236. A Flexible Stereoselective Synthesis of the Spirosesquiterpenes (±)-β-Acorenol, (±)-β-Acoradiene, (±)-Acorenone-B and (±)-Acorenone *via* an Intramolecular Ene-Reaction

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Summary

The racemic spirosesquiterpenes β-acorenol (**1**), β-acoradiene (**2**), acorenone-B (**3**) and acorenone (**4**) (*Scheme 2*) have been synthesized in a simple, flexible and highly stereoselective manner from the ester **5**. The key step (*Schemes 3* and *4*), an intramolecular thermal ene reaction of the 1,6-diene **6**, proceeded with 100% *endo*-selectivity to give the separable and interconvertible epimers **7a** and **7b**. Transformation of the '*trans*'-ester **7a** to (±)-**1** and (±)-**2** *via* the enone **9** (*Scheme 5*) involved either a thermal *retro*-ene reaction **10** → **12** or, alternatively, an acid-catalysed elimination **11** → **13** + **14** followed by conversion to the 2-propanols **16** and **17** and their reduction with sodium in ammonia into **1** which was then dehydrated to **2**. The conversion of the '*cis*'-ester **7b** to either **3** (*Scheme 6*) or **4** (*Scheme 7*) was accomplished by transforming firstly the carbethoxy group to an isopropyl group *via* **7b** → **18** → **19** → **20**, oxidation of **20** to **21**, then alkylative 1,2-enone transposition **21** → **22** → **23** → **3**. By regioselective hydroboration and oxidation, the same precursor **20** gave a single ketone **25** which was subjected to the regioselective sulfenylation-alkylation-desulfenylation sequence **25** → **26** → **27** → **4**.

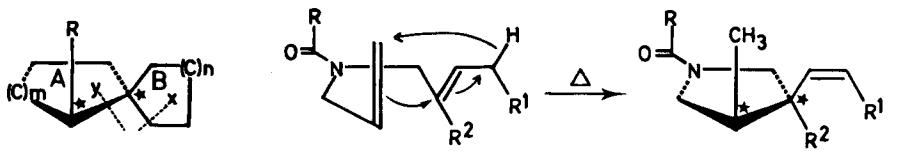
1. Introduction. – The interest in natural sesquiterpenoids with the spiro[4,5]decane skeleton I (*Scheme 1*) as constituents of essential oils, as stress metabolites and as proposed intermediates in terpene biogenesis has stimulated considerable synthetic efforts recently[1]) [1–7]. One of the major difficulties concerns the control of the relative configuration between the quaternary spiro center and an adjacent center carrying a C-atom substituent R.

Although this problem may be tackled by a regio-selective functional group manipulation of ring B [5f] [8a] the synthesis of natural spiro[4,5]decanes is accomplished most directly through a stereocontrolled spiroannelation step. Nearly all of the latter approaches rely on the steric bulk of the group R which directs more or less efficiently the formation of the bond x to the less hindered side of ring A[2]). This prin-

[1]) For a review see [1]; for more recent work on natural spiro[4,5]decanes see [2] (isolation) and [3–7] (synthesis).

[2]) For another potential route to spiro sesquiterpenoids *via* thermal cyclization of unsaturated ketones see [8b].

Scheme 1



Ia : m = 1, n = 2 **II** **a** : $R^1 = R^2 = H$ **III**
Ib : m = 2, n = 1 **b** : $R^1, = R^2 = -(CH_2)_3^-$

ciple, which applies to a variety of C-C bond forming processes, has been nicely exemplified *inter alia* in a brilliant synthesis of β-vetivone [6a].

We now wish to report an entirely different and versatile approach to sesquiterpenes of the acorane type **Ia** through formation of the bond **y** utilizing the stereoelectronic control of an intramolecular ene reaction. Its feasibility became apparent during systematic studies of the thermal conversion **II** → **III** [9]: pyrrolidines containing *cis*-related methyl- and vinyl-substituents were efficiently obtained stereospecifically under kinetic control (100% for the 2-azaspirodecene **IIIb**). Analogous construction of the carbocyclic spiro[4,5]decane system with functionality useful for further selective transformation into the racemic sesquiterpenes β-acorenol (**1**), β-acoradiene (**2**), acorenone-B (**3**) and acorenone (**4**) (*Scheme 2*) will be described here in detail.

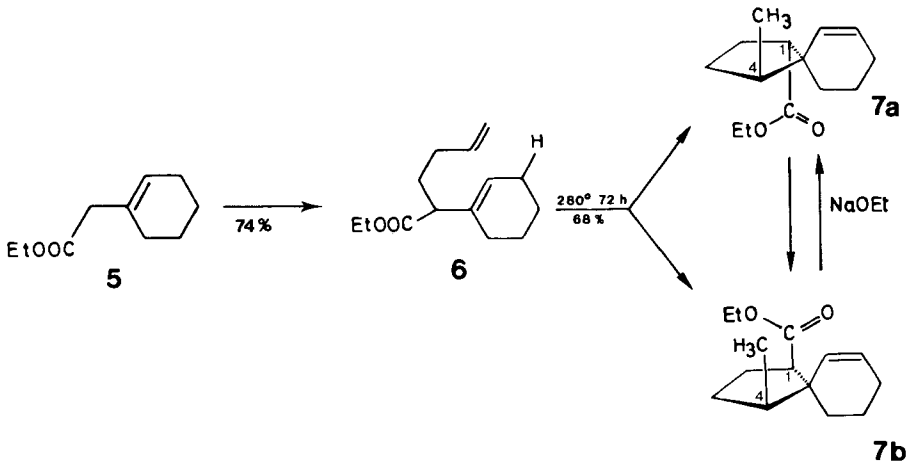
Scheme 2

(+)-β-ACORENOL (+)-β-ACORADIENE

(–)-ACORENONE B (–)- ACORENONE

2. Preparation of the Epimeric Spiroesters 7a and 7b by Intramolecular Ene Reaction of the Diene 6 (*Schemes 3 and 4*). – Ethyl 1-cyclohexenyl-acetate (**5**) [10] successively treated [11] with lithium cyclohexylisopropylamide and 1-bromo-3-butene gave the

