the solution was extracted with ether. The organic layer was separated, washed with 10% aqueous hydrochloric acid, saturated aqueous sodium bicarbonate and brine, dried over magnesium sulfate, and evaporated under reduced pressure. The residue was purified by preparative TLC (13% ethyl acetate in *n*-hexane) to produce 103 mg (80%) of sulfenylated ketone as an isomeric mixture: ir ($CHCl_3$) 1680, 1612, and 1585 cm^{-1}; NMR (CCl_4) 0.7–1.1 (m, 9 H), 1.1–2.4 (m, 9 H), 3.90–4.16 (m, 1 H), 5.97 and 6.00 (two d, J = 10 Hz, 1 H), 6.58 and 6.62 (two d, J = 10 Hz, 1 H), 7.1–7.5 (m, 5 H); MS *m/e* (rel %) 41 (58), 55 (44), 65 (33), 69 (72), 77 (52), 79 (32), 91 (44), 93 (47), 107 (55), 109 (37), 110 (60), 121 (100), 134 (30), 135 (80), 161 (33), 186 (30), 218 (12), 231 (12), 314 (50); mol wt (calcd for $C_{20}H_{26}OS$, 314.1704) 314.1705.

4,8-Dimethyl-1-isopropyl-9-phenylthiospiro[4.5]deca-6,8-diene (13). Methyllithium (0.40 ml of a 1.52 *M* *n*-hexane solution, 0.60 mmol) was added dropwise to a solution of 62 mg (0.20 mmol) of the sulfenylated ketone in 1.5 ml of dry ether cooled to −78°. After stirring at −78° for 1.5 hr, the reaction mixture was warmed to room temperature, diluted with ether, and quenched with 50% brine. The ethereal layer was dried over magnesium sulfate and evaporated in vacuo to give 63 mg (95%) of tertiary alcohol: ir ($CHCl_3$) 3600–3400, 1580 cm^{-1}; NMR (CCl_4) 0.7–1.0 (m, 9 H), 1.1–2.4 (m, 13 H), 3.20–3.60 (m, 1 H), 5.10–5.76 (m, 2 H), 7.0–7.5 (m, 5 H); MS *m/e* (rel %) 41 (47), 43 (100), 55 (35), 69 (35), 70 (30), 91 (32), 93 (32), 105 (35), 110 (47), 119 (40), 151 (52), 177 (27), 194 (20), 217 (25), 330 (19); mol wt (calcd for $C_{21}H_{30}OS$; 330.2017) 330.2016.

The tertiary alcohol (52 mg, 0.157 mmol) was heated in 8 ml of refluxing benzene in the presence of 4 mg of *p*-toluenesulfonic acid monohydrate with a Dean-Stark apparatus for 1.5 hr. After cooling, the solution was diluted with ether, washed with saturated aqueous sodium bicarbonate and brine, dried over magnesium sulfate, and evaporated in vacuo. The residual oil (50 mg) was submitted to preparative TLC (*n*-hexane, R_f 0.49) to give 28 mg (55% overall) as a colorless oil: ir ($CHCl_3$) 1640 and 1582 cm^{-1}; NMR (CCl_4) 0.8–1.0 (m, 9 H), 1.1–1.9 (m, 7 H), 2.00 (t, J = 2 Hz, 3 H), 2.15 (dm, J = 20 Hz, 1 H), 2.51 (dm, J = 20 Hz, 1 H), 5.35 (d, J = 10 Hz, 1 H), 5.89 (d, J = 10 Hz, 1 H), 7.1–7.4 (m, 5 H); MS *m/e* (rel %) 41 (55), 55 (38), 69 (33), 77 (32), 91 (100), 105 (58), 110 (56), 117 (38), 118 (53), 119 (56), 159 (40), 203 (71), 227 (25), 312 (31); mol wt (calcd for $C_{21}H_{28}S$, 312.1912) 312.1912.

Acorenone B. A mixture of 25 mg (0.08 mmol) of **13** and 174 mg (0.64 mmol) of mercuric chloride in 5 ml of 4:1 dioxane:water was refluxed for 48 hr. After cooling, the reaction mixture was diluted with ether. The ethereal layer was separated, washed with saturated aqueous sodium bicarbonate and brine, dried over magnesium sulfate, and evaporated in vacuo. The residue was triturated with *n*-hexane. The filtrate was evaporated in vacuo to give a pale yellow oil which was submitted to preparative TLC (8% ethyl acetate in *n*-hexane) to give 14 mg (56%) of recovered starting material and 5.5 mg (71% yield based on recovered starting material) of product. Comparison of its ir, uv, and NMR spectra with those of an authentic sample indicated their identity: MS *m/e* (rel %) 41 (76), 43 (38), 55 (50), 69 (48), 81 (30), 82 (63), 93 (37), 108 (33), 109 (100), 121 (42), 123 (30), 135 (80), 136 (43), 149 (33), 150 (19), 177 (55), 220 (75); mol wt (calcd for $C_{15}H_{24}O$, 220.1827) 220.1826.

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