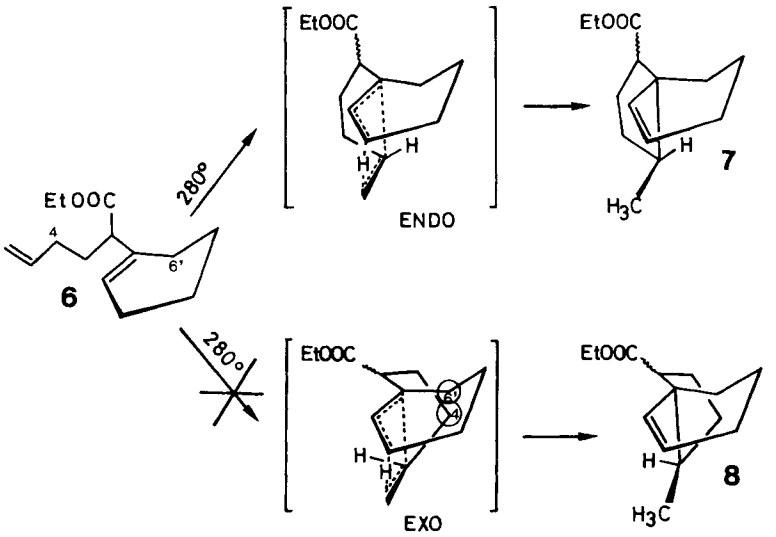
Scheme 3



C-alkylated 1,6-diene **6**. The latter cyclized at 290 ° to give a 1.7:1 mixture of the esters **7a** and **7b**. The two separated products, could be cleanly interconverted on basic treatment to give a 3:2 equilibrium mixture of **7a** and **7b**. Therefore the isomers **7a** and **7b** differ only with respect to their configuration at C(1). Although complete configurational assignment of **7a** and **7b** by ^{1}H-NMR. spectroscopy proved to be difficult[3]), the signals of the proton at C(1) are significantly different: the '*trans*'-ester **7a** shows a triplet (J = 7.0 Hz), δ = 2.78 ppm (no change after hydrogenation of the olefinic bond), whereas the '*cis*'-ester **7b** shows a triplet (J = 8.5 Hz) at higher field, δ = 2.61 ppm (shifted to δ = 2.48 ppm after hydrogenation). The stronger shielding and somewhat larger coupling constant of the H–C(1) triplet exhibited by the isomer **7b** may be attributed to the *cis*-relation of the methyl and carbethoxy groups which tend to occupy pseudoequatorial positions, forcing the H–C(1) more into an axial conformation. Olefin anisotropy effects do not play a major role here as shown by the hydrogenation experiments which do not give any information about the relative configuration of the methyl and the adjacent spiro center (identical in **7a** and **7b**). Nevertheless, the analogous cyclization of **IIb** to the 2-azaspirodecene **IIIb** [9], whose configuration has been established by X-ray analysis, strongly indicates that for **7a** and **7b**, the methyl and vinyl groups are on the same side of the five-membered ring. This also agrees with models (*Scheme 4*) which show nonbonding interactions between the bridge (C(4)) and the cyclohexene unit (C(6')) for the *exo* transition state, whereas the corresponding *endo* transition state is strain-free. The ene reaction of **6** should consequently proceed with an even higher *endo* selectivity than observed for the cyclization of the acyclic diene **IIa** [9]. In fact there was no trace (GC.) of the *exo* isomer **8**. Final unambiguous evidence for this configurational assignment was provided by the transformation of **7** into the spirosesquiterpenes **1** to **4** as described below; interconversion of the separable epimers **7a** and **7b** thus

[3]) No satisfactory stereochemical conclusions could be reached upon ^{1}H-NMR. comparison of the esters **7a** and **7b** or of their corresponding primary alcohols, using shift reagents.

Scheme 4



allowed the channeling of the synthetic pathway from a common precursor to both 1,4-*cis*- and 1,4-*trans*-substituted spiro[4,5]decane terpenes[4]).

3. Conversion of the *'trans'*-Ester 7a into (±) β-Acorenol (1) and (±)β-Acoradiene (2) (*Scheme 5*). – (+)-β-Acorenol (**1**) and (+)-β-acoradiene (**2**) were isolated from the wood of *Juniperus rigida* [12]. The total synthesis of their racemates from **7a** (preliminary communication [3a]), will be described here in detail[5]). Modification of the cyclohexene ring in **7a**, requiring alkylative 1,2-shift of the olefinic bond was accomplished as follows: Allylic oxidation [13] of **7a** furnished the enone **9** which reacted selectively with methyllithium; subsequent treatment with chlorodimethyl ether afforded the unstable acetal **10** as a mixture of epimers. In agreement with the thermolysis of various allylacetals [14][6]) the crude methoxymethyleneacetal **10** at 270° underwent a *retro*-ene reaction (*Scheme 5*) to give the ester **12** (36% from the enone **9**). Treatment of **12** with methyllithium finally gave (±)-β-acorenol (**1**) (identification by IR., ^{1}H-NMR. and GC. comparison with natural (+)-β-acorenol). Alternatively it appeared conceivable to convert the enone **9** to (±)-**1** *via* the dienes **13** and **14** obtained, together with the monoene **12** (in a ratio of 2:1:1) on heating the acetal **10** at a lower temperature (195°)[7]).

A simpler and more efficient route (94 to 96% yield) to the dienes **13** and **14** involved mild acid-induced (*p*-toluenesulfonic acid) dehydration of the alcohol **11**, prepared by reaction of **9** with methylmagnesium bromide. Thus, **11** led to the dienes

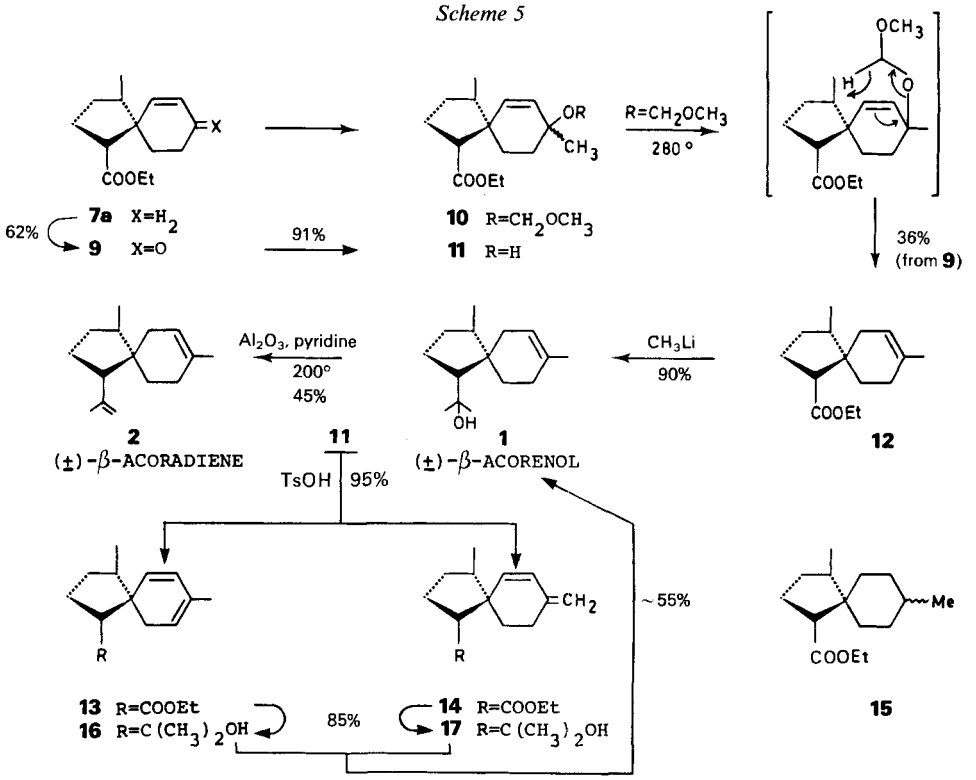
[4]) It may be pointed out that hydrolysis of **7a** and **7b** and separation of the free carboxylic acids into their enantiomers provides a potential route to the optically pure terpenes **1** to **4**. Indeed, preliminary experiments showed that saponification of **7a** and **7b** with NaOH, followed by reesterification with diazomethane could be carried out without epimerization at C(1).

[5]) A different non-stereoselective approach to (+)-β-acorenol has been achieved [3b].

[6]) Independent pyrolyses of allylic and propargylic acetals have been carried out recently in the laboratory of Prof. *D. Arigoni*, ETH Zürich. For an elegant application see [15].

[7]) At 270°, the dienes **13** and **14** presumably polymerize leaving the more stable monoene **12**.

Scheme 5



13 and **14** in a ratio of 7:3 or 1:3 depending on the solvent, dichloromethane or benzene, respectively[8]). Exposure of the latter 1:3 mixture to toluenesulfonic acid in dichloromethane refurnished a 7:3 mixture of **13** and **14** indicating the predominance of the endocyclic diene **13** under thermodynamically controlled reaction conditions (CH_2Cl_2), the formation of the diene **14** being favoured kinetically in benzene[9]). However, this point is of little relevance as far as the synthesis of (±)-β-acorenol is concerned as treatment of either diene **13** or **14** with methyllithium followed by reduction with sodium in ammonia furnished pure (±)-β-acorenol (**1**) in the same yield (54 to 57%)[10]).

Regioselective dehydration [12] of the synthetic (±)-β-acorenol afforded (±)-β-acoradiene (**2**) (identification by IR., ^{1}H-NMR. and GC. comparison with natural (+)-β-acoradiene).

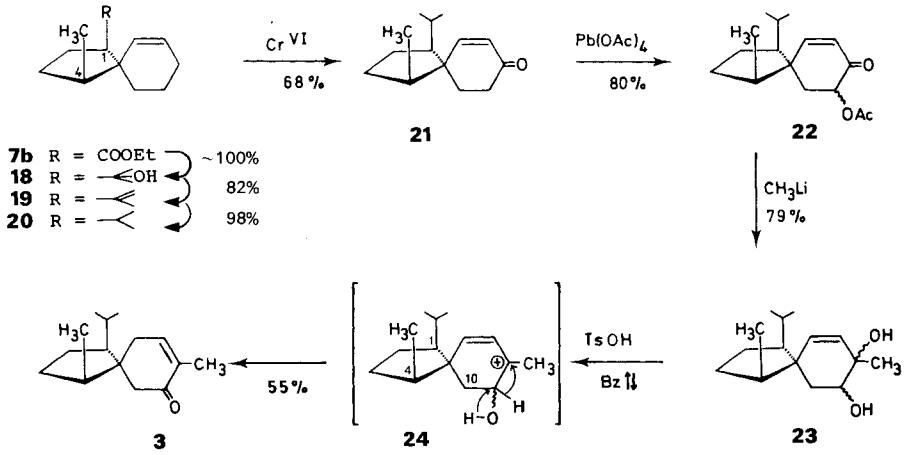
[8]) We thank Dr. *M. Pesaro*, *Givaudan SA*, for kindly communicating the application of these reaction conditions in a synthesis of (−)-acorenone-B (3) [16].

[9]) This solvent-dependent counterplay of thermodynamic *versus* kinetic control may be due to a better solvation of the transient allylcarbonium ion by dichloromethane as compared to benzene.

[10]) Hydrogenation of the dienic esters **13** and **14** proceeded rather slowly using *Lindlar* catalyst [17] in ethanol (no reaction in ethyl acetate) to give directly the saturated esters **15** without any monoene **12** (GC.) throughout the reaction. On the other hand the same conditions allowed partial reduction of the 2-propanols **16** and **17** to (±)-**1**; (50% by GC.); removal of a major unidentified side product was difficult and thus made the cleaner reduction of **16** and **17** with sodium in ammonia more attractive.

4. Conversion of the '*cis*'-Ester *7b* into (±)-Acorenone-B (3) (*Scheme 6*). – The spirocyclic sesquiterpene acorenone-B (**3**), isolated from *Bothriochloa intermedia* [18], has received considerable attention recently [5]. We describe here in detail the first

Scheme 6



(±)-ACORENONE B

stereoselective synthesis of racemic acorenone-B from the '*cis*'-ester **7b**[11]). With acorenone-B (**3**) and acorenone (**4**) in view it seemed appropriate to transform firstly the carbethoxy group of **7b** to an isopropyl substituent and to modify the cyclohexene ring at a later stage of the synthesis. Consequently the ester **7b** was treated with methyllithium; regioselective dehydration [19] of the crude 2-propanol derivative **18** gave the isopropenylspirodecene **19**, which, on selective hydrogenation [20], afforded the isopropyl spirodecene **20**[12]). This common precursor for acorenone-B and for acorenone, obtained in almost quantitative yield from the ester **7b**, was oxidized [13] to the cyclohexenone **21**. Conversion of **21** to (±)-acorenone-B (**3**) entails introduction of a methyl group in position 8 and 1,2-transposition of the enone system, accomplished as follows: α-acetoxylation of the enone **21** [21] afforded an epimeric mixture of acetates **22** which on reaction with methyllithium gave the stereoisomeric diols **23**. Dehydration of the diol mixture **23** afforded, after chromatography, pure (±)-acorenone-B (**3**) (identification by IR., NMR., MS. and GC. comparison with an authentic sample [5e]). The transformation **23** → **3** presumably involves a pinacol type hydrogen shift of the cation **24**[13]) followed by an acid-promoted migration of the olefinic bond. As side products, an inseparable mixture of 1-isopropyl-

[11]) Racemic acorenone-B was first synthesized with low stereoselectivity [5a]. After preliminary publication of our approach involving **7b** as the key intermediate [5b] other stereoselective routes to (±)-**3** [5c] and to enantiomerically pure (−)-**3** [5d] appeared. Very recently an alternative synthesis of (−)-**3** has been completed [16].

[12]) Under the homogenous hydrogenation conditions the inertness of the endocyclic double bond of **19** may be *inter alia* attributed to its steric shielding by the substituents at C(1) and C(4).

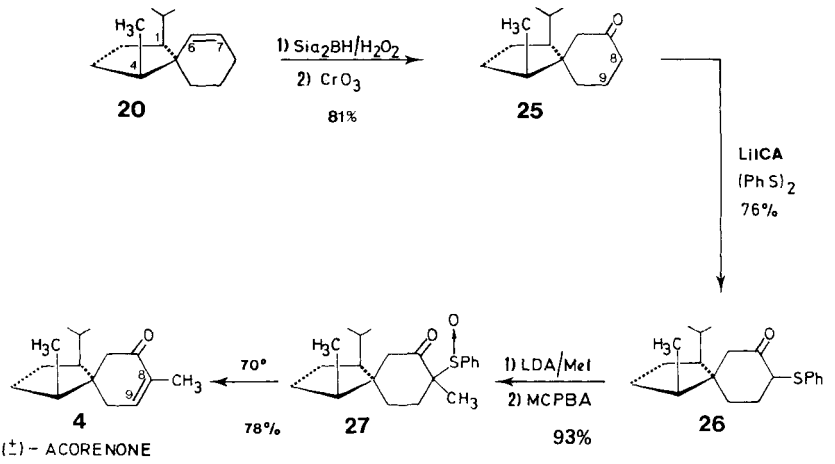
[13]) The intermediacy of the cation **24** is supported by a closely related study showing the ratio of arranged cyclohexenones to aromatic side products (*vide infra*) to be independent of the diol configuration [22].

4,6-dimethyl tetrahydronaphthalene and its 4-isopropyl-1,6-dimethyl isomer was isolated (18%) showing a minor competitive migration of C(1) and C(4); by contrast C(10) does not migrate under these conditions (absence of aldehyde signals in the ^{1}H-NMR. spectrum of the crude reaction mixture). Although not optimized, the efficiency of the alkylative 1,2-enone transposition **21** → **3** compares favourably with an alternative approach requiring $Hg(OAc)_2$ promoted hydrolysis of a dienylthioether [5c]. This new sequence applied to a variety of cyclohexenones proceeds in fair to excellent yields [22].

5. Conversion of the '*cis*'-1-Isopropyl-4-methyl-[4,5]-decene 20 into (±)-Acorenone (4) (*Scheme 7*)[14]. – (−)-Acorenone (**4**) is a constituent of the oil of sweet flag (*Acorus calamus*) [23]. It represents a spiro-epimer of (−)-acorenone-B (**3**) from which it was obtained by 1,3-enone transposition using the *Wharton* reaction [24][15]).

This formal inversion of the spiro-center served also to convert synthetic (±)-acorenone-B to (±)-**4** [5f].

Scheme 7



We describe here a more direct and simpler route to (±)-acorenone (**4**) from the easily accessible cyclohexene **20**. Models of **20** revealed a possible steric discrimination between the olefinic centers C(6) and C(7), the former being more hindered by the substituents at C(1) and C(4). In fact, hydroboration-oxidation of **20** using the bulky disiamylborane [25] and subsequent chromic oxidation afforded the single ketone **25**; in accord with this structure, four protons were smoothly exchanged on treatment with D_2O[16]).

The synthesis of (±)-acorenone (**4**) from **25** required the introduction of a methyl group at C(8), and unsaturation at C(8)–C(9) which was accomplished by a sulfenyla-

[14]) Reported by one of us (*W.O.*) at the 'Prelog-Symposium', Zürich, November 1976.

[15]) It is worth noting that the allylic alcohol coccinol, a metabolite of *Fusidium coccineum* was oxidized to the ketone coccinone, identical with (−)-acorenone [24].

[16]) No significant discrimination between the centers C(6) and C(7) was observed on reaction of **20** with diborane.

tion-alkylation-desulfenylation sequence [26]. After regioselective α-sulfenylation of the ketone **25**[17]), using lithium cyclohexylisopropylamide to generate the intermediate enolate, the phenylthioether **26** was treated with lithium diisopropylamide and methyl iodide to afford an alkylated thioether which was oxidized with *m*-chloroperbenzoic acid to the sulfoxide **27** (mixture of stereoisomers (93%). Heating **27** in carbon tetrachloride at 70° effected complete elimination to give (±)-acorenone (**4**) (identification by UV., IR., ^{1}H-NMR., ^{13}C-NMR. and MS. comparison with an authentic sample [5f] and with (−)-acorenone prepared either from coccinol or from (−)-acorenone-B[15]) [24])[18]).

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Experimental Part

General remarks. All reactions were carried out under an argon or nitrogen atmosphere. Abbreviations are used for the following solvents: DME for dimethoxyethane, HMPA for hexamethylphosphoramide and THF for tetrahydrofuran. The *usual work* up implied shaking of the crude reaction mixture with ether or CH_2Cl_2 and ice-water, washing of the organic layer with water, $NaHCO_3$ and/or sat. aq. NaCl-solution, drying over anhydrous Na_2SO_4 and removal of solvent *in vacuo* using a rotary evaporator. Preparative chromatography was carried out on silica gel (*Merck* 0.05–0.20 mm) unless specified otherwise. Melting points (m.p.) are not corrected. Gas chromatograms (GC.): steel column (2 mm/4 m), stationary phase on Chromosorb W, 2.5 atm N_2 or capillary column, 150 ft/0.01 inch *Perkin Elmer*, 3 atm N_2 unless specified otherwise; retention time in min. UV. spectra: λ_{max} in nm, log ε in parentheses. IR. spectra: film unless specified otherwise: ν_{max} in cm^{-1}. ^{1}H-NMR. spectra: in $CDCl_3$ at 100 MHz unless specified otherwise, internal standard tetramethylsilane (δ=0 ppm); abbreviations: *s*=singlet, *d*=doublet, *t*=triplet, *q*=quartet, *m*=multiplet, br., broad, *J*=spin-spin coupling constant (Hz). Mass spectra (MS.)=m/e, relative intensity in % in parentheses.

Preparation and Interconversion of the Spiroesters 7a and 7b (*Scheme 3*). – *Ethyl 2-(1-cyclohexenyl)-5-hexenoate* (**6**). To a stirred solution of freshly distilled cyclohexylisopropylamine (29.3 g, 0.2 mol) in dry DME (300 ml) was added dropwise at −70° a 2.15N solution of butyllithium in hexane (80 ml, 0.72 mol), dry HMPA (80 ml) and 10 min later a solution of ethyl 2-(1-cyclohexenyl)-acetate (**5**) (29 g, 0.172 mol) in DME (30 ml) followed 20 min later by 1-bromo-3-butene (28.0 g, 0.2 mol). The reaction mixture was stirred at −70° for 3 h, at 0° for 3 h, at 25° for 16 h and at 65° for 15 min, then subjected to the usual work-up, including washing of the organic layer with 10% citric acid, to give after distillation the pure alkylated product **6** as a colourless oil (28 g, 74%), b.p. 83–85°/0.4 Torr. – IR: 3085*w*, 1730, 1642*w*, 1035, 915. – ^{1}H-NMR.: 1.27 (*t*, *J*=7, 3H); 1.3–2.4 (12H); 2.93 (*m*, 1H); 4.15 (*q*, *J*=7, 2H); 4.8–5.2 (2H); 5.5–6.1 (2H).

$C_{14}H_{22}O_2$ (222.33) Calc. C 75.6 H 10.0 O 14.4% Found C 75.4 H 10.1 O 14.7%

Thermolysis of the 1,6-diene **6**. A solution of the diene **6** (10 g, 0.45 mmol) in dry toluene (54 ml) was heated in a sealed *Pyrex* ampule at 290° for 72 h. The evaporated reaction mixture (8 g), on chromatography (600 g SiO_2, toluene/pentane 2:1), furnished the less polar '*trans*'-ester **7a** as a colourless oil, (2.54 g, 25%). – b.p. 62° (bath)/0.1 Torr. – GC. (capillary SE-30, 150°): retention time 22.25. – IR.: 1730, 740. – ^{1}H-NMR.: 0.89 (*d*, *J*=6.5, 3H); 1.26 (*t*, *J*=7, 3H); 1.0–2.3 (11H); 2.78 (*t*, *J*=7, 1H); 4.16 (*d*×*q*, *J*=3 and 7, 2H, irradiation at 1.26 → *d*, *J*=3); 5.53 (*d*×*t*, *J*=10 and

[17]) Model experiments showed under these conditions highly regioselective sulfenylation of 4,4-dimethyl-2-cyclohexenone to give exclusively 4,4-dimethyl-6-phenylthio-2-cyclohexenone [27].

[18]) For the ^{13}C-NMR. and MS. spectra of acorenone-B and acorenone see [28].

1.5, 1 H, irradiation at 2.0 → *d*, *J* = 10); 5.76 (*d* × *t*, *J* = 10 and 3.5, 1 H, irradiation at 2.0 → *d*, *J* = 10). – MS.: 222 ($C_{14}H_{22}O_2^+$, 39), 177 (25), 176 (26), 149 (75), 148 (100), 122 (29), 101 (18).

$C_{14}H_{22}O_2$ (222.33) Calc. C 75.6 H 10.0% Found C 75.5 H 10.1%

Further elution afforded the more polar '*cis*'-ester **7b** (4.31 g, 43%). – GC. (capillary SE-30, 150°): retention time 21.75. – IR.: 1730, 738. – ^{1}H-NMR.: 0.89 (*d*, *J* = 6, 3 H); 1.23 (*t*, *J* = 7, 3 H); 1.1–2.4 (11 H); 2.61 (*t*, *J* = 8.5, 1 H); 4.10 (*q*, *J* = 7, 2 H); 5.46 (*d* × *t*, *J* = 10 and 1.5, 1 H, irradiation at 1.9 → *d*, *J* = 10); 5.84 (*d* × *t*, *J* = 10 and 3.5, 1 H, irradiation at 1.9 → *d*, *J* = 10). – MS.: 222 ($C_{14}H_{22}O_2^+$, 28), 176 (24), 149 (68), 148 (100), 122 (28), 107 (26), 101 (20), 93 (24), 91 (32), 79 (40).

$C_{14}H_{22}O_2$ (222.33) Calc. C 75.6 H 10.0% Found C 75.3 H 10.0%

A solution of the '*trans*'-ester **7a** (25 mg) in methanol (3 ml) was stirred with Pd/C (10%, 60 mg) under H_2 for 16 h. Filtration of the mixture, evaporation of the filtrate and distillation 62° (bath)/0.1 Torr furnished a saturated ester (19 mg). – ^{1}H-NMR.: 0.85 (*d*, *J* = 6, 3 H); 1.25 (*t*, *J* = 7, 3 H); 0.8–2.3 (15 H); 2.78 (*t*, *J* = 7.5, 1 H); 4.11 (*q*, *J* = 7, 2 H). Similar hydrogenation of the '*cis*'-ester **7b** (16 mg) afforded a saturated ester (13 mg). – ^{1}H-NMR.: 0.96 (*d*, *J* = 6, 3 H); 1.26 (*t*, *J* = 7, 3 H); 0.8–2.5 (15 H); 2.48 (*t*, *J* = 7.5, 1 H); 4.11 (*q*, *J* = 7, 2 H).

Interconversion of the epimeric esters **7a** *and* **7b**. A solution of the '*trans*'-ester **7a** (600 mg) in an anhydrous 1 N solution of sodium ethylate in ethanol (6 ml) was heated at 70° for 18 h in a sealed *Pyrex* tube. The evaporated mixture after usual work up and distillation 65° (bath)/0.1 Torr furnished a clean 2:3 mixture ^{1}H-NMR. of **7a** and **7b** (540 mg, 90%). The same mixture was obtained from the '*cis*'-ester **7b** under identical conditions.

Conversion of the '*trans*'-Ester 7a into (±)-β-Acorenol (1) and (±)-β-Acoradiene (2) (*Scheme 5*). – (*1R*, 4R*, 5S*)-1-Carbethoxy-4-methyl-spiro[4,5]-6-decen-8-one* (**9**). A mixture of the '*trans*'-ester **7a** (3.33 g, 15 mmol), sodium dichromate (6 g), acetic acid (30 ml), and acetic anhydride (18 ml) was stirred at 40° for 2 h. After further addition of sodium chromate (3 g), acetic acid (15 ml) and acetic acid anhydride (9 ml) the reaction mixture was stirred at 40° for 3 h, worked up as usual (3.08 g) and chromatographed (toluene/ethyl acetate 9:1) to give the unchanged ester **7a** (0.5) followed by the more polar enone **9** (1.75 g, 62% based on recovered **7a**), b.p. 100° (bath)/0.05 Torr. – UV. (methanol): 230 (4.05), 317 (1.58). – IR.: 1730, 1683, 1615 *w*. – ^{1}H-NMR.: 0.86 (*d*, *J* = 6.5, 3 H); 1.13 (*t*, *J* = 7, 3 H); 1.2–2.6 (9 H); 2.85 (*t*, *J* = 7, 1 H); 4.04 (*q*, *J* = 7, 2 H); 5.91 (*d*, *J* = 10, 1 H); 6.70 (*d*, *J* = 10, 1 H).

$C_{14}H_{20}O_3$ (236.31) Calc. C 71.2 H 8.5% Found C 71.1 H 8.3%

(*1R*, 4R*, 5S*)-1-Carbethoxy-8-methoxymethoxy-4,8-dimethyl-spiro-[4,5]-6-decene* (**10**). A 2N solution of methyllithium in ether (1 ml, 2.0 mmol) was added slowly at −70° to a stirred solution of the enone **9** (473 mg, 2.0 mmol) in anhydrous ether (4 ml). The mixture was allowed to warm to 25° then diluted with dry HMPA (4 ml). After dropwise addition of chlorodimethyl ether (0.3 ml, 4 mmol), the reaction mixture was stirred at 25° for 40 min, evaporated 3 times together with dry toluene (to remove the excess of chlorodimethyl ether) and finally shaken vigorously with pentane/aq. $NaHCO_3$. The organic layer was washed 3 times with aq. $NaHCO_3$, dried and evaporated to give the unstable acetal **10** (524 mg) which, without further purification was pyrolysed as described below. For identification a sample of the crude acetal (113 mg) was chromatographed on Al_2O_3 (neutral, activity II, toluene) to give pure **10** as an oily mixture of two stereoisomers (43 mg). – IR.: no OH, 1738, 1050. – ^{1}H-NMR.: 0.8–1.0 (3 H); 1.2–1.4 (6 H); 1.2–2.3 (9 H); 2.74 (*m*, 1 H); 3.37 (*s*, 3 H); 4.13 (*q*, *J* = 7, 2 H); 4.6–4.9 (2 H); 5.5–5.8 (2 H). The CH_3-signals at $\delta = 0.84/0.89$ and at $\delta = 1.25/1.30$ reveal the presence of two stereoisomers (2:3). – MS.: no $C_{17}H_{28}O_4$-peak, 281 (41), 161 (83), 160 (40), 145 (30), 119 (100), 105 (68), 93 (28), 91 (42).

(*1R*, 4R*, 5S*)-1-Carbethoxy-4,8-dimethyl-spiro[4,5]-7-decene* (**12**) *by Thermolysis of the Acetal* **10**. A solution of the crude acetal **10** (102 mg) in heptane (10 ml) was heated at 270–280° for 2 h in a sealed *Pyrex* ampule. The evaporated mixture (83 mg) afforded after chromatography (30 g SiO_2, toluene/petroleum ether 1:1) the olefinic ester **12** as a colourless oil (31 mg, 36% from the enone **9**). – IR.: 1735. – ^{1}H-NMR.: 0.83 (*d*, *J* = 6.5, 3 H); 1,24 (*t*, *J* = 7, 3 H); 1.24 (*s*, 3 H); 1.1–2.4 (11 H); 2.61 (*t*, *J* = 7, 1 H); 4.10 (*q*, *J* = 7, 2 H); 5.30 (*m*, 1 H). – After heating the crude acetal **10** (160 mg) in toluene (15 ml) at 195° for 16 h in a sealed ampule, chromatography of the evaporated solution furnished a mixture of **12**, **13** and **14** (107 mg).

(*1R**, *4R**, *5S**)-*1-Carbethoxy-4,8-dimethyl-6-decen-8-ol* (**11**). A 2N solution of methyl magnesium bromide in ether (1.1 ml, 2.2 mmol) was added over a period of 10 min at −10° to a stirred solution of the enone **9** (472 mg, 2 mmol) in THF (8 ml). After stirring the reaction mixture at −10° for a further 30 min it was poured into a mixture of ice and aq. buffer solution (sat. aq. NH_4Cl brought to pH = 8 by addition of NaOH). Extraction with ether, evaporation and distillation of the dried extracts furnished the alcohol **11** (460 mg, 91%) as an oily mixture of C(8)-epimers. – IR.: 3450 br., 1730, 762. – ^{1}H-NMR.: 0.8–1.0 (3H); 1.1–1.3 (6H); 1.1–2.4 (10H); 2.65 (*m*, 1H); 3.9–4.2 (2H); 5.3–5.8 (2H). Signals at $\delta = 0.84/0.89$ and $\delta = 1.25/1.30$ reveal the presence of two stereoisomers (2:3). – MS.: 252 ($C_{15}H_{24}O_3^+$, 1), 237 (13), 234 (12), 187 (12), 163 (16), 161 (29), 160 (27), 145 (13), 134 (16), 119 (42), 106 (21), 105 (33), 192 (71), 191 (100).

(*1R**, *4R**, *5S**)-*1-Carbethoxy-4-8-dimethyl-spiro[4,5]-6,8-decadiene* (**13**) and (*1R**, *4R**, *5S**)-*1-carbethoxy-4-methyl-8-methylene-spiro[4,5]-6-decene* (**14**). a) A mixture of the allylic alcohol **11** (50 mg, 0.2 mmol), toluenesulfonic acid monohydrate (10 mg) and CH_2Cl_2 (20 ml) was stirred at 20° for 4 h. Usual work-up (washing with $NaHCO_3$) and distillation of the reaction mixture at 110° (bath)/0.2 Torr furnished a 7:3 mixture (GC.) of the dienes **13** and **14**, respectively (44 mg, 94%). b) A mixture of the alcohol **11** (50 mg, 0.2 mmol), finely powdered toluenesulfonic acid monohydrate (10 mg) and dry benzene (20 ml) was stirred at 25° for 4 h. Usual work-up and distillation of the reaction mixture furnished a 1:3 mixture (GC.) of the dienes **13** and **14**, respectively (45 mg, 96%). c) Stirring a 1:3 mixture of **13** and **14** (50 mg) in CH_2Cl_2 (10 ml) with toluenesulfonic acid monohydrate (10 mg) at 20° for 4 h and usual work-up furnished **13** and **14** (38 mg) in a ratio of 7:3, respectively. For identification the mixture of **13** and **14** was separated by chromatography (hexane/toluene 4:1, sat. with ethanolamine). The diene **13** was eluted first, GC. (capillary, SE 30, 200°) retention time 12.49. – UV. (hexane): 262 (3.50). – IR.: 3040, 1735, 920. – ^{1}H-NMR.: 0.87 (*d*, $J = 6.5$, 3H); 1.22 (*t*, $J = 7$, 3H); 1.69 (*m*, 3H); 1.1–2.5 (7H); 2.66 (*t*, $J = 7$, 1H); 4.08 (*q*, $J = 7$, 2H); 5.38 (*m*, 1H); 5.62 (*d*, $J = 10$, 1H); 5.78 (*d* × *d*, $J = 10$ and 1.5, 1H). – MS.: 234 ($C_{15}H_{22}O_2^+$, 11), 188 (11), 160 (21), 145 (14), 119 (100), 105 (32), 91 (20).

Further elution gave the less polar diene **14**, GC. (capillary, SE 30, 200°): retention time 13.64. – UV. (hexane): 233 (4.33). – IR.: 3080*w*, 3030, 1738, 895. – ^{1}H-NMR.: 0.87 (*d*, $J = 6.5$, 3H); 1.24 (*t*, $J = 7$, 3H); 1.1–2.6 (9H); 2.82 (*t*, $J = 7$, 1H); 4.12 (*d* × *q*, $J = 1.5$ and 7, 2H); 4.81 (br., *s*, 2H); 5.65 (*d*, $J = 10$, 1H); 6.15 (*d*, $J = 10$, 1H). – MS.: 234 ($C_{15}H_{22}O_2^+$, 20), 188 (27), 161 (51), 160 (100), 119 (69), 105 (57), 91 (63).

(*1R**, *4R**, *5S**)-*1-(2-Hydroxypropyl)-4,8-dimethyl-spiro[4,5]-6,8-decadiene* (**16**) *and* (*1R**, *4R**, *5R**)-*1-(2-hydroxypropyl)-4-methyl-8-methylene-spiro[4,5]-6-decene* (**17**). a) A 2N solution of methylmagnesium bromide in ether (0.9 ml, 1.8 mmol) was added dropwise to a stirred solution of a 3:7 mixture of the dienes **13** and **14** (45 mg, 0.19 mmol) in dry THF (5 ml) at 0°. The reaction mixture was stirred at 25° for 2 h and worked up as described for the alcohol **11** to give after chromatography (toluene/ethyl acetate 9:1) a 3:7 mixture of the dienols **16** and **17** (36 mg, 85%). b) Under identical conditions a 1:3 mixture of the dienes **13** and **14** (38 mg, 0.16 mmol) furnished a 1:3 mixture of the dienols **16** and **17** (31 mg, 87%). c) Analogous reaction of the purified diene **13** (23 mg, 0.1 mmol) gave the pure dienol **16** (20 mg, 87%), GC. (5% Carbowax 20M, 180°): retention time 10.66. – UV. (hexane): 266 (3.31). – IR. (CCl_4): 3630, 3500 br., 3030, 950. – ^{1}H-NMR.: 0.84 (*d*, $J = 7$, 3H); 1.25 (*s*, 3H); 1.31 (*s*, 3H); 1.73 (*m*, 3H); 1.0–2.4 (8H); 2.73 (br. *d*, $J = 17$, 1H); 5.44 (br. *s*, 1H); 5.63 (*d*, $J = 10$, 1H); 5.74 (*d* × *d*, $J = 10$ and 1.5, 1H). – MS.: 220 ($C_{15}H_{24}O^+$, 0.6), 202 (26), 187 (5), 159 (17), 145 (38), 133 (73), 119 (100), 105 (75). d) Analogous reaction of the purified diene **14** (23 mg, 0.1 mmol) gave the pure dienol **17** (21 mg, 90%). – GC. (5% Carbowax 20M, 180°): retention time 14.72. – UV. (hexane): 234 (4.14). – IR. (CCl_4): 3630, 3090*w*, 3030, 1640*w*, 890. – ^{1}H-NMR.: 0.90 (*d*, $J = 6.5$, 3H); 1.21 (*s*, 3H); 1.27 (*s*, 3H); 1.1–2.6 (11H); 4.8 (br. *s*, 2H); 5.86 (*d*, $J = 10$, 1H); 6.25 (*d*, $J = 10$, 1H). – MS.: 220 ($C_{15}H_{24}O^+$, 10), 205 (34), 202 (61), 188 (18), 162 (30), 159 (63), 147 (39), 146 (33), 145 (31), 133 (43), 132 (35), 130 (31), 121 (36), 120 (69), 119 (66), 118 (35), 106 (30), 105 (87), 93 (38), 92 (38), 91 (100).

(±)-*β-Acorenol* (**1**). a) *Preparation from the ester* **12**. A 2N solution of methyllithium in ether (4 drops) was added to a stirred solution of the ester **12** (5 mg, 0.05 mmol) in ether (0.4 ml) at 25°. After 40 min at 25° usual work-up furnished racemic β-acorenol (**1**) (4 mg, 90%) as a colourless oil, GC. (5% Carbowax 20M, 180°): retention time 12.17. – IR. (KBr): 3450 br., 1450 br., 1372, 935,

805. – ^{1}H-NMR. (CCl_4): 0.83 (*d*, *J*=6.5, 3H); 1.22 (*s*, 3H); 1.29 (*s*, 3H); 1.72 (br.*s*, 3H); 1.0–2.3 (12H); 2.36 (br.*d*, *J*=17, 1H); 5.27 (br.*s*, 1H). – MS.: no $C_{15}H_{26}O^+$-peak, 204 (33), 189 (7), 161 (24), 121 (48), 119 (100), 105 (26), 93 (41). The IR. and ^{1}H-NMR. spectra and GC. of racemic **1** are identical to those of natural (+)-β-acorenol. b) *Preparation from the dienols* **16** *and* **17**. Na (100 mg) was added to a stirred solution of a 3:1 mixture of the dienols **16** and **17** (30 mg, 0.14 mmol) in liquid NH_3 (10 ml) at −40°. After stirring the blue solution at −40° for 3 h, successive addition of solid NH_4Cl, evaporation of the NH_3, usual work-up of the residue and chromatography (toluene/ethyl acetate 9:1) furnished pure (±)-β-acorenol (**1**) (17 mg, 57%). Analogous reduction of a 3:7 mixture of the dienols **16** and **17** (13 mg, 0.06 mmol) gave after chromatography pure (±)-β-acorenol **1** (7 mg, 54% yield).

(±)-β-Acoradiene (**2**). A homogeneous mixture of synthetic (±)-β-acorenol (**1**) (12 mg, 0.05 mmol), Al_2O_3 (*Merck*, neutral, activity I, 300 mg) and pyridine (0.4 g) was heated at 200° for 5 h in a sealed *Pyrex* ampoule. Extraction of the mixture (3×) with hot methanol, evaporation of the extracts and chromatography of the residue (hexane) gave pure (±)-β-acoradiene (**2**) as a colourless oil (5 mg, 45%). – GC. (capillary, SE 30, 180°): retention time 13.70; (5% Carbowax 20M, 180°): retention time 6.00. – IR. (KBr): 1645, 1460, 1380, 900, 820. – ^{1}H-NMR.: 0.84 (*d*, *J*=6.5, 3H); 1.0–2.4 (11H); 1.59 (br.*s*, 3H); 1.72 (*s*, 3H); 2.23 (*t*, *J*=7, 1H); 4.60 (br.*s*, 1H); 4.75 (br.*s*, 1H); 5.28 (br.*s*, 1H). The IR. and ^{1}H-NMR. spectra and GC. of (±)-**2** are identical to those of natural (+)-β-acoradiene.

(1R, 4R*, 5S*)-1-Carbethoxy-4,8-dimethyl-spiro[4,5]decane* (**15**). A 3:7 mixture of the esters **13** and **14** (34 mg, 0.15 mmol), *Lindlar* catalyst (*Fluka*, 30 mg) and ethanol (10 ml) was stirred at 25°. The reaction was followed by GC. (capillary SE 30, 200°) to show next to the unchanged dienes **13** and **14** (retention times of 12.49 and 13.68, respectively) the presence of only one peak, retention time 12.87. After 20 h further *Lindlar* catalyst (30 mg) was added to the reaction mixture which then was stirred under hydrogen for another 20 h. The filtrated and evaporated mixture afforded after chromatography (hexane/toluene 4:1, sat. with ethanolamine) the saturated ester **15** (10 mg), GC. (capillary SE 30, 200°): retention time 12.87. – IR. (CCl_4): 1740. – ^{1}H-NMR.: 0.7–1.0 (6H); 1.26 (*t*, *J*=7, 3H); 0.9–2.2 (14H); 2.9 (*t*, *J*=7, 1H); 4.14 (*d*×*q*, *J*=1.5 and 7, 2H). – MS.: 238 ($C_{15}H_{26}O_2^+$, 46), 192 (35, 34), 138 (63), 122 (49), 101 (68), 95 (100), 81 (69). Further elution gave only the more polar dienes **13** and **14** (7 mg) in the ratio of 3:1 (GC. analysis) indicating slower reduction of **13** as compared to **14**.

Conversion of the *'cis'*-Ester 7b into (±)-Acorenone-B (3) (*Scheme 6*). – *(1R*, 4S*, 5R*)-1-(2-Hydroxypropyl)-4-methyl-spiro[4,5]-6-decene* (**18**). A 1.5N solution of methyllithium in ether (4 ml, 6 mmol) was added to a stirred solution of the *'cis'*-ester **7b** (200 mg, 0.9 mmol) in ether (10 ml) over a period of 10 min at 25°. The reaction mixture was stirred for 40 min at 25°. Decomposition with sat. aq. ammonium sulfate solution followed by the usual work-up gave the alcohol **18** as a colourless oil (185 mg, 100%). – IR.: 3450 br., 3030*w*, 740, 700. – ^{1}H-NMR. (60 MHz): 0.85 (*d*, *J*=6, 3H); 1.22 (*s*, 3H); 1.32 (*s*, 3H); 0.75–2.5 (13H); 5.4–5.9 (2H).

(1R, 4S*, 5R*)-4-Methyl-1-(2-propenyl)-spiro[4,5]-6-decene* (**19**). A homogeneous mixture of Al_2O_3 (*Fluka*, neutral, activity I, 35 g), pyridine (7 g) and the alcohol **18** (1.0 g, 4.8 mmol) was heated in a sealed *Pyrex* ampoule at 220° for 9 h. Extraction with methanol (3×), usual work-up of the evaporated extracts (including washing of the organic layer with 10% citric acid) followed by chromatography (pentane) gave the diene **19**, (750 mg, 82%), GC. (capillary SE 30, 150°): retention time 11.61. – IR.: 3080*w*, 3030, 1645, 1460, 1380, 890. – ^{1}H-NMR.: 0.87 (*d*, *J*=6, 3H); 1.73 (*s*, 3H); 1.1–2.2 (11H); 2.32 (*m*, 1H); 4.80 (br.*s*, 2H); 5.5 (*d*×*t*, *J*=10.5 and 2, 1H; irradiation at 1.8 → *d*, *J*=10.5); 5.82 (*d*×*t*, *J*=10.5 and 3.5, 1H, irradiation at 1.8 → *d*, *J*=10.5). – MS.: 190 ($C_{14}H_{22}^+$, 58), 175 (32), 161 (13), 147 (26), 134 (73), 121 (53), 119 (42), 108 (89), 105 (74), 93 (73), 91 (55), 79 (100), 67 (37).

$C_{14}H_{22}$ (190.33) Calc. C 88.5 H 11.7% Found C 88.4 H 11.6%

Further elution with benzene afforded the unreacted alcohol **18** (250 mg).

(1R, 4S*, 5R*)-1-Isopropyl-4-methyl-spiro[4,5]-6-decene* (**20**). A solution of the diene **19** (450 mg, 2.3 mmol) in benzene (2 ml) was injected into a solution of tris-(triphenylphosphine)-chlororhodium(I) (300 mg) in benzene previously saturated with H_2. The mixture was stirred under H_2 for 5 h (uptake 60 ml H_2 at 1 atm.) to give after filtration through Al_2O_3 and distillation of the

evaporated filtrate the isopropyl derivative **20**, (445 mg, 98%). – GC. (capillary SE 30, 150°): retention time 14.85. – IR.: 3020 *w*, 1460, 1395, 1385, 1375, 750, 710. – ^{1}H-NMR.: 0.7–1.0 (9H); 1.0–2.1 (13H); 5.44 (*d* × *t*, *J* = 10.5 and 2, 1H); 5.82 (*d* × *t*, *J* = 10.5 and 3.5, 1H). – MS.: 192 ($C_{14}H_{24}^+$, 15), 190 (10), 149 (100), 136 (13), 121 (39), 108 (66), 93 (42), 91 (26), 79 (50), 69 (19).

(*1R*, 4S*, 5R*)-1-Isopropyl-4-methyl-spiro[4,5]-6-decen-8-one* (**21**). A mixture of the hydrocarbon **20** (180 mg, 0.93 mmol), sodium chromate (400 mg), acetic acid (2 ml) and acetic anhydride (1.2 ml) was heated at 40° for 4 h. Then further sodium chromate (200 mg), acetic acid (1 ml) and acetic anhydride (0.5 ml) were added to the reaction mixture which was heated at 40° for 2 h and finally left at 25° for 16 h. Usual work-up and chromatography (pentane) gave the unchanged hydrocarbon **20** (70 mg). Further elution with toluene/ethyl acetate 19:1 afforded the enone **21** as a pale yellow liquid (80 mg, 68% base on recovered **20**), b.p. 80–82° (bath) 0.3 Torr. – GC.: (3 m/3 mm-glass column, 5% OV 225, 200°): retention time 11.59; (capillary SE 30, 175°): retention time 21.02. – UV. (methanol): 238 (4.0), 318 (1.7). – IR.: 3040 *w*, 1680, 1630 *w*. – ^{1}H-NMR.: 0.75–1.05 (9H); 1.1–2.6 (11H); 6.10 (*d*, *J* = 10.5, 1H); 6.80 (br. *d*, *J* = 10.5, 1H). – MS.: 206 ($C_{14}H_{22}O^+$, 4), 191 (85), 149 (60), 139 (45), 125 (41), 112 (100), 97 (42), 84 (36), 69 (51).

$C_{14}H_{22}O$ (206.33) Calc. C 81.5 H 10.7% Found C 81.5 H 10.7%

(*1R*, 4S*, 5R*)-9-Acetoxy-1-isopropyl-4-methyl-spiro[4,5]-6-decen-8-one* (**22**). A mixture of the enone **21** (100 mg, 0.48 mmol), lead tetraacetate (90%, 500 mg, 1.12 mmol) and dry toluene (6 ml) was heated under reflux for 7 h. Usual work-up and chromatography (toluene/ethyl acetate 19:1) gave the pure acetate **22** (100 mg, 80%) as a mixture of two epimers. – IR.: 3040 *w*, 1750, 1700, 1670, 1620 *w*, 1240. – ^{1}H-NMR.: 0.6–1.1 (9H); 2.2 (*s*, 3H); 1.1–2.7 (9H); 5.5–7.0 (3H). – MS.: 264 ($C_{16}H_{24}O_3^+$, 1), 223 (3), 221 (4), 206 (3), 205 (4), 204 (22), 162 (17), 161 (100), 135 (24), 134 (28), 133 (24), 121 (43), 120 (45), 107 (23), 92 (20), 91 (34).

(±)-*Acorenone-B* (**3**). A 2N solution of methyllithium in ether (2 ml, 4 mmol) was added to a solution of the acetate **22** (85 mg, 0.32 mmol) in ether (5 ml) at −70°. The reaction mixture was left at 25° for 16 h. Decomposition with sat. aq. NH_4Cl solution and usual work-up gave the diol **23** as an oily mixture of epimers (60 mg, 79%). – IR.: 3400 br., 925. – A mixture of the crude diol **23** (60 mg, 0.25 mmol), TsOH (150 mg) and dry benzene (6 ml) was heated under reflux for 15 min. Usual work-up and chromatography (toluene) gave an inseparable mixture of 1-isopropyl-4,6-dimethyl-1,2,3,4-tetrahydro-naphthalene and 4-isopropyl-1,6-dimethyl-1,2,3,4-tetrahydro-naphthalene (9 mg, 18%), GC. (5% OV 225, 200°): retention time 3.91. – IR. ($CHCl_3$): no OH, 1510, 1470, 1390, 1350, 815, 805. – ^{1}H-NMR.: 0.6–3.0 (16H); 2.31 (*s*, 3H); 6.7–73 (3H). – MS.: 202 ($C_{15}H_{22}^+$, 14), 173 (5), 160 (14), 159 (100). Further elution with toluene afforded (±)-acorenone-B (**3**) as a sweet smelling colourless liquid (30 mg, 55%), b.p. 80–81° (bath)/0.5 Torr. – UV., IR., ^{1}H-NMR. and MS. spectra were superimposable on those of (±)-acorenone-B prepared by another route; the samples were also indistinguishable on co-injection in the GC.: (5% OV 225, 200°): retention time 9.90.

Conversion of *'cis'*-1-Isopropyl-4-methyl-spiro[4,5]-6-decene (20) into (±)-Acorenone (4) (*Scheme 7*). – (*1R*, 4S*, 5R*)-1-Isopropyl-4-methyl-spiro[4,5]decan-7-one* (**25**). A solution of 2-methyl-2-butene (860 mg), 12.0 mmol) in THF (6 ml) was slowly injected into a stirred 1N solution of freshly prepared diborane in ether (6 ml, 6 mmol) at −10°. The mixture was stirred at 0° for 2 h, and, after dropwise addition of a solution of the olefin **20** (400 mg, 2.0 mmol) in THF (2 ml), it was stirred at 25° for 56 h. Successive addition of water (2 ml), aq. 3N NaOH solution (2 ml) and 30% aq. hydrogen peroxide (2.4 ml, 18.0 mmol), further stirring of the reaction mixture at 25° for 30 min at 25° followed by usual work-up and chromatography (pentane) afforded the unreacted olefin **20** (50 mg). Further elution with $CHCl_3$ gave an alcohol (40 mg, 90%), GC. (5% OV 225, 170°): retention time 11.37. – IR.: 3350 br., which was dissolved in ether (10 ml). A solution of aq. chromic acid (prepared from sodium dichromate dihydrate (190 mg, 0.63 mmol) and 96% sulfuric acid (0.14 ml, 2.5 mmol) diluted to 1 ml with water) was added to the stirred etheral solution of this alcohol (40 mg) at 25° over 5 min. After 2 h stirring at 25° usual work-up of the ether layer afforded the ketone **25** as a colourless oil (320 mg, 81%), b.p. 80–84° (bath) 0.8 Torr. – GC. (5% OV 225, 220°): retention time: 7.49. – IR.: 1710. – ^{1}H-NMR.: 0.7–1.2 (9H); 1.2–2.5 (11H); 2.2–2.4 (4H). – MS.: 208 ($C_{14}H_{24}O^+$, 8), 165 (4), 150 (6), 124 (10), 122 (9), 97 (16), 91 (14), 58 (47), 43 (100); after treatment of **25** with D_2O (9 h) a M^+-peak of 212 ($C_{14}H_{20}D_4O^+$) was observed.

(*1R*, 4S*, 5R*)-1-Isopropyl-4-methyl-8-phenylthio-spiro[4,5]decan-7-one* (**26**). A 1.23N solution of butyllithium in hexane (0.80–0.81 ml, 1.0 mmol) was added dropwise at −78° to a stirred solution

of freshly distilled isopropyl-*N*-cyclohexylamine (151 mg, 1.0 mmol) in THF (2 ml). After 30 min at −78° a solution of the ketone **25** (186 mg, 0.89 mmol) in THF (2 ml) was added to the mixture during 5 min. The light yellow solution was stirred at −78° for 40 min and then injected at 25° into a solution of diphenyldisulfide (292 mg, 1.34 mmol) in THF (2 ml). After stirring at 25° for 2 h the reaction mixture was shaken with ether (20 ml) and 10% aq. HCl (10 ml). The organic phase after usual work-up and chromatography (pentane/ether 95:5) gave the sulfide **26** as an oily mixture of epimers (150 mg, 76% based on the recovered ketone **25**) followed by the unchanged ketone **25** (56 mg). – IR. ($CHCl_3$): 1710. – ^{1}H-NMR.: 0.7–1.1 (9H); 1.1–2.4 (12H); 2.92 (*d*, *J*=15, 1H); 3.75 (*m*, 1H); 7.2–7.6 (5H). – MS.: 316 ($C_{20}H_{28}OS^+$, 0.5), 248 (26), 209 (100), 205 (48), 191 (55), 178 (27), 109 (68), 95 (85), 81 (55).

(*1*R*, *4*S*, *5*R*)-*1-Isopropyl-4,8-dimethyl-8-phenyl-sulfinyl-spiro[4,5]decan-7-one* (**27**). A 1.33N solution of butyllithium in hexane (0.33 ml, 0.44 mmol) was added to a solution of dry diisopropylamine (45 mg, 0.44 mmol) in THF/HMPA (4:1, 1 ml) at −78°. After 30 min a solution of the ketosulfide **26** (118 mg, 0.37 mmol) in THF/HMPA (4:1, 1 ml) was slowly added, 20 min later the bath temperature was raised to 0°. Dropwise addition of a solution of methyl iodide (104 mg, 0.74 mmol) in THF (1 ml), stirring of the reaction mixture at 25° for 3 h, shaking with ether and aq. 2N HCl and usual work-up of the organic layer afforded the (1 *R**, 4 *S**, 5 *R**)-1-isopropyl-4,8-dimethyl-8-phenylthio-spiro[4,5]decan-7-one as an oily mixture of C(8)-epimers (120 mg, 93%). – IR.: 1715, 1600*w*, 1050. – ^{1}H-NMR. (60 MHz): 0.8–1.1 (9H); 1.1–2.9 (15H); 3.3 (*d*, *J*=11, 1H); 7.0–7.5 (5H). A solution of *m*-chloroperbenzoic acid (*Fluka*, 90%, 70 mg, 0.33 mmol) in CH_2Cl_2 (1 ml) was added to a stirred solution of this sulfide (110 mg, 0.33 mmol) in CH_2Cl_2 (2 ml) over a period of 5 min at −78°. After 15 min the cold reaction mixture was shaken with ether (10 ml) and 10% aq. $NaHSO_3$ solution (10 ml). Usual work-up of the organic layer and chromatography (ether) afforded the sulfoxide **27** as an oily mixture of epimers (80 mg, 62% from the ketone **25**). – IR. ($CHCl_3$): 1715. – ^{1}H-NMR. (60 MHz): 0.8–1.1 (9H); 1.1–2.7 (15H); 3.70 (*d*, *J*=13, 1H); 7.2–7.7 (5H).

(±)-*Acorenone* (**4**). A solution of the ketosulfoxide **27** (60 mg, 0.17 mmol) in CCl_4 (2 ml) was heated at 70° for 3 h. Evaporation and chromatography (pentane/ether 95:5) of the reaction mixture afforded (±)-acorenone (**4**) as a sweet smelling mobile liquid (30 mg, 79%), b.p. 100° (bath)/0.05 Torr. – GC. (5% FFAP, 160°): retention time 12.1. UV., IR., ^{13}C-NMR. and MS. spectra were identical to those of a sample prepared from (±)-acorenone-B [5f]. UV., IR. and ^{1}H-NMR. spectra of synthetic (±)-**4** were also superimposable on those of (−) coccinone, obtained by oxidation of the natural coccinol[15]) [24].

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